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Types of Dietary Fat and Cardiovascular Disease: A Systematic Review

2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee

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Nutrition Evidence Systematic Review
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This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee in collaboration with the Nutrition Evidence Systematic Review (NESR) team at the Center for Nutrition Policy and Promotion, Food and Nutrition Service, U.S. Department of Agriculture (USDA). All systematic reviews from the 2020 Advisory Committee Project are available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews.

Conclusion statements drawn as part of this systematic review describe the state of science related to the specific question examined. Conclusion statements do not draw implications, and should not be interpreted as dietary guidance. This portfolio provides the complete documentation for this systematic review. A summary of this review is included in the 2020 Advisory Committee's Scientific Report available at www.DietaryGuidelines.gov.

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USDA and HHS implemented a process to identify topics and scientific questions to be examined by the 2020 Dietary Guidelines Advisory Committee. The Committee conducted its review of evidence in subcommittees for discussion by the full Committee during its public meetings. The role of the Committee members involved establishing all aspects of the protocol, which presented the plan for how they would examine the scientific evidence, including the inclusion and exclusion criteria; reviewing all studies that met the criteria they set; deliberating on the body of evidence for each question; and writing and grading the conclusion statements to be included in the scientific report the 2020 Committee submitted to USDA and HHS. The NESR team with assistance from Federal Liaisons and Project Leadership, supported the

[i] Under contract with the Food and Nutrition Service, United States Department of Agriculture.

Committee by facilitating, executing, and documenting the work necessary to ensure the reviews were completed in accordance with NESR methodology. More information about the 2020 Dietary Guidelines Advisory Committee, including the process used to identify topics and questions, can be found at www.DietaryGuidelines.gov. More information about NESR can be found at NESR.usda.gov.

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INTRODUCTION

This document describes a systematic review conducted to answer the following question: What is the relationship between types of dietary fat consumed and risk of cardiovascular disease? This systematic review was conducted by the 2020 Dietary Guidelines Advisory Committee, supported by USDA's Nutrition Evidence Systematic Review (NESR).

More information about the 2020 Dietary Guidelines Advisory Committee is available at the following website: www.DietaryGuidelines.gov.

NESR specializes in conducting food- and nutrition-related systematic reviews using a rigorous, protocol-driven methodology. More information about NESR is available at the following website: NESR.usda.gov.

NESR's systematic review methodology involves developing a protocol, searching for and selecting studies, extracting data from and assessing the risk of bias of each included study, synthesizing the evidence, developing conclusion statements, grading the evidence underlying the conclusion statements, and recommending future research. A detailed description of the systematic reviews conducted for the 2020 Dietary Guidelines Advisory Committee, including information about methodology, is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews. In addition, starting on page 336, this document describes the final protocol as it was applied in the systematic review. A description of and rationale for modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Part D: Chapter 9. Dietary Fats and Seafood.

The systematic review described in this document builds on evidence reviewed by the 2015 Dietary Guidelines Advisory Committee. Information about the 2015 Dietary Guidelines Advisory Committee's review of the evidence for the question "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" can be found in their report[ii] (see Part D. Chapter 6: Cross-Cutting Topics of Public Health Importance, page 337).

[ii] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

List of abbreviations

Abbreviation	Full name
AA	Arachidonic acid
ALA	Alpha-linolenic acid
BMI	Body mass index
CAD	Coronary artery disease
CHD	Coronary heart disease
CNPP	Center for Nutrition Policy and Promotion
CVD	Cardiovascular disease
DHA	Docosahexaenoic acid
DISC	Dietary Intervention Study in Children
DPA	Docosapentaenoic acid
EPA	Eicosapentaenoic acid
FFQ	Food frequency questionnaire
FNS	Food and Nutrition Service
HDI	Human Development Index
HDL	High-density lipoprotein
HHS	United States Department of Health and Human Services
LA	Linoleic acid
LDL	Low-density lipoprotein
MI	Myocardial infarction
MUFA	Monounsaturated fatty acid
N	Sample size
n-3	Omega-3
n-6	Omega-6
NCC	Nested case-control
NESR	Nutrition Evidence Systematic Review

Abbreviation	Full name
NRCT	Non-randomized controlled trial
OASH	Office of the Assistant Secretary for Health
ODPHP	Office of Disease Prevention and Health Promotion
PAD	Peripheral artery disease
PCS	Prospective cohort study
PUFA	Polyunsaturated fatty acid
RCT	Randomized controlled trial
SFA	Saturated fatty acid
STRIP	Special Turku Coronary Risk Factor Intervention Project
UFA	Unsaturated fatty acid
U.K.	United Kingdom
U.S.	United States
USDA	United States Department of Agriculture

WHAT IS THE RELATIONSHIP BETWEEN TYPES OF DIETARY FAT CONSUMED AND RISK OF CARDIOVASCULAR DISEASE?

PLAIN LANGUAGE SUMMARY

What is the question?

- The question is: What is the relationship between types of dietary fat consumed and risk of cardiovascular disease?

What is the answer to the question?

Cardiovascular disease intermediate outcomes (blood lipids and blood pressure): Children

- Strong evidence demonstrates that diets lower in saturated fatty acids and cholesterol during childhood result in lower levels of total blood and low-density lipoprotein cholesterol throughout childhood, particularly in boys.
- Moderate evidence indicates that diets higher in polyunsaturated fatty acids during childhood result in lower levels of total blood cholesterol throughout childhood, particularly in boys.
- Insufficient evidence is available to determine the relationship between monounsaturated fatty acid intake during childhood and total blood and low-density lipoprotein cholesterol throughout childhood.
- Insufficient evidence is available to determine the relationship between intake of types of dietary fat during childhood and blood pressure throughout childhood.

Cardiovascular disease endpoint outcomes (cardiovascular disease event, diagnosis, or mortality): Children

- Insufficient evidence is available to determine the relationship between intake of types of dietary fat during childhood and cardiovascular disease health outcomes during adulthood.

Cardiovascular disease intermediate outcomes (blood lipids): Adults

- Strong and consistent evidence from randomized controlled trials demonstrates that replacing saturated fatty acids with unsaturated fats, especially polyunsaturated fatty acids, in adults significantly reduces total and low-density lipoprotein cholesterol. Replacing saturated fatty acids with carbohydrates (sources not defined) also reduces total and low-density lipoprotein cholesterol, but significantly increases triglycerides and reduces high-density lipoprotein cholesterol. Since the 2015 Dietary Guidelines Advisory Committee review, evidence remains inadequate to differentiate among sources of carbohydrate and their impact on blood lipids.
- Insufficient evidence is available to determine an independent relationship between dietary cholesterol intake in adults and blood lipids, given the co-occurrence of cholesterol with saturated fats in foods.

Cardiovascular disease endpoint outcomes (cardiovascular disease event, diagnosis, or mortality): Adults

- Strong evidence demonstrates that replacing saturated fatty acids with polyunsaturated fatty acids in adults reduces the risk of coronary heart disease events and cardiovascular disease mortality.
- Insufficient evidence is available to determine whether replacing saturated fatty acids with polyunsaturated fatty acids in adults affects the risk of stroke or heart failure.
- Insufficient evidence is available to determine whether replacing saturated fatty acids with different types of carbohydrates (e.g., complex, simple) in adults affects the risk of cardiovascular disease.
- Limited evidence is available regarding whether replacing saturated fatty acids with monounsaturated fatty acids in adults confers overall cardiovascular disease endpoint health benefits. Main sources of monounsaturated fatty acids in a typical American diet are animal fats, with co-occurrence of saturated fatty acids and monounsaturated fatty acids in these foods thereby obscuring the independent association of monounsaturated fatty acids with cardiovascular disease. Evidence reviewed from randomized controlled trials and prospective studies demonstrated benefits of plant sources of monounsaturated fats, including olive oil and nuts on cardiovascular disease risk.
- Moderate evidence indicates that total intake of omega-3 polyunsaturated fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid from food sources, by adults is associated with lower risk of cardiovascular disease.
- Limited evidence suggests that intake of linoleic acid, but not arachidonic acid, during adulthood may be associated with lower risk of cardiovascular disease, including cardiovascular disease mortality.
- Insufficient evidence is available from randomized controlled trials to quantify an independent relationship between dietary cholesterol intake in adults and overall risk of cardiovascular disease.

Why was this question asked?

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.

How was this question answered?

- The 2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.

What is the population of interest?

- For the intervention or exposure, generally healthy children, age 18 years and younger, and adults, age 19 years and older. For the outcome, those who had blood pressure measured during childhood, blood lipids measured during childhood

or adulthood, and/or had CVD endpoint outcomes measured during adulthood.

What evidence was found?

- This review identified 228 articles that met inclusion criteria: 37 in children and 191 in adults.
- Children:
  - Most studies found that lower childhood intake of saturated fatty acids (SFA) and dietary cholesterol, as well as higher intake of polyunsaturated fatty acids (PUFA), were beneficial for total blood cholesterol and/or low-density lipoprotein (LDL) cholesterol. Results were more consistent in boys. The 2020 Committee determined this evidence was strong for SFA and dietary cholesterol and moderate for PUFA.
  - Few studies examined monounsaturated fatty acid (MUFA) intake during childhood and its relationship to blood lipids and a conclusion could not be drawn.
  - Few studies examined types of dietary fat during childhood and either blood pressure or risk of CVD and a conclusion could not be drawn.
- Adults:
  - Most studies reported a beneficial effect of replacing SFA with MUFA or PUFA on total and LDL cholesterol. Most studies did not find an effect of replacing SFA with MUFA or PUFA on high-density lipoprotein (HDL) cholesterol or triglycerides.
  - Many studies found that replacement of SFA with PUFA was related to lower risk of CVD mortality and CHD. No consistent relationship between replacement of SFA with MUFA or carbohydrates and risk of CVD was found.
  - The 2020 Committee could not draw a conclusion about replacement of SFA with PUFA and heart failure or stroke due to a lack of evidence.
  - Several studies observed a beneficial relationship between higher omega-3 PUFA intake and lower risk of CVD, most consistently for eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).
  - Few studies assessed the relationship between omega-6 PUFA intake and risk of CVD, tending to observe benefits with higher intake of linoleic acid but not with arachidonic acid.
  - The 2020 Committee could not draw a conclusion about the relationship between dietary cholesterol intake and blood lipids or risk of CVD due to a small number of studies and inconsistent results. Additionally, dietary cholesterol is commonly found in foods that also contain SFA, making it difficult to assess dietary cholesterol independently.
  - This systematic review builds and expands on the work of the 2015 Committee. The 2020 Committee concurs with and updates the conclusions drawn by the 2015 Committee.

How up-to-date is this systematic review?

This review searched for studies in children from January 1990 to October 2019 and studies in adults from January 2010 to October 2019.

TECHNICAL ABSTRACT

Background

- This important public health question was identified by the U.S. Departments of Agriculture (USDA) and Health and Human Services (HHS) to be examined by the 2020 Dietary Guidelines Advisory Committee.
- The 2020 Dietary Guidelines Advisory Committee, Dietary Fats and Seafood Subcommittee conducted a systematic review to answer this question with support from the Nutrition Evidence Systematic Review (NESR) team.
- The goal of this systematic review was to examine the following question: What is the relationship between types of dietary fat consumed and risk of cardiovascular disease?

Conclusion statements and grades

Cardiovascular disease intermediate outcomes: Children

- Strong evidence demonstrates that diets lower in saturated fatty acids and cholesterol during childhood result in lower levels of total blood and low-density lipoprotein cholesterol throughout childhood, particularly in boys. (Grade: Strong)
- Moderate evidence indicates that diets higher in polyunsaturated fatty acids during childhood result in lower levels of total blood cholesterol throughout childhood, particularly in boys. (Grade: Moderate)
- Insufficient evidence is available to determine the relationship between monounsaturated fatty acid intake during childhood and total blood and low-density lipoprotein cholesterol throughout childhood. (Grade: Grade not assignable)
- Insufficient evidence is available to determine the relationship between intake of types of dietary fat during childhood and blood pressure throughout childhood. (Grade: Grade not assignable)

Cardiovascular disease endpoint outcomes: Children

- Insufficient evidence is available to determine the relationship between intake of types of dietary fat during childhood and cardiovascular disease health outcomes during adulthood. (Grade: Grade not assignable)

Cardiovascular disease intermediate outcomes: Adults

- Strong and consistent evidence from randomized controlled trials demonstrates that replacing saturated fatty acids with unsaturated fats, especially polyunsaturated fatty acids, in adults significantly reduces total and low-density lipoprotein cholesterol. Replacing saturated fatty acids with carbohydrates (sources not defined) also reduces total and low-density lipoprotein cholesterol, but significantly increases triglycerides and reduces high-density lipoprotein cholesterol. Since the 2015 Dietary Guidelines Advisory Committee review, evidence remains inadequate to differentiate among sources of carbohydrate and their impact on blood lipids. (Grade: Strong)
- Insufficient evidence is available to determine an independent relationship between dietary cholesterol intake in adults and blood lipids, given the co-occurrence of

cholesterol with saturated fats in foods. (Grade: Grade not assignable)

Cardiovascular disease endpoint outcomes: Adults

- Strong evidence demonstrates that replacing saturated fatty acids with polyunsaturated fatty acids in adults reduces the risk of coronary heart disease events and cardiovascular disease mortality. (Grade: Strong)
- Insufficient evidence is available to determine whether replacing saturated fatty acids with polyunsaturated fatty acids in adults affects the risk of stroke or heart failure. (Grade: Grade not assignable)
- Insufficient evidence is available to determine whether replacing saturated fatty acids with different types of carbohydrates (e.g., complex, simple) in adults affects the risk of cardiovascular disease. (Grade: Grade not assignable)
- Limited evidence is available regarding whether replacing saturated fatty acids with monounsaturated fatty acids in adults confers overall cardiovascular disease endpoint health benefits. Main sources of monounsaturated fatty acids in a typical American diet are animal fats, with co-occurrence of saturated fatty acids and monounsaturated fatty acids in these foods thereby obscuring the independent association of monounsaturated fatty acids with cardiovascular disease. Evidence reviewed from randomized controlled trials and prospective studies demonstrated benefits of plant sources of monounsaturated fats, including olive oil and nuts on cardiovascular disease risk. (Grade: Limited)
- Moderate evidence indicates that total intake of omega-3 polyunsaturated fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid from food sources, by adults is associated with lower risk of cardiovascular disease. (Grade: Moderate)
- Limited evidence suggests that intake of linoleic acid, but not arachidonic acid, during adulthood may be associated with lower risk of cardiovascular disease, including cardiovascular disease mortality. (Grade: Limited)
- Insufficient evidence is available from randomized controlled trials to quantify an independent relationship between dietary cholesterol intake in adults and overall risk of cardiovascular disease. (Grade: Grade not assignable)

Methods

- Two literature searches were conducted using 4 databases (PubMed, Cochrane, Embase, CINAHL) to identify articles that evaluated the intervention or exposure of intake of types of dietary fat and the outcomes of cardiovascular disease (CVD) intermediate outcomes (blood lipids in children and adults; blood pressure in children) and CVD endpoint outcomes. Because this systematic review built on evidence reviewed by the 2015 Dietary Guidelines Advisory Committee, one search was designed to identify articles in children from January 1990 to December 2009 and the other search was designed to identify articles in children and adults from January 2010 to October 2019. A manual search was conducted to identify articles that may not have been included in the electronic databases searched. Articles were screened by two NESR analysts independently for inclusion based on pre-determined criteria.

- Data extraction and risk of bias assessment were conducted for each included study, and both were checked for accuracy. The Committee qualitatively synthesized the body of evidence to inform development of conclusion statements, and graded the strength of evidence using pre-established criteria for risk of bias, consistency, directness, precision, and generalizability.

Summary of the evidence

Children

- This systematic review includes 37 articles, 22 articles from 7 randomized controlled trials (RCTs) and 16 articles from 14 prospective cohort studies (PCSs), published between January 1990 and October 2019 that examined the relationship between intake of types of dietary fat during childhood and cardiovascular disease (CVD) risk. (Note: One article from an RCT was also analyzed as a PCS.)
  - The RCTs modified child fat intake either through dietary counseling that focused primarily on reducing saturated fatty acids (SFA) and dietary cholesterol intake, with additional encouragement to increase polyunsaturated fatty acid (PUFA) intake, or through provision of food products (i.e., eggs, extra virgin olive oil, or oily fish) that differed in types of fat including SFA, monounsaturated fatty acids (MUFA), PUFA, and/or dietary cholesterol.
  - The PCSs primarily assessed SFA or PUFA intake, with fewer studies on MUFA or dietary cholesterol intake; only two studies modeled replacement between different types of fat or macronutrients.

- Most included studies assessed the relationship between intake of types of dietary fat during childhood and blood lipids.
  - Evidence from RCTs predominantly indicated that consuming less SFA and dietary cholesterol resulted in lower blood total cholesterol and low-density lipoprotein (LDL) cholesterol throughout childhood, particularly in boys; evidence from PCSs was consistent with the RCTs.
  - Although reduction of SFA intake was the primary focus of most RCTs, evidence from these RCTs also showed that higher PUFA intake resulted in decreased total blood cholesterol, particularly in boys; evidence from PCSs was broadly consistent with the RCTs.
  - Few studies, RCTs or PCSs, focused on the relationship between MUFA intake and blood lipids and the results were predominantly null.
  - The majority of studies assessed blood lipids during childhood; few assessed intake of types of fat during childhood and blood lipids into early adulthood.

- Fewer studies assessed the relationship between intake of types of dietary fat during childhood and blood pressure.
  - It was difficult to discern the effect of consuming different types of fat in the RCT that contributed the most evidence due to additional advice to reduce sodium consumption.
  - Few PCSs were conducted on this topic and results were predominantly null.

- Only one study included in this review assessed the relationship between intake of types of dietary fat during childhood and CVD endpoint outcomes and methodological limitations related to the dietary assessment confounded interpretation of results. Therefore, no conclusion could be drawn.

- Limitations of this body of evidence:
  - Most articles did not report race and ethnicity, but those that did included predominantly White or Caucasian participants.
  - Some studies specifically recruited children with elevated or higher than average blood lipid levels, reducing generalizability.
  - RCTs had predominantly low risk of bias, but few pre-registered their analysis intentions and several RCTs did not provide information on allocation of randomization sequences.
  - Although many PCSs accounted for most or many key confounders, all PCSs did not account for at least one key confounder.
  - Approximately half of the diet assessment methods used in the PCSs were not validated; many PCSs had high attrition rates and did not provide information on those lost to follow-up.

Adults

Adults: CVD intermediate outcomes

- This systematic review includes 97 articles that examined the relationship between intake of types of dietary fat during adulthood and CVD intermediate outcomes, published between January 2010 and October 2019. Of these, 47 were from 47 parallel design RCTs, 46 were from 44 crossover design RCTs, and 5 were from non-randomized controlled trial designs. (Note: One parallel design RCT was also analyzed as a crossover design RCT.)
  - The articles examined intake of SFA, MUFA, PUFA, and dietary cholesterol.
  - The majority of articles specifically examined types of fat from different food sources, including food sources that are predominantly fat (e.g., butter and olive oil).

- The relationship between types of dietary fat and blood lipids varied by the type of fat examined and the comparator.
  - <u>SFA intake:</u> Predominantly null effects were reported for SFA intake when replacement was not considered or when SFA was partially replaced by carbohydrates. However, among the studies that detected significant effects, all reported significantly higher total, LDL, and high-density lipoprotein (HDL) cholesterol with higher intake of SFA, compared to either lower intake of SFA or substitution with carbohydrate.
  - <u>Replacement of SFA with MUFA:</u> More than half of articles reported a beneficial effect of replacing a portion of SFA intake with MUFA intake on total and LDL cholesterol. Predominantly null effects were reported for HDL cholesterol and triglycerides.
  - <u>Replacement of SFA with PUFA:</u> More than half of articles reported a beneficial effect of replacing a portion of SFA intake with PUFA intake on total and LDL cholesterol. Predominantly null effects were reported for HDL cholesterol and triglycerides.
  - <u>MUFA intake:</u> Predominantly null effects were reported for MUFA intake when replacement was not considered or when MUFA was partially replaced with carbohydrates.
  - <u>Replacement of MUFA with PUFA:</u> Predominantly null effects were reported in articles that examined partial replacement of MUFA intake with PUFA intake.

        - Among the studies that found significant effects, the majority detected significantly lower levels of or significant decreases in total and LDL cholesterol when PUFA intake replaced a portion of MUFA intake.
        - Studies replacing a portion of MUFA intake with PUFA intake predominantly detected significant decreases or greater decreases in HDL cholesterol and significantly higher levels of, smaller decreases in, or greater increases in triglycerides.
    - PUFA intake: The vast majority of articles that assessed the effect of PUFA intake (without considering replacement) on total, LDL, or HDL cholesterol and triglycerides were null. However, among the few articles that detected significant effects, total and LDL cholesterol were significantly lower with greater PUFA intake, compared with lower PUFA intake; HDL cholesterol significantly increased or had smaller decreases with greater PUFA intake; and triglycerides were significantly lower or had greater decreases with greater PUFA intake.

- Few articles published during the search years of the present review assessed the relationship between dietary cholesterol intake and blood lipids.
    - Predominantly null effects were reported for dietary cholesterol. However, among the few articles that found significant results, higher intake of dietary cholesterol, compared to lower intake, significantly increased or resulted in higher levels of total, LDL, and HDL cholesterol.
    - In several articles, it was not possible to isolate the independent effect of dietary cholesterol on blood lipids due to simultaneous changes in the total amount of fat or proportion of different types of fatty acids in the study diet.

- Limitations of this body of evidence:
    - Several articles involved small sample sizes and lacked sufficient power.
    - Race or ethnicity was not consistently reported, but among those studies that provided this information, the majority included participants who were predominantly White or Caucasian.
    - It was not possible to isolate the independent effect of SFA, MUFA, or PUFA on blood lipids in several articles due to simultaneous changes of those three types of fat.
    - The majority of articles did not control for other dietary components beyond the intervention or test meal.

- This systematic review builds and expands on the work of the 2015 Dietary Guidelines Advisory Committee, which answered the question "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" and considered evidence from RCTs and PCSs from the 1960s to 2010.[iii] This systematic review concurs with and updates the conclusions drawn by the 2015 Dietary Guidelines Advisory Committee.

[iii] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

Adults: CVD endpoint outcomes

- This systematic review includes 94 articles that examined the relationship between intake of types of dietary fat during adulthood and CVD endpoint outcomes, published between January 2010 and October 2019. Of these, 90 were from 47 PCSs and 4 were from 3 nested case-control studies.
  - The articles primarily examined SFA, total PUFA, omega-3 (n-3) PUFA (including alpha-linolenic acid [ALA], eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA], or docosapentaenoic acid [DPA]), or MUFA intake. Fewer articles examined omega-6 (n-6) PUFA (including linoleic acid [LA] or arachidonic acid [AA]) or dietary cholesterol intake.
  - Several articles modeled replacement between different types of fats or macronutrients or, in some cases, between different sources of the same type of fat. Few articles specifically assessed food sources that are predominantly fat (i.e., butter and olive oil) or types of fat from different food sources.

- The relationship between types of dietary fat and CVD endpoint outcomes varied by the type of fat examined and the specific outcome assessed, with the most consistent results observed when replacement was modeled.
  - <u>Replacement of SFA with PUFA:</u> In this review, replacement of SFA with PUFA (predominantly total PUFA) in many studies was associated with significantly lower risk of CVD mortality and/or coronary heart disease (CHD) or associations were null. Fewer articles in this review reported data regarding the relationship between replacement of SFA with PUFA and other specific types of CVD including heart failure or stroke, and results were predominantly null.
  - <u>Replacement of SFA with carbohydrates:</u> In this review, replacement of SFA with carbohydrates and CVD outcomes were predominantly null. Most articles did not specify or differentiate between the types of carbohydrate replacing SFA (e.g., complex or simple carbohydrates/sugar).
  - <u>Replacement of SFA with MUFA:</u> In this review, predominantly null associations were observed between replacement of SFA with MUFA and total CVD and CHD. However, among the few articles that differentiated plant and animal sources, MUFA from plants tended to be associated with lower risk.

- In addition to articles that reported on total PUFA intake, many specifically assessed n-3 PUFA and some assessed n-6 PUFA.
  - <u>Total n-3 PUFA:</u> Predominantly null or beneficial associations were observed between total n-3 PUFA intake and CVD outcomes.
  - <u>Types of n-3 PUFA:</u> When “long chain” n-3 PUFA (EPA, DHA, and sometimes DPA), primarily from marine sources, were assessed separately from ALA, more consistent associations with lower risk of CVD were observed.
  - <u>Total n-6 PUFA:</u> Associations between total n-6 PUFA intake and CVD were predominantly null.
  - <u>Types of n-6 PUFA:</u> In the few articles specifically assessing LA and AA separately, beneficial associations were more often observed for LA as compared to AA.

- Few articles, with inconsistent results, assessed the independent relationship between dietary cholesterol intake and CVD endpoint outcomes, thereby further

confounding meaningful conclusions. Due to the co-occurrence of dietary cholesterol and SFA in animal source foods, disentangling independent associations between dietary cholesterol and CVD endpoint outcomes in these observational studies is challenging.

- Limitations of this body of evidence:
  - Many articles did not report race or ethnicity, but the majority of those that did involved participants who were predominantly White or Caucasian. Other important characteristics of participants in some included articles did not mirror those of the U.S. population, such as BMI and diet at baseline.
  - Although many articles accounted for the majority of key confounders, few accounted for all key confounders.
  - Some studies did not use validated dietary assessment methods or were limited by high attrition.
  - Although most studies included in this body of evidence were specifically designed to evaluate the relationship between diet and CVD, several articles were less direct as a result of being secondary analyses of RCTs or cohorts originally designed to assess outcomes other than CVD.

- This systematic review builds upon the work of the 2015 Dietary Guidelines Advisory Committee, which answered the question "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" and considered evidence from RCTs and PCSs from the 1960s to 2010.[iv]
  - Regarding the relationships between replacement of SFA with PUFA or carbohydrate, this systematic review concurs with and updates the conclusions drawn by the 2015 Dietary Guidelines Advisory Committee, providing additional context regarding specific CVD endpoint outcomes and the type of carbohydrate replacing SFA.
  - Regarding the relationship between replacement of SFA with MUFA, this systematic review concurs with and updates the conclusions drawn by the 2015 Dietary Guidelines Advisory Committee.

[iv] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

FULL REVIEW

Systematic review question

What is the relationship between types of dietary fat consumed and risk of cardiovascular disease?

Conclusion statements and grades

Cardiovascular disease intermediate outcomes: Children

Strong evidence demonstrates that diets lower in saturated fatty acids and cholesterol during childhood result in lower levels of total blood and low-density lipoprotein cholesterol throughout childhood, particularly in boys. (Grade: Strong)

Moderate evidence indicates that diets higher in polyunsaturated fatty acids during childhood result in lower levels of total blood cholesterol throughout childhood, particularly in boys. (Grade: Moderate)

Insufficient evidence is available to determine the relationship between monounsaturated fatty acid intake during childhood and total blood and low-density lipoprotein cholesterol throughout childhood. (Grade: Grade not assignable)

Insufficient evidence is available to determine the relationship between intake of types of dietary fat during childhood and blood pressure throughout childhood. (Grade: Grade not assignable)

Cardiovascular disease endpoint outcomes: Children

Insufficient evidence is available to determine the relationship between intake of types of dietary fat during childhood and cardiovascular disease health outcomes during adulthood. (Grade: Grade not assignable)

Cardiovascular disease intermediate outcomes: Adults

Strong and consistent evidence from randomized controlled trials demonstrates that replacing saturated fatty acids with unsaturated fats, especially polyunsaturated fatty acids, in adults significantly reduces total and low-density lipoprotein cholesterol. Replacing saturated fatty acids with carbohydrates (sources not defined) also reduces total and low-density lipoprotein cholesterol, but significantly increases triglycerides and reduces high-density lipoprotein cholesterol. Since the 2015 Dietary Guidelines Advisory Committee review, evidence remains inadequate to differentiate among sources of carbohydrate and their impact on blood lipids. (Grade: Strong)

Insufficient evidence is available to determine an independent relationship between dietary cholesterol intake in adults and blood lipids, given the co-occurrence of cholesterol with saturated fats in foods. (Grade: Grade not assignable)

Cardiovascular disease endpoint outcomes: Adults

Strong evidence demonstrates that replacing saturated fatty acids with polyunsaturated fatty acids in adults reduces the risk of coronary heart disease events and cardiovascular disease mortality. (Grade: Strong)

Insufficient evidence is available to determine whether replacing saturated fatty acids with polyunsaturated fatty acids in adults affects the risk of stroke or heart failure.

(Grade: Grade not assignable)

Insufficient evidence is available to determine whether replacing saturated fatty acids with different types of carbohydrates (e.g., complex, simple) in adults affects the risk of cardiovascular disease. (Grade: Grade not assignable)

Limited evidence is available regarding whether replacing saturated fatty acids with monounsaturated fatty acids in adults confers overall cardiovascular disease endpoint health benefits. Main sources of monounsaturated fatty acids in a typical American diet are animal fats, with co-occurrence of saturated fatty acids and monounsaturated fatty acids in these foods thereby obscuring the independent association of monounsaturated fatty acids with cardiovascular disease. Evidence reviewed from randomized controlled trials and prospective studies demonstrated benefits of plant sources of monounsaturated fats, including olive oil and nuts on cardiovascular disease risk. (Grade: Limited)

Moderate evidence indicates that total intake of omega-3 polyunsaturated fatty acids, particularly eicosapentaenoic acid and docosahexaenoic acid from food sources, by adults is associated with lower risk of cardiovascular disease. (Grade: Moderate)

Limited evidence suggests that intake of linoleic acid, but not arachidonic acid, during adulthood may be associated with lower risk of cardiovascular disease, including cardiovascular disease mortality. (Grade: Limited)

Insufficient evidence is available from randomized controlled trials to quantify an independent relationship between dietary cholesterol intake in adults and overall risk of cardiovascular disease. (Grade: Grade not assignable)

Summary of the evidence

Children

- This systematic review includes 37 articles,[1-37] 22 articles from 7 randomized controlled trials (RCTs) and 16 articles from 14 prospective cohort studies (PCSs), published between January 1990 and October 2019 that examined the relationship between intake of types of dietary fat during childhood and cardiovascular disease (CVD) risk. (Note: One article from an RCT was also analyzed as a PCS.)
    - The RCTs modified child fat intake either through dietary counseling that focused primarily on reducing saturated fatty acids (SFA) and dietary cholesterol intake, with additional encouragement to increase polyunsaturated fatty acid (PUFA) intake, or through provision of food products (i.e., eggs, extra virgin olive oil, or oily fish) that differed in types of fat including SFA, monounsaturated fatty acids (MUFA), PUFA, and/or dietary cholesterol.
    - The PCSs primarily assessed SFA or PUFA intake, with fewer studies on MUFA or dietary cholesterol intake; only two studies modeled replacement between different types of fat or macronutrients.
- Most included studies assessed the relationship between intake of types of dietary fat during childhood and blood lipids.
    - Evidence from RCTs predominantly indicated that consuming less SFA and dietary cholesterol resulted in lower blood total cholesterol and low-density

lipoprotein (LDL) cholesterol throughout childhood, particularly in boys; evidence from PCSs was consistent with the RCTs.
  - Although reduction of SFA intake was the primary focus of most RCTs, evidence from these RCTs also showed that higher PUFA intake resulted in decreased total blood cholesterol, particularly in boys; evidence from PCSs was broadly consistent with the RCTs.
  - Few studies, RCTs or PCSs, focused on the relationship between MUFA intake and blood lipids and the results were predominantly null.
  - The majority of studies assessed blood lipids during childhood; few assessed intake of types of fat during childhood and blood lipids into early adulthood.

- Fewer studies assessed the relationship between intake of types of dietary fat during childhood and blood pressure.
  - It was difficult to discern the effect of consuming different types of fat in the RCT that contributed the most evidence due to additional advice to reduce sodium consumption.
  - Few PCSs were conducted on this topic and results were predominantly null.

- Only one study included in this review assessed the relationship between intake of types of dietary fat during childhood and CVD endpoint outcomes and methodological limitations related to the dietary assessment confounded interpretation of results. Therefore, no conclusion could be drawn.

- Limitations of this body of evidence:
  - Most articles did not report race and ethnicity, but those that did included predominantly White or Caucasian participants.
  - Some studies specifically recruited children with elevated or higher than average blood lipid levels, reducing generalizability.
  - RCTs had predominantly low risk of bias, but few pre-registered their analysis intentions and several RCTs did not provide information on allocation of randomization sequences.
  - Although many PCSs accounted for most or many key confounders, all PCSs did not account for at least one key confounder.
  - Approximately half of the diet assessment methods used in the PCSs were not validated; many PCSs had high attrition rates and did not provide information on those lost to follow-up.

Adults

Adults: CVD intermediate outcomes

- This systematic review includes 97 articles that examined the relationship between intake of types of dietary fat during adulthood and CVD intermediate outcomes, published between January 2010 and October 2019.[38-134] Of these, 47 were from 47 parallel design RCTs, 46 were from 44 crossover design RCTs, and 5 were from non-randomized controlled trial designs. (Note: One parallel design RCT was also analyzed as a crossover design RCT.)
  - The articles examined intake of SFA, MUFA, PUFA, and dietary cholesterol.
  - The majority of articles specifically examined types of fat from different food sources, including food sources that are predominantly fat (e.g., butter and olive oil).

- The relationship between types of dietary fat and blood lipids varied by the type of fat examined and the comparator.
  - SFA intake: Predominantly null effects were reported for SFA intake when replacement was not considered or when SFA was partially replaced by carbohydrates. However, among the studies that detected significant effects, all reported significantly higher total, LDL, and high-density lipoprotein (HDL) cholesterol with higher intake of SFA, compared to either lower intake of SFA or substitution with carbohydrate.
  - Replacement of SFA with MUFA: More than half of articles reported a beneficial effect of replacing a portion of SFA intake with MUFA intake on total and LDL cholesterol. Predominantly null effects were reported for HDL cholesterol and triglycerides.
  - Replacement of SFA with PUFA: More than half of articles reported a beneficial effect of replacing a portion of SFA intake with PUFA intake on total and LDL cholesterol. Predominantly null effects were reported for HDL cholesterol and triglycerides.
  - MUFA intake: Predominantly null effects were reported for MUFA intake when replacement was not considered or when MUFA was partially replaced with carbohydrates.
  - Replacement of MUFA with PUFA: Predominantly null effects were reported in articles that examined partial replacement of MUFA intake with PUFA intake.
    - Among the studies that found significant effects, the majority detected significantly lower levels of or significant decreases in total and LDL cholesterol when PUFA intake replaced a portion of MUFA intake.
    - Studies replacing a portion of MUFA intake with PUFA intake predominantly detected significant decreases or greater decreases in HDL cholesterol and significantly higher levels of, smaller decreases in, or greater increases in triglycerides.
  - PUFA intake: The vast majority of articles that assessed the effect of PUFA intake (without considering replacement) on total, LDL, or HDL cholesterol and triglycerides were null. However, among the few articles that detected significant effects, total and LDL cholesterol were significantly lower with greater PUFA intake, compared with lower PUFA intake; HDL cholesterol significantly increased or had smaller decreases with greater PUFA intake; and triglycerides were significantly lower or had greater decreases with greater PUFA intake.

- Few articles published during the search years of the present review assessed the relationship between dietary cholesterol intake and blood lipids.
  - Predominantly null effects were reported for dietary cholesterol. However, among the few articles that found significant results, higher intake of dietary cholesterol, compared to lower intake, significantly increased or resulted in higher levels of total, LDL, and HDL cholesterol.
  - In several articles, it was not possible to isolate the independent effect of dietary cholesterol on blood lipids due to simultaneous changes in the total amount of fat or proportion of different types of fatty acids in the study diet.

- Limitations of this body of evidence:
  - Several articles involved small sample sizes and lacked sufficient power.

- Race or ethnicity was not consistently reported, but among those studies that provided this information, the majority included participants who were predominantly White or Caucasian.
- It was not possible to isolate the independent effect of SFA, MUFA, or PUFA on blood lipids in several articles due to simultaneous changes of those three types of fat.
- The majority of articles did not control for other dietary components beyond the intervention or test meal.

- This systematic review builds and expands on the work of the 2015 Dietary Guidelines Advisory Committee, which answered the question "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" and considered evidence from RCTs and PCSs from the 1960s to 2010.[v] This systematic review concurs with and updates the conclusions drawn by the 2015 Dietary Guidelines Advisory Committee.

Adults: CVD endpoint outcomes

- This systematic review includes 94 articles that examined the relationship between intake of types of dietary fat during adulthood and CVD endpoint outcomes, published between January 2010 and October 2019.[135-228] Of these, 90 were from 47 PCSs and 4 were from 3 nested case-control studies.
  - The articles primarily examined SFA, total PUFA, omega-3 (n-3) PUFA (including alpha-linolenic acid [ALA], eicosapentaenoic acid [EPA], docosahexaenoic acid [DHA], or docosapentaenoic acid [DPA]), or MUFA intake. Fewer articles examined omega-6 (n-6) PUFA (including linoleic acid [LA] or arachidonic acid [AA]) or dietary cholesterol intake.
  - Several articles modeled replacement between different types of fats or macronutrients or, in some cases, between different sources of the same type of fat. Few articles specifically assessed food sources that are predominantly fat (i.e., butter and olive oil) or types of fat from different food sources.

- The relationship between types of dietary fat and CVD endpoint outcomes varied by the type of fat examined and the specific outcome assessed, with the most consistent results observed when replacement was modeled.
  - <u>Replacement of SFA with PUFA:</u> In this review, replacement of SFA with PUFA (predominantly total PUFA) in many studies was associated with significantly lower risk of CVD mortality and/or coronary heart disease (CHD) or associations were null. Fewer articles in this review reported data regarding the relationship between replacement of SFA with PUFA and other specific types of CVD including heart failure or stroke, and results were predominantly null.
  - <u>Replacement of SFA with carbohydrates:</u> In this review, replacement of SFA with carbohydrates and CVD outcomes were predominantly null. Most articles did not specify or differentiate between the types of carbohydrate replacing SFA (e.g., complex or simple carbohydrates/sugar).
  - <u>Replacement of SFA with MUFA:</u> In this review, predominantly null associations

[v] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

were observed between replacement of SFA with MUFA and total CVD and CHD. However, among the few articles that differentiated plant and animal sources, MUFA from plants tended to be associated with lower risk.

- In addition to articles that reported on total PUFA intake, many specifically assessed n-3 PUFA and some assessed n-6 PUFA.
  - Total n-3 PUFA: Predominantly null or beneficial associations were observed between total n-3 PUFA intake and CVD outcomes.
  - Types of n-3 PUFA: When "long chain" n-3 PUFA (EPA, DHA, and sometimes DPA), primarily from marine sources, were assessed separately from ALA, more consistent associations with lower risk of CVD were observed.
  - Total n-6 PUFA: Associations between total n-6 PUFA intake and CVD were predominantly null.
  - Types of n-6 PUFA: In the few articles specifically assessing LA and AA separately, beneficial associations were more often observed for LA as compared to AA.

- Few articles, with inconsistent results, assessed the independent relationship between dietary cholesterol intake and CVD endpoint outcomes, thereby further confounding meaningful conclusions. Due to the co-occurrence of dietary cholesterol and SFA in animal source foods, disentangling independent associations between dietary cholesterol and CVD endpoint outcomes in these observational studies is challenging.

- Limitations of this body of evidence:
  - Many articles did not report race or ethnicity, but the majority of those that did involved participants who were predominantly White or Caucasian. Other important characteristics of participants in some included articles did not mirror those of the U.S. population, such as BMI and diet at baseline.
  - Although many articles accounted for the majority of key confounders, few accounted for all key confounders.
  - Some studies did not use validated dietary assessment methods or were limited by high attrition.
  - Although most studies included in this body of evidence were specifically designed to evaluate the relationship between diet and CVD, several articles were less direct as a result of being secondary analyses of RCTs or cohorts originally designed to assess outcomes other than CVD.

- This systematic review builds upon the work of the 2015 Dietary Guidelines Advisory Committee, which answered the question "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" and considered evidence from RCTs and PCSs from the 1960s to 2010.[vi]
  - Regarding the relationships between replacement of SFA with PUFA or carbohydrate, this systematic review concurs with and updates the conclusions drawn by the 2015 Dietary Guidelines Advisory Committee, providing additional context regarding specific CVD endpoint outcomes and the type of

[vi] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

carbohydrate replacing SFA.

- Regarding the relationship between replacement of SFA with MUFA, this systematic review concurs with and updates the conclusions drawn by the 2015 Dietary Guidelines Advisory Committee.

Description of the evidence: Children

Of the 228 articles that met inclusion criteria for this systematic review, 37 articles,[1-37] 22 from 7 randomized controlled trials (RCTs) and 16 from 14 prospective cohort studies (PCSs), examined the relationship between types of dietary fat consumed during childhood and risk of cardiovascular disease (CVD). (Note: One article from an RCT also was analyzed as a PCS.)[32]

RCT Characteristics

Seventeen articles from 2 RCTs used dietary counseling to change intake of dietary fat.

In the Special Turku Coronary Risk Factor Intervention Project (STRIP; N=1,062 at baseline) conducted in Finland, 7-month-old infants were randomized to receive either counseling which encouraged adherence to a diet with a saturated fatty acid (SFA) to monounsaturated fatty acid (MUFA) to polyunsaturated fatty acid (PUFA) intake ratio of 1:1:1, dietary cholesterol intake of <200 mg per day, and total fat intake of 30-35% energy, or to basic health education counseling which recommended a PUFA:SFA intake ratio of 0.3-0.4.[8,10,11,14,15,21-24,28-31] Counseling was delivered to the parents until children were age 7 years, after which, direct counseling to the children started to be incorporated STRIP assessed compliance via food diaries, which indicated that intervention children had consistently significantly lower SFA and dietary cholesterol intake and higher PUFA intake than control children. To date, follow-up and counseling for STRIP has continued through age 20 years.

In the Dietary Intervention Study in Children (DISC; N=663 at baseline) conducted in the U.S., children aged approximately 9.5 years with elevated LDL cholesterol were randomized to receive either counseling which encouraged adherence to a diet providing <8% of energy from SFA, up to 9% energy from PUFA, <75 mg per 1000 kilocalories of dietary cholesterol, and up to 28% energy from total fat, or to usual care.[6,13,25,32] DISC assessed compliance via multiple 24 hour recalls; these indicated that intervention children had consistently lower SFA intake than control children and that during the first three years of the study MUFA and dietary cholesterol intake were also lower for intervention children. Counseling for DISC continued for approximately 7 years.

The remaining 5 articles from 5 RCTs, 1 parallel design, 3 crossover design, and 1 cluster design, provided children (predominantly age 9-12 years) with different food products to achieve differences in intake of types of dietary fat including SFA, MUFA, PUFA, and dietary cholesterol.[2,5,7,18,36] These foods included oily fish (vs poultry),[36] whole eggs (vs egg whites),[2] products made with margarine (vs butter),[5] whole milk (vs milk preparation),[7] and extra-virgin olive oil (vs typical oil consumed).[18] Sample size ranged from N=54[2] to N=135.[18] These RCTs were conducted in Denmark,[36] Mexico, [2] Spain,[7,18] and the U.S.[5] In comparison to the RCTs that provided counseling,

these 5 RCTs which provided food products were of shorter duration, with intervention durations ranging from 4 weeks[2] to 7 months.[7]

Out of the 22 articles from RCTs, 20 reported on at least one blood lipid measurement (total cholesterol: 16; LDL cholesterol: 14; HDL cholesterol: 20; triglycerides: 16).[2,5-8,10,11,13-15,18,22-25,28-31,36] Most blood draws were conducted in a fasted state, the primary exception being STRIP, which, due to the young age of the participants, collected non-fasting blood draws until the children were age 5 years. Only 10 articles reported on systolic and diastolic blood pressure.[2,6,8,15,18,21,24,28,32,36] Most articles did not report race/ethnicity, a common practice in studies conducted in Europe. Of those studies that did report race/ethnicity, participants were predominantly White.[5,6,13,25,32]

PCS Characteristics

Of the 16 articles from 14 PCSs, 15 assessed intermediate outcomes[1,3,4,9,12,16,17,20,26,27,32-35,37] and one assessed CVD endpoint outcomes.[19] These studies were primarily conducted in the U.S.[1,27,32,37] and the U.K.,[3,4,19,20] with additional studies conducted in Australia,[16] Brazil,[17] Germany,[9] Ireland,[12] and the Netherlands.[26,33-35] Sample size varied greatly, with 3 articles with N<100,[12,17,27] 8 articles with N=100-1,000,[1,3,4,16,26,32,34,37] and 5 articles with N>1000.[9,19,20,33,35] Most PCSs did not report race/ethnicity of the participants, but among those that did, samples were predominantly White or Caucasian,[1,4,20,32,33,35] except one study which reported greater diversity, with 40% of participants African American and 40% of participants Hispanic.[37]

Among studies that reported on intermediate outcomes, exposure assessment predominantly occurred during childhood and adolescence (approximately age 4-13 years). Dietary assessment methods varied across the PCSs that assessed intermediate outcomes. These methods, approximately half of which were validated, included food frequency questionnaires (FFQs), 24 hour recalls, multiple day diet records or diet diaries, diet history interviews, and direct observation. Most studies measured SFA[1,4,9,12,16,17,20,26,27,32-35,37] or PUFA[1,4,9,12,20,26,27,32-35] intake, with fewer measuring MUFA[1,4,9,12,20,32,33,35,37] or dietary cholesterol[1,3,4,20,26,27,32,34] intake. Only two studies examined replacement between types of fat or other macronutrients.[9,33] Duration of follow-up for outcome assessment in these studies occurred primarily 1-5 years from baseline; however, several studies conducted follow-ups over a longer time period (approximately 15-20 years from baseline).[16,26,34] The PCSs primarily assessed non-fasting blood lipids, with 13 reporting on at least one blood lipid measurement (total cholesterol: 10; LDL cholesterol: 6; HDL cholesterol: 11; triglycerides: 4).[1,3,4,9,12,16,17,20,26,27,33,34,37] However, six of the PCSs assessed systolic and diastolic blood pressure.[3,17,26,32,35]

In the one study that examined CVD endpoint outcomes, follow-up lasted approximately 60 years, and stroke mortality and coronary heart disease (CHD) mortality were assessed.[19] Initiated in the late 1930s in the U.K., this study estimated child SFA intake at approximately age 7.5 years using a 7-day weighed household inventory, dividing the total food expenditure for the child's household by the total number of household members.[19]

Evidence synthesis: Children

Intermediate outcomes

The RCTs on this topic primarily addressed multiple types of fat within single studies, considering replacement, whereas the PCSs predominantly examined types of fat separately, without addressing replacement. Therefore, for RCTs, the evidence was synthesized by the type of intervention (i.e., diet counseling or provision of food products) and outcome. For PCSs, the evidence was synthesized by type of fat and outcome. Evidence from RCTs and PCSs are described in **Table 1** and **Table 2**, respectively. Risk of bias assessments from RCTs and PCSs are described in **Table 3** and **Table 4**, respectively.

RCTs

Blood lipids. Twenty articles from 7 RCTs examined the relationship between intake of types of fat during childhood and blood lipids.[2,5-8,10,11,13-15,18,22-25,28-31,36] Over half of these articles were from STRIP, unique in its early initiation of a dietary counseling intervention (beginning at age 7 months) and long duration of intervention and follow-up (approximately 19.5 years to date).[8,10,11,14,15,22-24,28-31] In STRIP, a predominantly beneficial effect of the intervention, which reduced SFA and dietary cholesterol intake while increasing PUFA intake throughout childhood, was observed for total cholesterol,[8,10,11,14,15,22-24,28-31] LDL cholesterol,[10,15,22,23,28,29] and triglycerides[10,11,15,22-24,28,29] in boys. Results were predominantly null for girls when analyzed separately from boys. HDL cholesterol was significantly lower in intervention group children, primarily girls, through age 5 years.[10,14,29-31] However, from age 7 years and older no statistically significant differences between the intervention and control group children were detected for HDL cholesterol.[8,10,11,15,22-24,28]

Similar, but less sustained, results were observed in DISC for blood lipids.[6,13,25] Children with LDL cholesterol levels at the 80th-98th percentile at baseline who received the intervention in DISC (dietary counseling to primarily reduce SFA and dietary cholesterol, with less emphasis on replacement) had lower total cholesterol and LDL cholesterol at the 1- and 3-year follow-ups (conducted at approximately age 10.5 and 12.5 years, respectively) compared to the control group [13]. However, no significant group differences were detected for total cholesterol or LDL cholesterol at the 5- and 7-year follow-ups (conducted at approximately 14.5 and approximately age 16.5 years, respectively) in the full cohort,[25] or at the 16- to 20-year follow-up conducted exclusively in female participants.[6] Triglycerides did not differ between groups at any time point, whereas HDL cholesterol was lower in the intervention group only at the 1-year follow-up.[6,13,25] Given that DISC enrolled children with elevated LDL cholesterol at baseline, the generalizability of this particular cohort is reduced.

The five remaining RCTs that examined blood lipids were heterogeneous, all providing food products to change child fat intake, but each focusing on different foods and types of fats.[2,5,7,18,36] One study increased long chain omega-3 (n-3) PUFAs (eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) by providing children with 300 grams per week of oily fish (compared to poultry with minimal long chain n-3 PUFA) for 12 weeks.[36] Although no differences in LDL cholesterol were detected between groups, increased long chain n-3 PUFA intake increased total cholesterol and HDL cholesterol and decreased triglycerides compared to controls.[36] Another study

that focused on PUFAs, in addition to SFA and dietary cholesterol, compared consumption of 25% energy from margarine, as spreads or bakery products, to butter for five weeks in a crossover trial.[5] Total cholesterol and LDL cholesterol were lower during the margarine period, which increased PUFA intake and decreased SFA and dietary cholesterol intake, compared to the butter period; no differences were detected between groups for HDL cholesterol or triglycerides.[5] In another crossover study that addressed replacement of SFA with unsaturated fatty acids, children consumed either 500 mL per day of whole milk or a commercially available powdered milk lower in SFA and dietary cholesterol and higher in MUFA and PUFA for 7 months.[7] Similar to the study comparing margarine to butter, total cholesterol and LDL cholesterol were lower following intake of the powdered milk higher in unsaturated fatty acids compared to intake of whole milk; no differences were detected for HDL cholesterol or triglycerides.[7] One crossover study modulated dietary cholesterol intake, in addition to SFA and MUFA intake, by comparing intake of two whole eggs per day to an egg white substitute for 4 weeks.[2] In this article, investigators categorized all participants as “hyper-" or “hyporesponders” to the dietary cholesterol intervention based on change in total blood cholesterol and this status was used as a variable in analyses.[2] Intake of whole eggs significantly increased both LDL and HDL cholesterol compared to egg substitutes, but the effect was stronger in “hyperresponders”; no effect on triglycerides was detected.[2] Finally, one cluster randomized study assessed replacement of typical oil consumed with extra virgin olive oil, which is rich in MUFAs.[18] No significant effect of the intervention was detected on total, LDL, or HDL cholesterol, or triglycerides.[18] However, because this study was conducted in Spain and refined olive oil would be the expected, predominant “typical oil consumed,” it is unlikely that the extra virgin olive oil increased MUFA intake at the expense of other types of fat in the intervention group.

Blood pressure. Ten articles from 5 RCTs examined the relationship between intake of types of fat during childhood and systolic or diastolic blood pressure.[2,6,8,15,18,21,24,28,32,36] In STRIP, dietary counseling that reduced SFA and dietary cholesterol intake had a beneficial effect or no effect on systolic and diastolic blood pressure.[6,8,21,24,28,32] However, the results for blood pressure in STRIP should be interpreted cautiously, as participants in the intervention group were also advised to reduce salt consumption as part of their counseling sessions.[6,8,21,24,28,32] Therefore, it is difficult to discern the independent effect of changing intakes of types of fat on blood pressure in this cohort.[6,8,21,24,28,32] In DISC, dietary counseling that targeted reduction of SFA intake, but not salt intake, had predominantly null effects on blood pressure.[6,32] The remaining 3 RCTs, which modulated child fat intake through provision of different food products (i.e., oily fish, eggs, or extra virgin olive oil), found predominantly null results for systolic and diastolic blood pressure.[2,18,36] In the study that compared intake of two whole eggs to egg substitutes for 4 weeks (modulating dietary cholesterol, SFA, and MUFA intake), a beneficial effect of the whole egg intervention was found for diastolic blood pressure, but not for systolic blood pressure.[2] Neither the study on oily fish (to increase long chain n-3 PUFA intake) nor the study on extra virgin olive oil detected a significant effect on blood pressure.[18,36] As noted previously, it is unlikely that the study on extra virgin olive oil provides a strong assessment of the effect of MUFA intake on blood pressure because the extra virgin olive oil likely replaced refined olive oil.[18]

PCSs

SFA and blood lipids. Twelve articles from 11 PCSs examined the relationship between SFA intake during childhood and blood lipids.[1,4,9,12,16,17,20,26,27,33,34,37] Of these, nine assessed total cholesterol,[1,4,16,17,20,26,33,34,37] six assessed LDL cholesterol,[4,9,16,17,27,33] ten assessed HDL cholesterol,[4,9,12,16,17,20,26,33,34,37] and four assessed triglycerides.[9,16,33,37] Broadly consistent with RCTs, results were predominantly null[1,9,16,33,37] or showed that higher intakes of SFA were associated with higher levels of total cholesterol[4,20,26,34] or LDL cholesterol.[4,17,27] Among the three studies that modeled replacement,[9,20,33] only one detected statistically significant results, finding that replacement of SFA with carbohydrate intake was associated with higher LDL cholesterol in females, but not males;[9] replacement of SFA with other types of fat in this study were non-significant.[9] In the case of HDL cholesterol and triglycerides, the majority of studies reported null associations between SFA intake and these blood lipids.[4,9,12,16,20,33,34,37] One study reported a statistically significant association between higher intake of SFA and higher HDL cholesterol,[26] whereas one study reported statistically significant associations between higher intake of SFA and lower triglycerides and between replacement of SFA with carbohydrate intake and higher triglycerides.[9]

SFA and blood pressure. Five articles from 4 PCSs examined the relationship between SFA intake during childhood and blood pressure.[17,26,32,33,35] The majority of these articles reported null associations between SFA intake and systolic or diastolic blood pressure,[17,26,32,33,35] including the one study that modeled replacement.[33] Only one study reported a statistically significant association between higher intakes of SFA at age 13 years and lower diastolic blood pressure at age 14 years.[26]

PUFA and blood lipids. Nine articles from 8 PCSs examined the relationship between PUFA intake during childhood and blood lipids.[1,4,9,12,20,26,27,33,34] Of these, six assessed total cholesterol,[1,4,20,26,33,34] four assessed LDL cholesterol,[4,9,27,33] seven assessed HDL cholesterol,[4,9,12,20,26,33,34] and two assessed triglycerides.[9,33] Broadly consistent with the results of RCTs, the association between PUFA intake and total cholesterol was predominantly beneficial[4,26,34] or null.[1,4,20,33] Among the articles that reported on HDL cholesterol, the majority reported null associations with PUFA intake[9,20,26,33,34]; only one reported a beneficial association and this was observed only in girls.[4] Of the few articles that assessed the relationship between PUFA intake and LDL cholesterol or triglycerides, including the three studies that examined replacement of other types of fat or macronutrients with PUFA, the majority of associations were null.[4,9,20,27,33] Only one study reported a significant association between replacement of other types of fat with unsaturated fatty acids (i.e., MUFA and PUFA) and higher total cholesterol after two years of follow-up.[20]

PUFA and blood pressure. Four articles from 3 PCSs examined the relationship between PUFA intake during childhood and blood pressure.[26,32,33,35] All articles reported null associations between PUFA intake and systolic or diastolic blood pressure,[26,32,33,35] including the one study that modeled replacement of other types of fats or macronutrients with PUFAs.[33]

MUFA and blood lipids. Seven articles from 7 PCSs examined the relationship between MUFA intake during childhood and blood lipids.[1,4,9,12,20,33,37] Of these, five assessed total cholesterol,[1,4,20,33,37] three assessed LDL cholesterol,[4,9,33] six assessed

HDL cholesterol,[4,9,12,20,33,37] and three assessed triglycerides.[9,33,37] All associations between MUFA intake and blood lipids were non-significant,[1,4,9,12,20,33,37] including studies that modeled replacement.[9,20,33]

MUFA and blood pressure. Three articles from 2 PCSs examined the relationship between MUFA intake during childhood and blood pressure.[32,33,35] One of these studies detected a significant association between higher MUFA intake and higher diastolic blood pressure, but did not detect a significant association with systolic blood pressure.[32] The other study reported null associations between MUFA intake and systolic or diastolic blood pressure,[33,35] including when replacement of other types of fat or macronutrients was modeled.[33]

Dietary cholesterol and blood lipids. Seven articles from 6 PCSs examined the relationship between dietary cholesterol intake during childhood and blood lipids.[1,3,4,20,26,27,34] Of these, six assessed total cholesterol,[1,3,4,20,26,34] two assessed LDL cholesterol,[4,27] five assessed HDL cholesterol,[3,4,20,26,34] and none assessed triglycerides. Broadly consistent with RCTs, associations between dietary cholesterol and total blood cholesterol were detrimental[1,26,34] or null.[1,3,4,20] All associations between dietary cholesterol and HDL cholesterol were null[4,20,26,34] except for one study that detected a significant association between higher dietary cholesterol and lower HDL cholesterol in girls, but not in boys.[3] LDL cholesterol was not significantly associated with dietary cholesterol in either study that assessed this relationship.[4,27] No study reported significant beneficial associations between dietary cholesterol and blood lipids.

Dietary cholesterol and blood pressure. Three articles from 3 PCSs examined the relationship between dietary cholesterol intake during childhood and blood pressure.[3,26,32] All three studies reported null associations between intake of dietary cholesterol and systolic or diastolic blood pressure.[3,26,32]

PUFA to SFA ratio and blood lipids. Three articles from 3 PCSs examined the relationship between the PUFA:SFA intake ratio during childhood and blood lipids.[3,4,34] Of these, all examined total cholesterol and HDL cholesterol,[3,4,34] one examined LDL cholesterol,[4] and none examined triglycerides. For total cholesterol, results were inconsistent with one study reporting a significant association between a higher PUFA:SFA intake ratio and lower total cholesterol,[34] another reporting a significant association with higher total cholesterol (but only in boys),[4] and the last reporting a null association.[3] In the one study that assessed LDL cholesterol, a higher PUFA:SFA intake ratios was significantly associated with higher LDL cholesterol in boys, but not in girls.[4] All three studies reported null associations between the PUFA:SFA intake ratio and HDL cholesterol.[3,4,34]

PUFA to SFA ratio and blood pressure. One article examined the relationship between the PUFA:SFA intake ratio during childhood and blood pressure.[3] This study reported a null association between the PUFA:SFA intake ratio and systolic or diastolic blood pressure.[3]

CVD endpoint outcomes

One article studying the relationship between intake of types of fat during childhood and CVD endpoint outcomes in adulthood met inclusion criteria.[19] Specifically, this

prospective cohort study (N=4,028) assessed the association between SFA intake at approximately age 7.5 years and CHD mortality or stroke mortality during approximately 60 years of follow-up.[19] In this cohort from the U.K., SFA intake was not significantly associated with either CHD mortality or stroke mortality. Results of this study were interpreted with caution due to serious limitations of the dietary assessment method. Specifically, child SFA intake was estimated by dividing total household intake, assessed with a 7-day weighed household inventory, by the number of household members. No information on the accuracy or validity of this assessment, conducted in the late 1930s, in regards to child intake was provided. Evidence and the risk of bias assessment for this study are described in **Table 2** and **Table 4**, respectively.

Assessment of the evidence[vii]

As outlined and described below, the body of evidence examining intake of types of dietary fat during childhood and CVD intermediate and endpoint outcomes was assessed for the following elements used when grading the strength of evidence.

Risk of Bias

As noted previously, the risk of bias assessment for RCTs and PCSs are described in **Table 3** and **Table 4**, respectively. The RCTs included in this portion of the review were generally of low risk of bias, with the exception of selection of the reported result for which most articles were assessed as having some concerns due to a lack of pre-registered statistical analysis plans or protocols. Information on the allocation of randomization sequences were not provided for the crossover and cluster RCTs.[2,5,7,18] Risk of bias across the PCSs were predominantly low or moderate for several domains including selection of participants, deviations from intended exposures, and outcome measurement. All PCSs were at serious risk of bias due to confounding as none accounted for all key confounders. However, several studies did account for the majority of key confounders, including sex, age, race/ethnicity, and total energy intake. Over half of the PCSs were at moderate or serious risk of bias for classification of exposures due to the use of dietary assessment tools with no confirmation of validity. The majority of PCSs were also at moderate risk of bias for missing data due to high attrition rates without information on those lost to follow-up.

Consistency

The results from RCTs that modulated SFA, PUFA, and dietary cholesterol intake were predominantly consistent with one another, showing primarily beneficial effects throughout childhood for total cholesterol and LDL cholesterol. The PCSs that assessed SFA, PUFA, and/or dietary cholesterol intake were broadly consistent with these RCTs, showing primarily either statistically significant associations in the same direction as predicted by RCTs or null associations.

[vii] A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

Directness
The majority of studies were designed to examine the relationship between dietary fat intake and risk of cardiovascular disease. However, the RCTs that provided dietary counseling were more directly focused on reduction of SFA and dietary cholesterol than changes in intake of MUFA or PUFA.

Precision
The majority of RCTs were powered to detect differences in blood lipids. Although sample size varied greatly across the PCSs, many had relatively large sample sizes.[3,9,19,20,32,33,35,37]

Generalizability
Most studies were conducted in the U.S., the U.K., and Scandinavia. Studies assessed dietary fat intake at a variety of ages during childhood, from infancy through adolescence. Many studies did not report race or ethnicity but those that did had samples that were predominantly White or Caucasian. The majority of studies included children with normal blood lipids at baseline, although some specifically recruited children with elevated or higher than average blood lipid levels.[6,13,25,27,32]

Other important considerations

A large, comprehensive search was conducted in multiple databases for this systematic review. Although risk of publication bias is always of potential concern, both small and large studies were included in this review, reporting both null and statistically significant results. Therefore, risk of publication bias is likely low across this body of evidence.

Description of the evidence: Adults (Cardiovascular disease intermediate outcomes)

Of the 228 articles that met inclusion criteria for this systematic review, 97 articles examined the relationship between types of dietary fat consumed during adulthood and CVD intermediate outcomes (i.e., total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides). Of these, 47 articles were from 47 parallel design RCTs,[38,41,44,47-53,59,61,63-65,67,70,71,73-75,78,81,82,84,88,89,92,93,95,96,99,100,104,106,110,112,113,120,125-127,129,130,132-134] 46 articles were from 44 crossover design RCTs,[39,42,43,45,46,49,54-58,60,62,66,68,69,72,76,77,79,80,83,85-87,90,91,94,97,98,101-103,105,107-109,111,115,118,119,121,122,124,128,131] 4 articles were from 4 crossover design non-randomized controlled trials (NRCT),[40,114,116,117] and 1 article was from a parallel design NRCT.[123] (Note: One parallel design RCT was also analyzed as a crossover design RCT.)[49] Except for four articles from two crossover design RCTs,[83,91,94,111] all articles reported on unique trials.

Detailed information on sample characteristics, intervention, comparator, including the distribution of types of fats in the intervention/comparator and dietary intake are described in **Table 5**. Sample sizes varied across articles, ranging from N=9[103] to N=164[91,111] for crossover designs and from N=17[129] to N=1,204[81] for parallel designs; the majority of articles had sample sizes of 100 participants or less. Participants were predominantly middle-aged or older adults with overweight or obesity and with normal blood lipids levels or mild hyperlipidemia. However, several studies specifically recruited participants at elevated risk for CVD, such as individuals with metabolic

syndrome[41,47,52,70,71,77,100,108,134] or multiple components of metabolic syndrome,[44,54,82,83,86,94,99,110] overweight or obese with one or more component of metabolic syndrome,[43,44,53,66,77,103,107] high blood pressure,[91,111] prediabetes,[107] polycystic ovary syndrome,[84] or who survived breast cancer.[123] Fourteen articles reported on studies that were conducted in younger adults, with mean ages less than 30 years[51,57,58,61,64,67,78,85,90,96,101,114,122,133]; these participants tended to have fewer risk factors for CVD and were predominantly of normal body mass index (BMI). Approximately 40% of the included studies were conducted in the U.S.; however, varieties of countries were represented across the body of evidence. These countries included:

- Australia[46,65,73,93,118,120]
- Brazil[63,71]
- Canada[39,42,54,55,66,83,94]
- China[57,96,119]
- Colombia[95]
- Denmark[51,68,75,110,132]
- Finland[81,108]
- France[134]
- Germany[47,62,67,92]
- Greece[90]
- Iran[41,70]
- Ireland[134]
- Italy[44,79,116,117]
- Japan[87]
- Malaysia[85,104,121,122]
- Netherlands[53,99,109,127,128,134]
- Norway[74,130,134]
- Poland[134]
- Spain[102,105,134]
- Sweden[50,78,134]
- Thailand[58]
- Turkey[114]
- U.K.[80,82,88,126,134]
- U.S.[38,40,43,45,48,49,52,54,56,59-61,64,69,72,76,77,83,84,86,89,91,94,97,98,100,101,103,106,107,111-113,115,123-125,129,131,133]

The type or types of dietary fat focused upon varied across the articles included in this body of evidence. Articles focused on a single type of fat, modulated multiple types of fat, or both. Of the articles that examined a single type of fat, 12 articles primarily examined SFA,[48,49,55,58,66,88,97,104,116,121,125,132] 12 articles primarily examined MUFA,[38,43,45,46,63,64,91,103,107,111,131] 11 articles primarily examined PUFA.[41,44,47,56,62,73,86,87,97,106,117] Additionally, 9 articles primarily addressed dietary cholesterol as the exposure,[42,52,56,61,80,101,113,115,127] although other types of fat often were not controlled for and varied between groups in these articles. Most articles

modulated multiple types of dietary fat, such as by replacing one type of fat with another or by changing the proportions of multiple types of fat in relation to other macronutrients. Of these articles that modulated multiple types of dietary fat, 29 focused on SFA and MUFA,[39,40,49,51,53-55,57,59,68,72,76,79,81,82,88,95,96,98,99,102,105,108,118,119,122,126,134] 10 focused on SFA and PUFA,[50,55,65,71,78,79,81,96,102,126] 17 focused on MUFA and PUFA,[54,70,83-85,90,92,94,96,100,102,109,112,114,120,124,126] and 15 focused on SFA, MUFA, and PUFA.[60,67,69,74,75,77,89,93,110,117,123,128-130,133]

In most articles, dietary fat intake was manipulated by providing test foods varying in fatty acid content to participants. The majority of the test foods were provided in their natural form; few studies provided specially formulated oils that are not widely available or consumed by the public. Approximately one-third of articles reported on controlled feeding trials in which study investigators provided all food to be consumed during the study period to participants.[43-45,51,53,55,57,67,82,83,85,89,91,96,98,99,106,111,118,119,121-124,129,131,133] In both cases, the majority of studies provided the test foods or meals daily. Most articles specified the primary food source of the dietary fat under study. These foods included oil (e.g., coconut oil, olive oil, and rapeseed oil),[41,43,47,50,53-55,57,58,62,67,68,70,76,78,82,83,85,87,88,90,92,94-96,99,100,102,104,108,109,112,118,119,121,122,126,131] butter[50,55,65,68,71,88,102,108,112,125,126,132] and other dairy products,[39,48,49,59,66,79,105,110,116,125,128] nuts,[38,43,45,46,56,63-65,84,86,98,107,114,124] eggs,[42,52,56,61,101,113,115,127] meat,[40,49,60,72-75,97,106] and fish.[44,73-75,80,106,117] Few articles did not report information on the primary food source of the dietary fat under study.[51,69,77,81,89,91,93,103,111,120,123,129,130,133,134] Several studies were designed to induce weight gain,[78] maintain weight loss,[51] or induce weight loss in participants during the intervention trial.[89,93,120,129] Intervention durations ranged from 4 weeks (the minimum required for inclusion in this review) to 19.5 years in parents of STRIP participants[81]; however, most interventions were 4 to 8 weeks in duration, with crossover design trials tending to have shorter intervention periods than parallel design trials. Among crossover trials, the duration of washout periods ranged from 1 week[45,122] to 10 weeks.[62,116] A washout period was not reported in three studies,[46,69,114] two of which had intervention arm durations of only 4 weeks. Although the majority of studies measured compliance using food diaries or FFQs, 30 out of 97 studies did not report compliance to the dietary intervention.

All articles assessed fasting blood lipids as the outcome. The majority of studies examined total blood cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides. However, a few trials did not examine total blood cholesterol[40,77,96,112] or HDL cholesterol.[51]

Evidence synthesis: Adults (Cardiovascular disease intermediate outcomes)

Evidence was synthesized by type of fat. Evidence from RCTs and NRCTs are described in **Table 5**. The risk of bias assessments are described in **Table 6** (for RCTs) and **Table 7** (for NRCTs).

SFA

Twelve articles (6 from parallel design RCTs, 6 from crossover design RCTs) assessed the relationship between consumption of SFA, compared to either different types, amounts or sources of SFA or replacing a portion of SFA with carbohydrate, during adulthood and blood lipid levels.[48,49,55,58,66,88,97,104,116,121,125,132] (Note: One article reported on a study that was analyzed as both a parallel design and crossover design RCT.)[49] Across different amounts, types and sources of SFA, results were predominantly null for blood lipids.[48,49,55,58,66,88,97,104,116,121,132] However, the consistency and pattern of results varied by the type of blood lipid and comparator. Among articles that did detect statistically significant effects on total and LDL cholesterol, most reported significantly higher levels of total or LDL cholesterol with higher intake of SFA, compared to either lower amounts of SFA or substitution with carbohydrate.[55,66,125] Among the few articles that did detect statistically significant effects on HDL cholesterol, SFA intake, primarily replacing a portion of carbohydrates, resulted in significantly higher levels of HDL cholesterol.[55,58,121,125] The vast majority of articles that assessed effect of SFA intake on triglycerides were null. When examining different sources of SFA, SFA from butter[88] or red or white meat[49] significantly increased total or LDL cholesterol compared to SFA from tropical oils, whereas SFA from coconut oil[88] or red or white meat[49] significantly increased HDL cholesterol compared to SFA from butter and tropical oils, respectively. The one study that examined the effect of different types of SFA (palmitic vs stearic acids) did not find an effect on total, LDL, or HDL cholesterol, but reported a significant greater levels of triglycerides with palmitic acid.[104]

Replacement of SFA with MUFA

Twenty-nine articles (12 from parallel design RCTs, 16 from crossover design RCTs, and 1 NRCT) assessed the relationship between MUFA intake replacing a portion of SFA during adulthood and blood lipid levels.[39,40,49,51,53-55,57,59,68,72,76,79,81,82,88,95,96,98,99,102,105,108,118,119,122,126,134] The consistency and pattern of results varied by outcome. Over half of articles reported a statistically significant effect of MUFA intake replacing a portion of SFA on total and LDL cholesterol, most of which reported a beneficial effect of MUFA on total cholesterol and LDL cholesterol,[39,49,53-55,68,76,81,82,88,95,98,102,108,121,122,126] and only one article finding higher LDL cholesterol when SFA was replaced with MUFA.[96] Among articles that examined the effect of replacing SFA intake with MUFA intake, the vast majority detected no effect on HDL cholesterol.[39,49,53-55,57,59,68,81,82,88,95,96,98,99,102,105,108,118,119,121,126,134] Those articles that did detect significant effects were mixed, some finding higher HDL cholesterol with higher MUFA intake,[40,72,122] but others finding higher HDL cholesterol with higher SFA intake.[76,88] Compared to other blood lipids, fewer articles detected a significant effect of MUFA intake on triglycerides. As with HDL cholesterol, the effects of MUFA intake replacing a portion of SFA on triglycerides were predominantly null.[39,49,51,53-55,59,68,72,76,79,81,82,88,95,96,98,99,102,105,108,118,119,121,126,134] Among the articles that detected a significant effect, all studies reported lower triglycerides or greater decreases in triglycerides with MUFA intake replacing a portion of SFA intake.[40,57,99,122]

Replacement of SFA with PUFA

Ten articles (7 from parallel design RCTs, 3 from crossover design RCTs) assessed

the relationship between PUFA intake replacing a portion of SFA during adulthood and blood lipid levels.[50,55,65,71,78,79,81,96,102,126] The consistency and pattern of results varied by outcome. Over half of articles reported a statistically significant effect of PUFA intake replacing a portion of SFA on total and LDL cholesterol, all of which reported a beneficial effect of PUFA on total cholesterol or LDL cholesterol.[50,55,81,96,102,126] All articles reported null effects of PUFA intake replacing a portion of SFA on HDL cholesterol.[50,55,65,71,78,79,81,96,102,126] The vast majority of articles that assessed effect of SFA intake on triglycerides were null, with only one study reporting a significantly higher levels of triglycerides after SFA consumption compared to PUFA intake.[55]

MUFA

Fourteen articles (5 from parallel design RCTs, 9 from crossover design RCTs) assessed the relationship between MUFA intake, compared to either different amounts or sources of MUFA or replacing a portion of MUFA with carbohydrate, during adulthood and blood lipid levels.[38,43,45,46,63,64,91,103,107,111,131] Across different amounts, types and sources of MUFA, results were predominantly null.[38,43,45,46,51,63,64,82,91,103,107,111,131] However, the consistency and pattern of results varied by the type of blood lipids and dietary comparator. Among the few articles that detected a statistically significant effect on total and LDL cholesterol, MUFA intake, primarily replacing a portion of carbohydrates, resulted in significantly lower levels or had greater decreases in total or LDL cholesterol.[111,131] Among the few articles that detected a statistically significant effect on HDL cholesterol, all but one article reported that MUFA intake, primarily replacing a portion of carbohydrates, resulted in significantly higher levels or a smaller decrease in HDL cholesterol.[64,111,131] Similar to total and LDL cholesterol, the vast majority of articles that assessed the effect of MUFA intake on triglycerides were null. Only two studies reported significant effects, both of which reported greater decreases in triglycerides with higher MUFA intake.[111,131] Regarding source of MUFA, only one study maintained MUFA intake constant but varied the source of MUFA.[131] This article reported significantly greater decreases in total and LDL cholesterol after consumption of MUFA from avocado, compared to MUFA from sunflower and canola oil.[131]

Replacement of MUFA with PUFA

Eighteen articles (10 from parallel design RCTs, 7 from crossover design RCTs, 1 NRCT) assessed the relationship between PUFA intake replacing a portion of MUFA during adulthood and blood lipids.[47,54,70,83-85,90,92,94,96,100,102,109,112,114,120,124,126] Across different amounts, types and sources of PUFA, results were predominantly null for blood lipids.[47,54,70,83-85,90,92,94,96,100,102,109,112,114,120,124,126] However, the consistency and pattern of results of studies that detected significant effects varied by the type of blood lipid. Several articles detected a statistically significant effect on total and LDL cholesterol, the majority reporting that higher intake of PUFA replacing a portion of MUFA resulted in significantly lower levels of or significant decreases in total or LDL cholesterol.[83,94,96,120] The remaining articles reported significantly lower levels of or decrease in total or LDL cholesterol with higher intake of MUFA replacing a portion of PUFA.[70,114] Among the few articles that detected a statistically significant effect on HDL cholesterol, all articles reported that PUFA intake replacing a portion of MUFA, resulted in significant decreases or greater decreases in HDL cholesterol.[70,83,85,94] Similar to total, LDL, and HDL cholesterol, the vast majority of articles that assessed

the effect of PUFA intake replacing a portion of MUFA on triglycerides were null. Among the few articles that detected a statistically significant effect on triglycerides, majority of articles reported that PUFA intake replacing a portion of MUFA, resulted in significantly higher levels of, smaller decreases in, or greater increases in triglycerides.[70,83,85,94] Only one article reported a greater decrease with PUFA intake replacing a portion of MUFA.[47] Additionally, two articles from the COMIT I trial reported a beneficial change in HDL cholesterol or triglycerides with either higher MUFA or PUFA depending on the type of oil compared.[83,94]

PUFA

Ten articles (4 from parallel design RCTs, 5 from crossover design RCTs, 1 NRCT) assessed the relationship between PUFA intake, compared to either different amounts or sources of PUFA or replacing a portion of PUFA with carbohydrate, during adulthood and blood lipids.[41,44,56,62,73,86,87,97,106,117] Across different amounts, types and sources of PUFA results were predominantly null.[41,44,47,56,62,73,86,87,97,106,117] The vast majority of articles that assessed the effect of PUFA intake on total and LDL cholesterol were null.[41,44,56,62,73,86,97,106,117] Among the few articles that detected a statistically significant effect of amount of PUFA on HDL cholesterol, both studies reported either significantly higher levels of or smaller decreases in HDL cholesterol with greater PUFA intake.[62,106] Among the few articles that detected statistically significant effects of PUFA on triglycerides, all studies reported a significantly greater decrease or lower levels of triglycerides with greater PUFA intake.[56,62,106] When comparing types of PUFA (alpha-linolenic acid [ALA] vs linoleic acid [LA]), one study reported significantly higher total, LDL, and HDL cholesterol with higher ALA intake in a study conducted only in men.[87]

SFA, MUFA, and PUFA

The following articles were weighed less heavily in the synthesis due to weaknesses in the study design. In fifteen articles, it was not possible to isolate the independent effect of SFA, MUFA or PUFA on blood lipids due to simultaneous changes of those three types of fat.[60,67,69,74,75,77,89,93,110,117,123,128-130,133] Results of these articles were predominantly null.[60,67,69,74,75,77,89,93,110,117,123,128,129,133] Among these studies, five concurrently restricted the energy composition of the intervention and/or control diet, making it difficult to detect the independent effect of dietary fat modification.[89,93,123,129,130] In a study designed to maintain recent weight loss, participants in all intervention arms experienced significant weight gain during the intervention, potentially obscuring results related to fat modification.[51] However, among the studies that found significant effects, higher-fat diets, higher in all types of fat, tended to increase LDL and HDL cholesterol,[74,77] and lower-fat diets (typically higher in carbohydrates) tended to increase triglycerides.[69,77,123] There were mixed findings for total cholesterol, with one study[67] reporting significantly greater increases in total cholesterol with higher-fat diet and another reporting significantly greater decreases in total cholesterol with a higher-fat diet.[130]

Dietary cholesterol

Nine articles (4 from parallel design RCTs and 5 from crossover design RCTs) primarily assessed the relationship between dietary cholesterol intake and blood lipids.[42,52,56,61,80,101,113,115,127] Of these, most achieved differences in dietary cholesterol

intake by providing the intervention arm with meals or beverages that contained whole eggs or egg yolks and the comparator arm with dietary cholesterol-free alternatives such as egg substitutes, egg whites, or carbohydrate based breakfast foods (e.g., oatmeal).[42,52,56,61,101,113,115,127] However, in one article the source of dietary cholesterol was prawns, which also provided 0.6-0.7 grams of EPA and DHA.[80] Across the body of evidence, higher dietary cholesterol intake, compared to lower dietary cholesterol intake, had either null effects on blood lipids,[52,56,61,80,113,115,127] or increased or resulted in higher levels of total blood cholesterol,[42,56,101] LDL cholesterol,[42,101] HDL cholesterol,[42,101] and/or triglycerides.[56] One article, which compared consumption of standard or n-3 PUFA enriched eggs to walnuts (free of dietary cholesterol), reported mixed results that varied by the type of egg.[56] When intake of standard eggs was compared to walnuts, higher dietary cholesterol increased total blood cholesterol and triglycerides, whereas when intake of n-3 PUFA enriched eggs was compared to walnuts, no effect on blood lipids was detected.[56] In several articles, it was not possible to isolate the independent effect of dietary cholesterol on blood lipids due to between-group differences in total fat intake,[101,113] SFA intake,[101,113] MUFA intake,[101,127] or PUFA intake[56,80] also attributable to the intervention and comparator foods. Additionally, some articles did not report the fat content of the intervention and comparator foods.[42,52] Therefore, it was difficult to evaluate the independent effect of dietary cholesterol on blood lipids across this body of evidence.

Assessment of the evidence[viii]

As outlined and described below, the body of evidence examining intake of types of dietary fat by adults and CVD intermediate outcomes was assessed for the following elements used when grading the strength of evidence.

Risk of Bias

As noted previously, the risk of bias assessment for RCTs and NRCTs are described in **Table 6** and **Table 7**, respectively. All RCTs were assessed as having low risk of bias for outcome measurement and over half were assessed as having low risk of bias for missing outcome data and deviations from intended interventions. In contrast, there were some concerns regarding selection of the reported result for the majority of articles from RCTs, as few articles reported a pre-registered protocol with sufficient information to assess statistical analysis intentions. Over half of the articles from RCTs had some concerns regarding randomization, as many did not provide information on the randomization and concealment of the allocation sequence. Among the few NRCTs, risk of bias was primarily assessed as low; however, all articles were assessed as being at serious risk of bias for confounding and at moderate risk of bias for selection of reported result.

Consistency

Consistency in results was observed across the body of evidence. Although the

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[viii] A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

relationship between types of dietary fat and blood lipids varied by the type of fat examined, replacing macronutrient or other types of fat, or the specific blood lipid, significant effects within those categories tended to be in the same direction.

Directness

Although many studies in this body of evidence were specifically designed to evaluate the relationship between types of dietary fat and blood lipids, others were less direct due to the nature of the intervention. For example, many articles were primarily interested on the effect of foods rich in particular types of fat, such as dairy, nuts, or fish, on blood lipids. Because these foods commonly produced differences in intake of multiple macronutrients and/or multiple types of fat, it was sometimes difficult to assess precisely the relationship between types of dietary fat and blood lipids. Less frequently, studies were primarily interested in assessing the effect of replacing total fat with carbohydrates, reducing intake of all types of fat but primarily from SFA. Again, this made it difficult to attribute effects or lack of effects specifically to a single type of fat versus multiple types of fat or a total reduction in fat intake.

Precision

Fewer than half of included articles reported a power calculation specific to blood lipids. Of these articles, most reported having adequate power. The remaining articles did not report a power analysis or had calculated the power of the trial for an alternative outcome. Many of these studies had particularly small sample sizes, so the precision of these articles may not be strong.

Generalizability

Most articles reported on studies conducted in the U.S. (over one-third of articles), and in a variety of countries across Europe. Race and ethnicity were not commonly reported in this body of evidence. Most articles that did report race and ethnicity had participants who were predominantly White or Caucasian. Although participants were predominantly middle-aged or older adults with overweight or obesity and with normal blood lipid levels or mild hyperlipidemia, studies were conducted in a variety of populations such as younger adults with low risk of CVD or middle-aged adults at elevated risk of CVD (e.g., individuals with metabolic syndrome).

Other important considerations

Publication bias

A large, comprehensive search was conducted in multiple databases for this systematic review. Although risk of publication bias is always of potential concern, this body of evidence was composed primarily of small and moderately sized studies that reported both null and statistically significant results. Therefore, the risk of publication bias is likely low across this body of evidence.

Building on the 2015 Dietary Guidelines Advisory Committee report and conclusions

This systematic review builds and expands on the work of the 2015 Dietary Guidelines Advisory Committee, which answered the question, “What is the relationship between intake of saturated fat and risk of cardiovascular disease?” and considered evidence from systematic reviews and meta-analyses, which included RCTs and PCSs from the

1960s to 2010.[ix] The 2015 Committee drew one conclusion pertaining to intermediate CVD outcomes (i.e., blood lipids):

- "Strong and consistent evidence from RCTs shows that replacing SFA with unsaturated fats, especially PUFA, significantly reduces total and LDL cholesterol. Replacing SFA with carbohydrates (sources not defined) also reduces total and LDL cholesterol, but significantly increases triglycerides and reduces HDL cholesterol. (Grade: Strong)"

The evidence in the present review is broadly consistent with this conclusion drawn by the 2015 Committee. In articles that examined replacement of SFA with MUFA or PUFA, MUFA or PUFA intake replacing a portion of SFA intake predominantly showed lower levels of or larger decreases in total blood and LDL cholesterol or null effects. Relative to articles that looked at replacement of SFA with unsaturated fatty acids, few articles in this body of evidence examined the effect of replacing SFA with carbohydrates. Across these articles, results were null or showed effects consistent with conclusions from the 2015 Committee, mainly lower total blood, LDL, and HDL cholesterol when SFA was replaced with carbohydrates. Based on the evidence in the present review, the 2020 Committee concurred with and updated the conclusions drawn by the 2015 Committee regarding replacement of SFA with MUFA, PUFA, or carbohydrates, with edits to increase the specificity of the conclusions.

Description of the evidence: Adults (Cardiovascular disease endpoint outcomes)

Of the 228 articles that met inclusion criteria for this systematic review, 94 articles examined the relationship between intake of types of dietary fat and CVD endpoint outcomes in adults. Of these, 90 articles were PCS designs (47 cohorts)[135-171,173-188,190-194,196-208,210-228] and 4 articles were nested case-control (NCC) designs (3 cohorts).[172,189,195,209] Sample sizes across the PCSs varied greatly, ranging from N=495[176] to N=521,120,[226] although most studies had >10,000 participants. The NCC studies had relatively smaller sample sizes, ranging in size from n=97 cases and n=194 controls[195] to n=720 cases and n=1,568 controls.[172] Participants were predominantly healthy middle-aged or older adults with overweight and without CVD at baseline. Almost half of studies also excluded individuals with prevalent cancer or diabetes. Although two studies only recruited individuals at high risk for CVD,[163,164,184,202] the majority of studies recruited from the population more generally. Most articles excluded participants with prevalent CVD, but some did not.[136,139,142,147,152,173] Most studies were conducted in cohorts that included both men and women, although some studies enrolled only men[135,139,144,166,174,176,205,213,214,219] or only women.[140,141,143,145-147,152,179,181,182,194,200,208,220] Race or ethnicity was not consistently reported, particularly in studies conducted in Europe. Among studies that did report race or ethnicity, participants were predominantly White or Caucasian.

[ix] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

However, several cohorts from the U.S. reported more diverse samples.[156,157,161,168,173,201,224,225] Most studies were conducted in the U.S. and Scandinavia. Varieties of other countries were represented across the body of evidence, however. Countries represented in the body of evidence included:

- Australia[147,191,192]
- Czech Republic[207]
- Denmark[148,149,160,170,171,198,208,210-212]
- Finland[135,176,205,213,214]
- France[203]
- Greece[177]
- Italy[143,193,195]
- Japan[166,185-187,190,216,221,222]
- The Netherlands[153-155,162,196,197,215]
- Norway[169]
- Poland[207]
- Russia[207]
- Singapore[175,188,189,209]
- Spain[138,150,151,163,164,202,204]
- Sweden[137,144-146,158,165,167,174,178,179,181,182,194,206,217]
- U.K.[136,139,198]
- U.S.[140-142,152,156,157,159,161,168,172,173,180,183,184,199-201,218-220,223-228]

The majority of studies measured dietary fat intake with validated FFQs, administered once at baseline. However, 11 articles assessed dietary fat intake multiple times with validated FFQs.[139,152,163,164,180,183,202,218,223,227,228] Other dietary assessment methods reported in these studies included 24-hour recalls,[190,201,225] food diaries/diet records,[135,176,184,213,214] and weighed individual or household food records.[166,185,187,210] Of the 94 included articles, 39 assessed SFA intake,[136,139,140,147,152,156,161,163,167,168,170,178,179,183,186-188,190,191,195-199,201,204,205,212,213,215-218,220-222,226-228] 29 assessed MUFA intake,[139,152,161,163,168,179,183,186,188,190,195-199,201,204,205,212,213,215-218,220,222,226-228] 71 assessed PUFA intake (including total PUFA intake, n-3 PUFA intake, and/or omega-6 [n-6] PUFA intake),[136-142,144-146,148,149,152-155,157-160,163,165-169,171-175,178-183,185-190,192,195-202,204,205,208-213,215-220,222,223,225,226,228] and 11 assessed dietary cholesterol intake.[135,140,168,179,184,187,188,195,214,220,224] Several of these studies modeled replacement between different types of fats or macronutrients, or in some cases between different sources of the same type of fat.[152,156,163,170,196-198,201,204,205,212,213,215,218,222,226-228] Few articles specifically assessed types of fat from different food sources.[155,156,163,169,196-198,215,226,227] Furthermore, because the literature search predominantly focused on types of fat, and not food sources that contain fat, few articles directly assessed common food sources of fat, including butter (predominantly SFA)[162,176,193,194,206] and olive oil (predominantly MUFA).[143,150,151,164,177,203,207]

CVD endpoint outcomes were assessed primarily through linkage to national registries for hospital discharges, medical records, and cause of death, although in some cases presence of the outcome was also assessed through follow-up directly with participant

or next of kin. Average time of follow-up ranged from approximately 5 years[142,147,164,191,195] to approximately 30 years,[152,218] but most studies had an average follow-up of at least 10 years. Of the included studies, 41 articles reported on incident CVD, inclusive of multiple types of fatal and/or nonfatal cases or events including myocardial infarction (MI), CHD, and stroke, of which 28 assessed CVD mortality alone[136,142,150,158,159,161,163,164,166,173,175,185,186,188,192,193,199-202,207,216,218,222-226] and 18 assessed nonfatal cases or events or a combination of fatal and nonfatal cases or events.[140,156,157,163-165,167,168,177,184,191,200,204,206,208,217,221,224] Additionally, articles reported on more specific categories of CVD endpoint outcomes. Forty-nine articles reported on incident CHD, coronary artery disease (CAD), and/or MI, of which 15 assessed mortality alone[142,147,153,159,175,185,187,197,202,207,209,213,222,223,225] and 39 assessed nonfatal cases or a combination of fatal and nonfatal cases.[138,143-145,148,151,153-157,159,160,162,170-172,176,183,189,194-198,200,205,206,208-210,213-215,217,221,224,227,228] Twenty-six articles examined stroke, of which 7 articles reported on stroke mortality alone[175,185,202,207,222,223,225] and 19 articles reported on nonfatal stroke or a combination of fatal and nonfatal stroke outcomes.[135,139,146,149,155,159,162,174,179,190,200,203,206,211,212,217,220,221,224] Less commonly assessed outcomes in this body of evidence included heart failure (9 articles),[137,140,141,180-182,219,222,224] sudden cardiac death (3 articles),[152,202,221] peripheral artery disease (PAD; 1 article),[178] and venous thromboembolism (1 article).[169]

Evidence synthesis: Adults (Cardiovascular disease endpoint outcomes)

Evidence was synthesized by type of fat, outcome, and study design. Evidence from the PCSs are described in **Table 8** whereas evidence from the NCC studies are described in **Table 9**. The risk of bias assessments for both study designs are described in **Table 10**.

SFA

Thirty-nine articles (38 from PCSs and 1 from a NCC study) assessed the relationship between SFA intake during adulthood and risk of CVD endpoint outcomes.[136,139,140,147,152,156,161,163,167,168,170,178,179,183,186-188,190,191,195-199,201,204,205,212,213,215-218,220-222,226-228] Of these, 18 articles modeled replacement of SFA with other types of fat or macronutrients,[152,156,163,170,196-198,201,204,205,212,213,215,218,222,226-228] and six articles examined MUFA:SFA or PUFA:SFA intake ratios.[136,140,161,188,199,216] Most of the articles reported on either CVD, inclusive of multiple conditions,[136,140,156,161,163,167,168,186,188,191,199,201,204,216,217,221,222,226] or CHD, CAD, and MI.[147,156,170,183,187,195-198,205,213,215,217,218,221,222,227,228] Fewer articles reported on stroke,[139,179,190,212,217,220-222] heart failure,[140,222] PAD,[178] or sudden cardiac death.[152,221,222]

SFA and total CVD

Among articles that assessed the relationship between SFA intake and CVD without considering replacement, results were predominantly null,[140,163,167,168,186,188,191,216-218] but some detected associations between higher SFA intake and lower CVD risk,[188,216,221,222] all of which were conducted in Asia and had participants with, on average, BMI in the normal range. One article reported a statistically significant association between higher SFA intake and greater risk of CVD, but only in women.[218]

When replacement with other types of fat or macronutrients was considered, the pattern of results tended to differ by what macronutrient replaced SFA. When SFA was replaced by total PUFA, results primarily demonstrated associations with lower risk of CVD[163,201,226] or null associations,[204,226] with most studies focusing on CVD mortality. One study reported that replacement of SFA with arachidonic acid (AA) was associated with higher risk of CVD mortality, but also found that replacing SFA with LA and marine omega-3 fatty acids was significantly associated with lower risk.[226] When SFA was replaced with MUFA, results were predominantly null[201,204,226] or indicated an association with lower risk of CVD.[226] When SFA was replaced by carbohydrate, one article indicated null associations with CVD,[204] whereas when carbohydrate was replaced by SFA, two articles indicated associations with greater CVD risk (one only in men).[163,218] In addition to the studies that examined total SFA intake, two examined the relationship between SFA from food sources and risk of CVD and results were inconsistent.[156,163] One study (conducted in Spain) reported null associations for SFA from dairy, meat, and eggs, and statistically significant associations with lower risk of CVD with SFA from vegetables and fish/seafood.[163] The other study (conducted in the U.S.) reported null associations for SFA from butter and plants, and statistically significant associations with lower risk of CVD with SFA from dairy and higher risk of CVD with SFA from meat.[156] Articles that examined the relationship between the MUFA:SFA or PUFA:SFA intake ratio and CVD reported predominantly null associations,[136,140,161,188,199,216] although one study reported a higher risk of CVD mortality with a higher PUFA:SFA ratio in men[216] and another study reported a lower risk of CVD mortality with a higher MUFA:SFA ratio in men or higher total unsaturated fatty acid (UFA):SFA ratio in men and women.[199]

SFA and CHD, CAD, MI, or PAD

Several articles assessed the relationship between SFA intake, without considering replacement, and CHD, CAD, and/or MI, and these associations were primarily null[183,187,197,198,217,221,222,228] or indicated greater risk with higher SFA intake.[147,187,221,228] Only two of these non-replacement studies reported a statistically significant associations between higher SFA intake and lower risk of CHD, CAD, and/or MI.[198,217] Regarding types of SFAs, two studies found inconsistent associations between intake of either shorter-chain SFAs of 4 to 10 carbons or longer-chain SFAs of 12 to 18 carbons and risk of CHD/MI.[198,228] When replacement with other types of fat or macronutrients was considered, the pattern of results tended to differ by the replacing macronutrient. When SFA was replaced by total PUFA, the associated risk of CHD was primarily null[197,198,222] or lower.[213,228] Only one study reported a significant association between replacement of SFA with PUFA and higher risk of CHD; however, this article reported small ranges in both SFA and PUFA intake in their cohort.[196] When SFA was replaced by MUFA, most articles reported null associations with risk of CHD, CAD, or MI,[197,198,222,227,228] with only two articles reporting associations with higher risk.[196,213] When SFA was replaced by carbohydrates, including those that specified low, medium or high glycemic index carbohydrates, most articles reported null associations with the risk of CHD, CAD, or MI,[170,197,198,205,222] but others reported associations with higher risk (particularly with medium or high glycemic index carbohydrates)[170,196] or lower risk (with whole-grain carbohydrate).[228] In one study, when carbohydrate was replaced by SFA there was no significant association with fatal or non-fatal CHD.[213] In the only NCC study to examine the relationship between

SFA intake and CVD endpoint outcomes, null associations were detected for incident MI.[195] In addition to the studies that examined total SFA intake, 5 examined the relationship between SFA from specific food sources, most focusing on meat and dairy, and risk of CHD and MI [156,196-198,215]. Results tended to vary by the food source of the SFA. Specifically, associations between SFA from meat and CHD, CAD, and MI were null[156,196-198] or indicated greater risk with higher intake levels[156,198,215]; associations between SFA from dairy, including total dairy, butter, cheese, and milk and CHD, CAD, and MI were null[156,196,197,215] or indicated lower risk with higher intake levels.[156,196,215] However, due to the insufficient number of studies that reported on the relationship between SFA from different food sources and CHD, CAD, or MI, results regarding this particular topic remain inconclusive. Only one article addressed PAD, and it detected a null association between SFA intake and incident PAD.[178]

SFA and stroke

As indicated previously, few articles assessed the relationship between SFA intake and stroke and most did not model replacement. Among these articles, most exclusively reported null associations between SFA intake and incident total stroke or subtypes of stroke such as ischemic stroke or hemorrhagic stroke.[139,179,190,212,217,220-222] In three studies, all conducted in Japan among individuals with an average BMI less than 25, higher intake of SFA was associated with lower risk of stroke (one finding significant associations only in men).[190,221,222] The two studies that modeled replacement of SFA with other types of fat or macronutrients had inconsistent results. One found that replacement of SFA with PUFA, but not MUFA or carbohydrate, was associated with higher risk of stroke mortality,[222] whereas the other study reported replacement of SFA with LA not being significantly associated with total ischemic stroke and stroke subtypes.[212]

SFA and other CVD outcomes

For the remaining outcomes, little evidence was available to draw conclusions. Articles that assessed the relationship between SFA intake and heart failure all reported null associations.[140,222] Results for sudden cardiac death were inconsistent, with one article reporting greater risk in women with higher SFA intake (but only when replacement with carbohydrates was not modeled),[152] one article reporting lower risk with higher SFA intake,[221] and one article reporting null associations.[222]

Food sources of SFA and CVD

In addition to the 39 articles that directly assessed SFA intake (reviewed above), five articles (all from European cohorts) indirectly assessed SFA by measuring intake of butter, which is predominantly composed of SFA.[162,176,193,194,206] The majority of these articles reported null associations between butter intake and CVD,[193,206] CHD and MI,[162,176,194,206] or stroke,[162,206] with only one article reporting an association between higher butter intake and higher risk of CHD in women, but not in men.[162] However, due to the indirectness of assessing butter intake (compared to directly assessing SFA intake) and the unusual categorizations of butter intake used in one analysis,[194] these articles were weighed less heavily when drawing conclusions.

MUFA

Twenty-nine articles (28 from PCSs and 1 from a NCC study) assessed the relationship between MUFA intake during adulthood and risk of CVD endpoint

outcomes.[139,152,161,163,168,179,183,186,188,190,195-199,201,204,205,212,213,215-218,220,222,226-228] Of these, 16 articles modeled replacement of MUFA with other types of fat or macronutrients[152,163,196-198,201,204,205,212,213,215,218,222,226-228] and 3 articles examined MUFA:SFA intake ratios.[161,188,199] Most of the articles reported on either CVD, inclusive of multiple conditions,[161,163,168,186,188,199,201,204,216-218,222,226] or CHD, CAD, and MI.[183,195-198,205,213,215,217,222,227,228] Fewer studies assessed stroke[139,179,190,212,217,220,222] or sudden cardiac death.[152]

MUFA and total CVD

Among the articles that assessed the relationship between MUFA intake, without considering replacement, and CVD, results were predominantly null.[168,186,216-218]. However, two articles reported statistically significant associations between higher MUFA intake (one only in women) and lower risk of CVD.[163,218] Several articles modeled replacement of different types of fat or macronutrients with MUFA and its association with CVD. When SFA was replaced by MUFA, results were null[201,204] or indicated an association with lower risk of CVD.[163,226] All three articles that assessed replacement of carbohydrates with MUFA detected an association with lower risk of CVD,[163,218,226] whereas the one article that assessed replacement of PUFA with MUFA detected an association with higher risk of CVD mortality.[201] One article considered the food source of MUFA.[226] When replacement of carbohydrates or SFA with MUFA from plants was modeled, this was associated with lower risk of CVD mortality, whereas when replacement of carbohydrates or SFA with MUFA from animals was modeled, associations indicated higher risk or were null, respectively.[226]

MUFA and CHD or MI

Among the articles that assessed the relationship between MUFA intake and CHD or MI without considering replacement, associations were primarily null,[183,195,213,217,227] including the one NCC study on this topic.[195] Results were more inconsistent when replacement with other types of dietary fats or macronutrients was considered. Most articles reported null associations between replacement of SFA or carbohydrates with total MUFA, or different sources of MUFA, and CHD or MI.[197,198,205,222,227,228] However, one article detected higher risk of CHD when carbohydrates or SFA were replaced with total MUFA,[213] whereas one article detected lower risk of CHD when carbohydrates were replaced with total MUFA.[205] Two articles considered the food sources of MUFA in their replacement analyses. In one study, replacement of carbohydrate or SFA with MUFA from meat sources was associated with higher risk of CHD, whereas replacement of carbohydrate or SFA with MUFA from dairy sources was associated with lower risk of CHD.[215] However, in this same article, replacement of MUFA from dairy with MUFA from meat was not associated with CHD.[215] The other article that considered food sources of MUFA found that replacement of MUFA from animal sources with MUFA from plant sources was associated with lower risk of CHD.[227]

MUFA and other CVD outcomes

As indicated previously, few articles assessed the relationship between MUFA intake and stroke, and most did not model replacement. Among the articles that did not model replacement, most detected null associations between MUFA (or, in one case, total unsaturated fatty acid intake[139]) and incident stroke.[139,179,190,217,220] Only one of five studies detected a significant association between MUFA intake and lower risk of

intracerebral hemorrhage; however, this association was only observed in men and MUFA intake only represented intake at breakfast.[190] The two studies that modeled replacement primarily found that replacement of SFA with MUFA was not associated with stroke mortality,[212,222] but one study did detect a significantly lower risk of mortality due to small vessel occlusion (but not for other subtypes of stroke).[212] MUFA intake in women was not associated with sudden cardiac death in the one article that assessed this outcome.[152]

Food sources of MUFA and CVD

In addition to the 29 articles that directly assessed MUFA intake (reviewed above), seven articles indirectly assessed MUFA intake by measuring olive oil intake.[143,150,151,164,177,203,207] Consistent with articles that reported on MUFA from plant sources, results showed either statistically significant associations between greater olive oil intake or use and lower risk of CVD,[150,164,177] CHD,[143] or stroke,[203] or associations were null.[151,207] However, due to the indirectness of all articles examining MUFA intake by assessing olive oil intake and the non-quantitative categorizations of oil intake (e.g., olive oil used for cooking versus not used for cooking) used in some analyses,[177,203,207] these articles were weighed less heavily when drawing conclusions.

PUFA

Seventy-one articles (67 from PCSs and 4 from NCC studies) assessed the relationship between PUFA intake during adulthood and CVD endpoint outcomes.[136-142,144-146,148,149,152-155,157-160,163,165-169,171-175,178-183,185-190,192,195-202,204,205,208-213,215-220,222-226,228] Results were synthesized by type of exposure: total PUFA, n-3 PUFA, n-6 PUFA, and n-3:n-6 PUFA ratio.

Total PUFA

Thirty-two articles assessed the relationship between total PUFA intake and CVD endpoint outcomes.[136,139,140,152,163,167,168,178,179,183,186-190,195-199,201,204,205,213,215-218,220,222,226,228] Of these, 14 modeled replacement of other types of fat or macronutrients with total PUFA[152,163,196-198,201,204,205,213,215,218,222,226,228] and 4 articles examined PUFA:SFA or PUFA+MUFA:SFA intake ratios.[136,140,199,216] Most articles reported on CHD, CAD, or MI[183,187,189,195-198,205,213,215,217,218,222,228] or CVD,[136,140,163,167,168,186,188,199,201,204,216,217,222,226] but some reported on stroke,[139,179,190,217,220,222] heart failure,[140] PAD,[178] or sudden cardiac death.[152]

Total PUFA and total CVD. Among articles that examined the relationship between total PUFA intake, without consideration of replacement, and CVD, results were predominantly null[167,168,186,188,199,204,216,217] or showed associations with lower risk of CVD.[163,199,201,218] One study, which was conducted in Japanese men, reported a significant association between higher intake of PUFA and CVD mortality.[216] As described previously, replacement of SFA with total PUFA was predominantly associated with lower risk of CVD,[163,201,226] with one article reporting null results.[204] Similar associations with lower risk of CVD were observed when replacement of MUFA or carbohydrates with PUFA was modeled.[163,201,218,226] Among the few articles that examined the PUFA:SFA or total UFA:SFA intake ratio, most detected null associations.[136,140,216]

Total PUFA and CHD, CAD, MI, or PAD. Of the articles that examined the relationship between total PUFA intake, without considering replacement, and CHD,

CAD, or MI, all reported null[187,189,195,213,217] associations (including the 2 NCC studies on this topic[189,195]) or beneficial associations.[183,213] As described previously, when replacement of SFA with PUFA was modeled, primarily null associations[197,198,222] or associations with lower risk of CHD/MI[213,228] were detected. Only one article reported an association with higher risk of CHD when replacement of SFA with PUFA was modeled.[196] Among articles that examined replacement of carbohydrates with PUFA, results were null [205,213] or showed associations with lower risk of fatal CHD.[213] One article examined sources of PUFA, specifically from meat or dairy, and found that replacement of PUFA from dairy with PUFA from meat was not associated with risk of CHD.[215] However, when PUFA from meat replaced carbohydrates, the associated risk of CHD was higher.[215] Only one article assessed the relationship between total PUFA intake, without considering replacement, and PAD, and it did not detect a statistically significant association between them.[178]

Total PUFA and stroke or other CVD outcomes. Fewer articles reported on stroke and other CVD outcomes. Of the articles that assessed the relationship between total PUFA intake and risk of stroke without replacement, all detected null associations.[139,179,190,217,220] Only one article examined the relationship between replacement of SFA with total PUFA and stroke, detecting a statistically significant association with higher risk of mortality.[222] One study assessed the relationship between total PUFA intake and risk of sudden cardiac death, detecting associations with lower risk, with and without consideration of replacement of carbohydrates.[152] No articles reported on the relationship between total PUFA intake and heart failure; however, one study assessed the relationship between the PUFA:SFA intake ratio and heart failure and did not detect a statistically significant association.[140]

n-3 PUFA

Forty-seven articles assessed the relationship between n-3 PUFA intake and CVD endpoint outcomes.[137,138,141,142,144-146,148,149,152,153,155,157-160,165,166,169,171-175,179-182,185,186,188,189,192,199,200,202,208-211,216-219,223,225,226] Although some studies reported on total n-3 PUFA intake,[138,152,165,173,175,192,216,218,225,226] most focused on more specific categories of n-3 PUFAs, namely ALA[141,148,152,155,157,159,165,172,175,179-181,200,202,209,210,218,219,223,225,226] and EPA, DHA, and docosapentaenoic acid (DPA; alone or in combination as “long chain” n-3 PUFAs).[137,138,141,142,144-146,152,153,157,158,160,165,166,169,171,172,174,175,179,182,185,186,188,189,199,200,202,208-211,217-219,223,225,226]

Few articles modeled replacement between n-3 PUFAs and other types of fat or macronutrients.[152,218,226] Most articles reported on CHD, CAD, and/or MI,[138,142,144,145,148,153,155,157,159,160,171,172,175,185,189,200,202,209,210,217,218,223,225] CVD,[142,157-159,165,173,175,185,186,188,192,199,200,202,208,216,217,223,225,226] or stroke.[146,149,155,159,174,175,179,185,200,202,211,217,223,225] Fewer articles reported on heart failure,[141,180-182,219] sudden cardiac death,[152,166,202] PAD,[137] or venous thromboembolism.[169]

Total n-3 PUFA. Among articles that assessed total n-3 PUFA intake, including one that considered replacement of carbohydrates or SFA with n-3 PUFA,[226] most examined CVD incidence and mortality[165,173,175,192,216,218,225,226] with fewer articles examining CHD, CAD, and/or MI,[138,175,225] stroke,[175,225] or sudden cardiac death.[152] Results were predominantly null across all outcomes,[138,165,173,175,192,216,218,225,226] with two articles reporting beneficial associations between higher total n-3 PUFA intake and

CVD and CHD mortality[175] or sudden cardiac death.[152]

ALA. Among the articles that examined the relationship between ALA intake and CVD endpoint outcomes, most focused on CHD, CAD, and/or MI,[148,155,157,159,172,175,200,202,209,210,225] CVD (inclusive of multiple types of outcomes),[157,159,165,175,200,202,210,218,225,226] and stroke.[149,155,159,175,179,200,202,225] Fewer reported on heart failure[141,180,181,219] and sudden cardiac death.[152,202] In the case of CHD, CAD, or MI and CVD, the majority of articles did not report statistically significant associations with ALA intake[148,155,157,159,165,172,200,202,209,210,218,219,225,226]; only one article reported a beneficial association.[175] In the case of stroke, results were predominantly null[149,159,179,200,202] or indicated a beneficial association between ALA intake and stroke.[155,175,225]

EPA, DHA, and DPA. Among the articles that examined EPA, DHA, and/or DPA, most combined EPA and DHA, or EPA, DHA, and DPA, into a single dietary exposure, commonly referring to them collectively as “marine” or “long chain” n-3 PUFAs.[137,141,142,144-146,152,153,157,158,160,165,166,169,171,174,175,179,182,185,188,189,199,200,202,208-211,217-219,223,225,226] Fewer articles examined EPA,[138,157,160,171,172,211] DHA,[138,157,160,171,172,185,211] and DPA[157,160,171,211] individually. Across articles that assessed the relationship between long chain n-3 PUFA (EPA, DHA, with or without DPA) and CVD endpoint outcomes, most focused on CHD, CAD, and MI or CVD and showed predominantly beneficial associations[144,145,153,157,158,175,199,202,208-210,223,225,226] (including the one study that modeled replacement of carbohydrates or SFA[226]) or null associations.[142,153,157,160,165,166,171,185,200,210,217] Only two articles reported detrimental associations with incident CVD.[217,218] Similar results were observed for articles that assessed the relationship between long chain n-3 PUFA intake and incident stroke, with most reporting null associations[174,179,200,202,211,217] or beneficial associations.[146,174,175,179,223,225] One article reported a statistically significant association between greater long chain n-3 PUFA intake and higher risk of stroke; however, this was only observed for cardioembolism and no other types of stroke.[211] Few articles were included that examined the relationship between total long chain n-3 PUFA intake and heart failure,[137,141,182,219] sudden cardiac death,[152,202] or venous thromboembolism[169] and results were predominantly null across these outcomes, although some reported beneficial associations.[137,152] When EPA, DHA, or DPA were examined individually, results were less consistent than when they were assessed collectively as long chain n-3 PUFA. In the case of EPA, associations with CHD, CAD, or MI were predominantly null,[138,157,160,171,172] with only one article showing a detrimental association at the highest quartile of intake for women.[171] Only one article each examined the relationship between EPA intake and incident CVD and stroke. A beneficial association was detected for CVD[157] and mixed results were observed for stroke, with a beneficial association detected for stroke due to large artery atherosclerosis, a detrimental association detected for cardioembolism, and null associations detected for small vessel occlusion and total ischemic stroke.[211] Similar results were seen for DHA, with exclusively null associations detected for CHD, CAD, or MI,[138,157,160,171,172,185] beneficial associations detected for CVD[157,185] and associations that varied in direction and statistical significance by type of stroke.[185,211] Fewer articles assessed DPA individually and results were inconsistent between outcomes. Predominantly null associations were detected between DPA and CHD and MI,[160,171] although one article reported a beneficial association between them.[157] In the

one article that assessed CVD, an association between higher DPA intake and lower risk of CVD was detected.[157] In the one article that reported on stroke, predominantly detrimental associations between DPA intake and types of stroke were detected.[211]

n-6 PUFA

Sixteen articles assessed the relationship between n-6 PUFA intake and CVD endpoint outcomes.[152,154,157,165,172,173,179,181,192,210,212,216-218,225,226] Few of these articles modeled replacement between n-6 PUFA and other types of dietary fat or macronutrients.[152,212,218,226] The majority of articles reported on total n-6 PUFA intake,[152,157,165,173,179,192,216-218,225,226] but others reported LA intake[152,154,157,165,172,210,212,218,225,226] and AA intake[152,157,172,218,225,226] individually. Most articles reported on CHD, CAD, or MI[154,157,172,210,217,218,225] or CVD.[157,165,173,192,216,217,225,226] Fewer articles addressed stroke,[179,212,217,225] heart failure,[181] or sudden cardiac death.[152]

Total n-6 PUFA. Most articles that examined total n-6 PUFA intake assessed its relationship to CVD, with inconsistent results, detecting beneficial,[173,218,226] null,[157,192,216,217,225] and detrimental associations[165,216] across the articles. Associations between total n-6 PUFA intake and CHD or stroke were null.[157,179,217,225] Only two articles examined replacement of carbohydrates or SFA with n-6 PUFA, one detecting associations with lower risk of CVD mortality[226] and the other detecting an association with lower risk of sudden cardiac death.[152]

LA. Associations between LA intake and CVD were predominantly null[157,225] or indicated lower risk of CVD,[218,226] with only one article reporting an association with higher risk of CVD.[165] Associations between LA intake and CHD or stroke were predominantly null,[154,157,172,210,212,225] with the exception of one article, which reported an association with lower risk of stroke due to small vessel occlusion when MUFA was replaced with LA.[212] All other associations between replacement of carbohydrates, SFA, or MUFA with LA and total or subtypes of stroke were null.[212] Only one article reported sudden cardiac death, detecting an association between higher LA intake and lower risk of sudden cardiac death.[152]

AA. Relatively few articles assessed the relationship between AA and CVD endpoint outcomes, with most reporting on CHD or CVD. The majority of articles detected null associations between AA intake on CHD[157,172] or CVD,[157,218] however one article reported statistically significant associations with lower risk of CHD and CVD,[225] whereas another article reported statistically significant associations with higher risk of CVD mortality when carbohydrates or SFA was replaced with AA.[226] One article each reported on sudden cardiac death[152] and stroke mortality,[225] both detecting null associations with AA intake.

n-3 to n-6 PUFA Ratio

Three articles, all from PCSs, assessed the relationship between the n-3:n-6 PUFA intake ratio and CVD endpoint outcomes.[165,225,226] All articles examined incident CVD or CVD mortality,[165,225,226] with one additionally examining CHD mortality and stroke mortality.[225] All associations between the n-3:n-6 PUFA intake ratio and CVD endpoint outcomes were null.

Dietary Cholesterol

Eleven articles (10 articles from 8 PCSs and 1 article from a NCC study) assessed the relationship between dietary cholesterol intake and CVD endpoint outcomes.[135,140,168,179,184,187,188,195,214,220,224] Of these, five examined CVD, inclusive of multiple types of outcomes,[140,168,184,188,224] four examined CHD or MI,[187,195,214,224] four examined stroke,[135,179,220,224] and two examined heart failure.[140,224] For CVD, results were inconsistent. One article, which included multiple large and well-characterized cohorts and used validated diet assessment methods, reported statistically significant associations between higher intake of dietary cholesterol and increased risk of CVD and CVD mortality,[224] whereas other articles reported statistically significant associations with decreased risk of CVD,[140,184] or reported null associations.[168,184,188] Results were also inconsistent for stroke, with some single-sex studies reporting null associations between dietary cholesterol intake and incident stroke in women[220] and men,[135] and others reporting statistically significant associations with higher risk of incident stroke.[179,224] Of the two articles that assessed heart failure, one did not detect significant associations with dietary cholesterol intake,[224] whereas the other detected a statistically significant association between higher dietary cholesterol intake and lower risk of heart failure in women.[140] All articles that assessed the relationship between dietary cholesterol intake and CHD or MI reported null associations.[187,195,214,224] Due to the co-occurrence of dietary cholesterol in foods that are also high in SFA and the relatively low dietary cholesterol intake in several articles,[140,168,220] it was difficult to disentangle the independent associations between dietary cholesterol and CVD endpoint outcomes in this body of evidence.

Assessment of the evidence[x]

As outlined and described below, the body of evidence examining intake of types of dietary fat by adults and CVD endpoint outcomes was assessed for the following elements used when grading the strength of evidence.

Risk of Bias

As noted previously, the risk of bias assessment for PCSs and NCC studies in adults are described in **Table 10**. Nearly all articles were at serious risk of bias due to confounding, with few accounting for all key confounders. In particular, race or ethnicity and family history of CVD or diabetes were not commonly accounted for in this body of evidence. However, many articles accounted for the majority of key confounders, including age, sex, physical activity, smoking, alcohol intake, and total energy intake. All articles were at moderate risk of bias due to selection of reported results as none reported a pre-registered protocol with sufficient information on statistical analysis intentions. Across other domains, the majority of articles were assessed as having low risk of bias.

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[x] A detailed description of the methodology used for grading the strength of the evidence is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

Consistency

The level of consistency across the included articles depended on the type of fat examined, the replacing macronutrient or type of fat (when replacement was modeled), and the CVD outcome assessed. In the case of replacement of SFA with PUFA, findings indicated associations with lower risk of CHD or total CVD or null associations. In the case of replacement of SFA with MUFA or carbohydrates, associations were predominantly null. Because these articles typically only modeled replacement with total MUFA or total carbohydrates, versus differentiating between animal and plant sources of MUFA or simple and complex carbohydrates, this may contribute to the predominantly null results for those analyses. For example, in the few articles that examined specific sources of MUFAs, beneficial associations tended to be observed with plant sources of MUFA, but not with animal sources of MUFA. In the case of PUFA, results tended to vary in consistency by the type of n-3 or n-6 PUFA examined. Although articles that examined total n-3 PUFA showed predominantly null associations with CVD endpoint outcomes, associations between total long chain n-3 PUFA (primarily EPA and DHA) and CVD endpoint outcomes showed more consistent benefits with higher intake. Similarly, although articles that examined total n-6 PUFA intake or LA intake alone tended to show beneficial or null associations with CVD endpoint outcomes, articles that examined AA intake alone were less consistent.

Directness

Most studies in this body of evidence were specifically designed to evaluate the relationship between diet and chronic diseases, inclusive of CVD, or CVD specifically. However, several studies were less direct due to a variety of factors. First, although butter and olive oil derive the majority of its calories from dietary fats and are predominantly composed of SFA and MUFA, respectively, articles that examined these foods as exposures were necessarily less direct.[143,150,151,162,164,177,193,194,203,206,207] Second, several articles were secondary analyses of RCTs originally designed to evaluate exposures or interventions besides types of dietary fats.[142,147,163,164,200,202,205,219] Third, several cohorts were initially designed to assess outcomes other than CVD, particularly cancer.[148,149,160,162,165,167,170,171,178,191,195,198,203,205,206,208,211,212,217,221]

Precision

Power analyses were not reported across this body of evidence. However, although some studies had relatively small sample sizes, the majority of studies had sample sizes greater than 10,000 participants (up to approximately 525,000 participants).

Generalizability

The majority of articles reported on studies conducted in the U.S. or in Europe, particularly Scandinavian countries such as Denmark, the Netherlands, and Sweden. Many articles, particularly studies conducted in Europe, did not report race or ethnicity of the cohort. Most articles that did report race or ethnicity had participants who were predominantly White or Caucasian. However, several cohorts from the U.S. had more diverse participants.[156,157,161,168,173,201,224,225] Few cohorts exclusively recruited participants at high risk of developing CVD,[163,164,184,202] with most studies enrolling participants across the spectrum of risk. Because several articles excluded individuals with prevalent diabetes, those results may be less generalizable to the overall U.S. population. Several studies conducted in Asia had participants with average BMI in the

normal range and lower than the average BMI commonly observed in U.S. cohorts[166,175,185-190,209,216,221,222]; articles from these studies may not be as generalizable to the overall U.S. population in this regard. The majority of articles examined dietary fat intake in adults of middle age or older, therefore, it is possible that results are less generalizable to younger adults.

Other important considerations

Publication bias

A large, comprehensive search was conducted in multiple databases for this systematic review. Although risk of publication bias is always of potential concern, both relatively small and large studies were included in this review, reporting both null and statistically significant results. Therefore, the risk of publication bias is likely low across this body of evidence.

Building on the 2015 Dietary Guidelines Advisory Committee report and conclusions

This systematic review builds and expands on the work of the 2015 Committee, which answered the question, "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" and considered evidence from systematic reviews and meta-analyses, which included RCTs and PCSs from the 1960s to 2010.[xi] The 2015 Committee drew two conclusions pertaining to CVD endpoint outcomes:

- "Strong and consistent evidence from RCTs and statistical modeling in prospective cohort studies shows that replacing SFA with PUFA reduces the risk of CVD events and coronary mortality. For every 1 percent of energy intake from SFA replaced with PUFA, incidence of CHD is reduced by 2 to 3 percent. However, reducing total fat (replacing total fat with overall carbohydrates) does not lower CVD risk. Consistent evidence from prospective cohort studies shows that higher SFA intake as compared to total carbohydrates is not associated with CVD risk. (Grade: Strong)"
- "Evidence is limited regarding whether replacing SFA with MUFA confers overall CVD (or CVD endpoint) benefits. One reason is that the main sources of MUFA in a typical American diet are animal fat, and because of the co-occurrence of SFA and MUFA in foods makes it difficult to tease out the independent association of MUFA with CVD. However, evidence from RCTs and prospective studies has demonstrated benefits of plant sources of monounsaturated fats, such as olive oil and nuts on CVD risk. (Grade: Limited)"

The evidence in the present review is broadly consistent with these conclusions drawn by the 2015 Committee. In articles that assessed replacement of SFA with PUFA, associations predominantly indicated lower risk of CHD and CVD mortality or were null. However, fewer articles examined outcomes such as heart failure or stroke. In articles that assessed replacement of SFA with carbohydrates, results were inconsistent but predominantly showed null associations with CVD outcomes. Although

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[xi] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

some articles separated low-, moderate-, and high-glycemic index carbohydrates, most articles did not specify or differentiate between the type of carbohydrate replacing the SFA, including complex carbohydrates or simple carbohydrates. Therefore, little evidence is available to draw conclusions regarding whether the association between replacement of SFA with carbohydrate varies by type of carbohydrate. Based on the evidence in the present review, the 2020 Committee concurred with and updated the conclusions drawn by the 2015 Committee, electing to develop new conclusion statements pertaining to replacement of SFA with PUFA or with carbohydrates to increase specificity of the conclusions. In articles that assessed replacement of SFA with MUFA in the present review, results were predominantly null and did not often differentiate between MUFA from plant sources and MUFA from animal sources. As such, the 2020 Committee concurred with and updated the conclusion drawn by the 2015 Committee regarding replacement of SFA with MUFA.

Research recommendations

In order to better assess the relationship between intake of dietary fats and risk of CVD, additional research is warranted to:

- Assess whether establishing patterns of dietary fat intake during childhood is predictive of blood lipids and risk of CVD during adulthood
- Examine how pubertal status and sex hormones may modify the effect of dietary fat intake during childhood on blood lipids and risk of CVD during adulthood
- Assess the relationship between replacement of SFA with other types of dietary fats or macronutrients during childhood and risk of CVD
- Examine whether the effect of replacing SFA with carbohydrates on risk of CVD varies by the type of carbohydrate (e.g., simple vs complex carbohydrates)
- Assess the effect of n-6 PUFA, both LA and AA, on risk of CVD
- Assess the effect of n-3 PUFA from plant sources (ALA) on risk of CVD
- Assess whether the relationship between type of dietary fat and blood lipids or risk of CVD varies by the food source or food matrix of the dietary fat
- Employ highly controlled methods (e.g., feeding trials) to examine the effect of dietary cholesterol, independent of SFA, on blood lipids and risk of CVD
- Assess the effect of percentage of types of dietary fats relative to calories within a dietary pattern on blood lipids and risk of CVD during childhood and adulthood
- Assess the effect of participant characteristics, including BMI, race and ethnicity, and chronic disease status, during childhood and adulthood on the relationship between types of dietary fat and blood lipids and risk of CVD
- Provide sufficient control of sodium intake to examine the independent relationship between dietary fat intake and blood pressure during childhood
- Examine the relationship between intake of types of dietary fat intake and specific CVD outcomes, such as heart failure and stroke, in adults instead of assessing CVD in aggregate

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Table 1. Evidence from randomized controlled trials examining types of dietary fat consumed during childhood and cardiovascular disease intermediate and endpoint outcomes*

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
RCT: Parallel Design			
Dietary Intervention Study in Children (DISC)			
Kwiterovich, 1995[13] **RCT, DISC, U.S.** Baseline N=663 Analytic N=623 (Attrition: 6%) **Participant characteristics at baseline:** • Children with LDL at the 80th – 98th percentile for age and sex at study entry • Age: Boys, Mean=9.7y; Girls, Mean=9.0y • Sex (female): 45% • Race/ethnicity: White ~86.5%, Black ~8.5%, Other ~5.0% • SES: NR • Anthropometry: BMI, Mean~17.5 **Blood lipids at baseline, Mean:** • TC (mmol/L): ~5.17 • LDL (mmol/L): ~3.38 • HDL (mmol/L): ~1.48 • Triglycerides (mmol/L): ~0.90 • No baseline differences between intervention and control group at baseline **Summary of findings:** *In children with elevated LDL cholesterol, counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, and less than 75mg/kcal of cholesterol, compared to usual care, reduced total and LDL cholesterol, but not HDL cholesterol or triglycerides, after 3y of follow-up.*	**Interventions/Comparators:** • Intervention (n=320): Counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, less than 75mg/1000kcal of cholesterol, and 28%E from total fat. • Control (n=303): Usual care Intervention duration: 3 years (Intervention group: 6 weekly and 5 biweekly sessions during 1st 6mo; 6 sessions during 2nd 6mo; 4-6 sessions during 2nd and 3rd years) Intervention compliance: Fat intake measured at 1y and 3y follow-up via multiple 24hr recalls, Mean (SD) for intervention vs control: • SFA (%E): 1y, 9.8 (2.7) vs 12.4 (2.6), p<0.001; 3y, 10.2 (2.6) vs 12.3 (2.2), p<0.001 • MUFA (%E): 1y, 10.7 (2.5) vs 12.3 (2.4), p<0.001; 3y, 10.7 (2.5) vs 12.3 (2.1), p<0.001 • PUFA (%E): 1y, 5.8 (1.8) vs 5.9 (1.9), p=0.88; 3y, 5.5 (1.9) vs 5.9 (1.8), p=0.03 • Cholesterol (mg/1000kcal): 1y, 90.0 (42.6) vs 113.9 (51.9), p<0.001; 3y, 95.0 (47.8) vs 112.9 (48.0), p<0.001 **Outcomes and assessment methods**: • Assessed at baseline (~9.5y), 1y, and 3y follow-ups • Blood lipids: TC, LDL, HDL, triglycerides (NR if fasting or non-fasting)	***Blood lipids at 1y, 3y follow-up*** **TC,** mmol/L, Mean (SD) Intervention: 4.95 (0.54), 4.74 (0.56) Control (ref): 5.10 (0.55), 4.82 (0.58) **Group differences**, Mean (95% CI): **1y F/U: -0.16 (-0.23, -0.08), p<0.001** **3y F/U: -0.08 (-0.17, -0.004), p=0.04** **LDL,** mmol/L, Mean (SD) Intervention: 3.17 (0.47), 2.98 (0.48) Control (ref): 3.29 (0.50), 3.07 (0.50) **Group differences**, Mean (95% CI): **1y F/U: -0.13 (-0.19, -0.06), p<0.001** **3y F/U: -0.09 (-0.16, -0.02), p=0.02** **Group differences in change:** **Greater decrease in LDL in the intervention group from baseline to 1y (p<0.001) and to 3y (p<0.05) compared to control** **HDL,** mmol/L, Mean (SD) Intervention: 1.44 (0.29), 1.36 (0.26) Control (ref): 1.47 (0.29), 1.36 (0.27) **Group differences**, Mean (95% CI): **1y F/U: -0.03 (-0.06, -0.004), p=0.03** 3y F/U: -0.005 (-0.03, 0.02), p=0.75 **Triglycerides,** mmol/L, Mean (SD) Intervention: 0.97 (0.44), 1.12 (0.52) Control (ref): 0.98 (0.44), 1.12 (0.51) **Group differences**, Mean (95% CI): 1y F/U: -0.01 (-0.07, 0.05), p=0.84 3y F/U: 0.02 (-0.05, 0.08), p=0.62	**Model adjustments:** Baseline blood lipid level, sex **Limitations:** • Although dietary fats was the focus of the intervention, increased dietary fiber with an emphasis on fruits, vegetables, and whole grains was also encouraged • None to report **Funding sources:** NHLBI

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Simons-Morton, 1997[32] **RCT, DISC, U.S.** Baseline N=663 Analytic N=583 (Attrition: 12%) **Participant characteristics at baseline:** • Children with LDL cholesterol values at the 80th – 98th percentile for age and sex at study entry • Age: Mean=9.6y, SD=0.72 • Sex (female): 46% • Race/ethnicity: White ~86.5%, Black ~8.5%, Other ~5.0% • SES: NR • Anthropometry: Height, Mean=136.4 cm, SD=6.9; Weight, Mean=32.9 kg, SD=6.8 **BP at baseline, Mean:** • SBP (mmHg): ~97.4 • DBP (mmHg): ~61.9 • No statistically significant differences between intervention and control groups at baseline **Summary of findings:** *In children with elevated LDL cholesterol, counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, and less than 75mg/kcal of cholesterol, compared to usual care, did not reduce SBP or DBP after 3y of follow-up.*	**Interventions/Comparators:** • Intervention (n=302): Counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, less than 75mg/1000kcal of cholesterol, and 28% energy from total fat. • Control (n=281): Usual care Intervention duration: 3 years (Intervention group: 6 weekly and 5 biweekly sessions during 1st 6mo; 6 sessions during 2nd 6mo; 4-6 sessions during 2nd and 3rd years) Intervention compliance: DISC intervention significantly reduced total fat, saturated fat, and cholesterol intake compared to usual care (See Kwiterovich, 1995) **Outcomes and assessment methods**: • Assessed at baseline (~9.6y), 1y, and 3y follow-ups • BP: SBP, DBP; Measured in duplicate	***BP at 1y, 3y follow-up*** **SBP,** mmHg, Mean (SD) Intervention: 96.9 (8.2), 100.0 (9.1) Control (ref): 97.3 (8.3), 100.4 (8.6) **Group differences**, Mean (95% CI): 1y F/U: -0.4 (-1.51, 0.69), p=0.47 3y F/U: -0.5 (-1.69, 0.78), p=0.47 **DBP,** mmHg, Mean (SD) Intervention: 60.5 (9.2), 63.4 (9.1) Control (ref): 61.0 (9.9), 64.3 (8.1) **Group differences**, Mean (95% CI): 1y F/U: -0.6 (1.94, 0.80), p=0.42 3y F/U: -1.0 (-2.35, 0.38), p=0.16	**Model adjustments:** Baseline BP, sex **Limitations:** • Although dietary fats was the focus of the intervention, increased dietary fiber with an emphasis on fruits, vegetables, and whole grains was also encouraged • No preregistered statistical analysis plan for SBP and DBP available **Funding sources:** NHLBI

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Obarzanek, 2001[25] **RCT, DISC, U.S.** Baseline N=663 Analytic N=548 (Attrition: 17%) **Participant characteristics at baseline:** • Children with LDL cholesterol values at the 80th – 98th percentile for age and sex at study entry • Age: Mean=9.5y, SD=0.72y • Sex (female): 45% • Race/ethnicity: White ~86.5%, Black ~8.5%, Other ~5.0% • SES: Parental education – some college or higher, 53.3%; Household income ≥$50,000, 35.6% • Anthropometry: BMI, Mean~17.5 **Blood lipids at baseline, Mean:** • TC (mmol/L): ~5.17 • LDL (mmol/L): ~3.38 • HDL (mmol/L): ~1.48 • Triglycerides (mmol/L): ~0.90 • No statistically significant differences between intervention and control groups at baseline **Summary of findings:** *In children with elevated LDL cholesterol, counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, and less than 75mg/kcal of cholesterol, compared to usual care, reduced total, LDL, and HDL cholesterol or triglycerides after 5y and ~7y of follow-up.*	**Interventions/Comparators:** • Intervention (n=283): Counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, less than 75mg/1000kcal of cholesterol, and 28% energy from total fat. • Control (n=265): Usual care Intervention duration: ~7 years (Intervention group: 6 weekly and 5 biweekly sessions during 1st 6mo; 6 sessions during 2nd 6mo; 4-6 sessions during 2nd and 3rd years; 4 sessions annually from 4th year on) Intervention compliance: Fat intake measured at Final (Median: 7.2y, range: 6.5-9.3y) follow-up via multiple 24hr recalls, Mean for intervention vs control: • SFA (%E): 10.2 vs 11.3, p<0.001 • Cholesterol (mg/1000kcal): 99 vs 103, p>0.05 **Outcomes and assessment methods**: • Assessed at baseline (~9.5y of age), 1y*, 3y*, 5y, and Final (Median: 7.2y, range: 6.5-9.3y) follow-ups • Blood lipids: TC, LDL, HDL, triglycerides (NR if fasting or non-fasting) *1y and 3y blood lipid results reported in Kwiterovich, 1995	***Blood lipids at 5y, 7.2y of follow-up*** **TC,** mmol/L, Mean (SD) Intervention: 4.54 (0.58), 4.64 (0.62) Control (ref): 4.60 (0.67), 4.66 (0.68) **Group differences**, Mean (95% CI): 5y F/U: -0.07 (-0.16, 0.03), p=0.18 7.2y F/U: -0.03 (-0.13, 0.07), p=0.59 **LDL,** mmol/L, Mean Intervention: 2.84, 2.95 Control (ref): 2.90, 3.00 **Group differences**, Mean: 5y F/U: Data NR in mmol/L, p=0.11 7.2y F/U: Data NR in mmol/L, p=0.25 **HDL,** mmol/L, Mean (SD) Intervention: 1.31 (0.29), 1.29 (0.29) Control (ref): 1.32 (0.26), 1.27 (0.25) **Group differences**, Mean (95% CI): 5y F/U: -0.02 (-0.06, 0.02), p=0.28 7.2y F/U: 0.01 (-0.03, 0.04), p=0.62 **Triglycerides,** mmol/L, Mean (SD) Intervention: 1.13 (0.66), 1.13 (0.58) Control (ref): 1.07 (0.53), 1.10 (0.50) **Group differences**, Mean (95% CI): 5y F/U: 0.07 (-0.02, 0.17), p=0.12 7.2y F/U: 0.04 (-0.05, 0.12), p=0.30	**Model adjustments:** Sex, baseline value of outcome variable, age at final visit (for final visit only) **Limitations:** • Although dietary fats was the focus of the intervention, increased dietary fiber with an emphasis on fruits, vegetables, and whole grains was also encouraged • No preregistered statistical analysis plan for 5y and Final follow-up analyses **Funding sources:** NHLBI

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Dorgan, 2011[6] **RCT, DISC, U.S.** Baseline N=301 Analytic N=214 (Attrition: 29%) **Participant characteristics at baseline:** • Female children with LDL cholesterol values at the 80th – 98th percentile for age and sex at study entry • Age: Mean=9.2y • Sex (female): 100% • Race/ethnicity: White ~90%, Black ~6%, Other 4% • SES: NR • Anthropometry: BMI z-score, Mean=0.2 **Blood lipids and BP at baseline:** • NR **Summary of findings:** *In female children with elevated LDL cholesterol, counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, and less than 75mg/kcal of cholesterol, compared to usual care, did not affect LDL and HDL cholesterol, or triglyceride levels at ~27y of age after 16-20y of follow-up. The intervention group had lower SBP at ~27y of age compared to the control group, but no difference in DBP.*	**Interventions/Comparators:** • Intervention (n=108): Counseling to adhere to a diet providing less than 8% energy from SFA, up to 9% energy from PUFA, less than 75mg/1000kcal of cholesterol, and 28% energy from total fat. • Control (ref, n=106): Usual care Intervention duration: ~7 years (Intervention group: 6 weekly and 5 biweekly sessions during 1st 6mo; 6 sessions during 2nd 6mo; 4-6 sessions during 2nd and 3rd years; 4 sessions annually from 4th year on) Intervention compliance: Fat intake measured at 16-20y follow-up via 3, non-consecutive 24hr recalls, Median (IQR) for intervention vs control: • SFA (%E): 9.8 (7.9-12.0) vs 11.3 (9.5-13.3), p<0.001 • MUFA (%E): 11.1 (9.0-13.0) vs 11.8 (10.2-13.6), p=0.07 • PUFA (%E): 6.6 (5.4-8.2) vs 6.2 (5.4-7.3), p=0.18 **Outcomes and assessment methods**: • Assessed at 16-20y follow-up (~27y of age) • BP: SBP, DBP; Measured in triplicate • Fasting blood lipids: LDL, HDL, triglycerides	***Blood levels at 16-20y of follow-up*** **LDL,** mg/dL, Mean (SD) Intervention: 119.9 (27.8) Control (ref): 118.1 (24.3) P=0.62 **HDL,** mg/dL, Mean (95% CI) Intervention: 59.5 (57.0, 62.0) Control (ref): 59.6 (57.1, 62.2) P=0.94 **HDL <50 mg/dL,** % Intervention: 24.4% Control (ref): 24.8% P=0.99 **Triglycerides,** mg/dL, Mean (95% CI) Intervention: 82.6 (76.2. 89.4) Control (ref): 82.4 (76.0, 89.4) P=0.98 **Triglycerides ≥150 mg/dL,** % Intervention: 12.2% Control (ref): 17.4% P=0.35 **SBP,** mmHg, Mean (95% CI) **Intervention: 107.7 (105.8, 109.6)** **Control (ref): 110.3 (108.3, 112.2)** **P=0.02** **DBP,** mmHg, Mean (95% CI) Intervention: 67.6 (65.8, 69.4) Control (ref): 68.2 (66.4, 70.0) P=0.59 **BP ≥130/≥85 mmHg or using BP medication,** % Intervention: 3.4% Control (ref): 7.1% P=0.25 *Note: No significant differences between groups detected in unadjusted analyses.	**Model adjustments:** Age at randomization, baseline BMI, baseline value of metabolic syndrome component, age at visit, race, education, hormone use, number of full-term pregnancies, leisure physical activity during past year, alcohol ingestion, cigarette smoking, current BMI, current intake of energy, SFA, PUFA, MUFA, cholesterol, insoluble and soluble fiber; carbohydrates (HDL and triglycerides only); sodium, calcium, potassium, magnesium (BP only) **Limitations:** • Although dietary fats was the focus of the intervention, increased dietary fiber with an emphasis on fruits, vegetables, and whole grains was also encouraged • No preregistered statistical analysis plan for 16-20y follow-up **Funding sources:** NCI

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
FiSK (Fish, children, health and cognition) Junior			
Vuholm, 2019[36] **RCT, FiSK Junior, Denmark** Baseline N=199 Analytic N=197 (Attrition: 1%) **Participant characteristics at baseline:** • Age: Median~9.6y • Sex (female): ~49% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI, Mean~16.4 **Blood lipids and BP at baseline, Mean:** • TC (mmol/L): ~4.15 • LDL (mmol/L): ~2.24 • HDL (mmol/L): ~1.54 • Triglycerides (mmol/L): Median~0.50 • SBP (mmHg): ~101 • DBP (mmHg): ~62 **Summary of findings:** *Children randomized to consume food rich in LCPUFAs (oily fish) for 12 weeks, compared to children randomized to consume food low in LCPUFAs (poultry), had higher total cholesterol, higher HDL cholesterol, and lower triglycerides. LDL cholesterol, SBP, and DBP were not affected by the intervention.*	**Interventions/Comparators:** • Oily fish (n=99): ~300g/wk (**1.4-4.1g n-3 LCPUFA/100g**); served 2x/wk for dinner and ≥3x/wk for lunch • Poultry (ref; n=98): ~300g/wk **(0.0-0.3g n-3 LCPUFA/100g**); served 2x/wk for dinner and ≥3x/wk for lunch Intervention duration: 12 weeks Intervention compliance: Assessed with precoded, daily recording sheets and FFQs (baseline and endpoint) completed by parents • Oily fish and poultry consumption increased in their respective groups • Oily fish group EPA+DHA intake: Baseline, 135 (141) mg/d; Endpoint, 913 (278) mg/d **Outcomes and assessment methods**: • Assessed at baseline and endpoint (12 wk) • Fasting blood lipids: TC, LDL, HDL, triglycerides • BP: SBP and DBP; Measured in triplicate	***Between-group differences at endpoint, adjusted for baseline values*** **TC,** mmol/L, Mean difference (95% CI) **Poultry (ref) vs Oily fish: 0.15 (0.03, 0.28), P=0.02** **LDL,** mmol/L, Mean difference (95% CI) Poultry (ref) vs Oily fish: 0.08 (-0.02, 0.17), P=0.10 **HDL,** mmol/L, Mean difference (95% CI) **Poultry (ref) vs Oily fish: 0.07 (0.01, 0.13), P=0.02** **Triglycerides,** mmol/L, Mean difference (95% CI) **Poultry (ref) vs Oily fish: -0.05 (-0.11, -0.00), P=0.04** **SBP,** mmHg, Mean difference (95% CI) Poultry (ref) vs Oily fish: -0.7 (-2.0, 0.6), P=0.29 **DBP,** mmHg, Mean difference (95% CI) Poultry (ref) vs Oily fish: -0.1 (-1.1, 0.9) P=0.79 Results were similar when stratified by sex except for triglycerides, where an effect of group was detected in boys but not girls.	**Model adjustments:** Blood lipids: Baseline value Blood pressure: Baseline value, Baseline height and device used **Limitations:** • Fish intake used as a proxy for LCPUFAs; Other types of fat (SFA, MUFA, cholesterol) not reported or considered • No preregistered statistical analysis plan for 5y and Final follow-up analyses **Funding sources:** Nordea-fonden; Food provided at discount from Skagenfood A/S, Sodam A/S, REMA1000 Danmark A/S; Food provided in kind from Amanda Seafoods A/S

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Special Turku Coronary Risk Factor Intervention Project (STRIP)			
Lapinleimu, 1995[14] **RCT, STRIP, Finland** Baseline N=1,062 Analytic N=807 (Attrition: 24% from 7mo to 13mo) **Participant characteristics at baseline (7mo):** • Age: ~7mo • Sex (female): 51.3% • Race/ethnicity: NR • SES: NR • Anthropometry: Weight-for-height: ~4% higher than Finnish mean based on Finnish growth curve; No group differences in growth from 7mo to 13mo **Fat intake at baseline (8mo), Mean (subset of formula-fed infants):** • SFA: ~13%E; ~11.8 g/day • MUFA: ~9%E; ~7.9 g/day • PUFA: ~5%E; ~4.4 g/day • Cholesterol: ~71.3 mg/day • No group differences at baseline **Blood lipids at baseline (7mo), Mean:** • Total cholesterol: ~3.98 mmol/L • HDL cholesterol: ~0.89 mmol/L • No group differences at baseline **Summary of findings:** *Total cholesterol and HDL cholesterol decreased significantly more in the intervention group than in the control group between 7 months and 13 months.*	**Intervention/Control:** • Intervention (n=403): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10 and 13 months • Control (n=404): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7 and 13 months Intervention duration: 6 months Intervention compliance: Assessed via 3-day food diary completed by family, assessed at 8 and 13 months Fat intake at **follow-up (13mo)**, Mean (SD), Intervention vs control: • SFA: 9%E (3) vs 13%E (3), P<0.001; 9.3 (3.5) g/day vs 14.5 (4.8) g/day, P<0.001 • MUFA: 10%E (3) vs 9%E (2), P=0.02; 10.4 (3.2) g/day vs 10.1 (3.3) g/day, P=0.66 • PUFA: 5%E (2) vs 4%E (1), P<0.001; 5.8 (2.2) g/day vs 4.4 (1.4) g/day, P<0.001 • Cholesterol (mg/d): 83.8 (36.6) vs 112.8 (44.2), P<0.001 **Outcomes and assessment methods:** • Assessed at 7mo (baseline) and 13mo • Non-fasting blood lipids: TC, HDL	**TC**, mmol/L, Mean (SD), Intervention vs Control ***Blood lipid levels at 13mo*** 3.96 (0.70) vs 4.22 (0.78), P=NR ***Change from 7mo to 13mo*** **-0.03 (0.72) vs 0.24 (0.64), P<0.001** **HDL**, mmol/L, Mean (SD), Intervention vs Control ***Blood lipid levels at 13mo*** 0.87 (0.19) vs 0.91 (0.19), P=NR ***Change from 7mo to 13mo*** **-0.04 (0.19) vs 0.01 (0.17), P<0.001**	**Model adjustments:** None **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity and avoidance of passive smoking • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Mannerheim League for Child Welfare, the Finnish Cardiac Research Foundation, the Medical Council of the Academy of Finland, the Yrjo Jahnsson Foundation, the Foundation for Paediatric Research, Finland, Piltti Foundation, the Juho Vainio Foundation, the Turku University Foundation, and Van den Bergh Foods Company

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations

Routi, 1996[30]
RCT, STRIP, Finland
Baseline N=1,062 Analytic N=784 (Attrition from 7mo to 24mo: 26%)
 	
Participant characteristics at follow-up (24mo):
• Age: ~24mo
• Sex (female): NR
• Race/ethnicity: NR
• SES: NR
• Anthropometry: NR
 	
Fat intake at follow-up (24mo), Mean (SD), Intervention vs Control:
• SFA (%E): 10.8 (2.8) vs 14.3 (3.0), P<0.001
• MUFA (%E): 10.4 (2.3) vs 10.8 (2.0), P<0.01
• PUFA (%E): 5.3 (1.4) vs 4.5 (1.4), P<0.001
  • LA (%E): 4.3 (1.2) vs 3.6 (1.3), P<0.001
  • LA (%FA): 14.5 (3.7) vs 11.0 (3.4), P<0.001
 	
Summary of findings:
Total cholesterol was significantly lower in the intervention group than in the control group at 2 years. HDL cholesterol was significantly lower in the intervention group than in the control group at 2 years.
	Intervention/Control:
	• Intervention (n=394): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 mo and 2y
	• Control (n=390): Basic health education of current PUFA/SFA ratio of 0.43 for children aged 1-2y at 7, 13 months, and 2 years
	
	Intervention duration: ~1.5 years
	Intervention compliance: Assessed via 3-day (8 and 13 months) or 4-day (2y) food diaries completed by family, assessed at 8mo, 13mo, and 2y
	
	Outcomes and assessment methods:
	• Assessed at 7mo (baseline), 13mo, and 2y
	• Non-fasting blood lipids: TC, HDL
		TC, mmol/L, Mean (SD), Intervention vs Control
		Blood lipid levels at 2y
		4.08 (0.69) vs 4.32 (0.77), P<0.001
		
		HDL, mmol/L, Mean (SD), Intervention vs Control
		Blood lipid levels at 2y
		0.97 (019) vs 1.02 (0.19), P<0.001
			Model adjustments:
			None
			
			Limitations:
			• Although intervention primarily focused on types of fats, dietary advice included importance of physical activity and avoidance of passive smoking
			• Some concern for risk of bias in missing outcome data due to attrition
			• Serious risk of bias in selection of the reported result due to multiple outcome measurements
			
			Funding sources:
			Turku University Foundation, the Cardiac Research Foundation, Finland, The Yrjo Jahnsson Foundation, the Varsinais-Suomi Fund of the Finnish Cultural Foundation, The Arvo ja Inkeri Suominen Fund, the Lydia Maria Julin Fund, the Medical Council of the Finnish Academy, the Juho Vainio Foundation, the Foundation for Pediatric Research, Finland, the Mannerheim League for the Wellfare of Children, Chymos Ltd, and Van den Bergh Foods, Finland

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Simell, 2000[31] **RCT, STRIP, Finland** Baseline N=1,062 Analytic N=843 (Attrition from 7mo to 3y: 30%) **Participant characteristics at follow-up (3y):** • Age: ~3y • Sex (female): 48% • Race/ethnicity: NR • SES: NR • Anthropometry: Growth from 7mo-3y: NS between groups **Fat intake at follow-up (3y), Mean (SD), Intervention vs Control:** • PUFA:SFA: 0.48 (0.17) vs 0.33 (0.13), P<0.0001, 95% CI: 0.12, 0.17 • Unsaturated FA:SFA: 1.38 (0.37) vs 1.08 (0.24), P<0.0001, 95% CI: 0.25, 0.34 • Cholesterol (mg/1000 kJ): 28 (10) vs 33 (11), P<0.0001, 95% CI: -6, -3 **Summary of findings:** *Total cholesterol was significantly lower by 3-6% in the intervention group than in the control group between 7 months and 3 years. This was significant only for males when stratified by sex. HDL cholesterol was significantly lower by 3-6% in the intervention group than in the control group from 7 months to 3 years.*	**Intervention/Control:** • Intervention (n=374; Boys, n=201; Girls, n=173): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 months, 2y to 3y, twice/year • Control (n=374; Boys, n=187; Girls, n=187): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13, 18 months, 2y, and 3y Intervention duration: ~2.5y Intervention compliance: Assessed via 3-day food diary (8, 13, and 18mo) or 4-day food diary (≥2y) completed by family, assessed at 8, 13, 18mo, and biannually ≥2y **Outcomes and assessment methods:** • Assessed at 7mo, 13mo, 2y, and 3y • Non-fasting blood lipids: TC, HDL	**TC**, mmol/L, Mean (SD), Intervention vs Control ***Blood lipid levels at 3y*** Boys: 4.12 (0.63) vs 4.44 (0.79), P=NR Girls: 4.45 (0.80) vs 4.49 (0.69), P=NR ***Mean difference from 13mo-3y, adjusted for 7mo*** **All** **TC was lower in intervention than control children between 7mo and 36mo, Data=NR, 95% CI: -0.27, -0.12, P<0.0001** **Boys: 0.32 (0.76) vs 0.57 (0.65)** **95% CI: -0.39, -0.20, P<0.0001** Girls: 0.23 (0.82) vs 0.37 (0.76) 95% CI: -0.21, 0.01, P=0.09 **HDL**, mmol/L, Mean (SD), Intervention vs Control ***Blood lipid levels at 3y*** Boys: 1.05 (0.23) vs 1.12 (0.22), P=NR Girls: 1.05 (0.20) vs 1.08 (0.21), P=NR ***Mean difference from 13mo-3y, adjusted for 7mo*** **All** **HDL was lower in intervention than in control children between 7mo and 3y, Data=NR, 95% CI: -0.07, -0.03, P<0.0001** **Boys: 0.15 (0.23) vs 0.21 (0.19)** **95% CI: -0.08, -0.03, P=0.0001** **Girls: 0.15 (0.20) vs 0.18 (0.20)** **95% CI: -0.07, -0.01, P=0.007**	**Model adjustments:** Baseline value (7mo) **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake. • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Mannerheim League for Child Welfare, the Finnish Cardiac Research Foundation, the Foundation for Paediatric Research, Finland, Piltti Foundation, the Juho Vainio Foundation, the Turku University Foundation, and Van den Bergh Foods Company

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Rask-Nissila, 2000[29] **RCT, STRIP, Finland** Baseline N=1,062 Analytic N=683 (Attrition from 7mo to 5y: 36%) **Participant characteristics at follow-up (5y):** • Age: ~5y • Sex (female): 49% • Race/ethnicity: NR • SES: NR • Anthropometry: Height-for-age, weight-for-height, and BMI at 5y did not vary by group **Fat intake at follow-up (5y), Mean (SD), Intervention vs Control:** • SFA (%E): Boys: 11.9 (2.2) vs 14.5 (2.5), P=0.0001; Girls: 11.7 (2.5) vs 14.3 (2.7), P=0.0001 • MUFA (%E): Boys, 10.7 (1.9) vs 11.2 (2.0), P=0.06; Girls, 10.7 (2.0) vs 11.0 (1.8), P=0.036 • PUFA (%E): Boys, 5.2 (1.2) vs 4.9 (1.2), P=0.02; Girls, 5.2 (1.1) vs 4.8 (1.2), P=0.001 • Cholesterol (mg): Boys, 168.2 (63.5) vs 193.0 (71.0), P=0.002; Girls, 163.9 (60.2) vs 188.1 (72.2), P=0.004 **Summary of findings:** *Total cholesterol was significantly lower in intervention boys than in control boys between 7 months and 5 years; this was not significant among girls. HDL cholesterol was significantly lower in the intervention group than in the control group between 7 months and 5 years. LDL cholesterol was significantly lower in intervention boys than in control boys at 5 years; this was not significant among girls. Triglycerides were not significantly different between groups.*	**Intervention/Control:** • Intervention (n=339; Boys, n=181; Girls, n=158): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7mo, 8mo, 10mo, 13mo, 15mo, 18mo, 21mo, 2y, 2.5y, 3y, 4y, and 5y • Control (n=344; Boys, n=170, Girls, n=174): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7mo,13mo, 24mo, 3y, 4y, and 5y Intervention duration: ~4.5 y Intervention compliance: Assessed via 3-day (<2y) or 4-day (≥2y) food diary completed by family ~biannually **Outcomes and assessment methods:** • Assessed at 7mo, 13mo, 2y, 3y, 4y, and 5y • Blood lipids: TC, HDL (Non-fasting <5y; fasting at 5y); LDL, triglycerides (only fasting at 5y)	**TC**, mmol/L, Mean (SD), Boys (Intervention vs Control): 4y: 4.09 (0.60) vs 4.40 (0.70) 5y: 4.14 (0.62) vs 4.41 (0.72) Change, 7mo-5y: 0.35 (0.77) vs 0.57 (0.65) ***Mean difference (95% CI), 13mo to 5y:*** **-0.39 (-0.52, -0.26), P<0.0001** Equality of slopes (13mo-5y): P=0.06 Girls (Intervention vs Control): 4y: 4.42 (0.65) vs 4.41 (0.79) 5y: 4.47 (0.72) vs 4.53 (0.74) Change, 7mo-5y: 0.32 (0.80) vs 0.35 (0.73) ***Mean difference (95% CI), 13mo to 5y:*** -0.146 (-0.293, -0.0001), P=0.052 Equality of slopes (13mo-5y): P=0.19 **HDL**, mmol/L, Mean (SD) Boys (Intervention vs Control): 4y: 1.11 (0.22) vs 1.16 (0.22) 5y: 1.19 (0.25) vs 1.22 (0.25) Change, 7mo-5y: 0.29 (0.23) vs 0.32 (0.22) ***Mean difference (95% CI), 13mo to 5y:*** **-0.07 (-0.11, -0.03), P=0.0007** Equality of slopes (13mo-5y): P=0.27 Girls (Intervention vs Control): 4y: 1.14 (0.18) vs 1.12 (0.22), 5y: 1.18 (0.21) vs 1.19 (0.23) Change, 7mo-5y: 0.29 (0.23) vs 0.28 (0.22) ***Mean difference (95% CI), 13mo to 5y:*** **-0.05 (-0.09, -0.01), P=0.007** **Equality of slopes (13mo-5y): Between-group differences decreased over time, P=0.023** **LDL**, mmol/L, Mean (SD) **Boys (5y): 2.62 (0.55) vs 2.87 (0.61)** **Difference at 5y: 95% CI: -0.39, -0.12, P=0.0002** Girls (5y): 2.94 (0.63) vs 2.99 (0.66) Difference at 5y: 95% CI: -0.21, 0.11, P=0.53 **Triglycerides**, mmol/L, Mean (SD), Intervention vs Control Boys (5y): 0.66 (0.23) vs 0.63 (0.21) Difference at 5y: P=0.25 Girls (5y): 0.69 (0.21) vs 0.69 (0.24) Difference at 5y: P=0.90	**Model adjustments:** Baseline (7mo) blood lipids **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Mannerheim League for Child Welfare; Finnish Cardiac Research Foundation; Foundation for Paediatric Research, Finland; Academy of Finland; Yrjo Jahnsson Foundation; Sigrid Juselius Foundation; Juho Vainio Foundation; Turku University Foundation; Finnish Cultural Foundation; Varsinais-Suomi Fund; City of Turku; Raisio Group; Van den Bergh Foods Company

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Kaitosaari, 2003[10] **RCT, STRIP, Finland** Baseline N=1,062 Analytic N=640 (Attrition from 7mo to 7y: 40%) **Participant characteristics at follow-up (7y):** • Age: ~7y • Sex (female): 45.3% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at follow-up (7y), Mean (SD, Intervention vs Control:** • SFA, Boys: 16.2g (4.9) vs 20.5g (5.5), P<0.0001 • SFA, Girls: 15.6g (4.6) vs 19.4g (5.0), P<0.0001 • PUFA:SFA, Boys: 0.48 (0.16) vs 0.34 (0.15), P<0.0001 • PUFA:SFA, Girls: 0.48 (0.17) vs 0.34 (0.11), P<0.0001 • Cholesterol, Boys: 118 mg/1000 kcal (40) vs 137 mg/1000 kcal (50), P=0.0002 • Cholesterol, Girls: 123 mg/1000 kcal (45) vs 137 mg/1000 kcal (44), P=0.008 **Summary of findings:** *Total cholesterol levels were lower in intervention children than control children at 7 years. When stratified by sex, intervention boys had significant decreases in total cholesterol between 7 months and 13 months, 48 months, and 7 years. Intervention girls had significant decreases in HDL cholesterol between 7 months and 13 months, but not between 7 months and 48 months and 7 years. LDL cholesterol and triglycerides were significantly lower in intervention boys than control boys. This was not significant among girls.*	**Intervention/Control:** • Intervention (n=315; Boys, n=134; Girls, n=112): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 months; from 2y to 7y, counseling twice/year • Control (n=325; Boys, n=140; Girls, n=125): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13 months, 2y to 7y twice a year Intervention duration: ~6.5 years Intervention compliance: Assessed via 3-day food diary (8, 13, and 18mo) or 4-day food diary (≥2y) completed by family/child, assessed biannually **Outcomes and assessment methods:** • Assessed at 7mo, 13mo, 3y, 5y, 7y mo • Blood lipids: TC, HDL, LDL, Triglycerides (Nonfasting at 7mo, 13mo and 3y; Fasting at ≥5y)	**TC**, mmol/L, Mean (SD), Intervention vs Control Male 13mo: 3.68 (0.61) vs 4.18 (0.70) **7y: 4.20 (0.64) vs 4.41 (0.66), P=0.003, 95% CI: -0.348, -0.071** Female 13mo: 4.19 (0.73) vs 4.31 (0.78) **7y: 4.55 (0.66) vs 4.57 (0.72), P=0.78, 95% CI: -0.181, 0.135** ***Change from 7mo to 7y:*** Male: 0.42 (0.70) vs 0.55 (0.63) Female: 0.40 (0.87) vs 0.43 (0.78) ***Difference in change from 7mo to:*** **Male: (Group*Time: P≤0.05)** **13mo: -0.394, 95% CI: -0.508, -0.280** **4y: -0.298, 95% CI: -0.401, -0.196** **7y: -0.200, 95% CI: -0.331, -0.069** ***Mean difference from 13mo to 7y*** Female: (Group*Time: P>0.05) -0.090, 95% CI: -0.213, 0.032, P=0.15 **HDL**, mmol/L, Mean (SD), Intervention vs Control Male 13mo: 0.86 (0.19) vs 0.92 (0.20) 7y: 1.29 (0.24) vs 1.29 (0.25), P=1.00, 95% CI: -0.053, 0.053 Female 13mo: 0.85 (0.19) vs 0.89 (0.17) 7y: 1.28 (0.20) vs 1.27 (0.22), P=0.82, 95% CI: -0.042, 0.052 ***Change from 7mo to 7y*** Male: 0.37 (0.21) vs 0.38 (0.21) Female: 0.39 (0.21) vs 0.38 (0.21) ***Difference in change from 7mo to:*** Female: (Group*Time: P≤0.05) **13mo: -0.049, 95% CI: -0.082, -0.016** 4y: -0.017, 95% CI:-0.047, 0.013 7y: 0.016, 95% CI: -0.030, 0.062 ***Mean difference from 13mo to 7y*** Male: -0.054, 95% CI: -0.086, -0.022, P=0.001 Group*Time: P>0.05	**Model adjustments:** Analyses of "Mean difference from 13mo to 7y": adjusted for 7mo (baseline) values **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake. • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Juho Vainio Foundation, the Yrjo Jahnsson Foundation, the Finnish Cardiac Research Foundation, the Foundation for Paediatric Research, Finland, the Academy of Finland, the Sigrid Juselius Foundation, the Turku University Foundation, the Finnish Cultural Foundation, City of Turku, EVO funds of Turku University Central Hospital, and the Raisio Group Research Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Kaitosaari, 2003 (CONTINUED) **RCT, STRIP, Finland** Baseline N=1,062 Analytic N=640 (Attrition from 7mo to 7y: 40%) **Participant characteristics at follow-up (7y):** • Age: ~7y • Sex (female): 45.3% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at follow-up (7y), Mean (SD, Intervention vs Control:** • SFA, Boys: 16.2g (4.9) vs 20.5g (5.5), P<0.0001 • SFA, Girls: 15.6g (4.6) vs 19.4g (5.0), P<0.0001 • PUFA:SFA, Boys: 0.48 (0.16) vs 0.34 (0.15), P<0.0001 • PUFA:SFA, Girls: 0.48 (0.17) vs 0.34 (0.11), P<0.0001 • Cholesterol, Boys: 118 mg/1000 kcal (40) vs 137 mg/1000 kcal (50), P=0.0002 • Cholesterol, Girls: 123 mg/1000 kcal (45) vs 137 mg/1000 kcal (44), P=0.008 **Summary of findings:** *Total cholesterol levels were lower in intervention children than control children at 7 years. When stratified by sex, intervention boys had significant decreases in total cholesterol between 7 months and 13 months, 48 months, and 7 years. Intervention girls had significant decreases in HDL cholesterol between 7 months and 13 months, but not between 7 months and 48 months and 7 years. LDL cholesterol and triglycerides were significantly lower in intervention boys than control boys. This was not significant among girls.*	**Intervention/Control:** • Intervention (n=315; Boys, n=134; Girls, n=112): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 months; from 2y to 7y, counseling twice/year • Control (n=325; Boys, n=140; Girls, n=125): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13 months, 2y to 7y twice a year Intervention duration: ~6.5 years Intervention compliance: Assessed via 3-day food diary (8, 13, and 18mo) or 4-day food diary (≥2y) completed by family/child, assessed biannually **Outcomes and assessment methods:** • Assessed at 7mo, 13mo, 3y, 5y, 7y mo • Blood lipids: TC, HDL, LDL, Triglycerides (Nonfasting at 7mo, 13mo and 3y; Fasting at ≥5y)	**LDL**, mmol/L, Mean (SD), Intervention vs Control Male (Interv: n=170; Cont: n=170) **2.63 (0.55) vs 2.82 (0.58), P=0.002, 95% CI: -0.312, -0.071** Female (Interv: n=145; Cont: n=155) 2.94 (0.60) vs 2.98 (0.65), P=0.59 95% CI: -0.181, 0.104 ***Mean difference from 5y and 7y*** Male: **LDL was lower in intervention than control boys between 5y and 7y. Difference: 95% CI: -0.333, -0.150, P<0.0001** Female: Data NR, P=0.18 **Triglycerides**, mmol/L, Mean (SD), Intervention vs Control Male Interv: n=170; Cont: n=170) 0.64 (0.26) vs 0.68 (0.30), P=0.30 Female (Interv: n=145; Cont: n=155) 0.71 (0.28) vs 0.68 (0.25), P=0.48 ***Mean difference from 5y to 7y*** Male: Triglyceride tended to decrease in intervention boys and increase in control boys, P=0.042 Female: Data NR, P=0.75	**Model adjustments:** Analyses of "Mean difference from 13mo to 7y": adjusted for 7mo (baseline) values **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake. • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Juho Vainio Foundation, the Yrjo Jahnsson Foundation, the Finnish Cardiac Research Foundation, the Foundation for Paediatric Research, Finland, the Academy of Finland, the Sigrid Juselius Foundation, the Turku University Foundation, the Finnish Cultural Foundation, City of Turku, EVO funds of Turku University Central Hospital, and the Raisio Group Research Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations

Kaitosaari, 2006[11]
RCT, STRIP, Finland
Baseline N=200 Analytic N=167 (Attrition: 17%); Subsample of children available for detailed laboratory measurements
 	
Participant characteristics at follow-up (9y):
• Age: ~9y
• Sex (female): 51%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: Weight-for-height (deviation from mean of healthy Finnish children): Boys: ~1.2%, Girls: ~4.6%, NS between groups
 	
Fat intake at follow-up (9y), Mean (SD), Intervention vs Control
• SFA (%E), Group difference: P<0.001
  ○ Boys: 11.2 (1.9) vs 12.8 (2.1)
  ○ Girls: 11.2 (2.8) vs 14.2 (2.3)
• MUFA (%E), Group difference: P=NS
  ○ Boys: 11.59 (1.79) vs 10.83 (1.75)
  ○ Girls: 10.39 (1.62) vs 11.06 (1.95)
• PUFA (%E), Group difference: P=0.0003
  ○ Boys: 6.03 (1.12) vs 5.39 (1.20)
  ○ Girls: 5.49 (1.19) vs 4.80 (1.02)
 	
Summary of findings:
Triglycerides were significantly lower in intervention children than control children at 9 years. Total cholesterol, HDL, and LDL were not different between groups.
	Intervention/Control:
	• Intervention (n=78; Boys, n=35; Girls, n=43): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 months; from 2y to 9y, counseling twice/year; dietary information were given directly to child beginning at 7y
	• Control (n=89; Boys, n=47; Girls, n=42): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7mo,13mo, 2y, 3y, 4y, and 5y; from 7mo to 7y twice/year; from 7y and older once/year
	Intervention duration: ~8.5 years
	Intervention compliance: Assessed via 3-day food diary (7mo to <2y) or 4-day food diary (≥2y) completed by family/child, assessed biannually
	
	Outcomes and assessment methods:
	• Assessed at 9y
	• Fasting blood lipids: TC, HDL, LDL, Triglycerides
		Blood lipid levels at 9y, Mean (SD), Intervention vs Control
		TC, mmol/L, Mean (SD)
		Male: 4.30 (0.66) vs 4.49 (0.85), P>0.05
		Female: 4.55 (0.65) vs 4.64 (0.65), Group difference: P>0.05
		HDL, mmol/L, Mean (SD)
		Male: 1.33 (0.25) vs 1.37 (0.28), P>0.05
		Female: 1.24 (0.20) vs 1.30 (0.24), Group difference: P>0.05
		LDL, mmol/L, Mean (SD)
		Male: 2.71 (0.48) vs 2.78 (0.76), P>0.05
		Female: 2.95 (0.61) vs 2.97 (0.56), Group difference: P>0.05
		Triglycerides, mmol/L, Mean (SD)
		Male: 0.57 (0.21) vs 0.75 (0.38)
		Female: 0.79 (0.36) vs 0.83 (0.29)
		Group difference: P=0.018
			Model adjustments:
			None
			
			Limitations:
			• Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake.
			• Some concern for risk of bias in missing outcome data due to attrition
			• Serious risk of bias in selection of the reported result due to multiple outcome measurements
			
			Funding sources:
			Juho Vainio Foundation, the Yrjo Jahnsson Foundation, the Finnish Cardiac Research Foundation, the Foundation for Paediatric Research, Finland, the Academy of Finland, the Sigrid Juselius Foundation, the Turku University Foundation, the Finnish Cultural Foundation, City of Turku, EVO funds of Turku University Central Hospital, and the Raisio Group Research Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Raitakari, 2005[28] **RCT, STRIP, Finland** Baseline N=453 Analytic N=369 (Attrition: 19%); Subset of children with ultrasound data at 11y (time-restricted cohort) **Participant characteristics at follow-up (11y):** • Age: ~11y • Sex (female): 50.7% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI: ~18 **Fat intake at follow-up (11y), Mean (SD), Intervention vs Control:** • SFA (%E), Boys: 10.8 (2.1) vs 13.2 (2.9), P<0.0001 • SFA (%E), Girls: 11.5 (2.9) vs 12.8 (2.7), P=0.001 • PUFA:SFA, Boys: 0.59 (0.19) vs 0.42 (0.14), P<0.0001 • PUFA:SFA, Girls: 0.53 (0.19) vs 0.41 (0.13), P<0.0001 **Summary of findings:** In this sub-study, total cholesterol and LDL were significantly lower in intervention boys than control boys at 11 years. These effects were not statistically significant in girls. There was no significant effect of the intervention on blood pressure, HDL cholesterol, and triglycerides at 11 years.	**Intervention/Control:** • Intervention (n=179; Boys, n=90; Girls, n=89): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21, 24, 30, 36, 48, and 60 months; biannually from 2y to 20y • Control (n=190, Boys, n=92; Girls, n=98): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13, 24, 36, 48, and 60 months; biannually from 7mo to 2y and annually from 2y to 20y Intervention duration: ~10.5 years Intervention compliance: Assessed via 4-day food diaries completed by family/child, assessed biannually **Outcomes and assessment methods:** • Assessed at 11y • BP: SBP and DBP; Measured in triplicate • Fasting blood lipids: TC, HDL, LDL, Triglycerides	***Blood lipid levels and BP at 11y*** **TC**, mmol/L, Mean (SD), Intervention vs Control **Boys: 4.37 (0.57) vs 4.58 (0.85), P=0.03** Girls: 4.53 (0.72) vs 4.58 (0.80), P=0.62 **LDL**, mmol/L, Mean (SD), Intervention vs Control **Boys: 2.64 (0.52) vs 2.92 (0.75), P=0.009** Girls: 2.84 (0.62) vs 2.87 (0.72), P=0.70 **HDL**, mmol/L, Mean (SD), Intervention vs Control Boys: 1.34 (0.28) vs 1.32 (0.28), P=0.86 Girls: 1.27 (0.23) vs 1.29 (0.26), P=0.41 **Triglycerides**, mmol/L, Mean (SD), Intervention vs Control Boys:0.82 (0.49) vs 0.78 (0.33), P=0.53 Girls: 0.91 (0.47) vs 0.87 (0.38), P=0.59 **SBP**, mmHg, Mean (SD), Intervention vs Control Boys: 105 (9) vs 104 (8), P=0.31 Girls: 103 (8) vs 105 (8), P=0.35 **DBP**, mmHg, Mean (SD), Intervention vs Control Boys: 63 (6) vs 63 (5), P=0.93 Girls: 63 (6) vs 63 (5), P=0.89	**Model adjustments:** None **Limitations:** • Although intervention primarily focused on types of fats, dietary advice was given on physical activity, avoidance of passive smoking, and salt intake • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Academy of Finland; City of Turku; Finnish Foundation for Pediatric Research; Finnish Foundation of Cardiovascular Research; Finnish Cultural Foundation; Government grants for Turku University Hospital; Juho Vainio Foundation; Mannerheim League for Child Welfare; Raisio Group Research Foundation; Social Insurance Institution of Finland; Turku University Foundation; Van den Bergh Foods Company; Yrjo Jahnsson Foundation; Sigrid Juselius Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations

Niinikoski, 2007[22]
RCT, STRIP, Finland
Baseline N=1062 Analytic N=532 (Attrition from 7mo to 14y: 50%)
 	
Participant characteristics at follow-up (14y):
• Age: ~14y
• Sex (female): 49%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI did not differ by study group between 7mo and 14y (P=0.28)
 	
Fat intake at follow-up (14y): Mean (SD), Intervention vs Control
• SFA (%E), P<0.001
  ○ Boys: 12 (3) vs 13 (3)
  ○ Girls: 12 (3) vs 13 (3)
 	
Summary of findings:
Total cholesterol, LDL cholesterol, and triglycerides in intervention boys were significantly higher between 7 months and 14 years than control boys. LDL cholesterol was significantly lower in intervention girls than control girls. HDL cholesterol did not differ between groups.
	Intervention/Control:
	• Intervention (n=254; Boys, n=135; Girls, n=119): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 months, 2y to 14y, counseling twice/year; dietary information were given directly to child beginning at 7y
	• Control (n=278; Boys, n=141; Girls, n=137): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7mo to 7y twice/year; from 7y to 14y once/year
	Intervention duration: ~13.5y
	Intervention compliance: Assessed via 3-day (<2y) or 4-day (≥2y) food diaries completed by family, assessed ~annually from 7mo to 14y
	Outcomes and assessment methods:
	• Assessed at 7, 13, months and 2y to 14y annually
	• Blood lipids: TC, HDL, LDL, Trig (Non-fasting from 7mo-4y; fasting at 5y to 14y)
		Blood lipid levels at 14y, Mean (SD)
		TC, mmol/L, Mean (SD), Intervention vs Control
		Boys: 3.91 (0.59) vs 4.11 (0.77)
		Mean difference from 7mo to 14y: P<0.001
		Girls: 4.23 (0.63) vs 4.30 (0.79)
		Mean difference from 7mo to 14y: P=0.12
		
		HDL, Intervention vs Control
		Boys: Data NR
		Mean difference from 7mo to 14y: P>0.05
		Girls: Data NR
		Mean difference from 7mo to 14y: P>0.05
		
		LDL, Intervention vs Control
		Boys: Data NR,
		Mean difference from 5y to 14y: P<0.05
		Girls: Data NR
		Mean difference from 5y to 14y: P<0.05
		
		Triglycerides, Intervention vs Control
		Boys: Data NR
		Mean difference from 5y to 14y: P<0.001
		Girls: Data NR
		Mean difference from 5y to 14y: P>0.05
			Model adjustments:
			Energy intake, SFA (%E) intake, height, and BMI
			
			Limitations:
			• Although intervention primarily focused on types of fats, dietary advice was given on physical activity, avoidance of passive smoking, and salt intake
			• Some concern for risk of bias in missing outcome data due to attrition
			• Serious risk of bias in selection of the reported result due to multiple outcome measurements
			
			Funding sources:
			Finnish Cardiac Research Foundation, Foundation for Pediatric Research, Finland, Academy of Finland, Yrjo Jahnsson Foundation, Sigrid Juselius Foundation, Special Federal Research Funds for Turku University Hospital, Turku University Foundation, Turku University Hospital Foundation, Juho Vainio Foundation, Finnish Cultural Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Niinikoski, 2009[21] **RCT, STRIP, Finland** Baseline N=1062 Analytic N=524 (Attrition from 7mo to 15y: 51%) **Participant characteristics at follow-up (15y):** • Age: ~15y • Sex (female): 48% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at follow-up (15y), Mean (SD), Intervention vs Control** • SFA (%E): 11.1 (2.4) vs 12.8 (3.0), P<0.001* • MUFA (%E): 10.9 (2.4) vs 10.6 (2.1), P=0.12* • PUFA (%E): 5.9 (1.6) vs 5.4 (.6), P<0.001* *Based on repeated measures ANOVA between 8mo and 15y **BP at baseline (7mo):** NR **Summary of findings:** *Diastolic and systolic blood pressure was significantly lower in intervention children than control children. When stratified by gender, girls and boys in the intervention group had significantly lower diastolic BP, but not systolic BP, than those in the control group.*	**Intervention/Control:** • Intervention (n=248; Boys, n=133; Girls n=115): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21 months, 2y to 15y biannually • Control (n=276; Boys, n=139; Girls, n=137): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7mo to 15y; biannually from 7mo to 7y and annually from 7y to 15y Intervention duration: ~14.5 years Intervention compliance: Assessed via 3-day (<2y) or 4-day (≥2y) food diaries completed by family/child, assessed biannually **Outcomes and assessment methods:** • Assessed annually from 7mo to 15y • BP: measured 1x per visit from 7mo to 7y, 2-4x per visit from 8-9y, 2x per visit after 9y; Mean values for each visit were used in statistical analyses	**SBP**, mmHg, Mean (SD), Intervention vs Control ***Blood pressure values at 15y*** Girls: 113.6 (10.2) vs 114.8 (11.9), P=0.38 Boys: 120.8 (13.2) vs 122.0 (12.3), P=0.42 **Mean difference from 7mo to 15y** **-1.0, 95% CI: -1.7, -0.2, P=0.018 (children in intervention group had lower systolic BP than children in control group)** **DBP**, mmHg, Mean (SD), Intervention vs Control ***Blood pressure values at 15y*** **Girls: 60.2 (6.0) vs 61.9 (6.9), P=0.048** **Boys: 60.8 (7.2) vs 62.7 (7.5), P=0.045** **Mean difference from 7mo to 15y** **-1.0, 95% CI: -1.5, -0.4, P<0.001 (children in intervention group had lower diastolic BP than children in control group)**	**Model adjustments:** None **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake, and ample use of vegetables, fruits, berries and whole grain products, and increase fiber • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Finnish Cardiac Research Foundation, Foundation for Pediatric Research, Finland, Academy of Finland, Mannerheim League for Child Welfare, Yrjo Jahnsson Foundation, Sigrid Juselius Foundation, Federal Research Funds for Turku University Hospital, Turku University Foundation, Turku University Hospital Foundation, Juho Vainio Foundation, Finnish Cultural Foundation, city of Turku

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Hakanen, 2010[8] **RCT, STRIP, Finland** Baseline N=1062 Analytic N=525 (Attrition from 7mo to 15y: 51%) **Participant characteristics at follow-up (15y):** • Age: ~15y • Sex (female): 48% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI: ~20.5 , P=0.31 between groups **Fat intake at follow-up (15y):** NR **Summary of findings:** *Diastolic blood pressure was significantly lower for intervention children than control children at 15 years. There were no significant effects of the intervention on HDL cholesterol, triglycerides, and systolic blood pressure at 15 years.*	**Intervention/Control:** • Intervention (n=249; Boys, n=133; Girls, n=116): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7mo, 8mo, 10mo, 13mo, 15mo, 18mo, 21mo, 2y, 2.5y, 3y, 4y, and 5y; biannually from 2y to 15y • Control (n=276; Boys, n=139; Girls, n=137): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13, 24, 36, 48, and 60 months; biannually from 7mo to 2y and annually from 2y to 15y Intervention duration: ~14.5 years Intervention compliance: Assessed via 4-day food diary completed by family/child, assessed biannually **Outcomes and assessment methods:** • Assessed at 15y • BP: SBP and DBP; Measured in duplicate • Fasting blood lipids: HDL, Triglycerides	***Blood lipid levels and BP at 15y*** **HDL**, mmol/L, Mean (SD), Intervention vs Control Boys: 1.08 (0.22) vs 1.08 (0.22) Girls: 1.23 (0.21) vs 1.21 (0.24) Group difference: P=0.43 **Triglycerides**, mmol/L, Mean (SD), Intervention vs Control Boys: 0.85 (0.49) vs 0.96 (0.48) Girls: 0.93 (0.41) vs 0.92 (0.54) Group difference: P=0.25 **SBP**, mmHg, Mean (SD), Intervention vs Control Boys: 121 (13) vs 122 (12) Girls: 114 (10) vs 115 (12) Group difference: P=0.25 **DBP**, mmHg, Mean (SD), Intervention vs Control **Boys: 61 (7.1) vs 63 (7.5)** **Girls: 60 (6.0) vs 62 (6.9)** **Group difference: P=0.005**	**Model adjustments:** None **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake, and ample use of vegetables, fruits, berries and whole grain products, and increase fiber • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Academy of Finland, Finnish Cardiac Research Foundation, Finnish Cultural Foundation, Special Federal Research Funds for Turku University Hospital, Research Foundation of Orion Corporation, C.G. Sundell Foundation, Yrjo Jahnsson Foundation, Maud Kuistila Foundation, Juho Vainio Foundation, Finnish Medical Society Duodecim and Foundation for Pediatric Research

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations

Niinikoski, 2012[23]
RCT, STRIP, Finland
Baseline N=1062 Analytic N=442 (Attrition from 7mo to 19y: 58%)
 	
Participant characteristics at follow-up (19y):
• Age: ~19y
• Sex (female): 49.8%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI: ~19.9
 	
SFA intake (%E) at follow-up (15y, 16y, 17y, 18y, 19y), Mean (SD), Intervention vs Control
• **15y:** Boys, 11.2 (2.3) vs 13.1 (2.9); Girls, 11.0 (2.5) vs 12.5 (3.2)
• **16y:** Boys,11.8 (2.6) vs 13.4 (2.9); Girls, 11.2 (2.5) vs 12.5 (2.8)
• **17y:** Boys, 11.7 (2.6) vs 13.1 (3.0); Girls, 11.6 (3.0) vs 12.2 (2.9)
• **18y:** Boys, 11.2 (2.6) vs 12.8 (3.0); Girls, 11.6 (2.7) vs 11.9 (3.1)
19y: Boys, 11.8 (2.5) vs 12.7 (3.2); Girls, 11.4 (2.4) vs 12.0 (2.8)
 	
Summary of findings:
Intervention boys who received nutrition counseling intervention (1:1:1 ratio of PUFA:MUFA:SFA) from 7 months to 20 years, compared to control boys who received basic health education at 7 months to 20 years, had significant lower total cholesterol, LDL, and triglycerides at 20 years. These effects were not significant in girls at 20 years. There were no significant effect of the intervention on HDL for both genders at 20 years.
	Intervention/Control:
	• Intervention (n=201): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21, 24, 30, 36, 48, and 60 months; biannually from 2y to 19y
	• Control (ref; n=241): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13, 24, 36, 48, and 60 months; biannually from 7mo to 2y and annually from 2y to 19y
	
	Intervention duration: ~18.5y
	Intervention compliance: 3-day or 4-day food diaries completed by family/child, assessed biannually or annually from 7mo-19y
	• SFA (%E), Group differences (95% CI) from 7mo-19y, Intervention vs Control (ref)
	  • Boys: -2.1 (-2.3, -1.9), P<0.001
	  • Girls: -1.9 (-2.1, -1.7), P<0.001
	
	Outcomes and assessment methods:
	• Assessed ~annually from 7mo to 19y
	• Blood lipids: TC, HDL, LDL, Triglycerides; Non-fasting 7mo-4y, Fasting from 5y-19y
		TC, mmol/L
		Mean (SD), Intervention vs Control (ref)
		Boys:
		15y: 3.64 (0.59) vs 3.89 (0.78)
		16y: 3.68 (0.57) vs 3.88 (0.75)
		17y: 3.71 (0.55) vs 3.91 (0.72)
		18y: 3.77 (0.57) vs 4.05 (0.78)
		19y: 4.00 (0.69) vs 4.16 (0.82)
		***Mean difference (95% CI) from 7mo-19y*:**
		-0.20 (-0.28, -0.13)
		Girls:
		15y: 4.11 (0.58) vs 4.22 (0.85)
		16y: 4.22 (0.71) vs 4.17 (0.79)
		17y: 4.41 (0.81) vs 4.31 (0.73)
		18y: 4.49 (0.77) vs 4.43 (0.76)
		19y: 4.57 (0.78) vs 4.56 (0.76)
		***Mean difference (95% CI) from 7mo-19y*:**
		-0.07 (-0.15, 0.02)
		
		HDL, mmol/L
		Mean (SD), Intervention vs Control
		Boys:
		15y: 1.08 (0.22) vs 1.08 (0.22)
		16y: 1.05 (0.22) vs 1.05 (0.23)
		17y: 1.07 (0.21) vs 1.06 (0.21)
		18y: 1.11 (0.24) vs 1.13 (0.22)
		19y: 1.20 (0.24) vs 1.14 (0.24)
		***95% CI of mean difference from 7mo-19y*:**
		-0.03, 0.02, P=0.81
		Girls:
		15y: 1.23 (0.21) vs 1.21 (0.69)
		16y: 1.26 (0.26) vs 1.22 (0.27)
		17y: 1.35 (0.29) vs 1.31 (0.25)
		18y: 1.42 (0.28) vs 1.38 (0.26)
		19y: 1.48 (0.28) vs 1.44 (0.30)
		***95% CI of mean difference from 7mo-19y*:**
		-0.02, 0.03, P=0.75
			Model adjustments:
			Age, age*study group if P<0.05
			
			Limitations:
			• Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake, and ample use of vegetables, fruits, berries and whole grain products, and increase fiber
			• Some concern for risk of bias in missing outcome data due to attrition
			• Serious risk of bias in selection of the reported result due to multiple outcome measurements
			
			Funding sources:
			Mannerheim League for Child Welfare; Finnish Cardiovascular Research Foundation; Foundation for Peadiatric Research, Finland; Academy of Finland; Public Health Challenge Research Programme; Juho Vainio Foundation; Yrjo Jahnsson Foundation; Sigrid Juselius Foundation; Turku University Foundation; Special Federal Research Funds for Turku University Hospital; Turku University Hospital Foundation; Finnish Cultural Foundation; Finnish Ministry of Education and Culture

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations

Niinikoski, 2012 (CONTINUED)
RCT, STRIP, Finland
Baseline N=1062 Analytic N=442 (Attrition from 7mo to 19y: 58%)
 	
Participant characteristics at follow-up (19y):
• Age: ~19y
• Sex (female): 49.8%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI: ~19.9
 	
SFA intake (%E) at follow-up (15y, 16y, 17y, 18y, 19y), Mean (SD), Intervention vs Control
• **15y:** Boys, 11.2 (2.3) vs 13.1 (2.9); Girls, 11.0 (2.5) vs 12.5 (3.2)
• **16y:** Boys,11.8 (2.6) vs 13.4 (2.9); Girls, 11.2 (2.5) vs 12.5 (2.8)
• **17y:** Boys, 11.7 (2.6) vs 13.1 (3.0); Girls, 11.6 (3.0) vs 12.2 (2.9)
• **18y:** Boys, 11.2 (2.6) vs 12.8 (3.0); Girls, 11.6 (2.7) vs 11.9 (3.1)
19y: Boys, 11.8 (2.5) vs 12.7 (3.2); Girls, 11.4 (2.4) vs 12.0 (2.8)
 	
Summary of findings:
Intervention boys who received nutrition counseling intervention (1:1:1 ratio of PUFA:MUFA:SFA) from 7 months to 20 years, compared to control boys who received basic health education at 7 months to 20 years, had significant lower total cholesterol, LDL, and triglycerides at 20 years. These effects were not significant in girls at 20 years. There were no significant effect of the intervention on HDL for both genders at 20 years.
	Intervention/Control:
	• Intervention (n=201): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7, 8, 10, 13, 15, 18, 21, 24, 30, 36, 48, and 60 months; biannually from 2y to 19y
	• Control (ref; n=241): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13, 24, 36, 48, and 60 months; biannually from 7mo to 2y and annually from 2y to 19y
	
	Intervention duration: ~18.5y
	Intervention compliance: 3-day or 4-day food diaries completed by family/child, assessed biannually or annually from 7mo-19y
	• SFA (%E), Group differences (95% CI) from 7mo-19y, Intervention vs Control (ref)
	  • Boys: -2.1 (-2.3, -1.9), P<0.001
	  • Girls: -1.9 (-2.1, -1.7), P<0.001
	
	Outcomes and assessment methods:
	• Assessed ~annually from 7mo to 19y
	• Blood lipids: TC, HDL, LDL, Triglycerides; Non-fasting 7mo-4y, Fasting from 5y-19y
		LDL*, mmol/L
		Mean (SD), Intervention vs Control
		Boys:
		15y: 2.18 (0.54) vs 2.38 (0.68)
		16y: 2.23 (0.52) vs 2.37 (0.66)
		17y: 2.22 (0.52) vs 2.39 (0.64)
		18y: 2.25 (0.50) vs 2.46 (0.70)
		19y: 2.33 (0.56) vs 2.52 (0.73)
		***95% CI of mean difference from 5y-19y*: -0.26, -0.10, P<0.001**
		Girls:
		15y: 2.45 (0.53) vs 2.59 (0.71)
		16y: 2.52 (0.58) vs 2.54 (0.68)
		17y: 2.58 (0.66) vs 2.57 (0.63)
		18y: 2.60 (0.64) vs 2.58 (0.68)
		19y: 2.57 (0.67) vs 2.62 (0.68)
		***95% CI of mean difference from 5y-19y*:** -0.17, -0.01, P=0.037
		
		*Additional analyses using alternative derivation of LDL reported with similar directionality and magnitude of group differences.
		
		Triglycerides, mmol/L
		Mean (SD), Intervention vs Control
		Boys:
		15y: 0.80 (0.48) vs 0.91 (0.48)
		16y: 0.87 (0.44) vs 0.96 (0.42)
		17y: 0.89 (0.39) vs 0.96 (0.49)
		18y: 0.89 (0.35) vs 1.01 (0.48)
		19y: 1.03 (0.74) vs 1.10 (0.46)
		***Mean difference (95% CI) from 5y-19y*: -0.06 (-0.10, -0.03), P=0.001**
		Girls:
		15y: 0.88 (0.40) vs 0.87 (0.53)
		16y: 0.94 (0.40) vs 0.87 (0.38)
		17y: 1.02 (0.46) vs 0.93 (0.39)
		18y: 1.04 (0.48) vs 1.00 (0.41)
		19y: 1.48 (0.28) vs 1.44 (0.30)
		***95% CI of mean difference from 5y-19y*:** -0.02, 0.03, P=0.75
			Model adjustments:
			Age, age*study group if P<0.05
			
			Limitations:
			• Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake, and ample use of vegetables, fruits, berries and whole grain products, and increase fiber
			• Some concern for risk of bias in missing outcome data due to attrition
			• Serious risk of bias in selection of the reported result due to multiple outcome measurements
			
			Funding sources:
			Mannerheim League for Child Welfare; Finnish Cardiovascular Research Foundation; Foundation for Peadiatric Research, Finland; Academy of Finland; Public Health Challenge Research Programme; Juho Vainio Foundation; Yrjo Jahnsson Foundation; Sigrid Juselius Foundation; Turku University Foundation; Special Federal Research Funds for Turku University Hospital; Turku University Hospital Foundation; Finnish Cultural Foundation; Finnish Ministry of Education and Culture

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Lehtovirta, 2018[15] **RCT, STRIP, Finland** Baseline N=554 Analytic N=417 (Attrition from 9y to 19y: 25%) **Participant characteristics at follow-up (19y):** • Age: ~19y • Sex (female): 48% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI ~22 **Fat intake at baseline (19y):** • SFA (%E): Boys: -2.0, 95% CI: -1.7, -2.3; Girls: -1.8, 95% CI: -1.5, -2.1, P<0.0001 (lower in intervention than control group for boys and girls) • MUFA (%E): NS between groups • PUFA (%E): Boys: 0.5, 95% CI: 0.4, 0.6; Girls: 0.6, 95% CI: 0.5, 0.8, P<0.0001 (higher in intervention than control group for boys and girls) **Summary of findings:** *Total cholesterol and LDL cholesterol were significantly lower for all intervention children than control children between 9 years and 19 years. When stratified by gender, there were no significant effect of the intervention on total cholesterol. LDL cholesterol and triglycerides were significantly lower in intervention boys than control boys. This was not significant for girls. No significant effects were found in HDL.*	**Intervention/Control:** • Intervention (n=NR): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day between 7 months and 19 years; Biannually from 2-19y • Control (n=NR): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7, 13 months, biannually from 7mo-7y and annually from 7y-20y Intervention duration: ~19.5y Intervention compliance: Assessed via 4-day food diary completed by child, assessed biannually **Outcomes and assessment methods:** • Assessed at 9, 11, 13, 15, 17, 19y • BP: NR • Fasting blood lipids: TC, HDL, LDL, Trig	***Differences in blood lipid between groups, Pooled analyses across 6 time points (9y n=554, 11y n=553, 13y n=508, 15y n=517, 17y n=457, 19y n=417)*** **TC**, mmol/L, Pooled mean (SD) **All: P=0.01** Boys: 3.64 (0.82), B: -0.114, P=0.07 Girls: 3.93 (0.87), B: -0.123, P=0.09 **HDL**, mmol/L, Pooled mean (SD) All: P=0.75 Boys: 1.32 (0.29), B: 0.018, P=0.46 Girls: P=0.87 **LDL**, mmol/L, Pooled mean (SD) **All: P=0.007** **Boys: 1.24 (0.42), B:-0.069, P=0.04** Girls: 1.37 (0.45), B: -0.071, P=0.08 **Triglycerides**, mmol/L, Pooled mean (SD) All: NR **Boys: 0.77 (0.34), B: -0.086, P<0.001** Girls: 0.84 (0.35), B: 0.011, P=0.69 **SBP**, mmHg, Mean (SD), Intervention vs Control Boys: 126.9 (12.1) vs 129.0 (13.4), P=NR Girls: 116.2 (10.2) vs 115.1 (12.6), P=NR **DBP**, mmHg, Mean (SD), Intervention vs Control Boys: 65.9 (7.8) vs 66.3 (8.2), P=NR Girls: 64.9 (6.3) vs 65.4 (7.7), P=NR	**Model adjustments:** Age, sex **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake, and ample use of vegetables, fruits, berries and whole grain products, and increase fiber • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Academy of Finland, Juho Vainio Foundation, Finnish Cultural Foundation, Finnish Foundation for Cardiovascular Research, Sigrid Juselius Foundation, Yrjo Jahnsson Foundation, Finnish Diabetes Research Foundation, Novo Nordisk Foundation, Strategic Research Funding from the University of Oulu, Finnish Ministry of Education and Culture, Special Governmental Grants for Health Sciences and Research, Turku University Hospital, University of Turku Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Nupponen, 2015[24] **RCT, STRIP, Finland** Baseline N=534 Analytic N=407 (Attrition from 15 to 20y: 24%) **Participant characteristics at follow-up (20y):** • Age: ~20y • Sex (female): 50% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI ~22.8 **Fat intake at follow-up (20y):** NR **Summary of findings:** Children who received a nutrition counseling intervention (1:1:1 ratio of PUFA:MUFA:SFA) from 7 months to 20 years, compared to children who received basic health education at 7 months to 20 years, had a lower risk of high blood pressure at 20y, but no effect was seen on continuous SBP or DBP from 15-20y. Intervention boys had a lower risk of high triglycerides at 20y and lower triglyceride levels from 15-20y compared to control boys. There were no significant effect of the intervention on HDL or triglycerides (in girls).	**Intervention/Control:** • Intervention (n=181): Nutrition counseling (20-45 minutes) aimed at a diet with 30-35% of energy from fat, proportions of PUFA, MUFA, SFA of 1:1:1, and cholesterol intake <200 mg/day at 7mo, 8mo, 10mo, 13mo, 15mo, 18mo, 21mo, 2y, 2.5y, 3y, 4y, and 5y months; biannually from 2y to 20y • Control (ref; n=226): Basic health education of current PUFA/SFA ratio of 0.3-0.4 at 7mo, 13mo, 2y, 3y 4y, and 5y months; biannually from 7mo to 2y and annually from 2y to 20y Intervention duration: ~19.5y Intervention compliance: 3-day or 4-day food diary, assessed biannually or annually from 7mo-19y **Outcomes and assessment methods:** • Assessed annually from 15 to 20y • BP: SBP and DBP; Measured in duplicate • Fasting blood lipids: HDL, Triglycerides • *Cut-offs for dichotomous outcomes set using cohort-based percentiles*	**HDL**, mmol/L, Mean (SD), Intervention vs Control (ref) **20y:** 1.35 (0.34) vs 1.33 (0.32) Group differences from 15-20y: P=0.17 **Low HDL,** RR (95% CI), Intervention vs Control (ref) ≤20th percentile: 0.96 (0.75, 1.23) ≤15th percentile: 0.95 (0.71, 1.27) ≤10th percentile: 0.80 (0.55, 1.16) **Triglycerides**, mmol/L, Mean (SD), Intervention vs Control (ref) **Girls:** **20y:** 1.10 (0.70) vs 1.00 (0.70) Group differences from 15-20y: P=0.19 **Boys:** **20y:** 0.80 (0.60) vs 1.00 (0.60) **Group differences from 15-20y: P=0.019** **High triglycerides**, RR (95% CI), Intervention vs Control (ref) **Girls:** ≥80th percentile: 1.25 (0.95, 1.65) ≥85th percentile: 1.25 (0.91, 1.71) ≥90th percentile: 1.44 (0.97, 2.15) **Boys:** **≥80th percentile: 0.71 (0.54, 0.94)** **≥85th percentile: 0.62 (0.44, 0.86)** ≥90th percentile: 0.67 (0.44, 1.00) **SBP**, mmHg, Mean (SD), Intervention vs Control (ref) **20y:** 121.1 (11.8) vs 121.9 (14.8) Group differences from 15-20y: P=0.47 **DBP**, mmHg, Mean (SD) **20y:** 65.4 (7.6) vs 66.5 (8.3) Group differences from 15-20y: P=0.25 **High SBP and/or DBP,** RR (95% CI), Intervention vs Control (ref) **≥80th percentile: 0.83 (0.70, 0.99)** **≥85th percentile: 0.77 (0.62, 0.95)** ≥90th percentile: 0.79 (0.61, 1.02)	**Model adjustments:** Sex by group interaction (triglycerides only) **Limitations:** • Although intervention primarily focused on types of fats, dietary advice included importance of physical activity, avoidance of passive smoking, and salt intake, and ample use of vegetables, fruits, berries and whole grain products, and increase fiber • Some concern for risk of bias in missing outcome data due to attrition • Serious risk of bias in selection of the reported result due to multiple outcome measurements **Funding sources:** Academy of Finland; Finnish Ministry of Education and Culture; Finnish Cultural Foundation; Finnish Cardiac Research Foundation; Sigrid Juselius Foundation; Yrjo Jahnsson Foundation; Juho Vainio Foundation; Special Governmental Grants for Health Sciences Research, Turku University Hospital; Turku University Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
RCT: Crossover Design			
Ballesteros, 2004[2] **RCT crossover, Mexico** Baseline N=60 Analytic N=54 (Attrition: 10%) **Participant characteristics at baseline:** • Age: Mean~10.4y • Sex (female): 54% • Race/ethnicity: NR • SES: 100% from low SES area of Hermosillo, Mexico • Anthropometry: BMI, Mean~19.6 **Blood lipids and BP at baseline, Mean:** • TC (mmol/L): ~3.5 • LDL (mmol/L): ~1.7 • HDL (mmol/L): ~1.3 • Triglycerides (mmol/L): ~1.2 • SBP (mmHg): ~102 • DBP (mmHg): ~64 **Summary of findings:** *In children, consuming 2 whole eggs (providing 518mg cholesterol, 3g SFA, and 6g MUFA) per day for 30 days lowered DBP (all participants) and increased LDL and HDL cholesterol (only among "hyperresponders") compared to a cholesterol and fat free egg white substitute.*	**Interventions/Comparators:** • Egg: Two whole eggs (110g) per day (518mg cholesterol, 3g SFA, 6g MUFA) • Substitute: 110 g egg white substitute per day (0mg cholesterol, 0g SFA, 0g MUFA) • *All subjects categorized as hyperresponders (increase TC ≥ 0.33 mmol/L) or hyporesponder (increase TC<0.29 mmol/L) in response to the Egg intervention* Intervention duration: 30 days (~4 weeks) Intervention compliance: Egg and substitute served at breakfast in school on weekdays; Parents monitored and interviewed to confirm consumption of egg and substitute on weekends; 98% compliance **Outcomes and assessment methods**: • Assessed at baseline/end of wash out period, after 30d of intervention • Fasting blood lipids: TC, LDL, HDL, triglycerides; Measured in duplicate • BP: SBP and DBP	***Blood lipids and BP post-intervention*** **LDL,** mmol/L, Mean (SD) Hyperresponders, Hyporesponders **Egg: 1.93 (0.36), 1.88 (0.42)** **Substitute (ref): 1.54 (0.38), 1.83 (0.44)** **Egg vs Substitute (ref): P<0.0001** **Responder: P<0.001** **Interaction: P<0.01** **HDL,** mmol/L, Mean (SD) Hyperresponders, Hyporesponders **Egg: 1.35 (0.29), 1.28 (0.19)** **Substitute (ref): 1.23 (0.26), 1.22 (0.19)** **Egg vs Substitute (ref): P<0.001** **Responder: P<0.001** **Interaction: P<0.05** **Triglycerides,** mmol/L, Mean (SD) Egg vs Substitute: p>0.05 **SBP,** mmHg, Mean (SD) Egg vs Substitute: p>0.05 **DBP,** mmHg, Mean (SD) Hyperresponders, Hyporesponders **Egg: 62.3 (3.2), 63.4 (4.5)** **Substitute (ref): 64.7 (4.0), 64.7 (5.2)** **Egg vs Substitute (ref): P<0.05**	**Model adjustments:** None **Limitations:** • No information randomization process • No preregistered statistical analysis plan and analyses without stratification by responder status NR **Funding sources:** American Egg Board; University of Connecticut Research Foundation

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Denke, 2000[5] **RCT crossover, U.S.** Baseline N=56 families, Analytic N=46 families (134 children), (Attrition: 18%) **Participant characteristics at baseline:** • Age: Mean=12y, SD=4 • Sex (female): 47% • Race/ethnicity: ~85% White, ~7% African American, ~4% Hispanic, ~2% Native American, ~2% Asian • SES: NR • Anthropometry: BMI, Mean=19.3, SD=4.3 **Blood lipids at baseline, Mean (SD):** • TC (mg/dL): 152 (25) • LDL (mg/dL): 95 (22) • HDL (mg/dL): 46 (11) • Triglycerides (mg/dL): 74 (41) **Summary of findings:** *In children approximately 12 years of age, providing 25% energy from margarine compared to butter daily for 5 weeks significantly reduced total and LDL cholesterol and had no effect on HDL and triglyceride levels.*	**Interventions/Comparators:** • Butter (ref): 25% energy from butter provided as spread or in specially formulated bakery product • Margarine: 25% energy from margarine provided as spread or in specially formulated bakery products • Expected intake: 21%E from test fat Intervention duration: 5 weeks (Washout: >1mo, 3mo during November-January holidays) Intervention compliance: 3-d diet record during third and fourth weeks of intervention by family; inventories of unconsumed products by study personnel; daily check sheets by family members • 3d diet record: Butter (18%E) vs Margarine period (21%E), P<0.01 • Inventory: Butter (83% of product) vs Margarine (88% of product), P=NR **Outcomes and assessment methods**: • Assessed at baseline and twice during last 2 weeks of each diet period. • Fasting blood lipids: TC, LDL, HDL, triglycerides	***Blood lipids post-intervention*** **TC**, mg/dl, Mean (SD) Butter (ref): 161 (32) Margarine: 150 (25) **Group differences, Mean (95% CI)** **-11.3 (-15.4, -7.2), P<0.001** **LDL**, mg/dl, Mean (SD) Butter (ref): 104 (30) Margarine: 93 (23) **Group differences, Mean (95% CI)** **-11.2 (-14.6, -7.7), P<0.001** **HDL**, mg/dL, Mean (SD) Butter vs Margarine: P=0.80 **Triglycerides**, mg/dL, Mean (SD) Butter vs Margarine: P=0.45	**Model adjustments:** Family membership, age, BMI, ad libitum LDL level, ApoE genotype, change in serum fatty acid CE levels **Limitations:** • The allocation sequence was not random and was not concealed • No information provided on missing data • No preregistered statistical analysis plan **Funding sources:** United Soybean Board; National Association of Margarine Manufacturers; University of Texas Southwestern GCRC grant.

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
Estevez-Gonzalez, 1998[7] **RCT Crossover, Spain** Baseline N=88 Analytic N=88 (Attrition: 0%) **Participant characteristics at baseline:** • Children 3-9y of age without family history of heart disease, metabolic disease, or hyperlipidemia • Age: 3-9y • Sex (female): 45.5% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI z-score, Mean=0.2 **Blood lipids at baseline:** • NR **Summary of findings:** *In children 3-9y of age, intake of a milk preparation with higher proportions of MUFAs and PUFAs, and lower proportions of SFAs and cholesterol than whole milk for 7mo, reduced total and LDL cholesterol and triglycerides compared to intake of whole milk for 7mo.*	**Interventions/Comparators:** • Control: ~500mL whole milk/d; 67% SFA, 30% MUFA, 3% PUFA; Cholesterol 107 mg/L • Intervention: ~500mL milk preparation/d; 15% SFA, 70% MUFA, 15% PUFA ; Cholesterol 22 mg/L • *Total fat in whole milk and milk preparation was equal* Intervention duration: 7 months Intervention compliance: NR **Outcomes and assessment methods**: • Assessed at end of each 7mo-period • Fasting blood lipids: TC, LDL, HDL, triglycerides	**TC,** mmol/L, Mean (SD) **Control: 4.53 (0.90)** **Intervention: 4.2 (0.67)** **p<0.001** **Children with elevated TC had a greater reduction in TC with the intervention compared to children with normal TC.** **LDL,** mmol/L, Mean (SD) **Control: 2.73 (0.73)** **Intervention: 2.47 (0.55)** **p<0.001** **Children with elevated TC had a greater reduction in LDL with the intervention compared to children with normal TC.** **HDL,** mmol/L, Mean (SD) Control: 1.41 (0.33) Intervention: 1.39 (0.28) p=NS **Triglycerides,** mmol/L, Mean (SD) **Control: 0.83 (0.39)** **Intervention: 0.72 (0.24)** **p<0.01**	**Model adjustments:** None **Limitations:** • No information on whether the allocation sequence was random • No preregistered statistical analysis plan **Funding sources:** NR

Study and Population Characteristics	Interventions, Comparators, Outcomes	Results†	Model Adjustments, Limitations
RCT: Cluster Design			
Muros, 2015[18] **RCT Cluster, Spain** Baseline N=162 Analytic N=135 (Attrition: 17%) **Participant characteristics at baseline:** • Age: Mean=10.7y, SD=0.5 • Sex (female): 49.6% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI, Mean=19.7, SD=3.7 **Blood lipids and BP at baseline, Mean (SD):** • TC (mg/dL): 156.7 (24.8) • LDL (mg/dL): 86.9 (20.1) • HDL (mg/dL): 56.0 (12.8) • Triglycerides (mg/dL): 79.1 (25.7) • SBP and DBP: NR **Summary of findings:** *Blood lipids and blood pressure did not differ between children who replaced their typical cooking oil with EVOO for 1mo while participating in a 6mo physical activity and nutritional education intervention and children who just participated in the physical activity and nutritional education intervention.*	**Interventions/Comparators:** • PA+NE+EVOO (n=20): Physical activity and nutritional education intervention with replacement of oil normally consumed with extra-virgin olive oil (EVOO) • PA+NE (n=25): Physical activity and nutritional education intervention • Other groups NA to review: control (n=41), physical activity alone (n=28), nutritional education alone (n=21) Intervention duration: 6 months (1 month of EVOO) Intervention compliance: Compliance to EVOO NR; Compliance to PA and NE assessed via attendance at sessions, <75% attendance excluded. **Outcomes and assessment methods**: • Assessed at baseline (~10.7y) and 6mo follow-up • Fasting blood lipids: TC, LDL, HDL, triglycerides • BP: SBP and DBP; Measured in triplicate	***Change in blood lipids or BP pre- to post-intervention:*** ***PA+NE vs PA+NE+EVOO*** **TC,** mg/dL, Mean (SD) P>0.05 **LDL,** mg/dL, Mean (SD) P>0.05 **HDL,** mg/dL, Mean (SD) P>0.05 **Triglycerides,** mg/dL, Mean (SD) P>0.05 **SBP,** mmHg, Mean (SD) P>0.05 **DBP,** mmHg, Mean (SD) P>0.05 ***BP at post-intervention:*** ***PA+NE vs PA+NE+EVOO*** **DBP,** mmHg, Mean difference (95% CI) P>0.05	**Model adjustments:** Baseline blood lipid level or blood pressure **Limitations:** • No information on randomization process • No information on timing of subject identification and recruitment relative to timing of randomization • No preregistered statistical analysis plan **Funding sources:** Mapfre Foundation; Direccion General de Investigacion and Gestion del Plan Ncional I+D+I; Consejeria de Innovacion de la Junta de Andalucia

* Abbreviations: BP – blood pressure, CI – confidence interval, DBP – diastolic blood pressure, F/U – follow-up, HDL – HDL cholesterol, kcal – kilocalorie(s), LDL – LDL cholesterol, NR – not reported, %E – percent energy, RCT – randomized controlled trial, ref – reference group, SBP – systolic blood pressure, SD – standard deviation, SES – socioeconomic status, TC – total cholesterol

† Statistically significant results bolded.

Table 2. Evidence from prospective cohort studies examining types of dietary fat consumed during childhood and cardiovascular disease intermediate and endpoint outcomes*

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Cowin, 2001[4] **PCS, ALSPAC, U.K.** Baseline N=1183, Analytic N=389 (Attrition: 67%) **Participant characteristics at baseline:** • Age: ~18mo • Sex (female): ~45% • Race/ethnicity: 100% Caucasian • SES: NR • Anthropometry: NR **Fat intake at baseline:** NR **Blood lipids baseline:** NR **Summary of findings:** *Associations between type and source of fat intake at 18mo and blood lipid levels at 31mo differed between boys and girls. Among boys, higher SFA intake was associated with higher TC, mean intake of PUFA was higher in those in the lowest quintile of TC compared to those in the highest quintile of TC, any consumption of butter was associated with higher TC, and weighed intake of non-polyunsaturated margarine was positively associated with TC. Among girls, higher PUFA intake was associated with higher HDL and weighed non-polyunsaturated margarine intake was associated with higher HDL. All other tested associations were not statistically significant.*	**Exposures:** • SFA (continuous; units NR) • PUFA (continuous; units NR) • MUFA (continuous; units NR) • PUFA:SFA ratio (continuous; units NR) • Cholesterol (continuous; units NR) • Butter (continuous and categorical [yes/no]; units NR) • Non-polyunsaturated margarine (continuous and categorical [yes/no]; units NR) • Polyunsaturated margarine (continuous and categorical [yes/no]; units NR) Assessment method and timing: • 3-day unweighted diet record followed by an interview with trained study personnel • Assessed at baseline (18mo) **Outcomes and assessment methods**: • Assessed at 31mo • Non-fasting blood lipids: TC, LDL, HDL	**TC**, Beta (SE) Boys (n=210)| **SFA: 0.0334 (0.010), P=0.001** MUFA, PUFA, Cholesterol: P>0.05 Girls (n=175) SFA, MUFA, PUFA, Cholesterol: P>0.05 **HDL**, Beta (SE) Boys (n=NR) SFA, MUFA, PUFA, Cholesterol: P>0.05 Girls (n=133) SFA: 0.0076 (0.004), P=0.080 **PUFA: 0.113 (0.056), P=0.045** MUFA, Cholesterol: P>0.05 ***FA intake between lowest 20% (ref) vs highest 20% TC levels*** **SFA**, g, Means, Difference (95% CI) **Boys: 21.1 vs 23.9, 2.8 (1.2, 4.5), P=0.001**; Girls: P>0.05 **MUFA**, g, Means, Difference (95% CI) Boys: P>0.05; Girls: P>0.05 **PUFA**, g, Geometric means **Boys: 5.66 vs 4.77, P=0.01;** Girls: P>0.05 **Cholesterol**, mg, Geometric means Boys: P>0.05; Girls: P>0.05 ***Correlation between blood lipids and FA intake (energy adjusted)*** **TC,** Correlation coefficient Boys (n=214): **PUFA:SFA ratio: 0.174, P=0.011** Girls (n=175): PUFA:SFA ratio: P>0.05 **LDL,** Correlation coefficient Boys (n=137) **SFA: 0.174, P=0.042** **PUFA:SFA ratio: 0.172, P=0.045** MUFA, PUFA, Cholesterol: P>0.05 Girls (n=109) All: P>0.05	**Key confounders NOT accounted for:** SES, family history of CVD or diabetes, physical activity **Key confounders accounted for:** Sex, age, TEI, race/ethnicity **Additional model adjustments:** Energy and the energy-adjusted intakes of SFA, MUFA, PUFA, cholesterol, starch, sugar, and vitamin C (backward regression models only), height (backward regression models in boys only) **Limitations:** • Did not account for all key confounders • Three day unweighted diet record not validated and method to assess exposures were not all clearly described • No preregistered statistical analysis plan and concern for selective reporting **Funding sources:** Northern and Yorkshire Regional Health Authority NHS Research and Development Programme on Cardiovascular Disease and Stroke.

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Cowin, 2001 (CONTINUED) **PCS, ALSPAC, U.K.** Baseline N=1183, Analytic N=389 (Attrition: 67%) **Participant characteristics at baseline:** • Age: ~18mo • Sex (female): ~45% • Race/ethnicity: 100% Caucasian • SES: NR • Anthropometry: NR **Fat intake at baseline:** NR **Blood lipids baseline:** NR **Summary of findings:** *Associations between type and source of fat intake at 18mo and blood lipid levels at 31mo differed between boys and girls. Among boys, higher SFA intake was associated with higher TC, mean intake of PUFA was higher in those in the lowest quintile of TC compared to those in the highest quintile of TC, any consumption of butter was associated with higher TC, and weighed intake of non-polyunsaturated margarine was positively associated with TC. Among girls, higher PUFA intake was associated with higher HDL and weighed non-polyunsaturated margarine intake was associated with higher HDL. All other tested associations were not statistically significant.*	**Exposures:** • SFA (continuous; units NR) • PUFA (continuous; units NR) • MUFA (continuous; units NR) • PUFA:SFA ratio (continuous; units NR) • Cholesterol (continuous; units NR) • Butter (continuous; units; NR) • Non-polyunsaturated margarine and polyunsaturated margarine (continuous; units NR) Assessment method and timing: • 3-day unweighted diet record followed by an interview with trained study personnel • Assessed at baseline (18mo) **Outcomes and assessment methods**: • Assessed at 31mo • Non-fasting blood lipids: TC, LDL, HDL	**Blood lipids by food consumption (yes vs no)** **HDL,** Correlation coefficient Boys (n=164): PUFA:SFA ratio: P>0.05 Girls (n=133): PUFA:SFA ratio: P>0.05 **TC**, mmol/L, Mean (SD) Girls and Boys: Butter, non-polyunsaturated margarine, polyunsaturated margarine: P>0.05 **HDL**, mmol/L, Mean (SD) Boys: **Butter: Yes (n=34), 0.91 (0.26) vs No (n=130), 0.83 (0.19), P=0.047** Non-polyunsaturated margarine, polyunsaturated margarine: P>0.05 Girls: Butter, non-polyunsaturated margarine, polyunsaturated margarine: P>0.05 **Correlations between blood lipids and foods consumption (weight)** **TC**, Correlation coefficient Boys **Non-polyunsaturated margarine: 0.219, P=0.047** Butter, polyunsaturated margarine: P>0.05 Girls Butter, polyunsaturated margarine, non-polyunsaturated margarine: P>0.05 **HDL**, Correlation coefficient Boys Butter, polyunsaturated margarine, non-polyunsaturated margarine: P>0.05 Girls **Non-polyunsaturated margarine: 0.368, P=0.021** Butter, polyunsaturated margarine: P>0.05	**Key confounders NOT accounted for:** SES, family history of CVD or diabetes, physical activity **Key confounders accounted for:** Sex, age, TEI, race/ethnicity **Additional model adjustments:** Energy and the energy-adjusted intakes of SFA, MUFA, PUFA, cholesterol, starch, sugar, and vitamin C (backward regression models only), height (backward regression models in boys only) **Limitations:** • Did not account for all key confounders • Three day unweighted diet record not validated and method to assess exposures were not all clearly described • No preregistered statistical analysis plan and concern for selective reporting **Funding sources:** Northern and Yorkshire Regional Health Authority NHS Research and Development Programme on Cardiovascular Disease and Stroke.

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Twisk, 1996[34] **PCS, Amsterdam Growth and Health Study, Netherlands** Baseline N=307 Analytic N=181 (Attrition: 41%) **Participant characteristics at baseline:** • Age: Mean=13.1y, SD=0.8 • Sex (female): 54% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at baseline, Mean (SD):** • SFA: Males, 16.6 (2.7) % of energy; Females, 15.5 (2.2) % of energy • PUFA: Males, 6.1 (2.0) % of energy; Females, 5.9 (2.5) % of energy • Cholesterol: Males, 29.4 (7.5) mg/MJ; Females, 30.2 (6.7) mg/MJ **Blood lipids at baseline:** • NR **Summary of findings:** *During adolescence and early adulthood, consumption of PUFA and a higher PUFA:SFA ratio was associated with lower total cholesterol whereas consumption of SFA and cholesterol was associated with higher total cholesterol. No type of fat was associated with HDL cholesterol.*	**Exposures:** • PUFA:SFA ratio (continuous) • SFA (continuous; % energy) • PUFA (continuous; % energy) • Cholesterol (continuous; mg/MJ) Assessment method and timing: • Cross-check dietary history interview assessing usual food consumption during past month, administered by a dietitian • Assessed at baseline (13y), 14y, 15y, 16y, 21y, and 27y of age **Outcomes and assessment methods**: • Assessed at baseline (13y), 14y, 15y, 16y, 21y, and 27y of age • Non-fasting blood lipids: TC, HDL	**PUFA:SFA ratio** **TC,** Beta (95% CI) **-0.07 (-0.12, -0.03), p=0.001** **HDL,** Beta (95% CI) Data NR, p=NS **SFAs** **TC,** Beta (95% CI) **0.05 (0.00, 0.10), p=0.04** **HDL,** Beta (95% CI) Data NR, p=NS **PUFAs** **TC,** Beta (95% CI) **-0.06 (-0.09, -0.02), p<0.01** **HDL,** Beta (95% CI) Data NR, p=NS **Cholesterol** **TC,** Beta (95% CI) **0.08 (0.03, 0.12), p=0.002** **HDL,** Beta (95% CI) Data NR, p=NS	**Key confounders NOT accounted for:** Race/ethnicity, SES, TEI, physical activity, family history of CVD or diabetes. **Key confounders accounted for:** Sex, age, TEI. **Additional model adjustments:** Time, body fatness, lean body mass, cardiopulmonary fitness **Limitations:** • Not all key confounders accounted for • Dietary history interview was not validated • 41% attrition without sufficient information on whether responders differed from nonresponders • No preregistered statistical analysis plan **Funding sources:** Dutch Heart Foundation; Dutch Prevention Fund; Dutch Ministry of Well Being and Public Health; Dairy Foundation on Nutrition and Health

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Post, 1997[26] **PCS, Amsterdam Growth and Health Study, Netherlands** Baseline N=307 Analytic N=182 (Attrition: 41%) **Participant characteristics at baseline:** • Age: ~13y • Sex (female): 54% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at baseline:** • NR **Blood lipids and BP at baseline:** • NR **Summary of findings:** *During adolescence and early adulthood, consumption of SFA was associated with higher total and HDL cholesterol, and lower DBP, consumption of PUFA was associated with lower total cholesterol, and consumption of cholesterol was associated with higher total cholesterol. All other diet-outcome associations were non-significant.*	**Exposures:** • SFAs (continuous; % energy) • PUFAs (continuous; % energy) • Cholesterol (continuous; mg/MJ) Assessment method and timing: • Cross-check dietary history interview assessing usual food consumption during past month, administered by a dietitian • Assessed at baseline (13y), 14y, 15y, 16y, 21y, and 27y of age **Outcomes and assessment methods**: • Assessed at baseline (13y), 14y, 15y, 16y, 21y, and 27y of age • BP: SBP, DBP • Non-fasting blood lipids: TC, HDL	**SFAs** **SBP,** Beta (95% CI)* Data NR, p=NS **DBP,** Beta (95% CI)* **-0.067 (-0.13, 0.00), p=0.049** **TC,** Beta (95% CI)** **0.60 (0.00, 0.12), p=0.03** **HDL,** Beta (95% CI)** **0.072 (0.02, 0.13), p=0.014** **PUFAs** **SBP,** Beta (95% CI)* Data NR, p=NS **DBP,** Beta (95% CI)* Data NR, p=NS **TC,** Beta (95% CI)** **-0.049 (-0.10, 0.00), p=0.042** **HDL,** Beta (95% CI)** Data NR, p=NS **Cholesterol** **SBP,** Beta (95% CI)* Data NR, p=NS **DBP,** Beta (95% CI)* Data NR, p=NS **TC,** Beta (95% CI)** **0.061 (0.01, 0.12), p=0.033** **HDL,** Beta (95% CI)** Data NR, p=NS *Results from univariate analyses (multivariate analyses not conducted) **Results from multivariate analyses	**Key confounders NOT accounted for:** Race/ethnicity, SES, physical activity, family history of CVD or diabetes. **Key confounders accounted for:** Sex, age, TEI. **Additional model adjustments:** Time, animal protein intake, SFA, PUFA, and cholesterol intake (multivariate analyses only). **Limitations:** • Not all key confounders accounted for • Dietary history interview was not validated • 41% attrition without sufficient information on whether responders differed from nonresponders • No preregistered statistical analysis plan **Funding sources:** NR

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

Ness, 2005[19]
PCS, Boyd Orr, U.K.
Baseline N=4,999 Analytic N=4,028 (Attrition: 19%)
 	
Participant characteristics at baseline:
• Age: Mean=7.5y, SD=4.8 (IQR: 3.5-11.2)
• Sex (female): 50.5%
• Race/ethnicity: NR
• SES: Father's social class: I 1.5%, II 7.2%, III 19.6%, IV 23.0%, V 14.3%, Unemployed 26.2%, Unclassifiable 8.2%; Townsend score (sum of standardized scores for levels of car ownership, house ownership, overcrowding, unemployment; negative values indicate less deprivation): -1.6 (range: -2.8 to 0.9)
• Anthropometry: NR
 	
Fat intake at baseline:
• See "Exposures" in next column.
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
Consumption of SFAs during childhood was not associated with CHD or stroke mortality after ~60y of follow-up.
	Exposures:
	• SFAs (quartiles), Mean (SD; range)
	  • Q1 (ref): 19.6 g/d (3.2; 8.8-24.0)
	  • Q2: 27.6 g/d (2.3; 24.0-31.4)
	  • Q3: 35.5 g/d (2.6; 31.4-40.4)
	  • Q4: 52.0 g/d (10.8; 40.6-108.9)
	
	Assessment method and timing:
	• Per capita intake calculated from seven-day weighed household inventory divided by number of household members and taking into account meals missed by family members and meals consumed by visitors
	• Assessed at baseline (1937-1939)
	
	Outcomes and assessment methods:
	• Assessed during ~60y of follow-up
	• CHD mortality and Stroke mortality: Determined from death certificate
		SFAs
		CHD mortality, Rate ratio (95% CI)
		Q1 (ref)
		Q2: 0.81 (0.54, 1.21)
		Q3: 0.68 (0.43, 1.08)
		Q4: 0.70 (0.39, 1.26)
		p-trend: 0.20
		Stroke mortality, Rate ratio (95% CI)
		Q1 (ref)
		Q2: 1.37 (0.74, 2.51)
		Q3: 0.71 (0.32, 1.58)
		Q4: 1.31 (0.49, 3.47)
		p-trend: 0.90
			Key confounders NOT accounted for:
			Race/ethnicity, physical activity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (father's social class, Townsend score), TEI.
			
			Additional model adjustments:
			Childhood family food expenditure, district of residence as child, period of birth, season when studied as child.
			
			Limitations:
			• Did not account for all key confounders
			• Start of exposure and follow-up did not coincide
			• SFA measured indirectly using 7d weighed household inventory divided by total number of household members irrespective of age or sex
			• 19% attrition without information on those lost to follow-up
			• No preregistered statistical analysis plan
			
			Funding sources:
			World Cancer Research Fund, Medical Research Council, British Heart Foundation

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Nicklas, 2002[20] **PCS, CATCH, U.S.** Baseline N=3,218 Analytic N=1,182 (Attrition: 63%) **Participant characteristics at baseline:** • Age: Mean~8.7y • Sex (female): 52% • Race/ethnicity: 71% White, 15% Hispanic-American, 10% African-American, 25 Asian, 2% other • SES: NR • Anthropometry: Weight, Mean~31.3 kg; Height, Mean~1.32 m **Fat intake at baseline, Mean**: • SFA (g): ~29g • MUFA (g): ~27g • PUFA (g): ~13g • Cholesterol (mg): ~221mg **Blood lipids at baseline, Mean:** • TC (mmol/L): ~77 • **HDL (mmol/L): ~23** **Summary of findings:** *Saturated fat and unsaturated fat intake was associated with increased serum TC in children 8 to 10 years of age. Dietary cholesterol intake was not significantly associated with serum TC.*	**Exposures:** • SFA (continuous; g) • MUFA (continuous; g) • PUFA (continuous; g) • Unsaturated FA (continuous; PUFA+MUFA; g) • Cholesterol (continuous; mg) Diet assessment method and timing: • Validated, food record-assisted 24-hour recalls • Assessed at baseline (~8.7y) and 2y follow-up (~11y) **Outcomes and assessment methods**: • Assessed at baseline (~8.7y) and 2y follow-up (~11y) • Non-fasting blood lipids: TC, HDL; absolute value assessed at baseline (~8.7y) and follow-up (~11y)	**Replacement of other types of fat with SFA** **TC,** mmol/L, Beta (SE) **0.004 (0.002), P<0.04** **HDL,** mmol/L, Beta (SE) Data NR, P>0.05 **Replacement of other types of fat with MUFA** **TC,** mmol/L, Beta (SE) P>0.05 **HDL,** mmol/L, Beta (SE) Data NR, P>0.05 **Replacement of other types of fat with PUFA** **TC,** mmol/L, Beta (SE) P>0.05 **HDL,** mmol/L, Beta (SE) Data NR, P>0.05 **Replacement of other types of fat with Unsaturated FA** **TC,** mmol/L, Beta (SE) **0.004 (0.002), P<0.03** **HDL,** mmol/L, Beta (SE) Data NR, P>0.05 **Cholesterol** **TC,** mmol/L, Beta (SE) Data NR, P>0.05 **HDL,** mmol/L, Beta (SE) Data NR, P>0.05	**Key confounders NOT accounted for:** SES, physical activity, family history of CVD or diabetes. **Key confounders accounted for:** Sex, age, race/ethnicity, TEI. **Additional model adjustments:** Height, weight, CATCH site, intervention group, semester, and school. **Limitations:** • Did not account for all key confounders • 63% attrition with no information on whether non-responders differed from responders • No preregistered statistical analysis plan **Funding sources:** NHLBI

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

Magnussen, 2011[16]
PCS, Childhood Determinants of Adult Health Study, Australia
Baseline N=2,809 Analytic N (including 9y olds)=539 (Attrition: 81%); Analytic N (excluding 9y olds)=302
 	
Participant characteristics at baseline:
• Age: Mean 11.9y, SD=2.5 (Note: Only 12y, 15y old children with dietary data)
• Sex (female): 50%
• Race/ethnicity: NR
• SES: Parental educational level: 40% School only, 29% Trade/vocational certificate, 31% University
• Anthropometry: BMI, Mean~18.5
 	
Fat intake at baseline:
• SFAs (%E): ~16%
 	
Blood lipids at baseline:
• TC (mg/dL): Mean~174
• LDL (mg/dL): Mean~105
• HDL (mg/dL): Mean~56
• Triglycerides (mg/dL): Median~58
 	
Summary of findings:
Change in saturated fat intake between approximately 12/15y and 32/35y of age was not associated with blood lipid risk categories from youth to adulthood.
	Exposures:
	• Change in SFA intake (continuous; age- and sex-specific z-score)
	
	Diet assessment method and timing:
	• 24hr record of food consumption; completed at baseline (12y and 15y of age)
	• Sum of 3 FFQ questions related to fat intake (type of milk usually consumed, frequency of trimming fat from meat, and type of spread usually used on bread); completed at 20y follow-up
	
	Outcomes and assessment methods:
	• Assessed at baseline (12y, 15y of age) and 20y follow-up
	• Fasting blood lipids: TC, LDL, HDL, triglycerides
	• Categorized based on pediatric and adult high-risk cut points:
	  • True-positive (TP): high-risk levels in youth and adulthood
	  • False-positive (FP): high-risk levels in youth, normal-risk levels in adulthood
	  • False-negative (FN): normal-risk levels in youth, high-risk levels in adulthood
	  • True-negative (TN): normal-risk levels in youth and adulthood
		Change in SFA intake z-score by blood lipid risk category
		
		TC
		No differences between any risk categories (TP, FP, FN, TN): All P>0.05
		LDL
		No differences between any risk categories (TP, FP, FN, TN): All P>0.05
		HDL
		No differences between any risk categories (TP, FP, FN, TN): All P>0.05
		Triglycerides
		No differences between any risk categories (TP, FP, FN, TN): All P>0.05
			Key confounders NOT accounted for:
			Race/ethnicity, SES, TEI, physical activity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age
			
			Additional model adjustments:
			None
			
			Limitations:
			• Did not account for all key confounders
			• SFA intake assessment method validity and reliability unknown
			• Analysis unlikely to have removed risk of bias arising from missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			Commonwealth Departments of Sport, Recreation and Tourism, and Health; the National Heart Foundation; Common-wealth Schools Commission; National Health and Medical Research Council; the Heart Foundation, the Tasmanian Com- munity Fund; Veolia Environmental Services; Sanitarium; ASICS; Target.

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Simons-Morton, 1997[32] **PCS, DISC, U.S.** Baseline N=663 Analytic N=583 (Attrition: 12%) **Participant characteristics at baseline:** • Children with LDL cholesterol values at the 80th – 98th percentile for age and sex who participated in RCT to assess effect of changing FA intake on CVD risk • Age: Mean=9.6y, SD=0.72 • Sex (female): 46% • Race/ethnicity: White ~86.5%, Black ~8.5%, Other ~5.0% • SES: NR • Anthropometry: Height, Mean=136.4 cm, SD=6.9; Weight, Mean=32.9 kg, SD=6.8 **Fat intake at baseline, Mean (SD):** • SFA: 24.9 g (8.6 g); 12.9%E (2.7%E) • MUFA: 24.9 g (8.3 g); 12.9%E (2.4%E) • PUFA: 11.4 g (4.0 g), 5.9%E (1.6% E) • Cholesterol: 201.8 mg (101.7 mg) **BP at baseline, Mean:** • SBP (mmHg): ~97.4 • DBP (mmHg): ~61.9 • No statistically significant differences between intervention and control groups at baseline **Summary of findings:** *In children with elevated LDL cholesterol participating in an RCT to assess the effect of changing FA intake on CVD risk, intake of SFA, MUFA, PUFA, and cholesterol intake were not associated with blood pressure except for a statistically significant relationship between higher MUFA intake and higher DBP.*	**Exposures:** • SFAs (continuous; g) • PUFAs (continuous; g) • MUFAs (continuous; g) • Cholesterol (continuous; mg) Assessment method and timing: • Three, non-consecutive 24-hr recalls conducted by trained dietitians at each time point • Assessed at baseline (~9.6y), 1y, and 3y follow-ups **Outcomes and assessment methods**: • Assessed at baseline (~9.6y), 1y, and 3y follow-ups • BP: SBP, DBP; Measured in duplicate	**SFAs** **SBP,** mmHg, Beta 0.065, p>0.05 **DBP,** mmHg, Beta -0.049, p>0.05 **MUFAs** **SBP,** mmHg, Beta 0.021, p>0.05 **DBP,** mmHg, Beta **0.13, p<0.05** **PUFAs** **SBP,** mmHg, Beta 0.027, p>0.05 **DBP,** mmHg, Beta 0.040, p>0.05 **Cholesterol** **SBP,** mmHg, Beta -0.0033, p>0.05 **DBP,** mmHg, Beta -0.0025, p>0.05	**Key confounders NOT accounted for:** Race/ethnicity, SES, physical activity, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, TEI **Additional model adjustments:** Height, weight, other macro- and micronutrients **Limitations:** • Not all key confounders accounted for • Intervention group was not controlled for in analyses • No preregistered statistical analysis plan **Funding sources:** NHLBI

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

van den Hooven, 2013[35]
PCS, Generation R, Netherlands
Baseline N=5,088 Analytic N=2,812 (Attrition: 45%)
 	
Participant characteristics at baseline:
• Age: Mean=14mo, SD=2mo
• Sex (female): 51.9%
• Race/ethnicity: Dutch ethnic background, 68.8%
• SES: Maternal educational level, Primary education 4.4%, Secondary 35.1%, Higher education 57.3%
• Anthropometry: Maternal BMI, Median=22.5, 95% range:18.3, 34.6
 	
Fat intake at baseline:
• See "Exposures" in next column.
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
Consumption of SFAs, MUFAs, or PUFAs at ~14mo of age were not associated with blood pressure at 6y of age.
	Exposures:
	• SFAs (tertiles)
	  • <13.3 g/d (ref)
	  • 13.3-16.5 g/d
	  • >16.5 g/d
	• MUFAs (tertiles)
	  • <11.5 g/d (ref)
	  • 11.5-14.6 g/d
	  • >14.6 g/d
	• PUFAs (tertiles)
	  • <7.0 g/d (ref)
	  • 7.0-8.6 g/d
	  • >8.6 g/d
	
	Diet assessment method and timing:
	• Self-administered, validated 211-item FFQ completed by parents/caregivers
	• Assessed at baseline (14 mo)
	
	Outcomes and assessment methods:
	• Assessed at 5.9y of age (Median, 95% range: 5.5, 6.6)
	• BP: SBP, DBP; Measured in quadruplicate
		SFAs
		SBP, mmHg, Beta (95% CI)
		<13.3 g/d (ref)
		13.3-16.5 g/d: 0.05 (-0.63, 0.72)
		>16.5 g/d: 0.29 (-0.39, 0.96)
		p-trend: 0.26
		DBP, mmHg, Beta (95% CI)
		<13.3 g/d (ref)
		13.3-16.5 g/d: 0.33 (-0.24, 0.89)
		>16.5 g/d: 0.10 (-0.47, 0.67)
		p-trend: 0.27
		
		MUFAs
		SBP, mmHg, Beta (95% CI)
		<11.5 g/d (ref)
		11.5-14.6 g/d: 0.27 (-0.41, 0.94)
		>14.6 g/d: 0.65 (-0.02, 1.33)
		p-trend: 0.15
		DBP, mmHg, Beta (95% CI)
		<11.5 g/d (ref)
		11.5-14.6 g/d: 0.40 (-0.18, 0.96)
		>14.6 g/d: 0.39 (-0.17, 0.96)
		p-trend: 0.20
		
		PUFAs
		SBP, mmHg, Beta (95% CI)
		<7.0 g/d (ref)
		7.0-8.6 g/d: 0.39 (-0.28, 1.06)
		>8.6 g/d: 0.26 (-0.41, 0.93)
		p-trend: 0.14
		DBP, mmHg, Beta (95% CI)
		<7.0 g/d (ref)
		7.0-8.6 g/d: 0.14 (-0.42, 0.70)
		>8.6 g/d: 0.10 (-0.46, 0.66)
		p-trend: 0.24
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (maternal education), TEI, physical activity.
			
			Additional model adjustments:
			Smoking during pregnancy, birth weight, current child BMI
			
			Limitations:
			• Not all key confounders accounted for
			• 45% attrition without information on whether non-responders differed from responders
			• No preregistered statistical analysis plan
			
			Funding sources:
			Erasmus Medical Center, Rotterdam; Erasmus University, Rotterdam; Dutch Ministry of Health, Welfare, and Sport; Netherlands Organization for Health Research and Development

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

Stroobant, 2017[33]
PCS, Generation R, Netherlands
Baseline N=5,088 Analytic N=2,967 (Attrition: 42%)
 	
Participant characteristics at baseline:
• Age: Median=12.9mo, 95% range: 12.2, 18.9
• Sex (female): 51.3%
• Race/ethnicity: Dutch ethnic background, 68.8%
• SES: Maternal educational level, None or primary education 5.5%, Middle school or <4y high school 36.0%, Higher education 58.6%; Monthly household income, <€1400 13.9%, €1400-2200 19.4%, >€2200 66.6%
• Anthropometry: Maternal BMI, Median=23.5, 95% range:18.8, 35.3
 	
Fat intake at baseline, Mean (SD):
• SFA: 11.5% (3.6%) of energy
• MUFA: 9.8% (3.1%) of energy
• PUFA: 5.5% (1.5%) of energy
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
Consumption of SFA, MUFA, or PUFA at the expense of CHO or protein, or consumption of MUFA or PUFA at the expense of SFA at ~13mo of age was not associated with blood pressure, and non-fasting total, LDL, or HDL cholesterol, or triglycerides at 6y of age.
	Exposures:
	• SFAs (continuous; per 5% energy)
	  • Replacement of CHO
	  • Replacement of protein
	• MUFAs (continuous; per 5% energy)
	  • Replacement of CHO
	  • Replacement of SFA
	  • Replacement of protein
	• PUFAs (continuous; per 5% energy)
	  • Replacement of CHO
	  • Replacement of SFA
	  • Replacement of protein
	
	Diet assessment method and timing:
	• Self-administered, validated 211-item FFQ completed by parents/caregivers
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed at 6.0y of age (Median, 95% range: 5.7, 6.6)
	• BP: SBP, DBP; Measured in quadruplicate; Converted to age and sex adjusted SD scores
	• Non-fasting blood lipids: TC, LDL, HDL, Triglycerides; Converted to age and sex adjusted SD scores
		SFAs replacing CHO
		SBP, SD score, Beta (95% CI)
		CHO: 0.074 (-0.065, 0.214)
		DBP, SD score, Beta (95% CI)
		CHO: 0.073 (-0.063, 0.209)
		HDL, SD score, Beta (95% CI)
		CHO: 0.043 (-0.119, 0.205)
		Triglycerides, SD score, Beta (95% CI)
		CHO: -0.073 (-0.236, 0.089)
		TC & LDL: NS, Data NR
		MUFAs replacing CHO or SFA
		SBP, SD score, Beta (95% CI)
		CHO: -0.065 (-0.241, 0.110)
		SFA: -0.139 (-0.443, 0.164)
		DBP, SD score, Beta (95% CI)
		CHO: -0.132 (-0.303, 0.039)
		SFA: -0.205 (-0.501, 0.091)
		HDL, SD score, Beta (95% CI)
		CHO: -0.010 (-0.217, 0.197)
		SFA: -0.053 (-0.408, 0.302)
		Triglycerides, SD score, Beta (95% CI)
		CHO: 0.028 (-0.179, 0.235)
		SFA: 0.102 (-0.253, 0.457)
		TC & LDL: NS, Data NR
		PUFAs replacing CHO or SFA
		SBP, SD score, Beta (95% CI)
		CHO: 0.109 (-0.053, 0.272)
		SFA: 0.035 (-0.124, 0.194)
		DBP, SD score, Beta (95% CI)
		CHO: 0.121 (-0.037, 0.272)
		SFA: 0.048 (-0.107, 0.203)
		HDL, SD score, Beta (95% CI)
		CHO: 0.053 (-0.138, 0.245)
		SFA: 0.010 (-0.178, 0.197)
		Triglycerides, SD score, Beta (95% CI)
		CHO: -0.038 (-0.230, 0.154)
		SFA: 0.035 (-0.152, 0.223)
		TC & LDL: NS, Data NR
		Replacement of protein with SFA, MUFA, or PUFA
		No associations between type of fat and blood lipids or BP (Data NR)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (maternal education, household income), TEI, physical activity (screen time, playing sports).
			
			Additional model adjustments:
			Energy from protein, energy from all types of fat (substitution of CHO), energy from CHO and all types of fat except SFA (substation of SFA), parity, prenatal alcohol intake, prenatal smoking, maternal BMI, maternal age, breastfeeding, birth weight.
			
			Limitations:
			• Not all key confounders accounted for
			• 42% attrition without information on whether non-responders differed from responders
			• No preregistered statistical analysis plan
			
			Funding sources:
			Erasmus Medical Center, Rotterdam; Erasmus University, Rotterdam; Dutch Ministry of Health, Welfare, and Sport; Netherlands Organization for Health Research and Development

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

Harris, 2017[9]
PCS, GINIplus and LISAplus, Germany
Baseline N=5,078 Analytic N=1,398 (Attrition: 72%)
 	
Participant characteristics at baseline:
• Age: Median=10.2y (IQR: 10.1, 10.3)
• Sex (female): 49%
• Race/ethnicity: NR
• SES: Parental education (high), 71.3%
• Anthropometry: BMI, Median=16.7 (IQR: 15.6, 18.4)
Fat intake at baseline, Median (IQR):
• SFA (%E): 12.6 (10.9, 14.7)
• MUFA (%E): 10.7 (9.3, 12.3)
• N-3 PUFA (%E): 0.54 (0.49, 0.62)
• N-6 PUFA (%E): 3.7 (3.2, 4.3)
Blood lipids, BP at baseline, Median (IQR):
• LDL (mmol/L): 2.1 (1.7, 2.5)
• HDL (mmol/L): 1.2 (1.1, 1.4)
• Triglycerides (mmol/L): 1.2 (0.9, 1.6)
Summary of findings:
Higher intake of SFA at 10y of age was associated with decreases in triglycerides from 10y to 15y of age, but was not associated with change in LDL or HDL cholesterol. Consumption of MUFA, N-3 PUFA, and N-6 PUFA at 10y were not associated with change in LDL and HDL cholesterol or triglycerides. Replacement of SFA consumption with either MUFA, N-3 PUFA, N-6 PUFA, or carbohydrate consumption was not associated with change in blood lipids except for two sex-stratified analyses: replacement of SFA consumption with carbohydrate consumption in females was associated with higher LDL cholesterol and triglycerides.
	Exposures:
	• SFA (continuous; per IQR increase in %E)
	• MUFA (continuous; per IQR increase in %E)
	• N-3 PUFA (continuous; per IQR increase in %E)
	• N-6 PUFA (continuous; per IQR increase in %E)
	• Replacement of SFA (continuous; per IQR increase in %E from substituting FA or CHO):
	  • MUFA
	  • N-3 PUFA
	  • N-6 PUFA
	  • CHO
	
	Assessment method and timing:
	• Self-administered, validated 80-item FFQ
	• Assessed at baseline (10y)
	
	Outcomes and assessment methods:
	• Assessed at baseline (10y) and 15y of age
	• Blood lipids: TC, LDL, HDL, triglycerides (17% fasted at 10y, 46.4% fasted at 15y)
		Change in blood lipids from 10y-15y
		
		SFAs
		LDL, mmol/L, Beta (95% CI)
		-0.36 (-0.075, 0.003), p=0.068
		HDL, mmol/L, Beta (95% CI)
		0.005 (-0.017, 0.027), p=0.638
		Triglycerides, mmol/L, Beta (95% CI)
		-0.38 (-0.75, -0.001), p=0.042
		
		MUFAs
		LDL, mmol/L, Beta (95% CI)
		-0.011 (-0.048, 0.025), p=0.534
		HDL, mmol/L, Beta (95% CI)
		0.011 (-0.009, 0.031), p=0.297
		Triglycerides, mmol/L, Beta (95% CI)
		-0.012 (-0.046, 0.023), p=0.503
		
		N-3 PUFAs
		LDL, mmol/L, Beta (95% CI)
		-0.027 (-0.057, 0.003), p=0.082
		HDL, mmol/L, Beta (95% CI)
		0.005 (-0.012, 0.022), p=0.540
		Triglycerides, mmol/L, Beta (95% CI)
		0.000 (-0.028, 0.029), p=0.981
		
		N-6 PUFAs
		LDL, mmol/L, Beta (95% CI)
		-0.003 (-0.034, 0.028), p=0.849
		HDL, mmol/L, Beta (95% CI)
		0.016 (-0.002, 0.033), p=0.074
		Triglycerides, mmol/L, Beta (95% CI)
		0.009 (-0.021, 0.038), p=0.559
		
		Results were similar when stratified by sex. See Harris, 2017 for more detail.
			Key confounders NOT accounted for:
			Race/ethnicity, physical activity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (parental education), TEI.
			
			Additional model adjustments:
			Study region, BMI, screen-time at 10y, fasting status at blood sampling, lipid concentration at 10y, pubertal onset, all energy bearing nutrients except SFA (replacement models)
			
			Limitations:
			• Not all key confounders accounted for
			• Did not control for GINIplus intervention group
			• 72% attrition with no information on bias due to loss to follow-up
			• No preregistered statistical analysis plan
			
			Funding sources:
			Federal Ministry for Education, Science, Research and Technology; Helmholtz Zentrum Munich; Research Institute at Marien-Hospital Wesel; LMU Munich; TU Munich; IUF-Leibniz Research Institute for Environmental Medicine at the University of Dusseldorf; Federal Ministry for Environment; Helmholtz Centre for Environmental Research; Commission of the European Communities, the 7th Framework Program: MeDALL project; Mead Johnson; Nestle

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

Harris, 2017 ***(CONTINUED)***
PCS, GINIplus and LISAplus, Germany
Baseline N=5,078 Analytic N=1,398 (Attrition: 72%)
 	
Participant characteristics at baseline:
• Age: Median=10.2y (IQR: 10.1, 10.3)
• Sex (female): 49%
• Race/ethnicity: NR
• SES: Parental education (high), 71.3%
• Anthropometry: BMI, Median=16.7 (IQR: 15.6, 18.4)
Fat intake at baseline, Median (IQR):
• SFA (%E): 12.6 (10.9, 14.7)
• MUFA (%E): 10.7 (9.3, 12.3)
• N-3 PUFA (%E): 0.54 (0.49, 0.62)
• N-6 PUFA (%E): 3.7 (3.2, 4.3)
Blood lipids, BP at baseline, Median (IQR):
• LDL (mmol/L): 2.1 (1.7, 2.5)
• HDL (mmol/L): 1.2 (1.1, 1.4)
• Triglycerides (mmol/L): 1.2 (0.9, 1.6)
Summary of findings:
Higher intake of SFA at 10y of age was associated with decreases in triglycerides from 10y to 15y of age, but was not associated with change in LDL or HDL cholesterol. Consumption of MUFA, N-3 PUFA, and N-6 PUFA at 10y were not associated with change in LDL and HDL cholesterol or triglycerides. Replacement of SFA consumption with either MUFA, N-3 PUFA, N-6 PUFA, or carbohydrate consumption was not associated with change in blood lipids except for two sex-stratified analyses: replacement of SFA consumption with carbohydrate consumption in females was associated with higher LDL cholesterol and triglycerides.
	Exposures:
	• SFA (continuous; per IQR increase in %E)
	• MUFA (continuous; per IQR increase in %E)
	• N-3 PUFA (continuous; per IQR increase in %E)
	• N-6 PUFA (continuous; per IQR increase in %E)
	• Replacement of SFA (continuous; per IQR increase in %E from substituting FA or CHO):
	  • MUFA
	  • N-3 PUFA
	  • N-6 PUFA
	  • CHO
	
	Assessment method and timing:
	• Self-administered, validated 80-item FFQ
	• Assessed at baseline (10y)
	
	Outcomes and assessment methods:
	• Assessed at baseline (10y) and 15y of age
	• Blood lipids: TC, LDL, HDL, triglycerides (17% fasted at 10y, 46.4% fasted at 15y)
		Change in blood lipids from 10y-15y
		
		Replacement of SFA with MUFA, PUFA, or CHO
		LDL, mmol/L, Beta (95% CI)
		MUFA: -0.034 (-0.082, 0.014), p=0.163
		n-3 PUFA: -0.026 (-0.063, 0.012), p=0.179
		n-6 PUFA: 0.017 (-0.021, 0.054), p=0.384
		CHO: 0.060 (-0.004, 0.123), p=0.064
		CHO-females: 0.125 (0.021, 0.229), p=0.019
		CHO-males: 0.012 (-0.064, 0.088), p=0.755
		
		HDL, mmol/L, Beta (95% CI)
		MUFA: 0.002 (-0.025, 0.029), p=0.894
		n-3 PUFA: -0.003 (-0.024, 0.018), p=0.775
		n-6 PUFA: 0.016 (-0.005, 0.038), p=0.129
		CHO: -0.001 (-0.037, 0.034), p=0.947
		CHO-females: -0.004 (-0.060, 0.052), p=0.891
		CHO-males: 0.000 (-0.045, 0.045), p=0.991
		
		Triglycerides, mmol/L, Beta (95% CI)
		MUFA: -0.041 (-0.086, 0.005), p=0.081
		n-3 PUFA: 0.002 (-0.034, 0.037), p=0.916
		n-6 PUFA: 0.018 (-0.018, 0.054), p=0.324
		CHO: 0.057 (-0.003, 0.117), p=0.063
		CHO-females: 0.098 (0.020, 0.176), p=0.014
		CHO-males: 0.020 (-0.069, 0.108), p=0.663
		
		Results for replacement of SFA with MUFA or PUFA were similar when stratified by sex. See Harris, 2017 for more detail.
			Key confounders NOT accounted for:
			Race/ethnicity, physical activity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (parental education), TEI.
			
			Additional model adjustments:
			Study region, BMI, screen-time at 10y, fasting status at blood sampling, lipid concentration at 10y, pubertal onset, all energy bearing nutrients except SFA (replacement models)
			
			Limitations:
			• Not all key confounders accounted for
			• Did not control for GINIplus intervention group
			• 72% attrition with no information on bias due to loss to follow-up
			• No preregistered statistical analysis plan
			
			Funding sources:
			Federal Ministry for Education, Science, Research and Technology; Helmholtz Zentrum Munich; Research Institute at Marien-Hospital Wesel; LMU Munich; TU Munich; IUF-Leibniz Research Institute for Environmental Medicine at the University of Dusseldorf; Federal Ministry for Environment; Helmholtz Centre for Environmental Research; Commission of the European Communities, the 7th Framework Program: MeDALL project; Mead Johnson; Nestle

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Williams, 2008[37] **PCS, The Healthy Start Project, U.S.** Baseline N~741, Analytic N=519 (Attrition: 30%) **Participant characteristics at baseline:** • Children enrolled in Head Start preschools • Age: Mean 3.9y, SD=1.8y • Sex (female): NR • Race/ethnicity: 40% African American, 40% Hispanic • SES: 90% families with annual income below the poverty line • Anthropometry: NR **Fat intake at baseline, Mean:** • SFA (%E): ~11.9 • MUFA (%E): ~11.2 • PUFA (%E): ~5.5 • Cholesterol (mg): ~176 **Blood lipids at baseline:** NR **Summary of findings:** *SFA and MUFA intake in children at 3.9 years was not significantly associated with triglycerides or total and HDL cholesterol at 8 years.*	**Exposures:** • SFA (continuous; %E) • MUFA (continuous; %E) Diet assessment method and timing: • Direct observation/plate waste measures during school and food record and telephone interviews with primary adult food provider to capture outside school intake over 24h period (validated and reliable) • Assessed at baseline (3.9y) **Outcomes and assessment methods**: • Assessed at 4y follow-up • Non-fasting blood lipids: TC, HDL, triglycerides; Continuous and by category (TC and HDL only)	**SFA** **TC** Continuous outcome: P>0.05 Intake by category (normal vs borderline vs high): P>0.05 **HDL** Continuous outcome: P>0.05 Intake by category (desirable vs borderline low vs low): P>0.05 **Trig** Continuous outcome: P>0.05 **MUFA** **TC** Continuous outcome: P>0.05 Intake by category (normal vs borderline vs high): P>0.05 **HDL** Continuous outcome: P>0.05 Intake by category (desirable vs borderline low vs low): P>0.05 **Trig** Continuous outcome: P>0.05	**Key confounders NOT accounted for:** SES, TEI, physical activity, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, race/ethnicity **Additional model adjustments:** Change in BMI **Limitations:** • Did not account for all key confounders • Did not account for intervention site (co-exposure) in analyses • No preregistered statistical analysis plan **Funding sources:** NIH

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Khalil, 2017[12] **PCS, Lifeways Cross-Generation Cohort Study, Ireland** Baseline N=1026 Analytic N=75 (Attrition: 93%) **Participant characteristics at baseline:** • Age: ~5y • Sex (female): 56% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI, Mean=16.96, SD=1.64 **Fat intake at baseline:** • NR **Blood lipids and BP at baseline:** • NR **Summary of findings:** *Consumption of SFAs, MUFAs, or PUFAs at 5y of age was not correlated with HDL cholesterol at 9y of age*	**Exposures:** • SFA (continuous; g) • MUFA (continuous; g) • PUFA (continuous; g) Assessment method and timing: • Self-administered, 52-item FFQ completed by the mother • Assessed at baseline (5y) **Outcomes and assessment methods**: • Assessed at follow-up (9y) • Non-fasting blood lipids: HDL	**SFAs** **HDL,** Pearson's correlation r=0.208, p=0.080 **MUFAs** **HDL,** Pearson's correlation r=0.151, p=0.207 **PUFAs** **HDL,** Pearson's correlation r=-0.076, p=0.524	**Key confounders NOT accounted for:** Sex, age, Race/ethnicity, SES, physical activity, family history of CVD or diabetes **Key confounders accounted for:** TEI **Additional model adjustments:** None **Limitations:** • Not all key confounders accounted for • FFQ was not validated • No information provided on how sub-group with blood lipids was assembled • No preregistered statistical analysis plan **Funding sources:** Health Research Board of the Republic of Ireland

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Altwaijri, 2009[1] **PCS, Project Heart Beat!, U.S.** Baseline N=678 Analytic N=NR (Attrition: NR%) **Participant characteristics at baseline:** • Age: 8y, 11y, and 14y • Sex (female): 49.1% • Race/ethnicity: 20.1% Black • SES: NR • Anthropometry: NR **Fat intake at baseline:** NR **Blood lipids at baseline:** NR **Summary of findings:** *In children and adolescents aged 8-18y of age, SFA, MUFA, and PUFA intake was not associated with total cholesterol. Greater cholesterol intake was associated with higher total cholesterol. When controlling for sexual maturation, dietary cholesterol intake was only associated with total cholesterol levels in boys.*	**Exposures:** • SFA (continuous; g) • MUFA (continuous; g) • PUFA (continuous; g) • Cholesterol intake (continuous; mg) Diet assessment method and timing: • Validated, semi-quantitative, 137-item FFQ (representing previous week's intake) administered by trained personnel • Assessed at baseline and annually for 4y **Outcomes and assessment methods**: • Assessed at baseline and annually for 4y • Fasting blood lipids: TC	**SFA** **TC**, mg/dL, Beta (SE) Data NR, P>0.05 **MUFA** **TC**, mg/dL, Beta (SE) Data NR, P>0.05 **PUFA** **TC**, mg/dL, Beta (SE) Data NR, P>0.05 **Cholesterol** **TC**, mg/dL, Beta (SE) **0.012 (0.005), P=0.013** Controlling for sexual maturation: Female: 0.009 (0.007), P=0.230 **Male: 0.014 (0.007), P=0.047**	**Key confounders NOT accounted for:** SES, TEI, physical activity, family history of CVD or diabetes. **Key confounders accounted for:** Sex, age, race/ethnicity. **Additional model adjustments:** BMI, sexual maturation (only analysis of dietary cholesterol) **Limitations:** • Did not account for all key confounders • No information provided on missing data • No preregistered statistical analysis plan **Funding sources:** NHLBI; CDC/Southwest Center for Prevention Research; Compaq Computer Corporation; UT Health Science Center at Houston, School of Public Health; USDA

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Boreham, 1999[3] **PCS, Young Hearts Project, U.K. (Northern Ireland)** Baseline N=509 Analytic N=459 (Attrition: 10%) **Participant characteristics at baseline:** • Age: ~12y • Sex (female): 51% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI, Mean~19 **Fat intake at baseline (12y), Mean (SD):** • PUFA:SFA ratio: Boys, 0.36 (0.15); Girls, 0.42 (0.17) • Cholesterol (mg/mJ/d): Boys, 18.7 (9.7); Girls, 17.8 (9.2) **Fat intake at 15y, Mean (SD):** • PUFA:SFA ratio: Boys, **0.42 (0.18)**; Girls, 0.46 (0.21) • Cholesterol (mg/mJ/d): Boys, **17.2 (8.1)**; Girls, **15.4 (9.0)** **Blood lipids and BP at baseline, Mean:** • TC (mmol/L): ~4.65 • HDL (mmol/L): ~1.39 • SBP (mmHg): ~111 • DBP (mmHg): ~69 **Summary of findings:** *In adolescents, the PUFA:SFA intake ratio at 12 and 15y of age was not associated with total and HDL cholesterol, or blood pressure. In boys, cholesterol intake was not associated with total and HDL cholesterol, or blood pressure. In girls, greater cholesterol intake was associated with lower HDL cholesterol.*	**Exposures:** • PUFA:SFA ratio (continuous) • Cholesterol (continuous; mg/mJ/d) Assessment method and timing: • Diet history with open-ended interview using photographic atlas to determine portion size • Assessed at baseline (12y) and 15y of age **Outcomes and assessment methods**: • Assessed at baseline (12y) and 15y of age • Non-fasting blood lipids: TC, HDL • BP: SBP and DBP; measured in duplicate	**PUFA:SFA ratio** **TC,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05 **HDL,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05 **SBP,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05 **DBP,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05 **Cholesterol** **TC,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05 **HDL,** Standardized beta (SE) Boys: Data NR, P>0.05 **Girls: -0.09 (0.04), P=0.042** **SBP,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05 **DBP,** Standardized beta (SE) Boys and Girls: Data NR, P>0.05	**Key confounders NOT accounted for:** Race/ethnicity, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, SES, TEI, physical activity, **Additional model adjustments:** Smoking, sexual maturation, vitamin C intake, carbohydrate (%E), total fat (%E) **Limitations:** • Did not account for all key confounders • Validity or reliability of diet history unknown • No preregistered statistical analysis plan **Funding sources:** Northern Ireland Chest, Heart and Stroke Association; British Heart Foundation; Wellcome Trust

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations

Masquio, 2015[17]
PCS, Brazil (Unnamed cohort)
Baseline N=77 Analytic N=60 (Attrition: 12%)
 	
Participant characteristics at baseline:
• Adolescents with obesity participating in 1 year of interdisciplinary therapy for weight loss
• Age: Mean~16.8y
• Sex (female): NR
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI, Mean~36.9
 	
Fat intake at baseline, Mean:
• SFA: ~18.9g; ~9.%E
• Participants with greater reductions in SFA intake had significantly higher SFA intake at baseline
 	
Blood lipids and BP at baseline, Mean:
• TC (mg/dL): ~168
• LDL (mg/dL): ~105
• HDL (mg/dL): ~44
• Mean BP (mmHg): ~94
 	
Summary of findings:
In adolescents with obesity participating in 1 year of interdisciplinary therapy, tertile of change in SFA intake was not associated with change in blood lipids or blood pressure. Continuous change in SFA intake was associated with change in total and LDL cholesterol.
	Exposures:
	• Change in SFA intake (categorical; tertiles)
	  • T1 (n=20): Increase or low reduction in SFA (<3.68g)
	  • T2 (n=20): Moderate reduction in SFA (3.8-13.67g)
	  • T3 (n=20): High reduction in SFA (>13.67g)
	• Change in SFA intake (continuous; g)
	
	Assessment method and timing:
	• Non-consecutive 3 day dietary record completed by adolescent with help from parents
	• Assessed at baseline and 1y follow-up
	
	Outcomes and assessment methods:
	• Assessed at baseline and 1y follow-up
	• Fasting blood lipids: TC, LDL, HDL
	• BP: Mean BP
		Change in blood lipids or BP
		
		TC, mg/dL
		T1 vs T2, T1 vs T3, T2 vs T3: All P>0.05
		Continuous: B=0.31, 95% CI: 0.06, 0.56), P=0.02
		
		LDL, mg/dL
		T1 vs T2, T1 vs T3, T2 vs T3: All P>0.05
		Continuous: B=0.27, 95% CI: 0.01, 0.53), P=0.04
		
		HDL, mg/dL
		T1 vs T2, T1 vs T3, T2 vs T3: All P>0.05
		
		Mean BP, mmHg
		T1 vs T2, T1 vs T3, T2 vs T3: All P>0.05
			Key confounders NOT accounted for:
			Sex, race/ethnicity, SES, TEI, physical activity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Age.
			
			Additional model adjustments:
			Visceral fat (analyses of continuous change in SFA intake only)
			
			Limitations:
			• Do not account for all key confounders
			• Only children who complied with interdisciplinary therapy (>75% attendance) selected for study
			• Three day dietary record unvalidated
			• All participating in interdisciplinary therapy for weight loss during study period
			• No preregistered statistical analysis plan
			
			Funding sources:
			CNPq; CAPES; UNIFESP; AFIP; CEPE; CEMSA

Study and Population Characteristics	Exposures, Comparators, Outcomes	Results†	Key Confounders, Study Limitations
Quivers, 1992[27] **PCS, U.S. (Unnamed cohort)** Baseline N=NA Analytic N=32 (Attrition: NA%); Selected from 259 who met blood lipid criteria and participated for ≥90d **Participant characteristics at baseline:** • Children with LDL cholesterol ≥110 mg/dL enrolled in the Cardiovascular Health Clinic for the Young prescribed National Cholesterol Education Program Step 1 Diet • Age: 2-16y • Sex (female): 50% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at baseline, Median (SD):** • SFA (%E): 9.03 (2.34) • PUFA (%E): 4.24 (2.52) • Cholesterol (mg/d): 132.46 (63.78) **Blood lipids at baseline, Median (SD):** • TC (mg/dL): 201.84 (31.18) • LDL (mg/dL): 147.69 (32.83) • HDL (mg/dL): 44.81 (7.79) • Triglycerides (mg/dL): 59.71 (23.60) **Summary of findings:** *In children with LDL cholesterol levels of at least 110mg/dL but normal triglycerides levels, reduction in grams of SFA intake (but not %E from SFA) was associated with decreased LDL cholesterol levels over ~1y of follow-up. This association was seen only when using Spearman correlations; no association was detected with Pearson correlations.Change in PUFA and dietary cholesterol intake were not associated with changes in LDL cholesterol.*	**Exposures:** • SFA (continuous; change from baseline to final; g and %E) • PUFA (continuous; change from baseline to final; g and %E) • Cholesterol (continuous; change from baseline to final; mg/d) Assessment method and timing: • 5 day diet diaries completed by children and parents • Assessed at baseline and final follow-up (~1.2y, range: ~0.4y to ~3.3y) **Outcomes and assessment methods**: • Assessed at baseline and final follow-up (~1.2y, range: ~0.4y to ~3.3y) • Blood lipids: LDL (NR if fasting or non-fasting)	**SFAs** **LDL,** Pearson correlation; Spearman Correlation ***Change in blood lipids from baseline to final*** g: 0.296, p=0.1; **0.396, p=0.025** %E: 0.015, p=0.936; 0.014, p=0.938 ***Rate of change (magnitude of change/time between baseline and final)*** g: 0.314, p=0.080; **0.494, p=0.004** %E: 0.048, p=0.793; 0.100, p=0.586 **PUFAs** **LDL,** Pearson correlation; Spearman Correlation ***Change in blood lipids from baseline to final*** g: 0.297, p=0.099; 0.161, p=0.380 %E: 0.135, p=0.463; 0.070, p=0.703 ***Rate of change (magnitude of change/time between baseline and final)*** g: **0.437, p=0.013**; 0.224, p=0.219 %E: 0.274, p=0.130; 0.126, p=0.492 **Cholesterol** **LDL,** Pearson correlation; Spearman Correlation ***Change in blood lipids from baseline to final*** mg: 0.142, p=0.437; 0.123, p=0.501 ***Rate of change (magnitude of change/time between baseline and final)*** mg: 0.035, p=0.850; 0.091, p=0.619	**Key confounders NOT accounted for:** Sex, age, race/ethnicity, SES, TEI, physical activity. **Key confounders accounted for:** Family history of CVD or diabetes. **Additional model adjustments:** None **Limitations:** • Not all key confounders accounted for • Only selected participants who participated in clinic for at least 90 days • 5 day diet diaries unvalidated • No information on missing data • No preregistered statistical analysis plan and relationships with most blood lipids NR **Funding sources:** NR

[*] Abbreviations: BP – blood pressure, CHO – carbohydrates, CI – confidence interval, DBP – diastolic blood pressure, HDL – HDL cholesterol, LDL – LDL cholesterol, NA – not applicable, NR – not reported, %E – percent energy, ref – reference group, SBP – systolic blood pressure, SD – standard deviation, SE – standard error, SES – socioeconomic status, TC – total cholesterol, TEI – total energy intake

[†] Statistically significant results bolded.

Table 3. Risk of bias for randomized controlled trials examining types of dietary fat consumed during childhood and cardiovascular disease intermediate and endpoint outcomes[*,†]

	Randomization	Identification of participants – randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Ballesteros, 2004,[2] Crossover RCT	Some Concerns		Low	Low	Low	Some Concerns
Denke, 2000,[5] Crossover RCT	High		Low	Some Concerns	Low	Some Concerns
Dorgan, 2011,[6] RCT	Low		Low	Low	Low	Some Concerns
Estevez-Gonzalez, 1998,[7] Crossover RCT	Some Concerns		Low	Low	Low	Some Concerns
Hakanen, 2010,[8] RCT	Low		Low	Some Concerns	Low	Some Concerns
Kaitosaari, 2003,[10] RCT	Low		Low	Some Concerns	Low	Some Concerns
Kaitosaari, 2006,[11] RCT	Low		Low	Some Concerns	Low	Some Concerns
Kwiterovich, 1995,[13] RCT	Low		Low	Low	Low	Low
Lapinleimu, 1995,[14] RCT	Low		Low	Low	Low	Some Concerns
Lehtovirta, 2018,[15] RCT	Low		Low	Low	Low	Some Concerns
Muros, 2015,[18] Cluster RCT	Some Concerns	Some Concerns	Low	Low	Low	Some Concerns
Niinikoski, 2007,[22] RCT	Low		Low	Some Concerns	Low	Some Concerns
Niinikoski, 2009,[21] RCT	Low		Low	Some Concerns	Some Concerns	Some Concerns
Niinikoski, 2012,[23] RCT	Low		Low	Some Concerns	Low	Some Concerns
Nupponen, 2015,[24] RCT	Low		Low	Low	Low	Some Concerns
Obarzanek, 2001,[25] RCT	Low		Low	Low	Low	Some Concerns
Raitakari, 2005,[28] RCT	Low		Low	Low	Low	Some Concerns
Rask-Nissila, 2000,[29] RCT	Low		Low	Low	Low	Some Concerns

[*] A detailed description of the methodology used for assessing risk of bias is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

[†] Possible ratings of low, some concerns, or high determined using the "Cochrane Risk-of-bias 2.0" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. *Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.)

	Randomization	Identification of participants – randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Routi, 1996,[30] RCT	**Low**		**Low**	**Low**	**Low**	**Some Concerns**
Simell, 2000,[31] RCT	**Low**		**Low**	**Low**	**Low**	**Some Concerns**
Simons-Morton, 1997,[32] RCT	**Low**		**Low**	**Low**	**Low**	**Some Concerns**
Vuholm, 2019,[36] RCT	**Low**		**Low**	**Low**	**Low**	**Low**

Table 4. Risk of bias for prospective cohort studies examining types of dietary fat consumed during childhood and cardiovascular disease intermediate and endpoint outcomes*

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Altwaijri, 2009[1]	Serious	Low	Low	Low	No information	Low	Moderate
Boreham, 1999[3]	Serious	Low	Moderate	Low	Low	Low	Moderate
Cowin, 2001[4]	Serious	Low	Serious	Low	Low	Low	Serious
Harris, 2017[9]	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Khalil, 2017[12]	Serious	Low	Moderate	Low	No information	Low	Moderate
Magnussen, 2011[16]	Serious	Low	Serious	Low	Moderate	Low	Moderate
Masquio, 2015[17]	Serious	Moderate	Moderate	Moderate	Low	Low	Moderate
Ness, 2005[19]	Serious	Moderate	Serious	Low	Moderate	Low	Moderate
Nicklas, 2002[20]	Serious	Low	Low	Low	Moderate	Low	Moderate
Post, 1997[26]	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Quivers, 1992[27]	Serious	Serious	Moderate	Low	No information	Low	Serious
Simons-Morton, 1997[32]	Serious	Low	Low	Serious	Low	Low	Moderate
Stroobant, 2017[33]	Serious	Low	Low	Low	Moderate	Low	Moderate
Twisk, 1996[34]	Serious	Low	Moderate	Low	Moderate	Low	Moderate
van den Hooven, 2013[35]	Serious	Low	Low	Low	Moderate	Low	Moderate
Williams, 2008[37]	Serious	Low	Low	Moderate	Low	Low	Moderate

* Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

Table 5. Evidence examining types of dietary fat consumed by adults and cardiovascular disease intermediate outcomes (blood lipids)*

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
RCT: Parallel Design			

Abbaspour, 2019[38]
RCT parallel, U.S.
Baseline N=54 Analytic N=48 (Attrition: 11%)
 	
Participant characteristics at baseline: Adults (40% female) ~30y of age with overweight or obesity
 	
Summary of findings:
Consuming mixed nuts for 8 weeks (which increased MUFA intake) did not significantly change blood lipids compared to consuming pretzels.
	Intervention and comparator:
	• Mixed nuts, 42.5g/d (n=24)
	  • Sources: almonds, cashews, hazelnuts, pecans, Brazil nuts, macadamia nuts, pistachios, walnuts, and peanuts
	• Pretzels, 69g/d (n=24)
	  • Sources: NA
	
	• *Mixed nuts and pretzels were isocaloric (250 kcal)*
	
	Duration of intervention: 8 wk
	Compliance: Monitored via 24h recalls at baseline, 4wk, and 8wk; Encouraged via weekly text reminders
	
	Total diet intake at 8 wk for Nuts vs Pretzels, Mean (SD), %E:
	SFA: 12.2 (3.8) vs 10.4 (2.9), P=NS
	MUFA: 18.2 (7.0) vs 11.8 (3.6), P<0.05
	PUFA: 10.2 (3.1) vs 8.3 (3.1), P=NS
	Cholesterol (g/d): 391 (286) vs 329 (171), P=NS
	Other components of diet differed significantly: Total fat (higher in Nuts), CHO (lower in Nuts), vitamin E and copper (higher in Nuts)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline, 4wk, and 8 wk
		
		Repeated measures ANOVA (Group*Time)
		
		TC, mmol/L, Baseline, 4wk, 8wk
		Nuts vs Pretzels: All P=NS
		
		LDL, mmol/L, Baseline, 4wk, 8wk
		Nuts vs Pretzels: P=NS
		
		HDL, mmol/L, Baseline, 4wk, 8wk
		Nuts vs Pretzels: P=NS
		
		Triglycerides, mmol/L, Baseline, 4wk, 8wk
		Nuts vs Pretzels: P=NS
			Model adjustments:
			Baseline blood lipid
			
			Limitations:
			• Allocation sequence was not concealed
			• No information on adherence
			• No preregistered statistical analysis plan
			
			Funding sources:
			AHA

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Akrami, 2018[41] **RCT parallel, Iran** Baseline N=60 Analytic N=52 (Attrition: 13%) **Participant characteristics at baseline:** Participants (37% female) aged mean 48 years with metabolic syndrome **Summary of findings:** *In adults with metabolic syndrome, consumption of flaxseed oil (higher in ALA), compared to sunflower seed oil (higher in LA), did not result in significant differences in total blood, LDL, HDL cholesterol, or triglycerides.*	**Intervention and comparator:** • Cold-pressed Flaxseed oil (n=26): 25 mL/day – SFA 15%, MUFA 28%, PUFA 58%, Oleic acid 27%, LA: 16%, ALA 41% • Cold-pressed Sunflower seed oil (n=26): 25 mL/day - SFA 14%, MUFA 28%, PUFA 58%, Oleic acid 28%, LA 58%, ALA0% • *Participants instructed to add test oils to their cold food or as salad dressings* Duration of intervention: 7 wk (3 week run-in) Compliance: measured at 2 and 6 wk follow-up **Dietary intake for Flaxseed vs Sunflower seed oil at end of intervention, Mean (SD), %E:** SFA: 7.5 (0.8) vs 7.6 (0.6), P=NS MUFA: NR PUFA: 17.3 (0.9) vs 16.5 (0.9), P=0.006 n-3 PUFA: 15.2 (1.2) vs 0.8 (0.1), P<0.001 Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids: Measured at baseline and 7wk follow-up Comparing difference in change between groups **TC**, mg/dL Flaxseed vs sunflower seed oil: NS **LDL**, mg/dL Flaxseed vs sunflower seed oil: NS **HDL**, mg/dL Flaxseed vs sunflower seed oil: NS **Triglycerides**, mg/dL Flaxseed vs sunflower seed oil: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No information on compliance • No information on whether missing data was different between groups • No preregistered statistical analysis plan **Funding sources:** Research Vice-chancellor of Shiraz University of Medical Sciences

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Annuzzi, 2014[44]
RCT parallel, Italy
Baseline N=86, Analytic N=78 (Attrition: 9%)
 	
Participant characteristics at baseline: Adults ~55y of age with overweight or obesity, high waist circumference, and at least one additional component of metabolic syndrome.
 	
Summary of findings:
In adults with overweight or obesity, high waist circumference, and at least one other component of metabolic syndrome, consumption of a diet high in n-3 PUFA (primarily EPA/DHA from fish) did not significantly change blood lipids compared to a diet lower in n-3 PUFA.
	Intervention and comparators:
	• High long chain n-3 PUFA: ~1.5%E from n-3 PUFA (primarily EPA/DHA)
	  • Source: Anchovies, Dentex (type of predatory fish) and/or Salmon
	  • Low polyphenol group (~363 mg/d): n=19
	  • High polyphenol group (~2861 mg/d): n=19
	• Low n-3 PUFA: ~0.5%E from n-3 PUFA
	  • Low polyphenol group (~365 mg/d): n=20
	  • High polyphenol group (~2903 mg/d): n=20
	
	• *All meals provided by researchers*
	• *All diets were weight maintaining*
	• *Macronutrient distribution same across all groups (50.7%E carbohydrates, 15.7%E protein, 33.6% total fat)*
	
	Duration of intervention: 8 wk (3 wk run-in)
	Compliance: Evaluated via 7 day dietary records at baseline, 4wk, and 8wk; reinforced by phone calls every 2-3 days from study dietitians; Participants were compliant with study diets
	
	Diet composition for High n-3 PUFA vs Low n-3 PUFA, Mean, %E:
	SFA: ~7.3% vs ~7.2%, P=NS
	MUFA: ~19.3% vs ~20.1%, P=NS
	n-6 PUFA: ~2.7% vs ~3%, P=NS
	n-3 PUFA: ~1.5% vs ~0.5%, P<0.0001
	EPA: ~0.45% vs ~0.03%, P<0.0001
	DHA: ~0.59% vs ~0.01%, P<0.0001
	Cholesterol: ~197 mg/d vs ~185 mg/d, P=NS
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Fasting blood lipids: Assessed at baseline and 8wk
		
		Comparing change in blood lipids between groups
		
		TC, mg/dL
		High n-3 vs Low n-3: P=NS
		n-3 by polyphenol interaction: P=NS
		
		LDL, mg/dL
		High n-3 vs Low n-3: P=NS
		n-3 by polyphenol interaction: P=NS
		
		HDL, mg/dL
		High n-3 vs Low n-3: P=NS
		n-3 by polyphenol interaction: P=NS
		
		Triglycerides, mg/dL
		High n-3 vs Low n-3: P=NS
		n-3 by polyphenol interaction: P=NS
			Model adjustments:
			Polyphenol group, polyphenol by n-3 group interaction, baseline blood lipid value
			
			Limitations:
			• No preregistered statistical analysis plan
			
			Funding sources: European Community's Seventh Framework Programme: Etherpaths Project; Foresid, Italian Society of Diabetology; Italian Diabetes Society; Food supplied by Lavazza, Nestle, Parmalat S.p.A., Zuegg S.p.A., Pompadour Te S.r.l., Coop. Nuovo Cilento s.c.r.l.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Baxheinrich, 2012[47]
RCT parallel, Germany
Baseline N=95 Analytic N=81 (Attrition: 15%)
 	
Participant characteristics at baseline: Adults (68% female) with metabolic syndrome, ~51 years, BMI ~34, no CVD
 	
Summary of findings:
Consumption of a rapeseed oil diet (high in ALA) versus olive oil diet (low in ALA), within a hypocaloric, low energy density dietary pattern for 26-weeks, resulted in a significant decrease in triglyceride levels, but no other significant between-group differences in lipids in persons with metabolic syndrome. Consumption of a rapeseed oil (30 g) and olive oil (30 g), replacing SFA with MUFA, significantly decreased total blood and LDL cholesterol and had no effect on HDL cholesterol.
	Intervention and comparator:
	• Rapeseed oil (RO) diet (30g/d oil plus 20g/d margarine), n=40
	  • Sources: Refined rapeseed oil and rapeseed-based commercial margarine (Types of fat NR)
	  • High MUFA; high ALA content
	• Olive oil (OO) diet (30g/d oil plus 20g/d margarine), n=41
	  • Sources: Refined olive oil and an olive oil-based margarine (Types of fat NR)
	  • High MUFA; low ALA content
	  • Once a week OO was replaced by sunflower oil to compensate for low LA in OO
	
	• *All participants on hypoenergetic diet (energy deficiency of 2·0–3·3MJ) with low energy density (ED), 42%E carbohydrates, 20% protein, and 38% fat (SFA<10% and MUFA 18%).*
	• *Participants received diet instruction and coaching from dietitians*
	
	Duration of intervention: 26 wk (~6 mo)
	Compliance: Good compliance based on diet records; however, 9 excluded (3 RO/6 OO) due to non-compliance
	
	Dietary intake for RO vs OO, Mean (SD):
	SFA: NS
	MUFA: NS
	PUFA (%E): 8.1 (1.9) vs 5.5 (0.9); P<0.001
	ALA (g/day): 3.46 (0.84) vs 0.78 (0.17); P<0.001
	LA (g/day): 10.8 vs 8.5, P=NS
	No significant difference in energy, macronutrient, and fiber intake.
		Outcomes and assessment methods:
		Fasting blood lipids: Assessed at baseline and at 6 mo.
		
		Difference in lipid values from baseline
		
		TC, mmol/l, mean difference
		RO: -0.30
		OO: -0.38
		RO vs OO: P=NS
		
		LDL, mmol/l, mean difference
		RO: -0.22
		OO: -0.28
		RO vs OO: P=NS
		
		HDL, mmol/l, mean difference
		RO: NS
		OO: NS
		RO vs OO: P=NS
		
		Triglycerides, mmol/l, mean difference
		RO: -0.45
		OO: -0.20
		RO VS OO: P=0.020
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• Potential missing data bias due to not statistically accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			Union for Promoting Oil and Protein Plants (UFOP); the International Foundation for the Promotion of Nutrition Research and Nutrition Education (ISFE)

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Beavers, 2010[48] **RCT parallel, U.S.** Baseline N=33 Analytic N=32 (Attrition: 0%) **Participant characteristics at baseline:** *Healthy, physically active, postmenopausal women aged ~54 years, BMI ~26, no hormone replacement therapy, no smoking* **Summary of findings:** *Consumption of three servings per day of soy versus dairy milk had no significant effect on blood total, LDL and HDL cholesterol and triglycerides in physically active postmenopausal women.*	**Intervention and comparator:** • 3 servings (8.25 fl oz)/d vanilla soy milk (n=16) • 3 servings (8 fl oz)/d reduced fat dairy milk (n=16) Duration of intervention: 4 wk (2 wk run-in, no washout period) Compliance: 98% compliance, after removal on one non-compliant subject (defined as <80% consumption), assessed via compliance logs. **Dietary intake soy vs dairy intervention at post-intervention, Mean (SD), g/day:** SFA: 20.39 (13.56) vs 28.27 (8.68), P<0.05 MUFA: 16.76 (8.51) vs 20.06 (9.10), P: NS PUFA: 13.47 (5.66) vs 8.72 (5.77), P: NS Cholesterol (mg/d): 168.36 (97.38) vs 291.56 (105.15), P: NS No other components of diet differed.	**Outcomes and assessment methods:** Fasting blood lipids at the start and end of each diet phase Blood lipid levels at follow-up **TC**, mg/dL Soy vs dairy: P=NS **LDL**, mg/dL Soy vs dairy: P=NS **HDL,** mg/dL Soy vs dairy: P=NS **Triglycerides,** mg/dL Soy vs dairy: P=NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** White-Wave Foods, Inc.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Bergeron, 2019[49]
RCT parallel (low vs high SFA), crossover (sources), U.S.
Baseline N=177 Analytic N=113 (Attrition: 36%)
 	
Participant characteristics at baseline: Participants (55% White, ~20% Asian) 43 y with BMI ~26 and normal lipid concentrations
 	
Summary of findings:
High SFA diet including sources from high-fat dairy products and butter, significantly increased total cholesterol, LDL cholesterol, but not HDL cholesterol and triglycerides.
Total blood cholesterol, LDL, and HDL cholesterol were significantly higher with red meat and white meat compared to nonmeat, independent of SFA content. There were no differences in blood lipids between red and white meat.
	Intervention and comparator:
	• Low SFA (~7%E), n=51
	  • Red meat: SFA: 8%E, MUFA 21%E, PUFA: 5% E, Cholesterol: 353 mg/day
	  • White poultry meat: SFA: 7%E, MUFA 18%E, PUFA: 6% E, Cholesterol: 424 mg/day
	  • Nonmeat: SFA: 7%E, MUFA 20%E, PUFA: 5% E, Cholesterol: 275 mg/day
	• High SFA (~14%E): n=62, high-fat dairy products and butter
	  • Red meat: SFA: 13%E, MUFA 12%E, PUFA: 5% E, Cholesterol: 403 mg/day
	  • White poultry meat: SFA: 14%E, MUFA 13%E, PUFA: 5% E, Cholesterol: 473 mg/day
	  • Nonmeat: SFA: 13%E, MUFA 12%E, PUFA: 5% E, Cholesterol: 403 mg/day
	
	Duration of intervention: 4 wk (2-7 wk washout)
	Compliance: menu checklists, grocery receipts, reported deviations from dietary instructions; "excellent" compliance
	
	Dietary intake for Intervention vs Control, Mean (SD), g/day: NR
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk follow-up (after each diet)
		
		Blood lipid levels after each diet period
		
		TC, mmol/L, Mean (SE)
		Mean difference:
		High - Low SFA: 0.22 (0.08), P=0.0002
		Red meat - White meat: P=NS
		Red meat - nonmeat: 0.18 (0.04), P<0.0001
		White meat - nonmeat: 0.18 (0.04), P<0.0001
		
		LDL, mmol/L, Mean (SE)
		Mean difference:
		High - Low SFA: 0.23 (0.06), P=0.0003
		Red meat - White meat: P=NS
		Red meat - nonmeat: 0.16 (0.03), P<0.0001
		White meat - nonmeat: 0.16 (0.03), P<0.0001
		
		HDL, mmol/L, Mean (SE)
		Mean difference:
		High - Low SFA: P=NS
		Red meat - White meat: P=NS
		Red meat - nonmeat: 0.03 (0.01), P=0.007
		White meat - nonmeat: 0.04 (0.01) P=0.0001
		
		Triglycerides, mmol/L, Mean (SE)
		Mean difference:
		High - Low SFA: P=NS
		Red meat - White meat: P=NS
		Red meat - nonmeat: P=NS
		White meat - nonmeat: P=NS
			Model adjustments:
			Dietary period
			
			Limitations:
			• Missing outcome data was unbalanced between groups
			• No preregistered statistical analysis plan
			
			Funding sources:
			NHLBI; National Center for Advancing Translational Sciences; University of California, San Francisco Clinical & Translational Science Institute

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Blesso, 2013[52] **RCT parallel, U.S.** Baseline N=40 Analytic N=37 (Attrition: 8%) **Participant characteristics at baseline:** Adults (~66% female) ~52y of age with overweight or obesity and with metabolic syndrome **Summary of findings:** *In adults with overweight or obesity and with metabolic syndrome following a CHO restricted diet, consumption of 3 eggs/d for 12 weeks (which increased cholesterol intake) did not significantly change blood lipids compared to consumption of an egg substitute devoid of dietary cholesterol and fat.*	**Intervention and comparator:** • Whole eggs (3 per day: 534 mg dietary cholesterol) while consuming a CHO restricted diet (25-30%E from CHO), n=20 • Egg substitute (0 mg dietary cholesterol, fat-free) while consuming a CHO restricted diet (25-30%E from CHO), n=17 • *Participants instructed to avoid eating eggs outside of the dietary intervention* Duration of intervention: 12 wk Compliance: Assessed via 5d dietary intake records at baseline, 6wk, and 12wk **Dietary intake at 12 wk for Egg vs Control, Mean (SD), %E:** SFA: NR MUFA: NR PUFA: NR Cholesterol (mg/d): 740.8 (139.7) vs 213.4 (83.3), P<0.0001 Other components of diet differed significantly: Choline (higher in Egg group)	**Outcomes and assessment methods**: Fasting blood lipids at baseline, 6wk, and 12wk Time*Group interaction **TC**, mg/dL Egg vs Control: P=NS **LDL**, mg/dL Egg vs Control: P=NS **HDL**, mg/dL Egg vs Control: P=NS **Triglycerides,** mg/dL Egg vs Control: P=NS	**Model adjustments:** None **Limitations:** • No information on randomization of allocation sequence • No information on compliance • No preregistered statistical analysis plan **Funding sources:** American Egg Board/Egg Nutrition Center

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Bjermo, 2012[50]
RCT parallel, HEPFAT, Sweden
Baseline N=67 Analytic N=61 (Attrition: 9%)
 	
Participant characteristics at baseline: Men and women were 51-63y, with abdominal diameter >25cm or waist circumference >88 cm (women) or >102 cm (men); no differences in BMI, lipids and cholesterol between groups at baseline.
 	
Summary of findings:
Participants who were assigned to the PUFA diet had significantly greater decrease in total cholesterol compared to those who were assigned to the SFA diet for 10 weeks.
	Intervention and comparator:
	• PUFA diet (n=32) – n-6 LA
	  • Instructed to consume ~15% of energy as LA
	  • Sources: Scones (baked on sunflower oil), margarine, sunflower oil, sunflower seeds
	• SFA diet (n=29)
	  • Sources: scones (baked-on butter) and butter
	
	Duration of intervention: 10 wk
	Compliance: 3-day weighed food records
	
	Change in dietary intake from baseline during intervention for Intervention (PUFA diet) vs Control (SFA diet), Mean (SD), g/day:
	Total fat: Increased more for SFA diet than PUFA diet, P<0.01
	SFA: Decreased in PUFA; Increased in SFA, Change between group, P<0.001
	MUFA: NR
	AA (20:4n-6): Change between group: P=NS
	LA: Increased in PUFA diet, decreased in SFA diet, Change between group, P<0.001
	PUFA: ALA (18:3n-6), Dihomo-gamma-linolenic acid (20:3n-6), AA (20:4n-6) did not differ between groups, P>0.36
	Cholesterol: NR
	Other components of diet differed significantly: Change in total fat was significantly different between groups (increased more for SFA diet);
		Outcomes and assessment methods:
		Fasting blood lipids at 10 wk
		
		TC, mmol/L, Mean (SD)
		Change (follow-up – baseline):
		PUFA: -0.2 (0.4)
		SFA: 0.0 (0.5)
		P=0.01
		
		LDL, mmol/L, Mean (SD)
		PUFA vs SFA diet: NS
		
		HDL, mmol/L, Mean (SD)
		PUFA vs SFA diet: NS
		
		Triglycerides, mmol/L, Mean (SD)
		PUFA vs SFA diet: NS
			Model adjustments:
			Baseline values
			
			Limitations:
			• No information provided on randomization method
			• Did not adjust for compliance in per protocol analyses
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Council for Working Life and Social Research

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Bladbjerg, 2011[51] **RCT parallel, MUFObes trial, Denmark** Baseline=131 Analytic N=99 (Attrition: 24%) **Participant characteristics at baseline:** ~28y, Obese (BMI~31), 61% female, recent loss of ≥8% body weight, non-smokers, no regular medications **Summary of findings:** *Consumption of a high MUFA diet, low fat diet or a control diet for 6 months to maintain weight loss, had no significant between-group differences in changes to blood lipids in overweight adults.*	**Intervention and comparators:** • High MUFA diet: Moderate (35-45%E) fat, high (>20%E) MUFA, and moderate (40-50%E in low-GI CHO, moderate (10-20%) protein (n=36) • High content of vegetable oils, whole-grain foods, nuts, and legumes • Low fat diet: 20-30%E fat, high (55-65%E) in mixed GI CHO, moderate (10-20%E) protein (n=40) • Control diet (average Danish diet): Moderate (30-40%E) fat, high SFA (>15%E), moderate (45-55%E) in high-GI CHO, low (<3%) fiber, moderate (10-20%) protein (n=23) • *Weight loss maintenance diets, all foods and beverages selected at study supermarket with feedback from dietitians and only these foods were to be consumed* Duration of intervention: 6 months (preceded by an 8- wk low energy (800-1000kcal/d) diet--only subjects who lost ≥8% body weight were randomized; followed by 3 week standardization diet similar to the control diet) Compliance: Monitored food selection, blood fatty acid analysis; compliance NR **Dietary composition for High-MUFA, LF diet vs Control diet, Mean (95% CI)**: Total fat: 38.4 (37.9, 39.0) vs 23.6 (23.1, 24.1) vs 32.1 (31.4, 32.7), P<0.001 SFA (%E): 7.1 (6.9, 7.4) vs 7.9 (7.6, 8.3) vs 15.1 (14.7, 15.5), P<0·001 MUFA (%E): 20.2 (19.8, 20.6) vs 8.4 (8.1, 8.6) vs 10.4 (10.0, 10.8), P<0·001 PUFA (%E): 7.8 (7.6, 8.1) vs 5.2 (5.1, 5.4) vs 4.0 (3.7, 4.3), P<0·001 CHO (%E): 43.3 (42.7, 43.9) vs 57.6 (57.0, 58.2) vs 49.8, (49.2, 50.5), P<0.001 Other components of diet that differed: Fiber, added sugar	**Outcomes and assessment methods**: Fasting blood lipids: At baseline and at 6 months Blood lipid levels at follow-up **TC,** mmol/L Between groups: NS **LDL,** mmol/L Between groups: NS **Triglycerides,** mmol/L Between groups: NS Subjects in all groups had a significant increase in BMI	**Model adjustments:** None **Limitations:** • No information provided about diet compliance • Potential bias from missing data • Trial registration is retrospective **Funding sources:** HA Foundation, the Danish Heart Association, the Danish Diabetes Association, Centre for Advanced Food Research, the State Research Councils, and the Danish Pork Council foundations, associations and research councils

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Bos, 2010[53] **RCT parallel, Netherlands** Baseline N=59 Analytic N=57 (Attrition: 3%) **Participant characteristics at baseline:** Participants (~58% female) between 40-65 years with mild abdominal obesity and slightly elevated total cholesterol and LDL cholesterol at baseline **Summary of findings:** *Participants who consumed high SFA diet, compared to high MUFA diet with refined olive oil, had significantly higher total blood and LDL cholesterol.*	**Intervention and comparator:** • High MUFA diet (20%E MUFA), n=18 – refined olive oil • High SFA diet (19%E SFA), n=19 – no food source reported • *Controlled-feeding trial; All meals provided to participants; 1 meal/d eaten under supervision of researchers* Duration of intervention: 8 wk (2 wk run-in on high SFA diet) Compliance: NR but indicates that participants had high compliance **Dietary intake for High MUFA, and High SFA diets, Mean (SD), %E:** SFA: 10.9 vs 19.2 MUFA: 20.3 vs 10.7 PUFA: 7.0 vs 5.4 n-3 PUFA: 0.6 vs 0.4 n-6 PUFA: 6.4 vs 5.0 Other components that differed between groups: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 8 wk follow-up **TC**, mmol/L, Difference, Mean (95% CI) **MUFA (ref) vs SFA (MUFA-SFA): -0.41 (-0.74, -0.09)** **(greater decreases in MUFA than SFA)** **LDL**, mmol/L, Difference, Mean (95% CI) **MUFA (ref) vs SFA (MUFA-SFA): -0.38 (-0.65, -0.11)** **(greater decreases in MUFA than SFA)** **HDL**, mmol/L, Difference, Mean (95% CI) MUFA vs SFA: NS **Triglycerides**, mmol/L, Difference, Mean (95% CI) MUFA vs SFA: NS	**Model adjustments:** Baseline levels, gender, participation in clamp measurements **Limitations:** • No information on compliance **Funding sources:** Netherlands Heart Foundation; Dutch Diabetes Research Foundation; Unilever R&D

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Chiu, 2014[59]
RCT parallel, U.S.
Baseline N=174 Analytic N=158 (Attrition: 9%)
 	
Participant characteristics at baseline: Participants ~38 years with BMI ~33 without history of diabetes or CVD with small but significant differences in total cholesterol at baseline
 	
Summary of findings:
Intake of high SFA from high-fat dairy (milk, cheese, yogurt, butter), compared to low SFA from low-fat dairy, did not alter TC, LDL, HDL cholesterol, and triglycerides.
	Intervention and comparators:
	• High SFA, high protein (n=32): SFA 15%E, MUFA 10%E, PUFA 7%, protein 30%E
	  • Source: High-fat dairy (milk, cheese, yogurt, butter)
	• Low SFA, high protein (n=36): SFA 7%E, MUFA 18%E, PUFA 7%, high protein 30%E
	  • Source: low-fat and non-fat dairy (milk, cheese, yogurt, butter)
	• High SFA, moderate protein (n=35): SFA 15%E, MUFA 20%E, PUFA 7%, protein 20%E
	  • Source: High-fat dairy (milk, cheese, yogurt, butter)
	• Low SFA, moderate protein (n=34): SFA (7%E), MUFA 29%E, PUFA 7%, protein 20%E
	  • Source: low-fat and non-fat dairy (milk, cheese, yogurt, butter)
	• Control (n=33)
	
	Duration of intervention: 4 wk
	Compliance: 5-point compliance score based on weekly interviews, menu checklists, grocery receipts; 95% of participants had dietary compliance score of 4 or 5
	
	Dietary intake for high SFA vs low SFA: NR
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk follow-up
		Difference in change
		
		TC, mmol/L, Mean (SE)
		High vs low SFA: NS*
		
		LDL, mmol/L, Mean (SE)
		High vs low SFA: NS*
		
		HDL, mmol/L, Mean (SE)
		High vs low SFA: NS*
		
		Triglycerides, mmol/L, Mean (SE)
		High vs low SFA: NS*
		
		*Inclusion of compliance score as a covariate did not significantly alter results
			Model adjustments:
			Sex
			
			Limitations:
			• No information provided on randomization method
			• Baseline differences in total cholesterol
			• No preregistered statistical analysis plan
			
			Funding sources:
			Dairy Management, Inc; National Center for Research Resources; National Center for Advancing Translational Sciences

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Clayton, 2015[61]
RCT parallel, U.S.
Baseline N=40, Analytic N=25 (Attrition: 37%)
 	
Participant characteristics at baseline: Recreationally active adults ~25y of age
 	
Summary of findings:
Among young adults participating in resistance training, consumption of an egg based breakfast daily for 12 weeks (which increased cholesterol intake within group; between-group NR) did not significantly change blood lipids compared to consumption of a bagel based breakfast.
	Intervention and comparator:
	• Egg-based breakfast (2 eggs/d) while participating in resistance training (3d/wk), n=11
	  • Sources: eggs
	• Bagel-based breakfast (9cm-diameter bagel/d) while participating in resistance training (3d/wk); Isoenergetic with egg-based breakfast, n=14
	  • Sources: NA
	
	• *Participants instructed not to eat eggs outside of the dietary intervention*
	
	Duration of intervention: 12 wk
	Compliance: Assessed via 3d food records at baseline, 6wk, and 12wk
	
	Dietary intake at 12wk for Intervention vs Control, Mean (SD), g/d:
	SFA: 24.61 (10) vs 26.29 (15), P=NR
	MUFA: 10.96 (6) vs 12.34 (8), P=NR
	PUFA: 4.26 (2) vs 6.09 (5), P=NR
	Cholesterol (mg/d): 446.04 (117) vs 292.97 (290), P=NR
	Other components of diet differed significantly: NR
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline, 6wk, and 12wk
		Repeated measures ANOVA
		
		TC, mg/dL
		Egg vs Control: P=NS
		
		LDL, mg/dL
		Egg vs Control: P=NS
		
		HDL, mg/dL
		Egg vs Control: P=NS
		
		Triglycerides, mg/dL
		Egg vs Control: P=NS
			Model adjustments:
			None
			
			Limitations:
			• No information on randomization of allocation sequence
			• No information on compliance
			• No information on whether missing data was different between groups
			• No preregistered statistical analysis plan
			
			Funding sources:
			Egg Nutrition Council

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

de Souza, 2018[63]
RCT parallel, Brazil
Baseline N=60 Analytic N=46 (Attrition: 23%)
 	
Participant characteristics at baseline: Women 20-59y of age with overweight or obesity.
 	
Summary of findings:
Women consuming 20g/d of baru almonds for 8 weeks, which increased MUFA intake, significantly increased HDL cholesterol relative to women consuming a baru-almond free diet. Almond intake did not have an effect on total or LDL cholesterol, or triglycerides.
	Intervention and comparator:
	• Baru almond-enriched diet (BAED), 20g/d daily (n=24)
	  • Sources: Roasted almonds
	• Baru almond-free diet (BAFD) (n=22)
	  • Sources: maltodextrin
	
	• *Both groups received individualized prescription of normocaloric and isoenergetic diet*
	
	Duration of intervention: 8 wk
	Compliance: Assessed via weekly phone calls, monthly consultations, and food records (NR); all participants completed the study
	
	Total dietary intake for BAED vs BAFD, Mean (SD), %E:
	SFA: 15.79 (8.74) vs 14.60 (5.92), P=NS
	MUFA: 15.67 (8.36) vs 9.08 (4.11), P=0.04, Time by Diet: P=0.05
	PUFA: 11.73 (8.48) vs 6.75 (2.86), P=0.00 , Time by Diet: P=NS
	Cholesterol: NR
	Other components of diet differed significantly: Total fat and dietary fiber (higher in BAED)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and at end of 8 wk.
		
		TC, mg/dL
		BAED vs BAFD: P=NS
		Time by Diet: P=NS
		
		LDL, mg/dL
		BAED vs BAFD: P=NS
		Time by Diet: P=NS
		
		HDL, mg/dL, Mean (SD), wk0, wk8
		BAED: 46.5 (8.98), 50.13 (9.40)
		BAFD: 44.73 (8.71), 43.54 (10.38)
		BAED vs BAFD: P=0.18
		Time by Diet: P=0.04
		
		Triglycerides, mg/dL
		BAED vs BAFD: P=NS
		Time by Diet: P=NS
			Model adjustments:
			Baseline blood lipid value; Included when p<0.05: sequence and period.
			
			Limitations:
			• No preregistered statistical analysis plan
			
			Funding sources: Foundation for Research Support of the State of Goias, Brazil

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Dhillon, 2018[64]
RCT parallel, U.S.
Baseline N=80 Analytic N=73 (Attrition: 9%)
 	
Participant characteristics at baseline: Normolipidemic first year college students ~18y of age; mean BMI: 25.5
 	
Summary of findings:
Young adults who consumed an almond snack daily for 8 weeks (increasing MUFA intake) had a smaller decrease in HDL cholesterol compared to young adults who consumed graham crackers. Almond intake did not have an effect on total or LDL cholesterol, or triglycerides.
	Intervention and comparator:
	• Almonds, 56.7g/d daily (n=38)
	  • Sources: dry-roasted almonds
	• Graham crackers, 77.5g/d (n=35)
	  • Sources: graham crackers
	
	Duration of intervention: 8 wk
	Compliance: Assessed via direct observation of consumption on weekdays and via text message on weekends and school breaks; Snack consumed ~6 days per week, no differences between groups
	
	Total dietary intake at wk8 for Almond vs Graham cracker, Mean (SD), g/d:
	SFA: 22.2 (11.7) vs 19.2 (9.8), P=NS
	MUFA: 31.8 (14.1) vs 22.0 (8.6), P=0.013,
	PUFA: 20.1 (9.9) vs 15.2 (7.7), P=NS
	Cholesterol: NR
	Other components of diet differed significantly: Total fat (higher in Almond), CHO (lower in Almond), alpha-tocopherol and magnesium (higher in Almond)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline, 4 wk, and 8 wk.
		Group*Time effect
		
		TC, mg/dL
		Almond vs Graham cracker: P=NS
		
		LDL, mg/dL
		Almond vs Graham cracker: P=NS
		
		HDL, mg/dL
		Almond vs Graham cracker: P<0.05
		Decrease in HDL was smaller for Almond group vs Graham cracker group
		
		Triglycerides, mg/dL
		Almond vs Graham cracker: P=NS
		
		Analyses stratified by weight status and fasting glucose were also conducted. See Dhillon, 2018 for more details
			Model adjustments:
			Subject at random effect, study week as within-subject factor
			
			Limitations:
			• No information provided on randomization method
			• No preregistered statistical analysis plan, analyzed outcome multiple ways
			
			Funding sources:
			Almond Board of California

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Dias, 2017[65] **RCT parallel, Australia** Baseline N=33 Analytic N=26 (Attrition: 21%) **Participant characteristics at baseline:** Healthy adults from 18 to 65 years without previous history of CVD and no differences in age, BMI, and blood lipids at baseline **Summary of findings:** *Total blood, LDL, HDL cholesterol and triglycerides was not significantly different between those who consumed foods high in SFA (butter and white chocolate) and n-6 PUFA (margarine and sunflower seeds).*	**Intervention and comparator:** • SFA (n=14): daily consumption of 24 g butter, 40 g white chocolate (30 g fat, 20.9 g SFA) • n-6 PUFA (n=12): daily consumption of 20 g margarine, 42 g sunflower seeds (30 g fat, 20 g n-6 PUFA) Duration of intervention: 6 wk Compliance: counting interventional food products provided; diet records; participants with low compliance (<80%) excluded from analysis; participants complied with study protocol based on plasma fatty acids **Dietary intake for SFA vs n-6 PUFA:** Total fat: NS between groups SFA: Increased for SFA group, decreased for n-6 PUFA group (within-group: both P<0.01) LA: decreased for SFA group; increased for n-6 PUFA group (within-group: both P<0.01) Total PUFA: NR Cholesterol: P=NS Other components of diet differed significantly: NR	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 6wk Difference in change **TC**, mmol/L, Median (IQR) SFA vs n-6 PUFA: NS **LDL**, mmol/L, Median (IQR) SFA vs n-6 PUFA: NS **HDL**, mmol/L, Median (IQR) SFA vs n-6 PUFA: NS **Triglycerides**, mmol/L, Median (IQR) SFA vs n-6 PUFA: NS	**Model adjustments:** None **Limitations:** • Attrition >10% • No preregistered statistical analysis plan **Funding sources:** Hunter Medical Research Institute; Faculty of Health, University of Newcastle, Australia

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Egert, 2010[67]
RCT parallel, Germany
Baseline=47 Analytic N=37 (Attrition: 21%)
 	
Participant characteristics at baseline: Healthy technical school students, ~23 y, 68% female, BMI ~21.5
 	
Summary of findings:
There was a significant between-group difference in change in total cholesterol among participants who consumed a high-MUFA, low-fat (~15%E MUFA) and a high-MUFA, high-fat (~20%E MUFA), over a 4 week period in young adults. No significant between-group differences were found in LDL- and HDL cholesterol and triglycerides.
	Intervention and comparator:
	• High-fat (40%E) MUFA-rich diet: 42.5g/day plant oils, 32.7g/day margarine (n=18)
	  • ~10% SFA, 20%E MUFA, ~9% PUFA
	• Low-fat (29%E) MUFA-rich diet: 25.7g/day plant oils, 24.1g/day margarine (n=19)
	  • ~8% SFA, ~15%E MUFA, ~7% PUFA
	
	• *All meals provided by researchers. Intervention diets isocaloric, with consistent fatty acid content: SFA, MUFA, and PUFA (26%, 51% and 23% total fatty acids, respectively) and consistency in type of carbohydrate content.*
	• *Principle source of fat: rapeseed oil and high-oleic sunflower oil and a MUFA-rich commercial margarine (MUFA, 48% of total fatty acids; 64 g fat/100 g) incorporated in sauces, desserts, curd and salad dressing*
	
	Duration of intervention: 4 wk (2 wk high-fat, high-SFA run-in diet)
	Compliance: Assessed via 3-day dietary records, reported to be high; no significant change in body weight
	
	Dietary composition of Low-fat vs High fat diets, Mean (SD):
	SFA (%E): 7.2 (0.2) vs 9.9 (0.4)
	MUFA (%E): 13.9 (0.4) vs 19.8 (0.3)
	PUFA (n-6) (%E): 5.3 (0.1) vs 7.0 (0.2)
	PUFA (n-3) (%E): 0.9 (0.0) vs 1.6 (0.1)
	Cholesterol (mg/MJ): 15.4 (0.9) vs 17.8 (0.9), P=NS
	No significant difference in fiber and antioxidants.
		Outcomes and assessment methods:
		Fasting blood lipids: Prewash-in, after wash-in, after 2 wk and after 4 wk of the study diet.
		
		Repeat measures with time (post wash-in, intervention diet wk 2 and wk 4) and group (high and low fat diet groups)
		
		TC, mmol/L, Mean (SD)
		Baseline (after run-in), 4 wk levels
		High-fat: 4.54 (0.75), 4.10 (0.68)
		Low-fat: 4.93 (0.66), 4.38 (0.77)
		Time*group interaction: P=0.037
		
		LDL, mmol/L
		High-fat vs low-fat: NS
		
		HDL, mmol/L
		High-fat vs low-fat: NS
		
		Triglycerides, mmol/L
		High-fat vs low-fat: NS
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• Attrition >10%
			• No preregistered statistical analysis plan
			
			Funding sources:
			German Union for the Promotion of Oil- and Protein-containing Plants

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Farajbakhsh, 2019[70]
RCT parallel, Iran
Baseline N=75 Analytic N=70 (Attrition: 7%)
 	
Participant characteristics at baseline: Adults (~64% female) ~49y of age with metabolic syndrome and who were (on average) with overweight or obesity.
 	
Summary of findings:
In adults with metabolic syndrome, consumption of sesame oil for 8 weeks (which increased MUFA intake) resulted in greater improvements in total blood and HDL cholesterol and triglycerides compared to sunflower oil (which increased PUFA intake).
	Intervention and comparators:
	• Sesame Oil enriched with Vitamin E (Vit E) (400mg), 30mL/d (n=23)
	  • SFA: 13%, MUFA: 43% (C18:1 43%), PUFA: 44%, LA: 42%, ALA: 1.2%
	• Sesame Oil, 30mL/d (n=24)
	  • SFA: 13%, MUFA 44% (C18:1 43%), PUFA: 44%, LA: 41%, ALA: 1.1%
	• Sunflower Oil, 30mL/d (n=23)
	  • SFA: 13%, MUFA: 31% (C18:1 31%), PUFA: 56%, LA: 54%, ALA: 0.2%
	
	• *Participants instructed to add test oils to their salad, rice, or other food components. All participants received dietary recommendations to consume 55% CHO, 15% protein, and 30% fat*
	
	Duration of intervention: 8 wk (2 wk run-in)
	Compliance: Monitored via weekly phone call or in person
	
	Total dietary intake at 8 wk for Sesame Oil + Vit E vs Sesame Oil vs Sunflower Oil, Mean (SD), %E:
	SFA: 13.4 (0.1) vs 12.8 (0.7) vs 12.8 (0.7), P=NS
	MUFA: 12.5 (0.8) vs 11.2 (0.2) vs 6.2 (0.2), P=0.02
	PUFA: 5.7 (0.4) vs 5.1 (0.2) vs 12.1 (0.2), P=0.01
	n-3 PUFA: 1.19 (0.4) vs 1.24 (0.3) vs 1.3 (0.2), P=NS
	Cholesterol: NR
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and at end of 8 wk.
		
		Comparing change in blood lipids
		
		TC, mg/dL, Mean (SD), Baseline, 8wk, change
		Sesame Oil + Vit E: 190.5 (34.7), 173.2 (32.1); -17.3
		Sesame Oil: 190.7 (53.9), 177.2 (45.3); -13.5
		Sunflower Oil: 186.8 (41.1), 189.8 (40.4); 3
		P=0.005 (pairwise comparisons NR)
		
		LDL, mg/dL
		Sesame Oil + Vit E vs Sesame Oil vs Sunflower Oil: P=NS
		
		HDL, mg/dL, Mean (SD), Baseline, 8wk, change
		Sesame Oil + Vit E: 34.8 (5.7), 36.8 (5.0); 4
		Sesame Oil: 35.9 (7.2), 36.4 (6.2); 0.5
		Sunflower Oil: 37.1 (8.4), 37.3 (7.6); 0.2
		P=0.002 (pairwise comparisons NR)
		
		Triglycerides, mg/dL Mean (SD) Baseline, 8wk, change
		Sesame Oil + Vit E: 149.3 (35.1), 128.1 (30.8); -21.2
		Sesame Oil: 170.9 (72.5), 157.7 (70.0); -13.2
		Sunflower Oil: 138.7 (60.4), 147.6 (69.7); 8.9
		P=0.001 (pairwise comparisons NR)
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• Information on compliance NR
			• No preregistered statistical analysis plan
			
			Funding sources:
			Shiraz University of Medical Sciences

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Gagliardi, 2010[71] **RCT parallel, Brazil** Baseline N=75 Analytic N=53 (Attrition: 29%) **Participant characteristics at baseline:** Participants (62% women) aged ~54 years with metabolic syndrome. No differences in clinical and biochemical parameters between groups **Summary of findings:** *Participants who consumed butter, compared to no-trans-fat margarine, did not have significant differences in total blood, LDL, HDL cholesterol, and triglycerides.*	**Intervention and comparator:** • Butter (n=18, 18 g/day): 67% SFA, 27% MUFA, 2% PUFA, 1% *trans* fat • No-*trans*-fat margarine (n=16, 36 g/day): 25% SFA, 22% MUFA, 53% PUFA, 0.5% *trans* fat Duration of intervention: 5 wk Compliance: telephone calls; compliance defined as minimum consumption of at least 30 days supply of spread product provided and less than 3 days of consecutive non-consumption of the spread **Dietary intake for Intervention vs Control at 5 wk, Mean (SD), g/day:** SFA: 12.9 (5.8) vs 9.8 (4.1) MUFA: 10.6 (4.3) vs 9.0 (3.0) PUFA: 6.5 (2.5) vs 7.5 (4.2) Cholesterol (mg/day): 212 (98) vs 326 (230) Other components of diet differed significantly: NR	**Outcomes and assessment methods**: Fasting blood lipids at 5 wk follow-up Difference in change **TC**, mg/dL, Median (min, max) Butter vs No-*trans*-fat margarine: NS **LDL**, mg/dL, Median (min, max) Butter vs No-*trans*-fat margarine: NS **HDL**, mg/dL, Median (min, max) Butter vs No-*trans*-fat margarine: NS **Triglycerides**, mg/dL, Median (min, max) Butter vs No-*trans*-fat margarine: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • Attrition >10% • No preregistered statistical analysis plan **Funding sources:** National Research and Scientific Council, Fundacao de Amparo a Pesquisa do Estado de Sao Paulo, Proap; USDA; spread provided by Unilever Corporation and Laticinios Aviacao-Goncalves Salles SA

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Grieger, 2014[73] **RCT parallel, Australia** Baseline N=83 Analytic N=80 (Attrition: 4%) **Participant characteristics at baseline:** Participants 64 years and older, BMI ~26, with slightly elevated blood lipids at baseline **Summary of findings:** *Fish intake, compared to red meat intake, did not affect total blood cholesterol, LDL, HDL cholesterol or triglyceride levels.*	**Intervention and comparator:** • Fish (n=43): 8 servings of mixed fish per 2 weeks (~800 mg/day of EPA+DHA); total fat from food: 7.0 g/day • Control (n=37): usual diet + 8 servings (68 g/day) of red meat per 2 weeks (~17 mg/day EPA; 4 mg/day DHA): total fat from food: 4.7 g/day Duration of intervention: 8 wk Compliance: participant interviews; 3-day weighed food records at wk 7; compliance met **Dietary intake from study fish or study red meat for Intervention (Fish) vs Control at wk 7, Mean (SD):** SFA (g): 2.6 (2.4) vs 3.4 (2.6) MUFA: NR very long chain n-3 PUFA (mg/day): 1,399 (1,244) vs 80 (60) Cholesterol: NR Other components of diet differed significantly: None **Overall dietary intake for Intervention (Fish) vs Control at wk 7, Mean (SD), g/day unless noted:** SFA: 28 (2) vs 28 (2), P=NS MUFA: 30 (2) vs 24 (1), P<0.05 PUFA: 13 (1) vs 9(1), P<0.05 Cholesterol: 271 (17) vs 288 (26), P=NS very long chain n-3 PUFA (mg): 1208 (156) vs 39 (6), P<0.01 EPA (mg): 446 (60) vs 11 (1), P<0.01 DPA (mg): 126 (19) vs 13 (2), P<0.01 DHA (mg): 636 (82) vs 15 (4), P<0.01 Other components of diet differed significantly: Zinc (greater in fish group), P<0.01	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 8 wk follow-up Levels at 8wk follow-up **TC**, mmol/L, Geometric Mean (SE) Fish vs control: NS **LDL**, mmol/L, Geometric Mean (SE) Fish vs control: NS **HDL**, mmol/L, Geometric Mean (SE) Fish vs control: NS **Triglycerides**, mmol/L, Geometric Mean (SE) Fish vs control: NS	**Model adjustments:** None **Limitations:** • No information on randomization of allocation sequence • No preregistered statistical analysis plan **Funding sources:** Australian Seafood Corporation Research Center

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Hagen, 2016[74] **RCT parallel, Norway** Baseline N=45 Analytic N=38 (Attrition: 16%) **Participant characteristics at baseline:** Participants aged 20-35y with normal BMI <25 **Summary of findings:** *Participants who consumed fatty fish, compared to lean meat, had significantly higher HDL cholesterol and triglycerides but there was no difference in total or LDL cholesterol. Participants who consumed fatty fish, compared to lean fish, had significantly higher HDL cholesterol. There were no differences between lean fish vs lean meat consumers in total blood cholesterol, LDL or HDL, cholesterol or triglycerides.*	**Intervention and comparators:** • Lean fish (cod) (n=14): 750 g (5 meals of 150 g) • Fatty fish (salmon) (n=15): 750 g (5 meals of 150 g) • Lean meat (chicken) (n=16): 750 g (5 meals of 150 g) Duration of intervention: 4 wk Compliance: participant interviews about intake; participants who did not comply with protocol were withdrawn from study **Dietary intake for Lean fish, fatty fish, lean meat, respectively, Median (25th-75th), g/day:** SFA (%E): 11 (9, 17), 14 (11, 16), 13 (10, 20), P=0.45 MUFA (%E): 11 (8, 16), 12 (10, 15), 13 (9, 17), P=0.21 PUFA: 5 (3, 9), 7 (5, 12), 6 (5, 9), P=0.55 Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4 wk follow-up Difference in change **TC**, mmol/L, Median (25th-75th) Lean fish vs fatty fish vs lean meat: NS **LDL**, mmol/L, Median (25th-75th) Lean fish vs fatty fish vs lean meat: NS **HDL**, mmol/L, Median (25th-75th) Lean fish: 1.6 (1.4, 1.9) Fatty fish: 1.7 (1.4, 2.0) Lean meat: 1.4 (1.3, 2.1) Lean fish vs lean meat: NS **Fatty fish vs lean meat: P=0.025** **Fatty fish vs lean fish: P=0.033** **Triglycerides**, mmol/L, Median (25th-75th) Lean fish: 0.64 (0.43, 0.80) Fatty fish: 0.73 (0.55, 0.84) Lean meat: 0.66 (0.50, 1.26) Lean fish vs lean meat: NS **Fatty fish vs lean meat: P=0.018** Fatty fish vs lean fish: NS	**Model adjustments:** None **Limitations:** • No information on randomization of allocation sequence • Missing data was different between groups • No preregistered statistical analysis plan **Funding sources:** Bergen Medical Research Foundation; KG Jebsen Center for Diabetes Research; fish and chicken from ICA Maxi;

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Hallund, 2010[75] **RCT parallel, Denmark** Baseline N=75 Analytic N=68 (Attrition: 9%) **Participant characteristics at baseline:** Healthy male aged 40-70 y with no history of CVD or diabetes and similar BMI, energy intake, protein, carbohydrate and fiber intake at baseline **Summary of findings:** *Consumption of farmed trout on marine feed, farmed trout on vegetable feed or chicken and rapeseed oil did not result in changes in total cholesterol, LDL, HDL cholesterol or triglycerides.*	**Intervention and comparators:** • Farmed trout on marine feed (150 g), daily meal, n=23 • Farmed trout on vegetable feed (150 g), daily meal, n=23 • Chicken (150 g) + 3.5 g rapeseed oil (to provide same amount of fat), daily meal, n=22 • *Weekly meal plan provided by researchers* **Fatty acid composition of marine trout, vegetable trout and chicken (%):** SFA: 25 (0.2) vs 15.2 (0.3) vs 20.8 (1.4) MUFA: 32.0 (1.0) vs 51.8 (1.0) vs 47.2 (1.8) PUFA: 35.7 (1.0) vs 30.3 (0.8) vs 32.1 (2.9) LA: 3.7 (0.1) vs 15.1 (0.2) vs 22.1 (1.7) AA: 0.7 (0.04) vs 0.8 (0.04) vs 1.8 (0.3) ALA: 1.2 (0.02) vs 3.5 (0.1) vs 3.2 (0.4) EPA: 6.9 (0.2) vs 1.3 (0.1) vs 0.3 (0.04) DHA: 16.3 (0.7) vs 5.1 (0.8) vs 0.5 (0.1) DPA: 2.6 (0.04) vs 0.5 (0.04) vs 0.8 (0.1) Duration of intervention: 8 wk Compliance: study diaries; 99% compliant **Dietary intake by intervention groups:** NR	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 8 wk follow-up Levels at 8wk follow-up, mixed ANOVA **TC**, mmol/L, Mean (SEM) Marine trout vs vegetable trout vs chicken: NS **LDL**, mmol/L, Mean (SEM) Marine trout vs vegetable trout vs chicken: NS **HDL**, mmol/L, Mean (SEM) Marine trout vs vegetable trout vs chicken: NS **Triglycerides,** mmol/L, Mean (SEM) Marine trout vs vegetable trout vs chicken: NS	**Model adjustments:** Baseline values **Limitations:** • No information on randomization of allocation sequence • No preregistered statistical analysis plan **Funding sources:** Danish Council for Strategic Research

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Iggman, 2014[78] **RCT parallel, LIPOGAIN, Sweden** Baseline N=39 Analytic N=39 (Attrition: 0%) **Participant characteristics at baseline:** Healthy, predominantly White (90%) adults (31% female) ~27y of age without overweight or obesity **Summary of findings:** *In healthy, young adults participating in an overfeeding trial, consumption of muffins high in n-6 PUFA from sunflower oil for 7 weeks (which increased PUFA intake) did not result in changes to blood lipids significantly different from changes in lipids from consumption of muffins high in SFA from palm oil (which increased SFA intake).*	**Intervention and comparator:** • Muffins high in n-6 PUFA (mainly LA) from refined sunflower oil, ~4, 240kcal muffins/d (n=19) • Muffins high in SFA from refined palm oil (mainly palmitic acid), ~4, 240kcal muffins/d (n=20) • *Both interventions aimed to induce 3% weight gain by end of study; Number of muffins/d added to habitual diet modulated to control weight gain* • *Each muffin contained 51%E fat* Types of fat in refined sunflower oil vs refined palm oil (%), previously reported: SFA: 11% vs 54% MUFA: 24% vs 37% PUFA: 65% vs 9% C16:0: 6% vs 48% Oleic acid: 24% vs 37% LA: 65% vs 9% ALA: 0.08% vs 0.23% Duration of intervention: 7 wk Compliance: Monitored via weekly phone call or in person; "good compliance" with diets **Change in dietary intake for PUFA muffin vs SFA muffin, Mean (SD), %E:** SFA: -1.6 (2.8) vs 4.9 (2.8), P=0.0001 MUFA: 0.9 (2.7) vs 3 (2.7), P=0.026 PUFA: 7.9 (2.1) vs 0.3 (1.3), P=0.0001 n-3 PUFA: 1.19 (0.4) vs 1.24 (0.3) vs 1.3 (0.2), P=NS Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids: Measured at baseline and at end of 7 weeks. Comparing between-group differences in change in blood lipids **TC**, mmol/L PUFA muffin vs SFA muffin: P=NS **LDL**, mmol/L PUFA muffin vs SFA muffin: P=NS **HDL**, mmol/L PUFA muffin vs SFA muffin: P=NS **Triglycerides,** mmol/L PUFA muffin vs SFA muffin: P=NS	**Model adjustments:** None **Limitations:** • No preregistered statistical analysis plan **Funding sources:** Swedish Research Council; Swedish Society of Medicine; Lennanders Foundation; Uppsala-Orebro Regional Research Council

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Jaakkola, 2017[81] **RCT parallel, Finland** Baseline N=2161 Analytic N=1204 (Attrition: 44%) **Participant characteristics at baseline:** 100% White parents of STRIP participants aged ~31y at baseline ***Summary of findings:*** *Intervention mothers, compared to control mothers, had significantly lower total blood cholesterol and LDL cholesterol after a dietary counseling intervention targeting the participants' child between ages 7mo to 20 years. These findings were not significant for fathers. There were no differences in HDL cholesterol and triglycerides between groups for mothers and fathers.*	**Intervention and comparator:** • Dietary counseling aimed to decrease saturated fat and increase unsaturated fat intake of the child; additionally, children were encouraged to consume more vegetables, fruits, berries, and whole-grain products and to lower salt intake • Usual care Duration of intervention: Child's age at 7 months to 20 years Compliance: 1-day food record recorded biennially between child's age 9 to 19 years **Dietary intake for Intervention vs Control, Mean (SE):** SFA: Mothers: 12.0 (0.18) vs 13.8 (0.16)%E, P<0.0001 Fathers: 12.3 (0.20) vs 13.9 (0.18)%E, P<0.0001 MUFA: Mothers: 12.2 (0.15) vs 11.6 (0.14)%E, P=0.01 Fathers, 12.8 (0.19) vs 12.2 (0.16)%E, P=0.04 PUFA: Mothers: 6.1 (0.08) vs 5.4 (0.07)%E, P<0.0001 Fathers: 6.4 (0.10) vs 5.8 (0.09)%E, P=0.0001 P/S ratio: Mothers: 0.56 (0.01) vs 0.44 (0.01), P<0.0001 Fathers: 0.56 (0.01) vs 0.47 (0.01), P<0.0001 Other components that differed between groups: Protein intake was higher in intervention fathers compared to control fathers (18.1 vs 17.6%E, P=0.02)	**Outcomes and assessment methods:** Fasting blood lipids: measured repeatedly during follow-up between child's age 9-19 years Levels at follow-up between the child's ages of 9 to 19 years **TC**, mmol/L, Mean (SE) Mothers: **Intervention: 5.01 (0.04)** **Control: 5.14 (0.04)** **P=0.03** Fathers: Intervention vs Control: NS **HDL**, mmol/L, Mean (SE) Mothers: Intervention vs Control: NS Fathers: Intervention vs Control: NS **LDL**, mmol/L, Mean (SE) Mothers: **Intervention: 3.18 (0.04)** **Control: 3.30 (0.03)** **P=0.02** Fathers: Intervention vs Control: NS **Triglycerides**, mmol/L, Mean (SE) Mothers: Intervention vs Control: NS Fathers: Intervention vs Control: NS	**Model adjustments:** Apo B cholesterol at baseline (for total cholesterol and LDL cholesterol for mothers) **Limitations:** • No preregistered statistical analysis plan **Funding sources:** The Academy of Finland; Finnish Cardiac Research Foundation, Juho Vainio Foundation; Finnish Cultural Foundation; Sigrid Juselius Foundation; Yrjo Jahnsson Foundation

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Jebb, 2010[82] **RCT parallel, RISCK trial, U.K.** Baseline=720 Analytic N=548 (Attrition: 24%) **Participant characteristics at baseline**: At risk for metabolic syndrome, ~52 y, 58% female, BMI ~28.5, 80% White, 80% central obesity, 25.5% low HDL, 72% high-TC, no CVD, no type 2 diabetes **Summary of findings:** *A low fat diet or a high monounsaturated fat diet consumed for 24 weeks, compared to a high saturated fat diet, significantly decreased total and LDL cholesterol in adults at risk for metabolic syndrome. The low fat diet lowered HDL cholesterol significantly more than diets high in monounsaturated fat or high in saturated fat. No significant differences in triglyceride changes were observed between groups.*	**Intervention and comparators:** • High-SFA, high glycemic index (HS/HGI) (n=85) • High-MUFA and HGI (HM/HGI) (n=111) • HM and low glycemic index (HM/LGI) (n=116) • Low-fat and HGI (LF/HGI) (n=116) • LF and LGI (LF/LGI) diets (n=121) **Analysis by fat type:** • High-SFA: Fat 38%E, CHO 45%E, SFA 16.6%E, MUFA 12%E (n=85) • High-MUFA: Fat 38%E, CHO 45%E, SFA 10%E, MUFA 20%E (n=227) • Low-fat: Fat 28%E, CHO 55%E, SFA 10%E, MUFA 12%E (n=236) • *Isocaloric diets, key sources of fat (i.e., spreads, cooking oils, and margarine) and carbohydrates (i.e., bread, pasta, rice, and cereals) provided by researchers with additional dietary information tailored to the study group* Duration of intervention: 24 wk (4 wk run-in on HS/HGI diet) Compliance: Assessed via food diaries; small decrease in weight with LF diet (~1kg); GI was ~8 GI points lower in LGI diets than the HGI diets compared to the target of 11–13 GI points. **Change in energy source from HS/HGI diet (ref) , Mean (95% CI), HS/HGI vs HM/LGI vs LF/HGI vs LF/LGI** HS/HGI Mean (SD) (ref) (%E): SFA: 16.5 (3.0), MUFA: 11.6 (2.1), PUFA: 5.8 (1.7), CHO: 43.0 (6.5) SFA (%E): -0.5 (-1.5, 0.6)a vs -7.0 (-7.9, -6.0)b vs -6.9 (-7.8, -6.0)b vs -7.3 (-8.3, -6.4)b,c vs -8.2 (-9.1, -7.3)c, a vs b vs c P<0.05 MUFA (%E): -0.1 (-1.2, 1.0)a vs 4.6 (3.6, 5.6)b vs 4.7 (3.7, 5.6)b vs -1.8 (-2.8, -0.8)c vs -1.9 (-2.8, -1.0)c, a vs b vs c P<0.05	**Outcomes and assessment methods**: Fasting blood lipids: At baseline and following the feeding period. **TC**, mmol/L, % Change from baseline. Mean (95% CI): **HS/HGI: -1.2 (-3.1, 0.6)** **HM/HGI: -3.9 (-5.7, -2.1)** **HM/LGI: -7.0 (-8.9, -5.0)** **LF/HGI: -5.7 (-7.4, -4.0)** **LF/LGI: -6.7 (-8.5, -4.8)** **Between groups P=0.0006** **HS/HGI vs HM/HGI, HM/LGI, LF/HGI, LF/LGI: P<0.001 (lower TC in comparator than HS/HGI)** **High SFA vs High MUFA: P=0.001** **High SFA vs Low-fat: P=0.001** High MUFA vs Low-fat: NS **LDL**, mmol/L, % Change from baseline, Mean (95% CI): **HS/HGI: -0.6 (-3.4, 2.1)** **HM/HGI: -5.2 (-7.8, -2.6)** **HM/LGI: -7.8 (-10.2, -5.5)** **LF/HGI: -7.0 (-9.2, -4.8)** **LF/LGI: -7.0 (-9.5, -4.5)** **Between groups: P=0.0015** **HS/HGI vs HM/HGI, HM/LGI, LF/HGI, LF/LGI: P<0.001 (lower LDL in comparator than HS/HGI)** **High SFA vs High MUFA: P=0.001** **High SFA vs Low-fat: P=0.001** High MUFA vs Low-fat: NS **HDL**, mmol/L, % Change from baseline, Mean (95% CI) HS/HGI: -2.0 (-4.3, 0.3) HM/HGI: -2.7 (-4.6, -0.9) HM/LGI: -4.3 (-6.3, -2.2) LF/HGI: -5.9 (-7.7, -4.0) LF/LGI: -7.2 (-8.9, -5.5)	**Model adjustments:** Center, ethnicity, baseline waist, baseline age, baseline HDL cholesterol, sex, and diet, weight change **Limitations:** • Attrition >10% • Study preregistration could not be located **Funding sources:** U.K. Food Standards Agency

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
	PUFA (%E): 0.0 (-0.7, 0.7)a,c vs 0.8 (0.2, 1.4)a,b vs 1.1 (0.5, 1.7)b vs -0.6 (-1.2, 0.0)c vs -0.7 (-1.4, -0.2)c, a vs b vs c P<0.05 CHO (%E): -1.0 (-3.1, 1.0)a vs 1.9 (0.1, 3.7)b vs 1.6 (-0.2, 3.4)b vs 8.1 (6.3, 9.9)c vs 8.5 (6.8, 10.2)c, a vs b vs c P<0.05 Glycemic index: 0.5 (-0.7, 1.8)a vs -0.2 (-1.3, 1.0)a vs -8.3 (-9.4, -7.2)b vs 0.9 (-0.3, 2.0)a vs -7.2 (-8.3, -6.1)b, a vs b vs c P<0.05	**Between groups: P=0.0009** High SFA vs High MUFA: NS **High SFA vs Low-fat: P=0.001** **High MUFA vs Low-fat: P=0.002** **Triglycerides,** mmol/L, %Change from baseline, Mean (95% CI): Between groups: NS	

Kalgaonkar, 2011[84]
RCT parallel, U.S.
Baseline N=36 Analytic N=31 (Attrition: 14%)
 	
Participant characteristics at baseline: Women ~33y of age (predominantly white) with PCOS and with overweight or obesity.
 	
Summary of findings:
In women with PCOS, consumption of walnuts for 6 weeks (which increased LA and ALA intake) did not significantly change blood lipids compared to consumption of almonds.
	Intervention and comparator:
	• Walnuts, 36g/day/1800kcal daily (n=17)
	  • Sources: walnuts
	• Almonds, 46g/day/1800kcal (n=14)
	  • Sources: almonds
	
	• *Both groups replaced 31 g/day dietary fat/1800kcal with nuts; counseled by study dietitian to maintain fat and energy intake constant*
	
	Duration of intervention: 6 wk
	Compliance: Assessed via return of unused portions of nuts; Participants consumed all the nuts.
	
	Dietary intake at 6 wk for Walnuts vs Almonds, Mean (SE), g/d, Comparing change between groups:
	SFA: 32 (3) vs 29 (5), P=NS
	MUFA: 19 (3) vs 35 (3), P=NS
	LA: 15.0 (1.0) vs 7.5 (0.6), P=0.0163
	ALA: 3.25 (0.3) vs 0.34 (0.07), P=0.0002
	Cholesterol (mg/d): 167 (30) vs 225 (26), P=NS
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and 4 wk
		
		Comparing change from baseline between groups
		
		TC, mmol/L
		Walnut vs Almond: P=NS
		
		LDL, mmol/L
		Walnut vs Almond: P=NS
		
		HDL, mmol/L
		Walnut vs Almond: P=NS
		
		Triglycerides, mmol/L
		Walnut vs Almond: P=NS
			Model adjustments:
			Baseline blood lipid
			
			Limitations:
			• No information on randomization of allocation sequence
			• Differential loss to follow-up with no information on whether results were robust to missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Center for Complementary and Alternative Medicine; ALSAM Foundation; UC Davis Clinical and Translational Science Center

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Khaw, 2018[88]
RCT parallel, U.K.
Baseline N=96 Analytic N=91 (Attrition: 5%)
 	
Participant characteristics at baseline: Participants (~67% women) aged 50-75 years, 98% European Caucasian with no history of cancer, CVD or diabetes
 	
Summary of findings:
Total cholesterol significantly increased in the butter group compared to the olive oil group. LDL cholesterol significantly increased in the butter group compared to the coconut oil and olive oil groups. HDL cholesterol significantly decreased in the butter group compared to the coconut oil group and significantly increased in the coconut oil vs olive oil group.
	Intervention and comparators:
	• Extra Virgin Coconut Oil (50 g/day), n=28
	  • 94% SFA: 48% lauric acid (C12:0), 19% myristic acid (C14:0), 9% palmitic acid (C16:0); 5% MUFA; 1% PUFA
	• Butter (50 g/day), n=33
	  • 66% saturated fat: 40% palmitic acid (C16:0) and stearic (C18:0); 26% MUFA; 3% PUFA (2% LA and 1% ALA); 4% *trans*-fat
	• Extra Virgin Olive Oil (50 g/day), n=30
	  • 19% SFA, 68% MUFA (oleic acid), 13% PUFA (LA); 14% PUFA
	
	• *Instructed to add test oils to usual diet*
	
	Duration of intervention: 4 wk
	Compliance: online 24-hour DietWebQ, defined as >75% adherence
	
	Dietary intake for intervention groups: NR
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk follow-up
		
		TC, mmol/L, Mean (SD), Difference
		Butter vs coconut oil: NS
		Butter vs olive oil: 0.38 (0.11, 0.64) (increased in butter)
		Coconut oil vs olive oil: NS
		
		LDL, mmol/L, Mean (SD), Difference
		Butter vs coconut oil: 0.45 (0.22, 0.68), P<0.0001 (increased in butter)
		Butter vs olive oil: 0.40 (0.17, 0.62), P<0.0001 (increased in butter)
		Coconut oil vs olive oil: NS
		
		HDL, mmol/L, Mean (SD), Difference
		Butter vs coconut oil: -0.19 (-0.31, -0.06) (increased in coconut oil)
		Butter vs olive oil: NS
		Coconut oil vs olive oil: 0.17 (0.04, 0.29) (increased in coconut oil)
		
		Triglycerides, mmol/L, Mean (SD), difference
		Butter vs coconut oil: NS
		Butter vs olive oil: NS
		Coconut oil vs olive oil: NS
			Model adjustments:
			Age, sex, BMI at baseline
			
			Limitations:
			• No preregistered statistical analysis plan
			
			Funding sources:
			Broadcasting Corporation; University of Cambridge

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Klempel, 2013[89] **RCT parallel, U.S.** Baseline N=35, Analytic N=32 (Attrition: 9%) **Participant characteristics at baseline:** Females ~43y of age with obesity with no history of cardiovascular disease **Summary of findings:** *In ~ 43y old women with obesity participating in a weight loss trial with alternate day fasting, intake of a high fat diet for 8 weeks did not significantly, change blood lipids compared to intake of a low fat diet.*	**Intervention and comparator:** • High Fat: 45% energy from total fat (14% SFA, 20% MUFA, 11% PUFA), n=15 • Low Fat: 25% energy from total fat (6% SFA, 13% MUFA, 6% PUFA), n=17 • *Both groups put on weight loss diet and practiced alternate day fasting (25% energy on fast days, 125% energy on feed days).* • *All meals provided by study* Duration of intervention: 10 wk (2 wk weight maintenance, 8 wk weight loss) Compliance: NR **Diet composition for High Fat vs Low Fat, %E:** SFA: 14% vs 6% MUFA: 20% vs 13% PUFA: 11% vs 6% Cholesterol: NR Other components of diet differed significantly: Carbohydrates (40% vs 60%)	**Outcomes and assessment methods**: Fasting blood lipids: Assessed at study weeks 1, 3, and 10, measured in duplicate Comparing % change **TC,** mg/dL High fat vs Low fat: P=NS **LDL,** mg/dL High fat vs Low fat: P=NS **HDL,** mg/dL High fat vs Low fat: P=NS **Triglycerides,** mg/dL High fat vs Low fat: P=NS	**Model adjustments:** Time by treatment interaction **Limitations:** • Energy restricted diet • No information on randomization of allocation sequence • No preregistered statistical analysis plan **Funding sources:** Departmental grant, Kinesiology and Nutrition, University of Illinois, Chicago

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Kruse, 2015[92]
RCT parallel, Germany
Baseline N=18 Analytic N=18 (Attrition: 0%)
 	
Participant characteristics at baseline: 100% overweight or obese men aged ~55 years with BMI ~29
 	
Summary of findings:
Consumption of 50 g/day of rapeseed/canola oil, compared to cold-pressed extra virgin olive oil, did not result in significant differences between groups in total blood, LDL- and HDL-cholesterol, and triglycerides among overweight adults.
	Intervention and comparator:
	• Refined rapeseed/canola oil (RA) (50 g/day); higher in PUFA, especially ALA and n-6 LA; not to be used for baking or frying
	  • Types of fat in oil: NR
	• Cold-pressed extra virgin olive oil (OL) (50 g/day); not to be used for baking or frying
	  • Types of fat in oil: NR
	
	Duration of intervention: 4 wk
	Compliance: 3-day food record at baseline and after 2nd week of intervention
	
	Dietary intake for Intervention vs Control: NR
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk follow-up
		
		Comparing change from baseline
		
		TC, mmol/L
		OL vs RA: NS
		LDL, mmol/L
		OL vs RA: NS
		HDL, mmol/L
		OL vs RA: NS
		Triglycerides, mmol/L
		OL vs RA: NS
			Model adjustments:
			None
			
			Limitations:
			• No preregistered statistical analysis plan
			
			Funding sources:
			Union zur Forderung von Oel-und Proteinpflanzen e. V., Germany; German Institute of Human Nutrition, Potsdam-Rehbruecke

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Lim, 2010[93] **RCT parallel, Australia** Baseline N=113 Analytic N=69 (Attrition: 49%) **Participant characteristics at baseline:** Participants (80% female) ~47 years who were overweight or obese with at least 1 CVD risk factor, no CVD, no diabetes **Summary of findings:** *After 15mo, intervention groups vs control had improved total cholesterol, LDL cholesterol, SBP, and DBP. However, there were no significant differences between intervention groups.*	**Intervention and comparators:** • Very Low Carbohydrate (VLC) diet: 35%E PRO, 60%E FAT, 20%E SFA, 4%E CHO • Very Low Fat (VLF) diet: 20%E PRO, 10%E FAT, 3%E SFA, 70%E CHO • High Unsaturated Fat (HUF) diet: 20%E PRO, 30%E FAT, 6%E SFA, 8%E PUFA, 50% CHO • Control: No dietary intervention received, intake NR • *All diets (except control) were energy-restricted and isocaloric with one another* Duration of intervention: 15mo (3 mo of intensive support followed by 12 mo of minimal support) Compliance: measured at 3, 6, 9, 12, and 15mo; lower compliance after 3 months **Dietary intake for VLC vs VLF vs HUF at 3mo,/15mo, Mean (SD), %E:** SFA: 17.7 (1.01)/13.2 (0.8), 5.1 (0.30)/10.7 (0.8), 6.0 (0.32)/9.9 (0.9) MUFA: 26.2 (1.41)/15.1 (1.4), 3.6 (0.21)/10.5 (0.9), 12.3 (0.51)/11.5 (0.6) PUFA: 6.5 (0.28)/5.5 (0.5), 1.8 (0.16)/4.3 (0.5), 7.2 (0.30)/5.6 (0.7) Cholesterol: 782.7 (24.7)/404.1 (58.1), 123.9 (5.4)/246.4 (31.4), 163.2 (17.2)/273.0 (33.1) Other components of diet differed significantly: CHO (%E): 12.4 (3.38)/36.5 (2.9), 66.0 (0.92)/50.5 (1.8), 48.7 (1.07)/43.2 (2.7) PRO (%E): 30.5 (0.91)/23.9 (1.5), 20.3 (0.55)/19.6 (0.9), 21.4 (0.51)/24.4 (1.66) FAT (%E): 54.3 (2.53)/37.1 (2.4), 12.5 (0.59)/28.3 (1.8), 28.0 (0.88)/30.3 (1.7)	**Outcomes and assessment methods:** Fasting blood lipids,: Measured at baseline, 3mo, 15mo Changes from baseline to 3mo (VLC, VLF, HUF), 15mo (VLC, VLF, HUF, control), different letters significantly different **TC**, mmol/L, Mean (SD) 3mo: NS differences between groups **15mo: Control: 0.5 (0.8)** **vs VLC: -0.4 (0.8), P<0.05** **vs VLF: -0.3 (0.8), P<0.05** **vs HUF: -0.3 (1.2), P<0.05** **P=0.042** NS between VLC, VLF, vs HUF **HDL**, mmol/L, Mean (SD) **3mo: Control: 0.1 (0.2) (NS)** **VLC: 0.1 (0.2)** **vs VLF: -0.1 (0.2), P<0.05** **vs HUF: -0.1 (0.2), P=0.025** NS between VLF vs HUF and between control vs all groups 15mo: NS differences between groups **LDL**, mmol/L, Mean (SD) **3mo: VLC: 0.3 (1.0)** **vs VLF: -0.4 (0.6), P<0.05** **vs HUF: -0.6 (1.1), P<0.05** **vs control: 0.4 (0.7), P<0.05** **P=0.015** **NS between VLF, HUF vs control** **15mo: -0.3 (0.7)a, -0.3 (0.7)a, -0.1 (1.1)a, 0.4 (0.7)b, p=0.022** **Triglycerides**, mmol/L, Mean (SD) **3mo: -0.7 (0.6)a, -0.1 (0.6)b, -0.2 (0.5)b, p=0.001** 15mo: NS differences between groups	**Model adjustments:** None **Limitations:** • Weight loss trial • No description of the randomization process and baseline imbalances in TC, and BP • Potential bias due to missing data • No preregistered statistical analysis plan **Funding sources**: National Heart Foundation, Australia and CSIRO Health Sciences and Nutrition

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Lucci, 2016[95] **RCT parallel, Colombia** Baseline N=160 Analytic N=145 (Attrition: 9%) **Participant characteristics at baseline:** Participants aged 50 years or older, mean BMI ~28, without prior CVD; normal to high LDL cholesterol, total cholesterol and triglycerides values at baseline; baseline blood lipid values did not differ between groups at baseline **Summary of findings:** *Consumption of extra virgin olive oil, compared to hybrid palm oil-rich diet, did not result in significant between-group differences in changes in total blood, LDL, and HDL cholesterol or triglycerides at 3 months.*	**Intervention and comparator:** • HPO: Hybrid palm oil-rich diet (25 mL/day, n=78) • EVOO: Rich extra-virgin olive oil diet (25 mL/day, n=82) **Types of fat in HPO vs EVOO (Mean, SD) %:** SFA: 30.8 (1.6) vs 15.4 (0.8) MUFA: 56.1 (1.0) vs 77.2 (1.2) PUFA: 11.1 (0.7) vs 6.1 (0.4) C16:0: 27.9 (1.2) vs 12.5 (0.8) Oleic acid: 55.2 (1.3) vs 76.0 (1.2) LA: 10.8 (0.5) vs 5.5 (0.8) ALA: 0.4 (0.0) vs 0.6 (0.1) Duration of intervention: 3 months Compliance: 24-hour food recall and FFQ at baseline and each follow-up visit (3) **Dietary intake for Intervention vs Control:** NR	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4, 8, and 12 wk follow-up Repeated measures ANOVA **TC**, mg/dL EVOO vs HPO: NS **LDL**, mg/dL EVOO vs HPO: NS **HDL**, mg/dL EVOO vs HPO: NS **Triglycerides**, mg/dL EVOO vs HPO: NS	**Model adjustments:** None **Limitations:** • No information on compliance • No preregistered statistical analysis plan **Funding sources:** Pontificia Universidad Javeriana and Hacienda la Cabana donated oil samples

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Lv, 2018[96] **RCT parallel, China** Baseline N=93 Analytic N=88 (Attrition: 5%) **Participant characteristics at baseline:** Participants aged ~21 with BMI ~21 with no history of CVD, HTN, diabetes or cancer **Summary of findings:** *LDL cholesterol was significantly different between cocoa butter, palm olein, and soybean oil diets (which groups differed was NR). HDL cholesterol and triglycerides did not significantly differ between cocoa butter, palm olein and soybean oil diets*	**Intervention and comparator:** • Palm olein (n=28): 30-36 g/day; 46% SFA, 44% MUFA, 10% PUFA, C16:0 29%, C18:0 3%, C18:1 50%, C18:2 15%, C18:3 0.3% • Soybean oil (n=29): 30-36 g/day; 23% SFA, 28% MUFA, 49% PUFA, C16:0 11%, C18:0 4%, C18:1 22%, C18:2 52%, C18:3 6.7% • Cocoa butter (n=31): 30-36 g/day; 94% SFA, 6% MUFA, 0.4% PUFA, C16:0 26%, C18:0 37%, C18:1 36%, C18:2 2%, C18:3 0% • SFA ratio of cocoa butter, palm olein, soybean oil: 4:2:1 • *5 days/wk all food provided by researchers; for weekend days, dietary advice was given on what foods to consume. Macronutrient and caloric compositions of test diets were identical.* • *Oil used for staple food (walnut cake, ujube cake, or Cantonese sponge cake) was partially replaced with cocoa butter and palm olein.* Duration of intervention: 16 wk Compliance: weighed food after intake **Dietary intake for Intervention vs Control:** % energy of lipids were similar between groups	**Outcomes and assessment methods**: Fasting blood lipids at baseline and wk follow-up Repeated ANOVA **LDL**, mmol/L, Mean (SE) Levels at 16 wk: **Cocoa butter: 2.21 (0.10)** **Palm olein: 2.24 (0.11)** **Soybean oil: 2.00 (0.08)** **Cocoa butter vs palm olein vs soybean oil: P=0.031** **HDL**, mmol/L, Mean (SE) Cocoa butter vs palm olein vs soybean oil: NS **Triglycerides**, mmol/L, Mean (SE) Cocoa butter vs palm olein vs soybean oil: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** Mutual fund of the Chinese Nutrition Society and Malaysian palm bureau; Capital Medical University provided diets

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Michielsen, 2019[99] **RCT parallel, Netherlands** Baseline N=60 Analytic N=47 (Attrition: 22%) **Participant characteristics at baseline:** Healthy adults (57% female), ~55 y, BMI~27, at risk for metabolic syndrome, TC<8mmol/L, no drug treatment for dyslipidemia or HTN, no diabetes **Summary of findings:** *None of the 3 test diets, 1) SFA-rich Western diet versus 2) MUFA rich diet (western type diet with SFA replaced by MUFA from olive oil) versus 3) Mediterranean diet (similar MUFA content) consumed for 8 weeks resulted in significant differences between groups in changes to total, LDL and HDL cholesterol among middle-aged adults at risk for metabolic syndrome. However, triglyceride levels decreased significantly more for the Mediterranean diet, compared to the SFA diet.*	**Intervention and comparator:** • SFA-rich diet (n=16) Western-type diet • MUFA-rich diet (n=17) Western-type diet with part of SFA replaced by MUFA from olive oil (MUFA 20%E) • Mediterranean (MED) diet (n=14) similar MUFA content (21%E) • Med diet higher in fatty fish, legumes, nuts, unrefined grain products, and red wine, and lower in dairy products and meat, compared with the other two intervention diets • *Diets isocaloric; 90% of calories provided by study personnel* • *Types of fat in diets NR* Duration of intervention: 8 wk (2 wk run-in on Western diet) Compliance: assessed via a food diary but NR Dietary intake for SFA vs MUFA vs Med Diet: NR	**Outcomes and assessment methods:** Fasting blood lipids assessed at baseline (after run-in) and after the 8 wk intervention Change in lipid values from baseline **TC,** mmol/l, Mean (SD), False discovery rate p-value (FDRp) Between-group: FDRp=NS **LDL,** mmol/l, Mean (SD), FDRp Between-group: FDRp=NS **HDL,** mmol/l, Mean (SD), FDRp Between-group: FDRp=NS **Triglycerides,** mmol/l, Mean (SD) FDRp **SFA diet: +0.069 (0.222)** MUFA diet: -0.111 (0.271) **Med diet: -0.257 (0.354)** Between-group: FDRp=0.037 SFA vs MUFA: NS **SFA vs Med: P<0.05**	**Model adjustments:** None **Limitations:** • No information provided on randomization method • Potential deviation from intended intervention since compliance is not reported • Registered protocol does not describe statistical analysis plan **Funding sources:** BioNH under Joint Programming Initiative; BBMRI-NL by Dutch government

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Miller, 2016[100] **RCT parallel, Muffin Study, U.S.** Baseline N=39 Analytic N=34 (Attrition: 13%) **Participant characteristics at baseline:** Middle-aged adults ~60.8 y with metabolic syndrome, 79% African-American, 60% women **Summary of findings:** *Diets that replaced SFA with PUFA versus MUFA over a 6 month period resulted in greater reductions in serum triglyceride levels and had no significant differential effect on blood total-, LDL- and HDL cholesterol in obese, middle-aged adults with* metabolic syndrome *following an AHA-type I diet to lose weight.*	**Intervention and comparator:** • MUFA (~12 grams high-oleic sunflower oil 3x/day) 10.3 g MUFA, 0.7 g PUFA, and 1.4 g SFA (n=15) • PUFA (~12 grams safflower oil 3x/day) 2 g MUFA, 9.2 g PUFA, 1 g SFA (n=19) • *All participants were following the AHA Step I hypocaloric diet (45%–50% carbohydrates, 15%–20% protein and 30%–35% of fat, reduced energy ~300 kcal/d).* • *Daily SFA intake reduced from 25-50% and replaced with either MUFA or PUFA* • *Participants consumed 3 MUFA- or PUFA-enriched muffins/day* Duration of intervention: 6 months (1-2 month run-in on AHA Step 1 diet) Compliance: Compliance NR; assessed by 7-day food records **Dietary intake for MUFA vs PUFA at 6 months, Mean (SD), %E:** Total SFA: NS Total MUFA: NR Total PUFA: NR C18:1 (Oleic acid, g): 24.8 (1.8) vs 13.1 (1.5), P<0.001 C18:2 (LA, g): 9.6 (0.9) vs 16.9 (1.2), P<0.001 C20:5 (EPA): NS C22:6 (DHA): NS MUFA/SFA (%): 167 (10) vs 104 (6); P=0.01 PUFA/SFA (%): 67 (5) vs 132 (11); P<0.0005 No significant between-group differences in total Energy, CHO, protein, total fat intake over the 6 mo intervention.	**Outcomes and assessment methods**: Fasting blood lipids: assessed at baseline and at 6 months Change in lipid values from baseline **TC**, mg/dL, Mean (SE) MUFA vs PUFA: P=0.48 **LDL**, mg/dL, Mean (SE) MUFA vs PUFA: P=0.92 **HDL**, mg/dL, Mean (SE) MUFA vs PUFA: P=0.85 **Triglycerides**, mg/dL, Mean (SE) **MUFA: +6 (5)** **PUFA: -30 (18)** **MUFA vs PUFA: P=0.01**	**Model adjustments:** Baseline value of the outcome measure, change in weight **Limitations:** • No information provided on randomization method • Potential missing data bias due to not statistically accounting for missing data • No preregistered statistical analysis plan **Funding sources:** VA Merit Grant Award; NHLBI

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Ng, 2018[104]
RCT parallel, Malaysia
Baseline N=85 Analytic N=85 (Attrition: 0%)
 	
Participant characteristics at baseline: Overweight participants (~75% women) ~35 years, BMI ~26
 	
Summary of findings:
Consumption of stearic acid, compared to palmitic oils, resulted in significantly reduced triglycerides. There were no significant differences in total blood, LDL, and HDL cholesterol between groups.
	Intervention and comparator:
	• Chemically-interesterified (CIE) oils baked into two test cupcakes and five pieces of test cookies with:
	  • IEPalm (n=29): Palmitic acid: C16:0 35%, C18:0 5%, C18:3 0.13% (refined, bleached and deodorized palm olein) ~20%E
	  • IEStear (n=28): Stearic acid: C16:0 8%, C18:0 39%, C18:3 0.04% (fully hydrogenated soybean oil, high oleic acid sunflower oil and sunflower oil) ~20%E
	  • NatPO (n=28): Natural palm olein: C16:0 38%, C18:0 4%, C18:3 0.23%; ~20%E
	
	• *Three test fats used to prepare daily snacks with a standard palm-based background diet. 5 days/wk meals provided by researchers.*
	
	Duration of intervention: 8 wk (3 wk run-in)
	Compliance: daily attendance list to record collection of test snacks and meal packs
	
	Dietary intake for IEPalm , IEStear and NatPO snacks, Mean (SD), kcal/day:
	SFA: 209.5 (2.0); 232.3 (3.2); 213.3 (19.6)
	MUFA: 221.6 (0.1); 200.3 (2.3); 215.1 (14.2)
	PUFA: 63.2 (2.0); 53.4 (1.2); 60.6 (5.4)
	Cholesterol: NR
	Other components of diet differed significantly: None (energy of SFA, MUFA, PUFA of background diets were similar)
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 6, and 8 wk follow-up
		Comparisons of between-group differences at 8 wk follow-up
		
		TC, mmol/L, Mean (SD)
		Palmitic vs Stearic vs Natural palm olein: NS
		LDL, mmol/L, Mean (SD)
		Palmitic vs Stearic vs Natural palm olein: NS
		HDL, mmol/L, Mean (SD)
		Palmitic vs Stearic vs Natural palm olein: NS
		Triglycerides, mmol/L, Mean (SD)
		Palmitic: 1.36 (0.69)
		Stearic: 1.16 (0.80)
		Natural palm olein: 1.39 (0.87)
		Palmitic vs Stearic: P=0.007
		Palmitic vs Natural palm olein: NS
		Stearic vs Natural palm olein: NS
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• No preregistered statistical analysis plan
			
			Funding sources:
			Malaysian Palm Oil Board

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Ooi, 2012[106]
RCT parallel, U.S.
Baseline N=NR Analytic N=20 (Attrition: NR)
 	
Participant characteristics at baseline: Participants ~66 years with BMI between 23-28 who had mild to moderate hypercholesterolemia at baseline; differences in blood lipid levels were observed at baseline
 	
Summary of findings:
High-fish diet, compared to low-fish diet, significantly decreased triglycerides and resulted in a smaller decrease in HDL cholesterol levels after 24 weeks. There was no significant difference between the two diets on total and LDL cholesterol after 24 weeks.
	Intervention and comparator:
	• High-fish diet (n=10): EPA+DHA 1.23 g/day, SFA:4.5%E (SD=0.7)
	  • Sources: Sole fillet, salmon, tuna
	• Low-fish diet (n=10): EPA+DHA 0.27 g/day, SFA: 4.0%E (SD=0.4)
	  • Sources: poultry
	
	• *All meals/snacks provided by researchers*
	
	Duration of intervention: 24 wk
	Compliance: NR
	
	Dietary intake for Intervention vs Control: NR
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 24 wk follow-up
		
		TC, mmol/L, Median (IQR)
		High-fish vs low-fish: NS
		
		LDL, mmol/L, Median (IQR)
		High-fish vs low-fish: NS
		
		HDL, mmol/L, Median (IQR)
		Levels at 24 wk
		High-fish: 1.04 (0.71, 1.52)
		Low-fish: 0.93 (0.71, 1.21)
		Median % change from baseline diet
		High-fish: -9
		Low-fish: -19
		Between-group difference: P=0.04
		
		Triglycerides, mmol/L, Median (IQR)
		Levels at 24wk
		High-fish: 1.46 (1.21, 1.79)
		Low-fish: 1.76 (1.30, 2.07)
		Median % change from baseline diet
		High-fish: -24
		Low-fish: -1
		Between-group difference: P=0.02
			Model adjustments:
			None
			
			Limitations:
			• Potential problem in randomization process due to baseline imbalances
			• No information on compliance
			• No preregistered statistical analysis plan
			
			Funding sources:
			NIH; USDA; National Health and Medical Research Council

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Raziani, 2016[110]
RCT parallel, Denmark
Baseline N=164 Analytic N=139 (Attrition: 15%)
 	
Participant characteristics at baseline: Adults (~66% female) ~53y of age at baseline, with BMI ~29, a high waist circumference and at least one additional risk factor for metabolic syndrome.
 	
Summary of findings:
Consuming regular fat cheese (higher in SFA) for 12 weeks did not significantly change blood lipids compared to reduced fat cheese (lower in SFA) or a carbohydrate control.
	Intervention and comparator diets:
	• Regular fat cheese (REG), n=45
	  • Sources: Riberhus and Sharp Cheddar Cheese
	• Reduced fat cheese (RED), n=48
	  • Sources: Reduced fat Riberhus and Sharp Cheddar Cheese
	• Carbohydrate control (CHO), n=46
	  • Sources: White bread and jam
	
	Duration of intervention: 12 wk (preceded by 2 wk run in)
	Compliance: Assessed via food diaries; >95% adherence to assigned intervention foods
	
	Total dietary intake for Regular fat cheese vs Reduced fat cheese vs Carbohydrate control, Mean (SD), g/d:
	SFA: 34.3 (2.3) vs 27.4 (1.2) vs 19.1 (1.4); REG vs RED P<0.01, REG vs CHO, P<0.001
	MUFA: 30.1 (2.1) vs 27.1 (1.6) vs 23.9 (1.6); REG vs RED P=0.10, REG vs CHO P<0.01
	PUFA: 13.7 (1.0) vs 13.0 (0.8) vs 13.3 (0.9); REG vs RED P=0.40, REG vs CHO P=0.60
	Cholesterol: NR
	Other components of diet differed significantly: Total fat (highest in REG and lowest in CHO), Carbohydrate (highest in CHO), Calcium (higher in REG compared to CHO)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and end of 12wk intervention
		
		TC, mmol/L, Mean (SD)
		REG vs RED: P=0.14
		REG vs CHO: P=0.11
		
		LDL, mmol/L, Mean (SD)
		REG vs RED: P=0.42
		REG vs CHO: P=0.17
		
		HDL, mmol/L, Mean (SD)
		REG vs RED: P=0.86
		REG vs CHO: P=0.07
		
		Triglycerides, mmol/L, Mean (SD)
		REG vs RED: P=0.11
		REG vs CHO: P=0.88
		
		***No comparison between RED and CHO**
			Model adjustments:
			Baseline outcome, age, sex, BMI, change in body fat
			
			Limitations:
			• None
			
			Funding sources: Danish Dairy Research Foundation; Danish Agriculture and Food Council; National Dairy Council (U.S.); Dairy Farmers of Canada; Centre National Interprofessionel de l'Economie Laitiere; Dairy Australia; Nederlandse Zuivel Organisatie

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Rozati, 2015[112] **RCT parallel, U.S.** Baseline N=44 Analytic N=41 (Attrition: 7%) **Participant characteristics at baseline:** Overweight or obese participants ≥65 years, ~70% Caucasian, 65% female **Summary of findings:** *Olive oil intake, compared to intake of corn oil, soybean oil and butter combined, did not significantly change LDL, HDL cholesterol and triglycerides.*	**Intervention and comparator:** • Olive oil (average intake: 39 g/day, SEM=7) (n=20) • Control oil (10% Corn oil, 90% soybean oil) and butter; average intake 41 g/day, SEM=8) (n=21) **Fatty acid composition of olive oil and control oil + control butter, %:** SFA: ~16.3 vs ~15.4 + ~62.8% Oleic acid: 68.3 vs 22.7 + 30.7 LA: 10 vs 54.2 + 4.1 ALA: 0.7 vs 6.3 + 0.5 Duration of intervention: 3 months Compliance: checklist of study oils consumed per week; dietary intake assessed via 3-day dietary record at baseline and 3 months **Dietary intake for Intervention vs Control at 3 months, Mean (SD), g/day:** SFA: 25 (2) vs 28 (3), P=0.33 MUFA: 44 (4) vs 29 (3), P<0.001 Oleic acid (18:1n9): 42 (4) vs 27 (3), P<0.001 PUFA: 15 (1) vs 28 (4), P=0.02 Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at 3 months **LDL**, mg/dL, Mean (SEM) Olive oil vs control: NS **HDL**, mg/dL, Mean (SEM) Olive oil vs control: NS **Triglycerides**, mg/dL, Mean (SEM) Olive oil vs control: NS	**Model adjustments:** Age, sex and baseline value **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** Deoleo Company (Spain), USDA

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Rueda, 2013[113]
RCT parallel, U.S.
Baseline N=73 Analytic N=48 (Attrition: 22%)
 	
Participant characteristics at baseline: Freshman in university (17-20y of age) with, on average, normal blood lipids and BMI at baseline.
 	
Summary of findings:
Among freshman in university, consumption of 2 eggs for breakfast, 5 times per week for 14 weeks (which increased cholesterol and SFA intake), did not significantly change blood lipids compared to consumption of egg-free breakfasts.
	Intervention and comparator:
	• Egg breakfast containing one serving of egg (equivalent to 2 whole eggs) 5x/wk, n=27
	  • One serving of scrambled eggs: 170 calories, 12 g fat, 3.5 g saturated fat, 385 mg cholesterol
	• Non-egg breakfast (5x/wk), n=21
	  • Sources: Pancakes (370 calories, 8 g fat, 0 g SFA and 0 g cholesterol) or ready-to-eat cereals (~115 calories, 1 g fat, 0 g SFA, 0 g cholesterol)
	
	Duration of intervention: 14 wk
	Compliance: Assessed via university-issued ID cards (frequency of breakfast consumption), immediate recall of breakfast items consumed at weeks 1, 4, 7, 10, and 13 (3d each week), and food diaries at weeks 3 and 14; acceptable level of compliance reported
	
	Breakfast dietary intake at 13 wk for Egg vs Control, Mean (SD), kcal/d:
	SFA: 60 (16) vs 33 (15), P<0.0001
	MUFA: NR
	PUFA: NR
	Cholesterol (mg/d): 404 (52) vs 68 (114), P<0.0001
	Other components of diet differed significantly: Total fat and protein (both higher in Egg)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at 2wk, 8wk, 14wk
		
		Differences at 2 wk, 8 wk, 14 wk and time*intervention interaction
		
		TC, mg/dL, Mean (SD)
		Egg vs no-egg breakfast: NS
		
		LDL, mg/dL, Mean (SD)
		Egg vs no-egg breakfast: NS
		
		HDL, mg/dL, Mean (SD)
		Egg vs no-egg breakfast: NS
		
		Triglycerides, mg/dL, Mean (SD)
		Egg vs no-egg breakfast: NS
			Model adjustments:
			None
			
			Limitations:
			• No information on randomization of allocation sequence
			• Co-interventions (other dietary components) not balanced between groups
			• No information on potential impact of missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			American Egg Board

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Tapsell, 2010[120] **RCT parallel, Australia** Baseline N=150 Analytic N=95 (Attrition: 37%) **Participant characteristics at baseline:** *Participants (men and women) aged mean 44 years who were overweight or obese* **Summary of findings:** *All groups significantly reduced total cholesterol, but the LC and PUFA groups had greater triglycerides reductions. HDL cholesterol increased in the LF-LC and LF-PUFA, but not in LF-PUFA-LC.*	**Intervention and comparators:** • Low-fat (LF) (n=26): isocaloric dietary advice, to target intake of 20% PRO, 50% CHO, and 30% FAT (5% PUFA, 15% MUFA, 10% SFA) • LF-PUFA (n=21): isocaloric dietary advice, to target foods high in PUFA, and 20% PRO, 50% CHO, and 30% FAT (10% PUFA, 10% MUFA, 10% SFA) • LF, low calorie (LFLC) (n=21): 2 MJ/d calorie restriction, to target intake of 20% PRO, 50% CHO, and 30% FAT (5% PUFA, 15% MUFA, 10% SFA) • LF-PUFA-LC (n=27): 2 MJ/d calorie restriction, to target foods high in PUFA, and 20% PRO, 50% CHO, and 30% FAT (10% PUFA, 10% MUFA, 10% SFA) Duration of intervention: 3 months Compliance: measured at baseline and 3mo **Dietary intake for Intervention diets: NR**	**Outcomes and assessment methods**: Fasting blood lipids: Measured at baseline, 3mo Change from baseline to 3mo (mean (SD), p-values for time, intervention, and diet effects (interaction effect) **TC (mmol/L):** LF: -0.25 (0.3) LF-PUFA: -0.50 (1.2) LF-LC: -0.27 (0.5) LF-PUFA-LC: -0.30 (1.0) **p=0.000, p=0.017,** p=0.716 (0.711) **LDL (mmol/L):** LF: -0.27 (0.4) LF-PUFA: -0.24 (0.6) LF-LC: -0.32 (0.4) LF-PUFA-LC: -0.44 (0.7) **p=0.000,** p=0.081, p=0.634 (0.533) **HDL (mmol/L):** LF: 0.02 (0.2) LF-PUFA: 0.05 (0.1) LF-LC: 0.16 (0.3) LF-PUFA-LC: 0.00 (0.2) **p=0.007,** p=0.744, **p=0.042 (0.069)** **Triglycerides (mmol/L):** LF: 0.09 (0.7) LF-PUFA: -0.47 (1.0) LF-LC: -0.26 (0.5) LF-PUFA-LC: -0.16 (0.4) **p=0.008**, p=0.091, p=0.056 (0.058)	**Model adjustments:** None **Limitations:** • Weight loss trial • No information on compliance reported • No preregistered statistical analysis plan **Funding sources**: National Health and Medical Research Council of Australia

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Utzschneider, 2013[125]
RCT parallel, U.S.
Baseline N=49 Analytic N=35 (Attrition: 29%)
 	
Participant characteristics at baseline: Participants aged ~69 years, BMI ~27 with no differences in diets at baseline
 	
Summary of findings:
Participants consuming high SFA diets from high-fat dairy and meat sources, compared to low SFA diet from low-fat dairy and mostly lean meats, had significantly higher total, LDL, and HDL cholesterol, and significantly lower triglycerides.
	Intervention and comparator:
	• Low SFA diet (n=20): Total fat 25%E, SFA 7%E
	  • Sources: low-fat and non-fat dairy, lean meats, bacon (to confuse participants to be able to guess which diet they were on)
	• High SFA diet (n=15): Total fat 45%, SFA 25%E
	  • Sources: butter, cheeses, fatty meats, cream
	
	Duration of intervention: 4 wk
	Compliance: weekly telephone calls and food record daily; all participants were compliant on macronutrient targets
	
	Dietary composition for Intervention vs Control at 4 wk, Mean (SEM), %E:
	SFA: 7.4 (0.2) vs 23.6 (0.2), P<0.001
	MUFA: 21.2 (1.5) vs 32.6 (1.5), P<0.001
	PUFA: 10.6 (0.7) vs 7.7 (0.3), P=0.50
	Cholesterol: 108 (6) vs 354 (14), P<0.001
	Other components of diet differed significantly: fat %E (higher in high SFA), carbohydrate %E (higher in low SFA), sugar (higher in low SFA), fructose (higher in low SFA), fiber (higher in low SFA), omega-3 FAs (higher in high SFA)
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk follow-up
		
		TC, mmol/L, Mean (SEM)
		Changes from baseline:
		Low SFA: -0.59 (0.10)
		High SFA: 0.63 (0.17)
		P<0.001
		
		LDL, mmol/L, Mean (SEM)
		Changes from baseline:
		Low SFA: -0.56 (0.08)
		High SFA: 0.52 (0.13)
		P<0.001
		
		HDL, mmol/L, Mean (SEM)
		Changes from baseline:
		Low SFA: -0.17 (0.04)
		High SFA: 0.14 (0.07)
		P<0.001
		
		Triglycerides, mmol/L, Mean (SEM)
		Changes from baseline:
		Low SFA: 0.31 (0.10)
		High SFA: -0.05 (0.06)
		P=0.01
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• No preregistered statistical analysis plan
			• Attrition >10%
			• Other components of diet differed between groups (carbohydrate, sugar, fructose, fiber)
			
			Funding sources:
			VA Office of Research and Development Medical Research Service; University of Washington Diagnostic Imaging Science Center

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Vafeiadou, 2015[126] **RCT parallel, DIVAS, United Kingdom** Baseline N=202 Analytic N=195 (Attrition: 3%) **Participant characteristics at baseline:** Non-smoking men (~28%) and women ~65 y with moderate CVD risk based on CVD risk score **Summary of findings:** *Participants on SFA diet from butter had significantly increased changes in total cholesterol and LDL cholesterol, compared to the MUFA and n-6 PUFA diets. There were no significant effects on HDL cholesterol and triglycerides.*	**Intervention and comparators:** • SFA diet (n=65): 17%E SFA, 9%E MUFA, 9%E N-6 PUFA (Source: Butter) • MUFA diet (n=64): 11%E SFA, 19%E MUFA, 13%E n-6 PUFA (Source: refined olive oil, olive oil/rapeseed oil blended spread) • N-6 PUFA diet (n=66): 4%E SFA, 4%E MUFA, 10%E N-6 PUFA (Source: Safflower oil and spread) • *All diets isoenergetic* Duration of intervention: 16 wk Compliance: 4-day weighed diet diaries at 0, 8 and 16 weeks; compliance goals were met **Change in dietary intake for SFA vs MUFA vs N-6 PUFA Diets, Mean (SEM), %total energy:** SFA: 6.1 (0.4) vs -4.1 (0.4) vs -3.6 (0.4), P≤0.001 (differed between SFA diet and MUFA or n-6 PUFA) MUFA: -0.9 (0.3) vs 6.8 (0.4) vs 0.7 (0.4), P≤0.001 (different between all groups) n-6 PUFA: -2.3 (0.2) vs -0.5 (0.2) vs 5.5 (0.4), P≤0.001 (differed between all groups) n-3 PUFA: -0.20 (0.07) vs 0.08 (0.05) vs 0.04 (0.05), P≤0.001 (differed between SFA diet and MUFA or n-6 PUFA) Total PUFA: -2.5 (0.3) vs -0.4 (0.2) vs 5.5 (0.4), P≤0.001 (differed between all groups) Cholesterol (mg/day): 13 (14) vs -64 (15) vs -47 (13), P≤0.001 (differed between SFA diet and MUFA or n-6 PUFA) Other components of diet differed significantly: energy (Changes in energy intake was significantly different in SFA diet (-0.0 (0.2)) than MUFA (-0.7 (0.2)) or n-6 PUFA (-0.4 (0.2)) diet)	**Outcomes and assessment methods**: Fasting blood lipids at 16 wk follow-up **TC**, mmol/L, Mean (SEM) Change: **SFA: 0.36 (0.08)** MUFA: -0.07 (0.09) n-6 PUFA: -0.11 (0.09) **SFA was significantly different from MUFA and n-6 PUFA P≤0.001** MUFA and n-6 PUFA did not significantly differ between groups **LDL**, mmol/L, Mean (SEM) Change: **SFA: 0.30 (0.07)** MUFA: -0.09 (0.08) n-6 PUFA: -0.16 (0.07) **SFA was significantly different from MUFA and n-6 PUFA P≤0.001** MUFA and n-6 PUFA did not significantly differ between groups **HDL**, mmol/L, Mean (SEM) SFA vs MUFA vs n-6 PUFA: NS **Triglycerides**, mmol/L, Mean (SEM) SFA vs MUFA vs n-6 PUFA: NS	**Model adjustments:** Baseline values, BMI, age, sex **Limitations:** • No preregistered statistical analysis plan **Funding sources:** United Kingdom Food Standards Agency; Department of Health Policy Research Programme

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

van der Made, 2014[127]
RCT parallel, Netherlands
Baseline N=101 Analytic N=88 (Attrition: 13%)
 	
Participant characteristics at baseline: Participants (~70% female) aged ~62 years, BMI ~26, who had early signs of macular degeneration
 	
Summary of findings:
Consumption of 1.5 egg yolks daily for 1 year did not significantly change total, LDL, HDL cholesterol or triglycerides compared to control.
	Intervention and comparator:
	• Daily consumption of buttermilk drink (80 mL) containing one of the following:
	  • 1.5 egg yolks (n=45): 323 mg cholesterol, 33% SFA, 50% MUFA, 18% PUFA, 0.3% *trans* fat, 1.4 mg lutein
	  • Control (n=43): 2 mg cholesterol, 67% SFA, 26% MUFA, 4% PUFA, 3% *trans* fat, 0 g lutein
	
	Duration of intervention: 1 year
	Compliance: validated FFQ; good compliance reported
	
	Dietary intake for Intervention vs Control, Mean (SD), (%E):
	SFA: Intervention: Baseline 13 (3.1), Change +0.9 (3.0); Control: Baseline 14 (3.0), Change -0.2 (3.6), P=NS
	MUFA: Intervention: Baseline 14 (4.0), Change +0.5 (3.5); Control: 14 (4.0), Change +1.1 (6.0), P=NS
	Oleic acid: Intervention: Baseline 12 (4.0), Change -1.2 (3.6); Control: Baseline 12 (3.9), Change +1.2 (5.6), Change differed from control group P<0.05
	PUFA: Intervention: Baseline 7.9 (3.2), Change +1.4 (3.3); Control: Baseline 8.2 (4.0), Change +0.3 (4.4), P=NS
	Cholesterol (mg/d): Intervention: Baseline 245 (99), Follow-up 296 (106); Control: Baseline 217 (103), Change -12 (83), Change differed from control group P<0.05
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 1 year follow-up
		Changes in lipids from baseline
		TC, mmol/L, Mean (SD)
		Egg yolk vs control: NS
		
		LDL, mmol/L, Mean (SD)
		Egg yolk vs control: NS
		
		HDL, mmol/L, Mean (SD)
		Egg yolk vs control: NS
		
		Triglycerides, mmol/L, Mean (SD)
		Egg yolk vs control: NS
			Model adjustments:
			None
			
			Limitations:
			• No information on randomization of allocation sequence
			• No preregistered statistical analysis plan
			
			Funding sources:
			Europees Fonds voor Regionale Ontwikkeling; Dutch Ministry of Economic Affairs, the Province of Limburg; Newtricious R&D B.V.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Varady, 2011[129] **RCT parallel, U.S.** Baseline N=20, Analytic N=17 (Attrition: 15%) **Participant characteristics at baseline:** Obese, BMI~33.5, 71% female, ~35 years, normal cholesterol, no diabetes, no CVD **Summary of findings:** *In adults with obesity participating in a weight loss trial, there was no significant group differences in change over time for total, LDL- and HDL-cholesterol and triglycerides between those who followed a high fat diet versus a low fat diet for 6 weeks.*	**Intervention and comparator:** • High Fat: 60%E from total fat (26% SFA, 24% MUFA, 9% PUFA), n=9 • Low Fat: 25% E from total fat (7% SFA, 9% MUFA, 9% PUFA), n=8 • *Energy restricted diets (25% baseline energy need) provided by researchers and distributed 3 times/week* • *Both groups lost weight from baseline* Duration of intervention: 6 wk Compliance: Subjects recorded foods added or missed from menu plan; noncompliant (>5% deviation) were excluded in analyses **Diet composition for High Fat vs Low Fat: NR** SFA (%E): 26% vs 7% MUFA (%E): 24% vs 9% PUFA: 9% vs 9% Cholesterol (mg): 448 vs 299 Other components of diet differed significantly: Carbohydrate (%E): 5% vs 55%, Protein (%E): 35% vs 20%, Fiber (g): 11 vs 30	**Outcomes and assessment methods**: Fasting blood lipids: Assessed at study weeks 1 and 6 Comparing change between groups with time by treatment interaction **TC,** mg/dL, Mean (SD) High fat vs Low fat: P=NS **LDL,** mg/dL, Mean (SD) High fat vs Low fat: P=NS **HDL,** mg/dL, Mean (SD) High fat vs Low fat: P=NS **Triglycerides,** mg/dL, Mean (SD) High fat vs Low fat: P=NS	**Model adjustments:** Time by treatment interaction **Limitations:** • Energy restricted diet • >10% attrition • No preregistered statistical analysis plan **Funding sources:** Kinesiology and Nutrition and Physical Therapy, University of Illinois, Chicago; NIH Clinical Research Center; NHLBI

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Veum, 2017[130] **RCT parallel, Norway** Baseline=46 Analytic N= 38 (Attrition: 17%) **Participant characteristics at baseline:** Men with abdominal obesity, 30-50 years, BMI >29, no diabetes **Summary of findings:** Among middle-aged men with abdominal obesity consuming moderately energy restricted diets for 12 weeks, a low-fat, high carbohydrate (LFHC) diet compared to a very high–fat, low-carbohydrate (VHFLC) diet, significantly reduced total cholesterol and LDL cholesterol and increased HDL cholesterol. There was no significant between-group difference in changes to triglyceride level.	**Intervention and comparator:** • Very high–fat, low-carbohydrate (VHFLC): 73%E fat, 10%E carbohydrate, 17% protein (n=20) • Low-fat, high-carbohydrate (LFHC): 30%E fat and 53%E carbohydrate, 17% protein (n=18) • *Modest isocaloric energy restricted diets; Diets emphasized low-processed, lower-glycemic foods* • *Subjects received diet instruction, individual coaching as desired and food donations* Duration of intervention: 12 wk Compliance: On-line dietary records 5-days/month and weight checks; noncompliant participants were excluded from analyses **Dietary intake for LFHC vs VHFLC, Mean (SD), (%):** SFA: 12.4 (1.1) vs 34.1 (3.1), P≤ 0.001 MUFA: 8.1 (1.0) vs 22.9 (1.9), P≤ 0.001 PUFA: 4.6 (1.0) vs 5.2 (1.0), P=NS No significant difference in energy, protein (17%E) or PUFA; fiber intake significantly lower in the VHFLC group	**Outcomes and assessment methods**: Fasting blood lipids: At baseline, 4 wk, 8 and 12 wk Change from baseline to 12 wk, Mean (95% CI), p-values for time and group interaction **TC**, mmol/L **LFHC: -0.96 (-1.23, -0.69)** VHFLC: +0.13 (-0.29, 0.55) **LFHC vs VHFLC: P<0.001** **LDL**, mmol/L **LFHC: -0.78 (-1.08, -0.49)** VHFLC: +0.26 (-0.08, 0.60) **LFHC vs VHFLC: P<0.001** **HDL**, mmol/L LFHC: -0.01 (-0.10, 0.07) **VHFLC: +0.14 (0.06, 0.22)** **LFHC vs VHFLC: P=0.034** **Triglycerides,** mmol/L **LFHC: -0.41 (-0.60, -0.21)** **VHFLC: -0.53 (-0.68, -0.37**) LFHC vs VHFLC: P=NS	**Model adjustments:** Age, baseline intake of energy, carbohydrate, added sugar, and cholesterol **Limitations:** • Energy restricted diet (subjects in both arms lost ~10.5kg) • Potential bias due to randomization process • >10% attrition • Preregistered statistical analysis plan describes 3 and 6 month outcome assessment (only short-term results reported) **Funding sources:** Western Norway Regional Health Authority, Meltzerfondet; Bergen Medical Research Foundation; University of Bergen

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Werner, 2013[132]
RCT parallel, Denmark
Baseline N=NR Analytic N=37 (Attrition: NR)
 	
Participant characteristics at baseline: Healthy participants from 50 to 70 years old (Mean ~62y), with normal BMI
 	
Summary of findings:
There were no differences in total cholesterol, LDL, HDL cholesterol and triglycerides between participants who consumed butter from mountain-pasture-grazing cows and butter from conventionally fed cows.
	Intervention and comparator:
	• Replacement of 15%E of daily fat intake with:
	  • Butter from mountain-pasture grazing cows (n=19); different FA composition (20% less of cholesterol-raising SFAs than in control butter)
	  • Butter from conventionally fed cows (n=18)
	
	Duration of intervention: 12 wk
	Compliance: 3-day weighed food records at 6 wk
	
	Dietary intake after 6 wk for Intervention vs Control, Mean (SD), g/day:
	SFA: 16.0 (0.7) vs 15.8 (0.7), P=NS
	MUFA: 10.2 (0.4) vs 10.6 (0.4), P=NS
	PUFA: 4.0 (0.2) vs 3.6 (0.2), P=NS
	Cholesterol: NR
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Differences in Fasting blood lipids
		
		TC: NS
		
		LDL: NS
		
		HDL: NS
		
		Triglycerides: NS
			Model adjustments:
			None
			
			Limitations:
			• No preregistered statistical analysis plan
			
			Funding sources:
			Strategic Research Council of Denmark, The Danish Dairy Research Foundation, Danish Cattle Federation and Arla Foods

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Young, 2017[133] **RCT parallel, U.S.** Baseline=78 Analytic N= 71 (Attrition: 9%) **Participant characteristics at baseline:** Healthy, ~26.6 y, 48% female, BMI ~23.7, 72% White, 14% African American, 10% Asian **Summary of findings:** *Among young, healthy, normal weight adults, consumption of higher n-3 and lower n-6 diets compared to the standard military food plan for 10 weeks had no significant effect on blood lipid levels or between-group differences.*	**Intervention and comparators:** • Experimental Moderate (EXP-Mod): less n-6 (3.7%E) and more dietary n-3 (1.3%E) (n=27) • Experimental High (EXP-High): EXP-Mod diet plus 1 smoothie supplemented with 1000 mg n-3 (1.7%E)/day (n=28) (supplementation arm not included in this analysis) • Both experimental diets were lower in SFA, higher in MUFA (particularly oleic acid) than the control diet. • Control: U.S. Military's Standard Garrison Dining Facility Menu (n=23) • *Participants consumed the same meals, but in intervention diets, high LA foods were replaced with high oleic acid/low LA and high n-3 fatty acid foods. Target foods included chicken, egg, oils, smoothies, and food ingredients.* • *Most meals were prepared in a metabolic kitchen, diets were isocaloric* Duration of intervention: 10 wk Compliance: Monitored by dietetic support staff and weight was monitored daily; high compliance reported **Dietary intake for Control vs EXP-Mod vs EXP-High, Mean (SD), g/day:** SFA: 16.6 (1.8) vs 14.4 (1.4) b vs 15.1 (1.3)b MUFA: 20.7 (2·6) vs 30.5 (5·1)b vs 31.9 (5·4) b PUFA, n-6: 22.8 (4.8) vs 8.1 (2.2)b vs 8.4 (2.1)b PUFA, n-3: 2.8 (0.8) vs 2.9 (0.9) vs 3.9 (1.0)a,b EPA+DPA+DHA (mg/d): 176 (73) vs 904 (482) b vs 1928 (736) a,b Cholesterol: NR No significant differences in macronutrient content of the diets.	**Outcomes and assessment methods**: Fasting blood lipids: At baseline and after the feeding period. Blood lipid levels at follow-up **TC**, mmol/L Exp-Mod vs Control: P=NS **LDL**, mmol/L Exp-Mod vs Control: P=NS **HDL**, mmol/L Exp-Mod vs Control: P=NS **Triglycerides**, mmol/L Exp-Mod vs Control: P=NS	**Model adjustments:** None **Limitations:** • Preregistered statistical analysis plan does not include lipid outcomes **Funding sources:** U.S. Army Medical Research and Materiel Command; Intramural Program of the National Institute on Alcohol Abuse and Alcoholism

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Yubero-Serrano, 2015[134] **RCT parallel (LIPGENE), Ireland, U.K., Norway, France, The Netherlands, Spain, Poland, Sweden** Baseline N=486 Analytic N=162 (Attrition: 66%) **Participant characteristics at baseline:** Participants (56% female) mean age 54 years with metabolic syndrome **Summary of findings:** *In adults with metabolic syndrome, consuming a diet rich in SFA, compared to a diet rich in MUFA, for 12 weeks did not affect blood lipids.*	**Intervention and comparators:** • High SFA (HSFA) (n=39): high-fat (38% energy) SFA-rich diet (16% SFA, 12% MUFA, 6% PUFA) • High monounsaturated fatty acids (HMUFA) (n=38): high-fat (38% energy), MUFA-rich diet (8% SFA, 20% MUFA, 6% PUFA) Groups that did not meet inclusion criteria for review: • Low-fat, high-complex carbohydrate (LFHCC) control (n=41): isoenergetic low-fat (28% energy), high-complex carbohydrate diet (8% SFA, 11% MUFA, 6% PUFA), with 1g/d high oleic sunflower oil supplement • LFHCC n-3 (n=44): isoenergetic low-fat (28% energy), high-complex carbohydrate diet (8% SFA, 11% MUFA, 6% PUFA), with 1.24 g/d VLC n-3 PUFA supplement Duration of intervention: 12 wk Compliance: measured at weeks 6 and 12 **Dietary intake for HSFA, HMUFA, LFHCC, LFHCCn-3, Mean (SEM), %E:** SFA: 17.50 (0.33), 10.38 (0.20), 8.56 (0.26), 8.65 (0.26) MUFA: 12.74 (0.26), 18.73 (0.37), 11.78 (0.30), 11.40 (0.28) PUFA: 6.25 (0.16), 6.66 (0.16), 6.00 (0.17), 5.67 (0.14) Cholesterol: NR n-3 PUFA (g/d): 1.84 (0.12), 1.90 (0.12), 1.89 (0.16), 3.05 (0.14) Other components of diet differed significantly: FAT: 39.83 (0.62), 38.92 (0.51), 29/63 (0.60), 29.12 (0.50) CHO: 41.24 (0.67), 42.07 (0.59), 49.35 (0.76), 50.22 (0.68) PRO: 17.42 (0.41), 16.87 (0.34), 19.18 (0.49), 18.34 (0.39)	**Outcomes and assessment methods**: Fasting blood lipids: Measured at baseline, 12 wk Between-group pre-post differences in intervention diet group, by tertile of insulin resistance (HOMA-IR) **Tertile 1 (HOMA-IR<1.90)**: • TC: NS • LDL: NS • HDL: NS • Triglycerides: NS **Tertile 2 (HOMA-IR 1.90-2.93)**: • TC: NS • LDL: NS • HDL: NS • Triglycerides: NS **Tertile 3 (HOMA-IR >2.93)**: • TC: NS • LDL: NS • HDL: NS • Triglycerides: NS	**Model adjustments:** None **Limitations:** • Information on compliance NR • No preregistered statistical analysis plan **Funding sources**: EU 6 Framework Food Safety & Quality Programme

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
RCT Crossover Design			

Abdullah, 2015[39]
RCT multi-center crossover, Canada
Baseline N=137 Analytic N=124 (Attrition: 9%)
 	
Participant characteristics at baseline: Healthy adults aged ~39, SD=16.4 years with mean BMI of 25.7, CVD free, no diabetes, no smoking
 	
Summary of findings:
Intake of 3 servings/d of conventional dairy products compared to a dairy free diet for 4 weeks significantly increased LDL cholesterol but did not have a significant effect on total and HDL cholesterol, or triglycerides.
	Intervention and comparator:
	• Diet with dairy products (total n=114)
	  • Sources: 3 servings/day of commercial dairy including 1% fat milk, 1.5% fat yogurt and 34% fat cheese
	• Dairy-free diet (total n=117)
	  • Sources: Energy-equivalent control including fruit and vegetable juice, cashews and a cookie
	
	Duration of intervention: 4 wk each diet (4-8 wk washout period)
	Compliance: validated Web-based FFQ and weekly report of daily consumption of dairy products; good compliance evident by FFQ mean 3.5 servings/d net difference between the intake of dairy and control products (P<0.0001)
	
	Dietary intake for Intervention vs Control, Mean (95%CI):
	SFA (%E): 10.7 (10.4, 11.1) vs 8.5 (8.2, 8.8), P<0.0001
	MUFA(%E): 12.0 (11.6, 12.5) vs 14.0 (13.4, 14.6), P<0.0001
	PUFA(%E): 5.3 (5.1, 5.6) vs 7.1 (6.9, 7.4), P<0.0001
	Cholesterol (mg): 209.8 (193.8, 227.1) vs 168.0 (150.0, 188.3), P<0.0001
	Trans FA: NS
	Other components of diet differed: carbohydrate, fiber, protein, calcium and vitamin D
		Outcomes and assessment methods:
		Fasting blood lipids at end of each dietary phase (4 wk follow-up)
		
		TC, mmol/L, Control vs Dairy, Mean (SE)
		Intervention: 5.08 (0.08)
		Control: 5.00 (0.08)
		Between-group: P=0.07
		
		LDL, mmol/L, Control vs Dairy, Mean (SE)
		Intervention: 2.99 (0.08)
		Control: 2.91 (0.08)
		Between-group: P=0.04
		
		HDL, mmol/L, Control vs Dairy, Mean (SE)
		Intervention: 1.53 (0.4)
		Control: 1.53 (0.04)
		Between-group: P=0.92
		
		Triglycerides, mmol/L, Control; Dairy, Mean (SE)
		Intervention: 1.23 (0.05)
		Control: 1.23 (0.06)
		Between-group: P=0.69
			Model adjustments:
			None
			
			Limitations:
			• No preregistered statistical analysis plan
			
			Funding sources:
			Dairy Research Cluster Initiative (Agriculture and Agri-Food Canada, Dairy Farmers of Canada, the Canadian Dairy Network, and the Canadian Dairy Commission)

Alphonse, 2017[42]
RCT crossover, Canada
Baseline N=55 Analytic N=49 (Attrition: 11%)
	Intervention and comparators:
	• Daily milkshake (240 mL) containing one of following:
	  • Egg yolk cholesterol (600 mg)
	  • Plant sterols (2 g)
	  • Control (no cholesterol and plant sterol)
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk follow-up
		TC, mmol/L, Mean (SEM)
		Levels at 4wk:
		Egg cholesterol: 5.03 (0.13)
			Model adjustments:
			Treatment, sequence and sex
			
			Limitations:
			• No information on randomization of allocation sequence

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Participant characteristics at baseline: Participants (57% female) with normal or slightly elevated cholesterol aged ~33 years, majority overweight, without history of CVD, CHF or diabetes **Summary of findings:** *Egg yolk cholesterol, compared to plant sterols, significantly increased total cholesterol, LDL and HDL cholesterol. Egg yolk cholesterol, compared to control (no cholesterol), significantly increased total cholesterol and HDL cholesterol, but not LDL cholesterol and triglycerides. There were no differences in blood lipids between plant sterols and controls (no plant sterol).*	• *Participants advised to maintain typical diet and physical activity levels* Duration of intervention: 4 wk each diet (4 wk washout) Compliance: weekly checklists, 3-day food records; all included participants completed all three phases and study requirements **Dietary intake:** NR	Plant sterols: 4.78 (0.14) Control: 4.76 (0.14) Change from control, mean % (SEM) Egg cholesterol: +4.76 (1.42) Plant sterol: -1.58 (1.43) **Egg cholesterol vs plant sterols: P<0.05** **Egg cholesterol vs control: P<0.05** **LDL**, mmol/L, Mean (SEM) Levels at 4wk: Egg cholesterol: 2.96 (0.13) Plant sterols: 2.72 (0.13) Control: 2.85 (0.13) Change from control, mean % (SEM) Egg cholesterol: +5.40 (2.61) Plant sterol: -2.86 (2.39) **Egg cholesterol vs plant sterols: P<0.05** Egg cholesterol vs control: NS **HDL**, mmol/L, Mean (SEM) Levels at 4wk: Egg cholesterol: 1.53 (0.06) Plant sterols: 1.45 (0.06) Control: 1.44 (0.06) Change from control, mean % (SEM) Egg cholesterol: +6.64 (2.06) Plant sterol: +1.28 (1.85) **Egg cholesterol vs plant sterols: P<0.05** **Egg cholesterol vs control: P<0.05** **Triglycerides**, mmol/L, Mean (SEM) Levels at 4wk: Egg cholesterol: 5.03 (0.13) Plant sterols: 4.78 (0.14) Control: 4.76 (0.14) Change from control, mean (%) **Egg cholesterol: +1.55 (3.12)** **Plant sterol: +7.95 (4.97)** Egg cholesterol vs plant sterols: NS Egg cholesterol vs control: NS	• No preregistered statistical analysis plan **Funding sources:** Dairy Farmers of Canada; Agri-Food Research and Development Initiative

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Andraski, 2019[43]
RCT crossover, U.S.
Baseline=NR Analytic N=12 (Attrition: NR)
 	
Participant characteristics at baseline: Overweight, BMI ~30.7, low HDL cholesterol (mean 44.4 mg/dl), ~42 y, 67% female
 	
Summary of findings:
Consumption of a high-fat, high-MUFA diet compared to a low-fat, high carbohydrate diet had no significant between-group differences in changes to blood lipids in overweight adults with low HDL cholesterol.
	Intervention diets:
	• High fat (high MUFA): 40% fat (23% MUFA, 7% PUFA, 10% SFA), 45% CHO, 15% protein, 180mg cholesterol
	  • MUFA from vegetable oil and nuts
	• Low fat (high carbohydrate): 20% fat (8% MUFA, 7% PUFA, 5% SFA), 65% CHO, 15% protein, 90 mg cholesterol
	  • Carbohydrate mainly from whole grains
	
	• *Isocaloric diets; all food and beverages provided by researchers*
	
	Duration of intervention: 32 days (3 wk washout, consumed self-selected diet)
	Compliance: NR
	
	Dietary intake for Low fat vs High fat diet: NR
		Outcomes and assessment methods:
		Fasting blood lipids: At baseline and after each feeding period.
		
		Difference at follow-up
		
		TC, mmol/L
		High fat vs low fat: NS
		
		LDL, mmol/L
		High fat vs low fat: NS
		
		HDL, mmol/L
		High fat vs low fat: NS
		
		Triglycerides, mmol/L
		High fat vs low fat: NS
			Model adjustments:
			None
			
			Limitations:
			• No information provided about randomization or period effects
			• No data available to asses attrition rate
			• No information provided about diet compliance
			• Potential bias from missing data
			• No preregistered statistical analysis plan for most blood lipid outcomes
			
			Funding sources:
			National Institutes of Health; Kowa Company Ltd; American Heart Association

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Baer, 2019[45]
RCT crossover, U.S.
Baseline N=42 Analytic N=40 (Attrition: 5%)
 	
Participant characteristics at baseline: Adults ~57y of age with BMI ~29 and total blood cholesterol ~206 mg/dL at baseline.
 	
Summary of findings:
Consumption of 42 g/d of cashews for 4 weeks, which increased MUFA intake, did not significantly change blood lipids compared to a cashew free diet.
	Intervention and comparator diets:
	• Base diet with cashews (42g/d) daily
	  • Sources: cashews
	• Control: Base diet without cashews
	  • Sources: NA
	
	• *Two treatment phases were isocaloric, other study foods reduced proportionately to incorporate cashews*
	• *All food provided to participants during study period*
	
	Duration of intervention: 4 wk (1 wk washout)
	Compliance: Monitored by dining facility staff for breakfast and dinner on weekdays and additionally assessed by checking food items and food weights.
	
	Diet composition for Cashew vs Control, Mean, %E:
	SFA: ~11 vs ~11, P=NR
	MUFA: ~11 vs ~9, P=NR
	PUFA: ~8 vs ~7, P=NR
	Cholesterol: NR
	Other components of diet differed significantly: Total fat (higher in Cashew), CHO (lower in Cashew)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured in duplicate at baseline and 4 wk
		
		Levels at 4 wk follow-up
		
		TC, mg/dL
		Cashew vs Control: P=NS
		
		LDL, mg/dL
		Cashew vs Control: P=NS
		
		HDL, mg/dL
		Cashew vs Control: P=NS
		
		Triglycerides, mg/dL
		Cashew vs Control: P=NS
			Model adjustments:
			Baseline blood lipid, BMI, age, sex, treatment sequence, treatment period
			
			Limitations:
			• Only one week washout between interventions
			
			Funding sources:
			USDA Agricultural Research Service; Global Cashew Council; International Nut and Dried Fruit Council

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Barbour, 2015[46]
RCT crossover, Australia
Baseline N=69 Analytic N=61 (Attrition: 12%)
 	
Participant characteristics at baseline: Nonsmoking adults ~65y of age with overweight or obesity without hypertension or CVD
 	
Summary of findings:
Consuming high oleic peanuts for 12 weeks (which increased MUFA intake) did not change blood lipids compared to a nut free diet.
	Intervention and comparator diets:
	• High oleic peanuts, 84g/d (men) or 56g/d (women) 6d/wk
	  • Sources: roasted, unsalted high oleic peanuts
	• Control: Nut-free regular diet
	  • Sources: NA
	
	Duration of intervention: 12 wk each diet (no washout period)
	Compliance: Monitored via diet diaries. 85% (women) and 80% (men) of peanuts consumed
	
	Total diet intake at 12 wk for Peanuts vs Control, Mean (SD), g/d:
	SFA: 31.8 (8.7) vs 29.6 (9.7), P=NS
	MUFA: 47.5 (11.3) vs 25.2 (7.7), P<0.001
	PUFA: 11.2 (3.3) vs 9.8 (3.3), P<0.001
	Cholesterol: NR
	Other components of diet differed significantly: Total fat and protein, fiber, and total energy intake (all higher in Peanut)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and 12 wk
		
		Difference at follow-up
		
		TC, mmol/L
		Peanut vs Control: P=NS
		
		LDL, mmol/L
		Peanut vs Control: P=NS
		
		HDL, mmol/L
		Peanut vs Control: P=NS
		
		Triglycerides, mmol/L
		Peanut vs Control: P=NS
			Model adjustments:
			Baseline blood lipid
			
			Limitations:
			• None to report
			
			Funding sources:
			Australian Research Council; Peanut Company of Australia

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Bowen, 2018[54]
RCT crossover, COMIT II, Canada and U.S.
Baseline N=174 Analytic N=119 (Attrition: 32%)
 	
Participant characteristics at baseline: Adults (63% female) with or at risk for metabolic syndrome, mean age ~44 y, BMI~32, ~30% with dyslipidemia
 	
Summary of findings:
Consumption of canola oil or *HOCO increased MUFA and decreased SFA intake, and significantly lowered blood total- and LDL cholesterol compared to a consumption of a control oil configured to mimic a Western-style diet over 6 weeks in adults for 6 weeks with* metabolic syndrome.
	Intervention and Comparators:
	• Participants consumed smoothies (2/d) containing one of the following oils:
	  • Canola oil
	  • High-oleic acid canola oil (HOCO)
	  • Control oil
	  • Sources:49% ghee, 29% safflower oil, 14% flaxseed oil, and 8% coconut oil
	
	Types of fat in canola oil vs HOCO vs Control, %:
	SFA 6.56 vs 6.43 vs 12.26
	MUFA: 17.45 vs 19.11 vs 10.50
	Oleic acid: 15.55 vs 17.86 vs 5.92
	PUFA: 9.21 vs 7.02 vs 9.96
	ALA: 2.10 vs 0.76 vs 1.73
	• *Oils provided ~18% of total energy for all calorie levels (e.g., for a 3,000 kcal diet, 60 g of oil was provided)*
	• *Controlled-feeding study: all meals/snacks provided by researchers*
	
	Duration of intervention: 6 wk each feeding period (≥4-wk washout periods)
	Compliance: NR
	
	Dietary intake for Canola oil vs HOCO vs Control, Mean (SD), g/day: NR
	Three experimental diets were identical in %E from macronutrients.
		Outcomes and assessment methods:
		Fasting blood lipids assessed at baseline (day 1 and 2) and the endpoint (days 41 and 42)
		
		Endpoint-to-endpoint comparisons
		
		TC, mmol/L, Mean (SEM)
		Levels at 6 wk:
		Canola: 4.54 (0.04)
		HOCO: 4.58 (0.04)
		Control: 4.74 (0.04)
		Canola vs Control P<0.0001
		HOCO vs Control P = 0.002
		Canola vs HOCO: NS
		Group difference: P<0.0001
		
		LDL, mmol/L, Mean (SEM)
		Levels at 6 wk:
		Canola: 2.64 (0.04)
		HOCO: 2.67 (0.04)
		Control: 2.83 (0.04)
		Canola vs Control P<0.0001
		HOCO vs Control P = 0.0002
		Canola vs HOCO: NS
		Group difference: P<0.0001
		
		HDL, mmol/L, Mean (SEM)
		Group difference: NS
		
		Triglycerides, mmol/L, Mean (SEM)
		Group difference: NS
			Model adjustments:
			Diet specific baseline value
			
			Limitations:
			• No information on compliance
			• Potential missing data bias due to not statistically accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			Agriculture and Agri-Food Canada; the Canola Council of Canada, Alberta Canola; SaskCanola; Dow Agro Sciences; Manitoba Canola Growers; the National Center for Research Resources; NIH

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Brassard, 2017[55]
RCT crossover, Canada
Baseline N=103 Analytic N=92 (Attrition: 11%)
 	
Participant characteristics at baseline: Predominantly white, overweight or obese men and women ~39y of age with high waist circumference and HDL concentrations below 75th percentile.
 	
Summary of findings:
Diets rich in SFA from cheese or butter, compared to diets rich in MUFAs, PUFAs or CHOs, increased total and LDL cholesterol. Compared to a diet higher in CHO, diets rich in SFA from cheese or butter increased HDL cholesterol. Triglycerides were increased by a diet rich in SFA from cheese compared to diets rich in SFA from butter or in PUFA, but triglycerides were reduced by a diet rich in SFA from butter compared to a diet higher in CHO.
	Intervention and comparator diets:
	• Diet rich in SFAs from cheese
	  • Sources: cheese
	• Diet rich in SFAs from butter
	  • Sources: butter
	• Diet rich in MUFAs
	  • Sources: refined olive oil
	• Diet rich in PUFAs
	  • Sources: corn oil
	• CHO: High-carbohydrate, low-fat diet
	  • Sources: NR
	
	• *All FA diets: 32%E FA, 52%E CHO, 16%E protein*
	• *High CHO, low fat diet: 25%E FA, 59%E CHO, 16% protein*
	• *Each participant consumed 5 isoenergetic diets for 4 wk each separated by ≥24 d washouts. 3 meals & 1 snack per day provided to participants*
	
	Duration of intervention: 4 wk each diet (washout ≥24 days)
	Compliance: Weekly checklist of study foods consumed and not consumed, self-reported compliance : 98.7% SD = 2.4%
	
	Nutritional composition of intervention diets for Cheese vs Butter vs MUFA vs PUFA vs CHO, Mean, %E:
	SFA: 12.6 vs 12.4 vs 5.8 vs 5.8 vs 5.8
	MUFA: 12.5 vs 12.3 vs 19.6 vs 12.6 vs 12.6
	PUFA: 4.8 vs 4.8 vs 4.8 vs 11.5 vs 4.8
	Cholesterol: All ~272mg/2500kcal
	Other components of diet differed significantly: CHOs higher (59%) in CHO diet vs all others (~52%); Calcium (higher in the cheese than other groups)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured in duplicate at end of 4wk intervention period
		TC, mmol/L, Mean (SD)
		Cheese: 5.00 (0.94); vs MUFA, PUFA or CHO: p<0.05
		Butter: 5.10 (0.95); vs MUFA, PUFA or CHO: p<0.05
		MUFA: 4.82 (0.89)
		PUFA: 4.60 (0.81)
		CHO: 4.89 (0.92)
		P-between diets: <0.0001
		LDL, mmol/L, Mean (SD)
		Cheese (ref): 3.19 (0.81); vs MUFA, PUFA or CHO: p<0.05
		Butter (ref): 3.30 (0.84); vs MUFA, PUFA or CHO: p<0.05
		MUFA: 3.03 (0.78)
		PUFA: 2.84 (0.69)
		CHO: 3.11 (0.79)
		P-between diets: <0.0001
		HDL, mmol/L, Mean (SD)
		Cheese: 1.10 (0.19); vs CHO, p<0.05
		Butter: 1.11 (0.21); vs CHO, p<0.05
		MUFA: 1.10 (0.19)
		PUFA: 1.10 (0.20)
		CHO: 1.06 (0.19)
		P-between diets: 0.0051
		Triglycerides, mmol/L, Mean (SD)
		Cheese: 1.43 (0.70); vs Butter or PUFA, p<0.05
		Butter: 1.36 (0.73); vs CHO, p<0.05
		MUFA: 1.38 (0.67)
		PUFA: 1.30 (0.62); vs Cheese, p<0.05
		CHO: 1.46 (0.71) ; vs Butter, p<0.05
		P-between diets: 0.0007
		
		*No comparison made between CHO, MUFA, and PUFA diets because were not primary objectives of study
			Model adjustments:
			When variable p<0.05: baseline blood lipid value, sex, age, BMI, center, sequence, WHR or waist circumference, ethnicity
			
			Limitations:
			• No information provided on randomization method
			• No preregistered statistical analysis plan for most blood lipid outcomes
			
			Funding sources:
			Dairy Research Cluster Initiative (Agriculture and Agri-Food Canada, Dairy Farmers of Canada, the Canadian Dairy Network, the Canadian Dairy Commission)

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Burns-Whitmore, 2014[56]
RCT crossover, U.S.
Baseline N=26, Analytic N=20 (Attrition: 23%)
 	
Participant characteristics at baseline: Nonsmoking, healthy lacto-ovo vegetarians (80% female, 50% White) ~38y of age with normal blood lipids and BMI ~23.
 	
Summary of findings:
Among healthy lacto-ovo vegetarians, consumption of walnuts for 8 weeks (which increased n-6 PUFA and ALA intake, and decreased dietary cholesterol intake) reduced total blood cholesterol and triglycerides compared to consumption of standard or n-3 FA enriched eggs. Blood lipids did not vary significantly between standard egg and n-3 FA enriched egg.
	Intervention and comparators:
	• n-3 FA enriched egg (6/wk)
	  • Sources: eggs from chickens fed diet containing flaxseed
	• Walnuts (28.4g, 6/wk)
	  • Sources: walnuts
	• Standard egg (6/wk)
	  • Sources: eggs
	
	Duration of intervention: 8 wk each diet (washout: 4 wk)
	Compliance: Monitored via counseling with dietitian, daily diary to record deviations in food intake, and 3, 24hr recalls per treatment period; compliance met through dietary intake
	
	Total dietary intake for n-3 enriched egg vs walnuts vs standard egg, Mean, %E:
	SFA: 7.71 vs 7.86 vs 7.55, P=NS
	MUFA: 10.4 vs 10.5 vs 10.4, P=NS
	PUFA: 6.53 vs 11.7 vs 6.98, P<0.0001 (walnut vs n-3 enriched egg or standard egg)
	n-6 PUFA: 5.21 vs 9.84 vs 5.84, P<0.0001 (walnut vs n-3 enriched egg or standard egg)
	LA: 5.16 vs 9.84 vs 5.79, P<0.0001 (walnut vs n-3 enriched egg or standard egg)
	AA: 0.54 vs 0.53 vs 0.50, P<0.0001 (all differ)
	n-3 PUFA: 0.55 vs 1.61 vs 0.66, P<0.0001 (walnut vs n-3 enriched egg or standard egg)
	ALA: 0.49 vs 1.61 vs 0.64, P<0.0001 (walnut vs n-3 enriched egg or standard egg)
	EPA: 0.06 vs 0.00 vs 0.00, P<0.0001 (n-3 enriched egg vs walnuts or standard egg)
	DHA: 0.06 vs 0.00 vs 0.00, P<0.0001 (n-3 enriched egg vs walnuts or standard egg)
	Cholesterol (mg/d): 214 vs 46 vs 136, P<0.0002 (walnut vs n-3 enriched egg or standard egg)
	Other components of diet differed significantly: Protein (lower in walnut)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and 4 wk
		
		Comparison between baseline adjusted values at 4 wk
		
		TC, mmol/L, Mean (95% CI)
		Standard egg: 5.09 (4.92, 5.26)
		n-3 enriched egg: 4.96 (4.79, 5.12)
		Walnuts: 4.77 (4.60, 4.94)
		Walnut vs Standard egg (ref): P<0.05
		n-3 enriched egg vs Walnut or Standard egg: P=NS
		
		LDL, mmol/L
		Standard egg vs n-3 enriched egg vs Walnut: All P=NS
		
		HDL, mmol/L
		Standard egg vs n-3 enriched egg vs Walnut: All P=NS
		
		Triglycerides, mmol/L
		Standard egg: 1.12 (1.00, 1.26)
		n-3 enriched egg: 0.97 (0.87, 1.08)
		Walnuts: 0.92 (0.83, 1.03)
		Walnut vs Standard egg (ref): P<0.05
		n-3 enriched egg vs Walnut or Standard egg: P=NS
			Model adjustments:
			Period effect, baseline values
			
			Limitations:
			• No information on randomization of allocation sequence
			• No information on missing data by intervention sequence
			• No preregistered statistical analysis plan
			
			Funding sources:
			American Egg Board Fellowship; Agriculture Research Institute (Grant) from California State Polytechnic University, Pomona; California Walnut Commission (donation of walnuts); Chino Valley Ranchers (donation of eggs)

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Cheng, 2019[57] **RCT crossover, China** Baseline N=72 Analytic N=67 (Attrition: 7%) **Participant characteristics at baseline:** Healthy Chinese participants (~50% female) aged ~23 years, with normal BMI and no history of CVD, hypertension or diabetes **Summary of findings:** *Consumption of palm olein, compared to cocoa butter and extra virgin olive oil resulted in significantly lower triglycerides in young Chinese adults. No other significant differences in blood lipids were observed.*	**Intervention and comparators:** • Palm olein (35% SFA) • Cocoa butter (64% SFA) • Extra virgin olive oil (17% SFA) • *Participants consumed standardized Chinese meals provided by researchers, enriched with one of the test oils* • *Each test oil accounted for ~40% of total fat intake and ~11.3% total energy intake* **Fatty acid composition of palm olein, CB and EVOO, g%:** SFA: 34.5 vs 64.4 vs 17.2 (EVOO < PO and CB, P<0.01) Palmitic acid: 29.4 vs 26.2 vs 13 Stearic acid: 3.4 vs 37.1 vs 3.9 MUFA: 50.7 vs 33.1 vs 77.5 (EVOO > PO and CB, P<0.01) Oleic acid: 50.3 vs 33.1 vs 76.3 PUFA: 14.8 vs 2.5 vs 5.3, P>0.05 ALA: 0.3 vs 0 vs 0.7 LA: 14.5 vs 2.5 vs 4.6 Duration of intervention: 4 wk each dietary period (2 week run-in and 2-wk washout periods) Compliance: All participants dined in cafeteria and researchers supervised compliance and intake behavior; all participants adhered to diet "closely" **Dietary intake for palm olein, cocoa butter, extra virgin olive oil, Mean (SD), g/day:** SFA: 18.2 (1.6) vs 24.7 (1.3) vs 13.9 (0.7), between all groups: P<0.05 MUFA: 24.8 (1.5) vs 20.8 (1.6) vs 31.2 (0.7), between all groups: P<0.05 PUFA: 9.7 (1.0) vs 7.7 (1.6) vs 9.2 (1.1), P=NS between groups Cholesterol: 489.1 (75.3) vs 498.2 (113.9) vs 493.6 (99.3), P=NS Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4 wk follow-up after each experimental diet Levels at 4 wk follow-up **TC**, mmol/L, Mean (SD) Palm olein vs cocoa butter vs EVOO: NS **LDL**, mmol/L, Mean (SD) Palm olein vs cocoa butter vs EVOO: NS **HDL**, mmol/L, Mean (SD) Palm olein vs cocoa butter vs EVOO: NS **Triglycerides**, mmol/L, Mean (SD) **Palm olein: 0.81 (0.28)** **Cocoa butter: 0.84 (0.31)** **EVOO: 0.88 (0.31)** **Palm olein vs cocoa butter: P<0.05** **Palm olein vs EVOO: P<0.05** Cocoa butter vs EVOO: NS	**Model adjustments:** Baseline indices, age, gender **Limitations:** • No preregistered statistical analysis plan **Funding sources:** Nutrition Fund Chinese Nutrition Society; Fundamental Research Funds for the Central Universities; Research Innovation Program for College Postgraduates in Jiangsu Province; National Key Project of Research and Development Plan

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Chinwong, 2017[58] **RCT crossover, Thailand** Baseline N=34 Analytic N=32 (Attrition: 6%) **Participant characteristics at baseline:** Participants (50% female) aged ~21 years with normal serum lipid levels at baseline, BMI ~21 **Summary of findings:** *Consumption of coconut oil (15 mL twice a day), compared to a 2% carboxymethylcellulose solution, significantly increased HDL cholesterol, but no other significant differences in changes in blood lipids were observed.*	**Intervention and comparator:** • Virgin coconut oil (15 mL/day x 2 times/day): lauric acid (12%) 50%, myristic acid (C14:0) 18%, caprylic acid (C8:0) 9%, palmitic acid (C16:0) 8% • 2% carboxymethylcellulose (CMC) solution (15 mL/day x 2 times/day) Duration of intervention: 8 wk each dietary period (washout: 8 wk) Compliance: daily food record throughout study period; participant interview; compliance NR **Dietary intake for Intervention vs Control:** NR	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 24 wk follow-up **TC**, mg/dL, Mean (SD) Difference in change: VCO vs control: NS **LDL**, mg/dL, Mean (SD) Difference in change: VCO vs control: NS **HDL**, mg/dL, Mean (SD) Baseline to follow-up VCO: 60.3 (9.2) to 64.2 (9.9) Control: 60.8 to 59.0 **Change:** **VCO: 3.91 (6.34)** **Control: -1.81 (6.49)** **Difference in change: 5.72 (9.01), P=0.001** **Triglycerides**, mg/dL, Mean (SD) Difference in change: VCO vs control: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No information on compliance • No preregistered statistical analysis plan **Funding sources:** Thailand Research Fund

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Choi, 2018[60] **RCT crossover, U.S.** Baseline N=15 Analytic N=12 (Attrition: 20%) **Participant characteristics at baseline:** Men ~68y and post-menopausal women ~61y with BMI ~27 **Summary of findings:** *Consumption of 18% fat ground-beef patties (less oleic acid and less dietary cholesterol), compared to 25% fat ground beef patties (more oleic acid and more dietary cholesterol) did not result in any changes in total blood cholesterol, LDL, HDL cholesterol, or triglycerides.*	**Intervention and comparator:** • 18% fat: Ground-beef patties containing 18% total fat (5 per week) (intervention first: n=6): SFA: 7.6 g/patty; MUFA: 9.2 g/patty; *trans* fat: 0.8 g/patty; each patty = 114 grams (~4 ounces) previously reported • 25% fat: Ground-beef patties containing 25% total fat (5 per week) (control first: n=6): SFA: 11.9 g/patty; MUFA: 11.3 g/patty; *trans* fat: 1.6 g/patty Duration of intervention: 5 wk (washout 4 wk) Compliance: 4-day record **Dietary intake for Intervention (18% fat patty) vs Control (25% fat patty) after each intervention period, Mean (SE), g/day:** SFA: 28 (4) vs 29 (3) MUFA: 26 (4) vs 28 (2) Oleic acid: 21 (3) vs 24 (2), P<0.05 (time*treatment) LA: 12 (3) vs 10 (1) ALA: 0.8 (0.1) vs 0.9 (0.1) EPA: 0.01 (0.01) vs 0.05 (0.02) DHA: 0.01 (0.01) vs 0.11 (0.05) PUFA: 13 (3) vs 12 (1) Cholesterol (mg/day): 241 (45) vs 310 (61), P<0.05 (time*treatment) Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 5 wk follow-up Two-factor (time and treatment) repeated-measures ANOVA **TC**, mmol/L, Mean (SE) 18% fat vs 25% fat: NS **LDL**, mmol/L, Mean (SE) 18% fat vs 25% fat: NS **HDL**, mmol/L, Mean (SE) 18% fat vs 25% fat: NS **Triglycerides**, mmol/L, Mean (SE) 18% fat vs 25% fat: NS	**Model adjustments:** None **Limitations:** • No information on randomization of allocation sequence • No information on compliance • No information on whether missing data was different between groups • No preregistered statistical analysis plan **Funding sources:** Texas AgriLife Research

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Dawczynski, 2010[62]
RCT crossover, Germany
Baseline N=51 Analytic N=40 (Attrition: 22%)
 	
Participant characteristics at baseline: Healthy adults aged 59.2, SD= 6.0 years with mean BMI of 29.7, no CVD, no diabetes, mildly hypertriglyceridemic (TAG: ≥1.5 mmol/L)
 	
Summary of findings:
The consumption of dairy products supplemented with 3g/d n-3 LC-PUFA for 15 weeks compared to a placebo significantly decreased blood triglyceride and increased HDL-cholesterol and had no effect on total and LDL cholesterol in adults with mild hypertriglyceridemia.
	Intervention and comparator:
	• 3g n- 3 LC-PUFA/d provided via supplemented dairy products (~40 g fat daily).
	  • Sources: 200 g yogurt (3.8% fat), 30 g cheese (~ 50% fat), and 20-30 g butter; milk fat partially replaced by fish oil/rapeseed oil (not detectable) + 0.1 g/100 g vit E
	• Placebo: dairy products not supplemented
	  • Sources: Same as above, un-supplemented
	
	Duration of intervention: 15 wk (10 wk washout period)
	Compliance: 9 persons excluded for non-compliance (increase in erythrocyte membrane EPA <50% after 15wk intervention); EPA increase in "consumers" 282%, SD=153
	
	Dietary intake for Intervention vs Control, Mean (SD), g/d:
	SFA: 33.8 (9.92) vs 37.9 (11.2), P≤0.05
	MUFA: 25.4 (8.70) vs 26.3 (9.63), P: NS
	PUFA: 13.5 (3.74) vs 11.0 (3.69), P≤0.01
	The intake of AA, EPA, DHA, MUFA, PUFA, n- 3 FA, and CLA was higher in the intervention period, but the intake of SFA was lower (p ≤0.05)
		Outcomes and assessment methods:
		Fasting blood lipids at start and end of each test period
		
		TC, mmol/L, Intervention; Control, Mean (SD)
		Intervention: 6.13 (0.97)
		Control: 6.23 (1.02)
		Between-group: P=NS
		
		LDL, mmol/L, Intervention; Control, Mean (SD)
		Intervention: 4.28 (0.92)
		Control: 4.34 (0.97)
		Between-group: P: NS
		
		HDL, mmol/L, Intervention; Control, Mean (SD)
		Intervention: 1.14 (0.28)
		Control: 1.06 (0.23)
		Between-group: P≤0.05
		
		Triglycerides, mmol/L, Intervention; Control, Mean (SD)
		Intervention: 1.56 (0.98)
		Control: 1.84 (1.03)
		Between-group: P≤0.01
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• Potential bias from missing data
			
			Funding sources:
			HERZGUT creamery

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Drouin-Chartier, 2015[66] **RCT crossover, Canada** Baseline N=29 Analytic N=27 (Attrition: 7%) **Participant characteristics at baseline:** Postmenopausal women with abdominal obesity, ~57years, with BMI of ~31.9, 63% with metabolic syndrome, no CVD, no diabetes, no smoking, no hormone replacement therapy **Summary of findings:** *Consumption of low fat milk in the context of a NCEP diet, compared to consuming a NCEP diet without milk, had significantly smaller decreases in total cholesterol, but had no significant effect on LDL and, HDL cholesterol and triglycerides in postmenopausal women with abdominal obesity.*	**Intervention and comparator:** • MILK diet: 3 portions 2% milk/day (20%E); diet consistent with National Cholesterol Education Program (NCEP) diet: 29%E fat, 10%SFA, CHO 55%, protein 17% • NCEP no milk diet: comparable isocaloric diet (7d-cycle menus, calories and macronutrient composition) – added animal protein (mostly red meat and white egg powder), carbohydrate (mostly fruits) and lipids (mostly lard) Duration of intervention: 6 wk (4wk run-in, 6-8wk washout period) Compliance: Daily compliance sheets maintained by subjects indicated >98% compliance. **Dietary intake for Intervention vs Control, Mean (SD), %E :** SFA: 9.4 vs 9.8, P<0.05 MUFA: 12.0 vs 12.6, P=NS PUFA: 4.8 vs 4.9, P=NS Cholesterol: NS between groups Other components of diet differed: carbohydrate, fat, calcium and vitamin D significantly higher in the MILK diet.	**Outcomes and assessment methods**: Fasting blood lipids: start and end of each phase **TC**, mmol/L, Mean (SD) at post-intervention, % change MILK: 5.6 (0.87) -2.6% NCEP: 5.53 (0.76); -5.8% **MILK vs NCEP: P=0.01** **LDL**, mmol/L, % change MILK vs NCEP: P=0.42 **HDL**, mmol/L, % change MILK vs NCEP: P=0.29 **Triglycerides**, mmol/L, % change MILK vs NCEP: P=0.14	**Model adjustments:** Diet specific baseline values, changes in waist circumference **Limitations:** • No information provided on randomization method **Funding sources:** Canadian Institutes of Health Research, Dairy Farmers of Canada; Provigo/Loblaws

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Engel, 2015[68] **RCT crossover, Denmark** **Baseline N=50 Analytic N=47 (Attrition: 6%)** **Participant characteristics at baseline:** Healthy participants with normal BMI at ~40 years of age without diagnosis of current or previous CVD, diabetes or other severe chronic diseases **Summary of findings:** *Intake of olive oil, compared to butter, was significantly associated with lower total cholesterol and lower LDL cholesterol.*	**Intervention and comparator:** • Butter (13.5 g fat; daily diet with **butter** baked in bread roll) • Refined olive oil (13.3 g; daily diet with **olive oil** baked in bread roll) Duration of intervention: 5 wk (run in: 2 wk; washout: 10 days) Compliance: 3-day dietary records (2 weekdays, 1 weekend) **Dietary intake for Intervention (butter) vs Control (olive oil), Mean (SD), g/day:** SFA: 37.5 (15.7) vs 30.6 (13.3), P<0.0001 MUFA: NS PUFA: NS Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids: measured in duplicate at baseline (before intervention) and after intervention **TC**, Mean (SD), mmol/L **Butter: 5.50 (0.98)** **Olive oil: 5.27 (0.95)** **P<0.05** **LDL**, Mean (SD), mmol/L **Butter: 3.04 (0.86)** **Olive oil: 2.87 (0.86)** **P<0.05** **HDL**, NS **Triglycerides,** NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • Insufficient washout period • No preregistered statistical analysis plan **Funding sources:** Danish Dairy Research Foundation; Butter provided by Arla Foods, Denmark; Olive oil provided by AarhusKarlshamn, Denmark A/S.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Faghihnia, 2010[69]
RCT crossover, U.S.
Baseline N=NR Analytic N=63 (Attrition: NR)
 	
Participant characteristics at baseline: Participants (3% female) aged mean 48 years who had body weight <130% ideal, and total and LDL <95th percentile for sex/age
 	
Summary of findings:
Consuming a low-fat high carbohydrate diet for 4 weeks compared to a high-fat, low carbohydrate diet resulted in significantly decreased HDL- and LDL cholesterol, and increased triglycerides. There was no significant change in total cholesterol.
	Intervention diets:
	• High-fat, Low-carbohydrate (HFLC) diet:
	  • 15%E PRO, 40%E FAT,(13%E SFA, 11%E MUFA, 14%E PUFA, 3%E trans fat), 45%E CHO
	• Low-fat, High-carbohydrate (LFHC) diet:
	  • 15%E PRO, 20%E FAT(5%E SFA, 10%E MUFA, 5%E PUFA, 2%E trans fat), 65%E CHO
	
	• *There were no differences in dietary cholesterol and the ratio of simple:complex carbohydrate (50:50) between the diets*
	
	Duration of intervention: 2 controlled feeding periods lasting 4 wk each, no washout period
	Compliance: Good; <5% deviations
	
	Dietary composition for HFLC and LFHC diets: see above
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and after each 4 wk feeding period
		
		Measures after HFLC, LFHC, and difference between interventions:
		TC, mg/dL, Mean (SD)
		192.0 (34.5), 187.0 (31.7), Difference: -5.0 (21.3), p=0.06
		LDL, mg/dL, Mean (SD)
		124.0 (31.3), 117.3 (30.7), Difference: -6.6 (22.0), p< 0.05
		HDL, mg/dL, Mean (SD)
		41.1 (7.7), 37.0 (7.4), Difference: -4.1 (3.8), p<0.0001
		Triglycerides, mg/dL, Mean (SD)
		134.0 (100.8), 165.4 (96.2), Difference: 31.4 (84.9), p<0.0001
			Model adjustments:
			None
			
			Limitations:
			• No description of the randomization process
			• No washout period between interventions
			• No information about weight change during the intervention
			• No description of baseline sample size, and whether any drop-out occurred after subjects were randomized
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Dairy Council and the Foundation Leducq.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Gilmore, 2011[72] **RCT crossover, U.S.** **Baseline** N=30 Analytic N=27 (Attrition: 10%) **Participant characteristics at baseline:** Normocholesterolemic men ~36y with BMI ~27 **Summary of findings:** *Participants who consumed high MUFA patties (lower in SFA, higher in MUFA and oleic acid), compared to low MUFA patties, had greater positive change from baseline in HDL cholesterol. There were no differences in total blood cholesterol, LDL cholesterol and triglycerides.*	**Intervention and comparator:** • Low MUFA ground patties (5/wk): pasture-fed cattle (MUFA:SFA 0.70; Oleic acid: 10.1 g/114 g ground beef; LA: 0.55 g/114 g ground beef; ALA: 0.09 g/114 g ground beef) • High MUFA ground patties (5/wk): cattle fed grain-based diets (MUFA:SFA 1.10; Oleic acid: 13.3 g/114 g ground beef; LA: 0.56 g/114 g ground beef; ALA: 0.03 g/114g ground beef) Duration of intervention: 5 wk (4 wk washout) Compliance: 3-day diet record **Dietary intake for Intervention (low MUFA) vs Control (high MUFA) at 5 wk, Mean (SD), g/day:** Total fat: 97 (9) vs 97 (8), NS between groups SFA: 39 (4) vs 36 (2), P=NR; Greater in low MUFA group MUFA: 31 (4) vs 32 (3), P=NR; Greater in high MUFA group Oleic acid: 27 (3) vs 27 (2), Higher in MUFA group PUFA: 11 (1) vs 12 (2), P=NR LA: 8 (1) vs 9 (2), NS between groups ALA: 1 (1) vs 1 (1), NS between groups Cholesterol: 325 (44) vs 325 (43), NS between groups Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 5 wk follow-up **TC**, mmol/L, Mean (SD) Change from baseline: Low MUFA vs High MUFA: NS **LDL**, mmol/L, Mean (SD) Change from baseline: Low MUFA vs High MUFA: NS **HDL**, mmol/L, Mean (SD) Change from baseline: **Low MUFA vs High MUFA: P<0.05** (high MUFA patties had greater positive change from baseline, compared to low MUFA patties) **Triglycerides**, mmol/L, Mean (SD) Change from baseline: Low MUFA vs High MUFA: NS	**Model adjustments:** None **Limitations:** • No information on randomization of allocation sequence • No information on compliance • No preregistered statistical analysis plan **Funding sources:** Beef Checkoff through National Cattlemen's Beef Association

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Harris, 2017[76] **RCT crossover, U.S.** Baseline N=14 Analytic N=12 (Attrition: 14%) **Participant characteristics at baseline:** Postmenopausal women (mean age 59 y) with BMI ~26 and normal fasting lipids at baseline **Summary of findings:** *Consumption of virgin coconut oil for 4 weeks resulted in significant increases in total blood cholesterol, LDL, and HDL cholesterol; whereas consumption of safflower oil resulted in significant decreases in total blood and LDL cholesterol. The between-group difference in change was significant for total blood, LDL, and HDL cholesterol. There were no significant differences between groups in triglycerides.*	**Intervention and comparator:** • Virgin coconut oil (VCO) (30 mL/d): 97% SFA, 3% Oleic acid, <1% LA • Safflower oil (SO) (30 mL/d): 6% SFA, 80% Oleic acid, 13% LA • *Participants instructed to add test oils to already-prepared foods as toppings or dressings (not to cook with them).* • *Participants instructed to maintain current diet* Duration of intervention: 4 wk each dietary period (washout: 4 wk) Compliance: 8 days/month food records (total of 28 day food journals); "high rate" reported **Dietary intake for Intervention vs Control, Mean (SD), g/day:** SFA: NR MUFA: NR PUFA: NR Cholesterol: NR Other components of diet differed significantly: Protein: VCO (before; after): 83 (62); 96 (62); SO: 69 (15); 68 (18), P≤0.05	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4 wk follow-up Difference in change between groups **TC**, mg/dL, Mean (SD) Before; after values **VCO: 219.6 (32.6), 237.8 (24.1), Change: +18.20** **SO: 222.8 (25.6), 219.3 (22.8), Change: -3.50** **VCO vs SO (change): P≤0.05** **LDL**, mg/dL, Mean (SD) Before; after values **VCO: 124.0 (24.7), 137.5 (27.2), Change: +13.50** **SO: 130.7 (25.6), 126.8 (25.7), Change: -3.90** **VCO vs SO (change): P≤0.05** **HDL**, mg/dL, Mean (SD) Before; after values **VCO: 63.9 (16.2), 70.5 (18.8), Change: +6.60** SO: 63.2 (14.7), 62.9 (14.5), Change: -0.30 **VCO vs SO (change): P≤0.05** **Triglycerides**, mg/dL, Mean (SD) VCO vs SO (change): NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** University of Colorado, Colorado Springs' Committee on Creative and Research WorkSeed Grant Program; Tropical Traditions donated oils

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Hyde, 2019[77] **RCT crossover, U.S.** Baseline N=21 Analytic N=16 (Attrition: 24%) **Participant characteristics at baseline:** Participants (38% female) aged mean 41 years who were obese (BMI) diagnosed with metabolic syndrome **Summary of findings:** *After 4wk, there were no significant group differences in LDL cholesterol. All subjects combined and men had significantly decreased HDL cholesterol and decreased triglycerides after the HC diet.*	**Intervention diets:** • Low Carbohydrate (LC) diet: 20%E PRO, 74%E FAT, 6%E CHO, 100 g/d SFA • Moderate Carbohydrate (MC) diet: 20%E PRO, 48%E FAT, 32%E CHO, 70 g/d SFA • High Carbohydrate (HC) diet: 20%E PRO, 23%E FAT, 57%E CHO, 40 g/d SFA • *Controlled feeding trial* • *Isocaloric diets* Duration of intervention: 2 wk run-in on a standard American diet, followed by 3 controlled feeding periods lasting 4 wk each, with 2 wk washout period in between Compliance: measured daily; compliance NR **Dietary intake for Intervention diets (HC, MC, LC), Mean (Range), g (mg cholesterol):** SFA: 40 (28–51), 70 (48–89), 100 (69–127) MUFA: 21 (15–27), 54 (37–69), 86 (59–110) PUFA: 6 (5–8), 21 (14–26), 35 (24–45) Cholesterol: 334 (231–425), 503 (347–639), 1,015 (701–1291) Other components of diet differed significantly: CHO: 420 (290–534), 234 (161–297), 45 (31–58) PRO: 144 (100–184), 146 (101–185), 150 (103–190) FAT: 77 (53–97), 159 (110–202), 242 (167–307)	**Outcomes and assessment methods:** Fasting blood lipids: Measured at baseline and after each 4 wk feeding period Measures at baseline, and after LC, MC, HC (a vs b vs c denotes significant between group differences): Comparing difference in change **LDL**, mg/dL All: NS Men: NS Women: NS **HDL**, mg/dL **All: 37 (9), 40 (11)b, 35 (9)c, 34 (8)c, p=0.009** **Men: 33 (9), 35 (9)b, 32 (7)b, 30 (7)c, p=0.027** Women: NS **Triglycerides**, mg/dL **All: 177 (58), 120 (38)b, 189 (103)c, 199 (70)c, P=0.006** **Men: 188 (57), 114 (32)b, 181 (85)bc, 217 (83)c, P=0.019** Women: NS	**Model adjustments:** None **Limitations:** • No description of the randomization process • Potential bias from missing data • No preregistered statistical analysis plan **Funding sources:** National Dairy Council and the Dutch Dairy Association

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Intorre, 2011[79]
RCT crossover, Italy
Baseline N=30, Analytic N=30 (Attrition: 0%)
 	
Participant characteristics at baseline: Normolipidemic adults (~66% female) 20-40y of age and with mean BMI of ~23.
 	
Summary of findings:
In participants self-selecting their diet, consumption of cheese lower in SFA, and higher in MUFA and PUFA, for 4 weeks did not change fasting blood lipids compared to consumption of conventional cheese higher in SFA and lower in MUFA and PUFA.
	Intervention and comparator diets:
	• Experimental cheese lower in SFA and higher in MUFA and PUFA, three 50g serving/wk
	  • Sources: From cows fed diet with added linseed oil
	• Control cheese higher in SFA and lower in MUFA and PUFA, three 50g serving/wk
	  • Sources: From cows fed diet without added linseed oil
	
	Duration of intervention: 4 wk (preceded by 2 wk run in; 1mo washout between interventions)
	Compliance: Monitored via food records and 24 hour recalls; Cheese was consumed "as indicated"
	
	Total dietary intake for Control cheese vs Experimental cheese, Mean (SD), %E:
	SFA: 12.0 (2.5) vs 12.7 (2.9), P=NS
	MUFA: 18.4 (4.5) vs 18.8 (4.0), P=NS
	PUFA: 5.3 (0.9) vs 5.2 (1.0), P=NS
	Cholesterol: NR
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Changes in Fasting blood lipids:
		Measured at beginning and end of 4wk period
		
		TC, mmol/L, Mean (SD)
		Experimental vs Control: P=NS
		
		LDL, mmol/L, Mean (SD)
		Experimental vs Control: P=NS
		
		HDL, mmol/L, Mean (SD)
		Experimental vs Control: P=NS
		
		Triglycerides, mmol/L, Mean (SD)
		Experimental vs Control: P=NS
			Model adjustments:
			None
			
			Limitations:
			• No information on method of randomization
			• No preregistered statistical analysis plan
			
			Funding sources:
			TRUEFOOD project (European Commission under the 6th Framework Programme for RTD)

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Isherwood, 2010[80] **RCT crossover, U.K.** Baseline N=25 Analytic N=23 (Attrition: 8%) **Participant characteristics at baseline:** Normo-lipidemic men aged ~41 with BMI ~26, free of dietary supplements **Summary of findings:** *Consumption of 8 ounces of prawns (which increased dietary cholesterol), daily for 4 weeks, compared to 8 ounces of fish sticks, did not significantly change total cholesterol, LDL, HDL cholesterol or triglycerides.*	**Intervention and comparator:** • 225 g/day (~8 oz) cold water prawns daily: dietary cholesterol 295 mg, EPA+DHA: 0.6-0.7 g • 225 g/day (~8 oz) of fish ('crab') sticks: traces of dietary cholesterol and n-3 PUFA Duration of intervention: 4 wk each diet (washout 4 wk) Compliance: 3-day diet diaries; participants were compliant with study protocol **Dietary intake for Intervention vs Control, Mean (SD), g/day:** SFA: 19 (5) vs 21 (10) MUFA: 22 (6) vs 22 (10) PUFA: 14 (8) vs 11 (7) Cholesterol (mg/d): 794 (186) vs 275 (92), P<0.001 Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4 wk follow-up Difference in change **TC**, mmol/L, Mean (SD) Prawn vs control: NS **LDL**, mmol/L, Mean (SD) Prawn vs control: NS **HDL**, mmol/L, Mean (SD) Prawn vs control: NS **Triglycerides,** mmol/L, Mean (SD) Prawn vs control: NS	**Model adjustments:** None **Limitations:** • No preregistered statistical analysis plan **Funding sources:** European Fisheries Fund and Sea Fish Industry Authority

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Jones, 2014[83] **RCT crossover, COMIT I, U.S. and Canada** Baseline N=170 Analytic N=130 (Attrition: 24%) **Participant characteristics at baseline:** Nonsmoking adults ~46y of age with at least one cardiovascular risk factor and who were, on average, overweight (BMI, 29.8). **Summary of findings:** *Among adults with at least one cardiovascular risk factor, consuming oils with different FA profiles had different effects on blood lipids after 4 weeks. Corn-safflower (high in LA), flax-safflower (high in ALA), and canola-oleic (high in oleic acid) reduced total blood and LDL cholesterol compared to canola-DHA (high in DHA). Canola-DHA increased HDL cholesterol and decreased triglycerides compared to canola, corn-safflower, flax-safflower, and canola-oleic.*	**Intervention and comparator:** • Canola oil (59% oleic acid, 20% LA, 10% ALA) • Canola-DHA oil (63% oleic acid, 6% DHA) • Corn-Safflower oil (18% oleic acid, 69% LA) • Canola-Oleic oil (72% oleic acid, 15% LA) • Flax-Safflower oil (18% oleic acid, 38% LA, 32% ALA) **Fatty acid composition of Canola, Canola DHA, CornSaff, FlaxSaff, and Canola Oleic, (% fat):** SFA: 7.3 vs 9.0 vs 7.9 vs 8.1 vs 6.9 MUFA: 60.3 vs 64.7 vs 17.7 vs 17.9 vs 73.2 Oleic acid: 58.6 vs 63.2 vs 17.6 vs 17.9 vs 71.5 PUFA: 29.3 vs 23.1 vs 69.6 vs 69.5 vs 17.0 LA: 19.5 vs 12.7 vs 69.3 vs 37.5 vs 14.7 ALA: 9.8 vs 2.0 vs 0.3 vs 32.0 vs 2.3 EPA: 0 vs 0.2 vs 0 vs 0 vs 0 DPA: 0 vs 2.4 vs 0 vs 0 vs 0 DHA: 0 vs 5.8 vs 0 vs 0 vs 0 • *All diets weight-maintaining with fixed macronutrient composition: 15% protein, 50% CHO, 35% fat* • *All food provided by study* Duration of intervention: 4 wk each dietary period (4 wk wash-out) Compliance: Assessed by study coordinators by completion of meals provided under supervision and by presence of food not consumed in returned meal bags for off-site consumption **Diet composition for Canola vs Canola-DHA vs Corn-Safflower vs Canola-Oleic vs Flax-Safflower, Mean, %E:** SFA: 6.6 vs 6.9 vs 6.7 vs 6.5 vs 6.8 MUFA: 17.6 vs 17.8 vs 9.5 vs 19.3 vs 9.6 PUFA: 9.1 vs 8.0 vs 16.3 vs 6.9 vs 16.3 Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids: Measured at start of dietary phase and 4 wk. Different letters indicate different at P<0.05 **TC**, Mean (SE) ***At 4 wk, mmol/L:*** **Canola: 4.81 (0.14) ab** **Canola-DHA: 4.87 (0.14) a** **Corn-Safflower: 4.74 (0.14) bc** **Flax-Safflower: 4.69 (0.14) c** **Canola-Oleic: 4.77 (0.14) bc** ***Percentage change, %:*** **Canola: -8.5 (2.5) a** **Canola-DHA: -7.4 (2.5) a** **Corn-Safflower: -11.7 (2.5) b** **Flax-Safflower: -11.4 (2.5) b** **Canola-Oleic: -9.4 (2.5) ab** **LDL**, Mean (SE) ***At 4 wk, mmol/L:*** **Canola: 2.91 (0.08) b** **Canola-DHA: 3.02 (0.08) a** **Corn-Safflower: 2.85 (0.08) b** **Flax-Safflower: 2.84 (0.08) b** **Canola-Oleic: 2.86 (0.08) b** ***Percentage change, %:*** **Canola: -11.3 (2.8) ab** **Canola-DHA: -7.0 (2.8) b** **Corn-Safflower: -15.4 (2.8) a** **Flax-Safflower: -12.9 (2.8) a** **Canola-Oleic: -12.5 (2.8) a** **HDL**, Mean (SE) ***At 4 wk, mmol/L:*** **Canola: 1.20 (0.02) b** **Canola-DHA: 1.30 (0.02) a** **Corn-Safflower: 1.20 (0.02) b** **Flax-Safflower: 1.17 (0.02) b** **Canola-Oleic: 1.18 (0.02) b** ***Percentage change, %:*** **Canola: -4.2 (1.8) a**	**Model adjustments:** Age, sex, center (random effect), last treatment (random effect) **Limitations:** • No information on whether analyses were robust to missing data • No preregistered statistical analysis plan **Funding sources:** Canola Council of Canada; Flax Council of Canada; Agriculture and Agri Food Canada; Dow Agrosciences; Canada Research Chairs; Western Grains Research Foundation; National Center for Research Resources; National Center for Advancing Translational Sciences

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
		Canola-DHA: +3.5 (1.8) b **Corn-Safflower: -4.4 (1.8) a** **Flax-Safflower: -6.8 (1.8) a** **Canola-Oleic: -5.0 (1.8) a** **Triglycerides,** Mean (SE) ***At 4 wk, mmol/L:*** **Canola: 1.60 (0.10) a** **Canola-DHA: 1.25 (0.10) b** **Corn-Safflower: 1.56 (0.10) a** **Flax-Safflower: 1.56 (0.10) a** **Canola-Oleic: 1.64 (0.10) a** ***Percentage change, %:*** **Canola, Corn-Safflower, Flax-Safflower, Canola-Oleic: All NR, a** **Canola-DHA: -20.7 (3.8) b**	

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Karupaiah, 2016[85] **RCT crossover, Malaysia** Baseline N=34 Analytic N=34 (Attrition: 0%) **Participant characteristics at baseline:** Young adults (53% female), ~23y of age, with BMI ~25. **Summary of findings:** *In young adults, consumption of soybean oil based mayo for 4 weeks (which increased n-6 PUFA intake and decreased SFA and MUFA intake) significantly reduced total blood and LDL cholesterol relative to a palm olein based mayo. The soybean oil based mayo also decreased HDL cholesterol compared to the palm olein based mayo, and had no between-group effect on triglycerides*	**Intervention and comparator:** • Mayonnaise (~20g/d) made with soybean oil (high LA) • Mayonnaise (~20g/d) made with palm olein • *All meals provided by the study (fixed total fat and cholesterol content)* **Fatty acid composition for Soybean vs Palm olein-mayo; duplicated total diet (%):** SFA: 14.0 vs 41.7; 35.1 vs 41.9, P<0.05 MUFA: 24.5 vs 45.3; 38.5 vs 42.8, P<0.05 PUFA: 58.7 vs 12.6; 25.7 vs 14.4, P<0.05 Palmitic acid: 10.4 vs 37.7; 28.0 vs 34.6, P<0.05 Stearic acid: NS Oleic acid: 24.3 vs 45.1; 37.5 vs 41.8, P<0.05 LA: 53.1 vs 12.3; 23.4 vs 13.0, P<0.05 C18:3n6: Mayo: not detected; 0.18 vs 0.04, P<0.05 ALA: 5.6 vs 0.3; 1.05 vs 0.77, P=NS Total n-6: 53.1 vs 12.3; 24.0 vs 13.2, P<0.05 Total n-3: 5.6 vs 0.3; 1.05 vs 0.77, P<0.05 Duration of intervention: 4 wk each dietary period (Wash-out: 2 wk) Compliance: Monitored via meal time attendance records, 3, 24 hour recalls per crossover period **Total diet for Soybean Oil Mayonnaise vs Palm Olein Mayonnaise, Mean (SD), % of FA:** SFA: 35.1 (2.8) vs 41.9 (1.3), P<0.05 MUFA: 38.5 (1.3) vs 42.8 (1.8), P<0.05 PUFA: 25.7 (3.6) vs 14.4 (0.9), P<0.05 n-6 PUFA: 24.0 (3.7) vs 13.2 (1.0), P<0.05 n-3 PUFA: 1.05 (0.41) vs 0.77 (0.87), P=NS Cholesterol: NR Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids: Measured at baseline and in duplicate at 4 wk. *Between group differences at 4 wk* **TC**, mmol/L, Mean (SD) **Baseline: 5.20 (0.56)** **Soybean Oil: 4.80 (0.65)** **Palm Olein: 5.06 (0.61)** **Between group differences P=0.001** **LDL**, mmol/L, Mean (SD) **Baseline: 3.37 (0.52)** **Soybean Oil: 3.05 (0.57)** **Palm Olein: 3.22 (0.57)** **Between group differences P=0.016** **HDL**, mmol/L, Mean (SD) **Baseline: 1.39 (0.27)** **Soybean Oil: 1.21 (0.27)** **Palm Olein: 1.34 (0.30)** **Between group differences P<0.001** **Triglycerides,** mmol/L, Mean (SD) Soybean Oil vs Palm Olein: P=NS	**Model adjustments:** Change in body weight **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** Kewpie Corporation, Japan

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Katz, 2012[86]
RCT crossover, U.S.
Baseline N=46 Analytic N=40 (Attrition: 13%)
 	
Participant characteristics at baseline: Nonsmoking adults (~61% female) ~57y of age with overweight or obesity, high waist circumference, and one or more additional risk factors for metabolic syndrome
 	
Summary of findings:
In adults with overweight or obesity and at risk for metabolic syndrome, consuming a walnut enriched diet for 8 weeks (which increased PUFA intake) did not significantly change blood lipids relative to a diet without walnuts.
	Intervention and comparator diets:
	• Walnut enriched ad libitum diet, 56g/d daily; Counseled to substitute walnuts for other foods in diet to keep weight stable
	  • Sources: unroasted English walnuts
	• Control: Ad libitum diet without walnuts
	  • Sources: NA
	
	Duration of intervention: 8 wk (4 wk run in; 4 wk washout)
	Compliance: Assessed via diet records and consumption log sheets; 1 participant dropped out due to inability to comply with protocol
	
	Dietary intake during Walnut diet vs Control diet, Mean (SD), %E:
	SFA: 11.8 (3.5) vs 11.6 (3.6), P=NS
	MUFA: 10.8 (3.0) vs 10.7 (3.2), P<0.01
	PUFA: 13.2 (6.0) vs 6.0 (2.8), P<0.01
	n-3 PUFA: 2.1 (0.8) vs 0.6 (1.1), P<0.01
	n-6 PUFA: 10.7 (5.1) vs 4.8 (2.5), P<0.01
	Cholesterol (mg/d): 297.1 (176.5) vs 321.9 (172.0), P=NS
	Other components of diet differed significantly: Total fat (higher in walnut), protein and CHO (lower in walnut).
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and 8 wk
		
		Comparing change from baseline between groups
		
		TC, mg/dL
		Walnut vs Control: P=NS
		
		LDL, mg/dL
		Walnut vs Control: P=NS
		
		HDL, mg/dL
		Walnut vs Control: P=NS
		
		Triglycerides, mg/dL
		Walnut vs Control: P=NS
			Model adjustments:
			Age, race, BMI, hypertensive status, dyslipidemia, treatment sequence
			
			Limitations:
			• No information on randomization of allocation sequence
			• No information on whether results were robust to missing data
			• Trial register does not contain sufficient information to assess selection of reported results
			
			Funding sources:
			California Walnut Commission

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Kawakami, 2015[87] **RCT crossover, Japan** Baseline N=21 Analytic N=15 (Attrition: 29%) **Participant characteristics at baseline:** Participants (0% female) aged ~45 with BMI ~25 **Summary of findings:** *Consumption of flaxseed oil (higher in ALA), compared to corn oil, resulted in significant between group differences in total blood, LDL, and HDL cholesterol. There were no significant differences in triglycerides between groups.*	**Intervention and comparator:** • Flaxseed oil (high ALA) (10 g/day) • Corn oil (10 g/day) • *Participants instructed to consume test oils (10 g/d) using a spoon once daily with dinner* **Fatty acid composition of flaxseed oil and corn oil (g/100g):** Palmitic acid: 5.2 vs 12.0 Stearic: 3.8 vs 2.0 Oleic: 18.9 vs 29.1 LA: 16.2 vs 54.5 ALA: 54.9 vs 0.9 AA: 0.2 vs 0.5 n6:n3 ratio: 0.3 vs 60.6 Duration of intervention: 12 wk (washout: 8 wk) Compliance: food diary every 2 wk and remaining volumes of oil; all subjects consumed >97% of oil **Dietary intake for flaxseed vs corn oil at 12wk, Mean (SD), units/day:** Total fat (g): 64.1 (4.1) vs 71.4 (3.2), P=NS ALA (mg): 6,032.0 (140.0) vs 1,606.0 (136.0), P<0.05 EPA (mg): 225 (75) vs 153 (59), P=NS DHA (mg): 383 (109) vs 288 (85), P=NS LA (mg): 8,106 (775) vs 15,675 (688), P<0.05 n6:n3 ratio: 1.2 (0.1) vs 8.3 (0.8), P<0.05 Other components of diet differed significantly: alpha-tocopherol: 8.1 (0.6) vs 5.4 (0.5), P<0.05	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4 and 12 wk follow-up **TC**, mg/dL, Mean (SD) **Flaxseed oil: 202.3 (7.3)** **Corn oil: 216.9 (7.7)** **Between group difference at 12wk: P<0.05** **LDL**, mg/dL, Mean (SD) **Flaxseed oil: 127.7 (7.2)** **Corn oil: 137.9 (7.7)** **Between group difference at 12wk: P<0.05** **HDL**, mg/dL, Mean (SD) **Flaxseed oil: 49.2 (2.7)** **Corn oil: 54.9 (3.0)** **Between group difference at 12wk: P<0.05** **Triglycerides**, mmol/L, Mean (SD) Flaxseed oil vs corn oil: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No information on whether missing data was different between groups • No preregistered statistical analysis plan **Funding sources:** Ministry of Agriculture, Forestry, and Fisheries; Sadamitsu Food Industry Limited

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Kontogianni, 2013[90] **RCT crossover, Greece** Baseline N= 53 Analytic N=37 (Attrition: 30%) **Participant characteristics at baseline:** Healthy, normal weight adults (78% female) mean 25.6y and 22 BMI, free of CHD, diabetes, MedDietScore 34 **Summary of findings:** *Diets enriched with flaxseed oil versus olive oil did not significantly change blood total, LDL and HDL cholesterol and triglycerides in adults who traditionally use olive oil as the main dietary oil.*	**Intervention and comparator:** • Flaxseed oil (15mL/d or 13.8g) • Olive oil (extra virgin) (15mL/d) • *Diets enriched: Participants instructed to incorporate oils into their daily dietary intake without substituting any of their current oil intakes* **Fatty acid composition of flaxseed oil vs olive oil (g/day):** Oleic acid: 3 vs 11.3 ALA: 8 vs 0.13 Duration of intervention: 6 wk each diet (6 wk washout) Compliance: 7 non–compliant with flaxseed oil (change in erythrocyte membrane ALA concentration < 0.06%E) Mean change: 0.18 (range -0.04-.043) **Dietary intake for Flaxseed vs Olive oil, Mean (SD):** SFA (%E): NS MUFA (%E): NS PUFA (%E): 8.4 (1.9) vs 6.0 (5.9), P<0.001 n-3/n-6 FA ratio: 1.4 (1.2) vs 8.3 (3.5), P<0.001 ALA (g/d): 8.7 (2.2) vs 0.8 (0.3), P<0.001 EPA (g/d): 0.05 (0.09) vs 0.08 (0.12), P=0.02 DHA (g/d): NS No differences observed in macronutrients, fiber and alcohol.	**Outcomes and assessment methods**: Fasting blood lipids assessed the first and last day of each intervention Levels after dietary intervention **TC**, flaxseed vs olive oil, P=NS **LDL**, flaxseed vs olive oil, P=NS **HDL**, flaxseed vs olive oil, P=NS **Triglycerides**, flaxseed vs olive oil, P=NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • Proportion of missing outcome data not balanced • No preregistered statistical analysis plan **Funding sources:** NR, (Minerva S.A supplied olive oil)

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Kovell, 2019[91] **RCT crossover, OmniHeart, U.S.** Baseline=191 Analytic N= 164 (Attrition: 14%) **Participant characteristics at baseline:** ~53.6 y, 45% female, BMI ~30.2, 55% African American, 100% high BP or HTN, no HTN or hyperlipidemia medication, no CVD, no diabetes **Summary of findings:** *Replacement of 10% carbohydrate by unsaturated fat for 6 weeks did not significantly affect blood LDL cholesterol levels in healthy adults with pre- or stage 1 hypertension.*	**Intervention diet:** • Carbohydrate-rich diet (CARB): 58% carbohydrate, 15% protein, 27% fat, 6% SFA, 13% MUFA, 8%PUFA) • Protein-rich diet (PROT): 10% CHO replaced by protein (48% CHO, 25% protein, 27% fat, 6% SFA, 13% MUFA, 8%PUFA) • Unsaturated fat-rich diet (UNSAT): 10% CHO replaced by unsaturated fat (48% CHO, 15% protein, 37% fat, 6% SFA, 21% MUFA, 10%PUFA) • *All diet interventions were weight maintenance, low in saturated fat, cholesterol, and sodium.* • *Meals prepared in a research kitchen.* Duration of intervention: 6 wk (2-4 wk washout) Compliance: 95% of trial person days, i.e. complete consumption of all study foods without any non-study foods **Dietary intake for CARB vs PROT vs UNSAT, Mean (SD), (%):** SFA: 6 vs 6 vs 6 MUFA: 13 vs 13 vs 21 PUFA: 8 vs 8 vs 10 Cholesterol: NR (NS) Other components of diet differed significantly: CHO: 58 vs 48 vs 48	**Outcomes and assessment methods**: Fasting blood lipids: At baseline and after each feeding period. Comparisons between groups at end of each feeding period **LDL**, mg/dl, Mean change from baseline UNSAT vs CARB: P=0.22	**Model adjustments:** None **Limitations:** • Attrition >10% **Funding sources:** NIH/NHLBI

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Liu, 2018[94] **RCT crossover, COMIT, Canada and U.S.** Baseline N=130 Analytic N= 101 (Attrition: 25%) **Participant characteristics at baseline:** Adults (50% female) with or at risk for metabolic syndrome, mean age ~50 y, with a BMI of ~29.4 and central obesity **Summary of findings:** *After 4 weeks, five oil interventions (canola, canola oleic, and canola DHA oils, corn and safflower oil blend, and fax and safflower oil blend), which were low in SFAs and high in MUFAs or PUFAs, significantly decreased total- and LDL cholesterol and triglyceride concentrations from baseline in adults with or at risk for metabolic syndrome. Canola DHA had a significantly greater effect on increasing HDL cholesterol and decreasing triglycerides than the other four oil types.*	**Intervention and comparators:** • Conventional Canola oil (3.8 g ALA) • Canola Oleic: High oleic acid–canola oil (1.2 g ALA) • Canola DHA: DHA-enriched high oleic acid–canola oil (1.2 g ALA and 3.6 g DHA) • Corn oil and safflower oil blend (Corn/Saff) • Flax oil and safflower oil blend (Flax/Saff) (6.9 g ALA) • *Participants consumed 2 smoothies per day (each containing treatment oil) as part of an isocaloric diet.* • *Treatment oils provided ~18% of total fat energy per day; for a 3,000kcal diet, 60 g treatment oil/day was incorporated into smoothies.* **Fatty acid composition of Canola vs Canola Oleic vs Canola DHA, CornSaff and FlaxSaff (% of total fat):** SFA: 7.2 vs 6.5 vs 8.6 vs 7.9 vs 8.1 MUFA: 62.8 vs 72.0 vs 63.8 vs 17.7 vs 17.9 PUFA: 29.5 vs 17.0 vs 23.3 vs 69.6 vs 69.4 ALA: 9.8 vs 2.3 vs 2.2 vs <1.0 vs 32.0 DHA: 0 vs 0 vs 5.8 vs 0 vs 0 LA: 19.5 vs 14.7 vs 12.7 vs 69.3 vs 37.5 All food was provided to participants (3 meals and a snack daily) during the feeding period. All diets (%E): 50% CHO, 15% Protein, 35% fat (18% from treatment oil) Duration of intervention: 4 wk each treatment period (2-4 wk washout) Compliance: NR; assessed via based remaining amounts of treatment shakes in pre-packaged food packs, weekly diet questionnaires and change in serum DHA **Dietary intake for all groups, Mean (SD):** SFA: NR MUFA: NR PUFA: NR Cholesterol: NR	**Outcomes and assessment methods**: Fasting blood lipids: assessed at day 1 and days 29 and 30 (endpoint) for each treatment period. *Changes in lipid values from baseline in response to treatment oils* **TC**, mmol/L, Mean (SEM) Canola oil: −0.58 (0.051) Canola Oleic: −0.61 (0.06) Canola DHA: −0.54 (0.06) Corn/Saff: −0.62 (0.06) Flax/Saff: −0.68 (0.04) **All differences from baseline P<0.05** **Group differences: Canola DHA vs Corn/Saff; Flax/Saff P<0.05** **LDL**, mmol/L, Mean (SEM) Canola oil: −0.54 (0.05) Canola Oleic: −0.55 (0.05) Canola DHA: −0.58 (0.054) Corn/Saff: −0.59 (0.05) Flax/Saff: −0.60 (0.048) **All differences from baseline P<0.05** NS differences between groups **HDL**, mmol/L, Mean (SEM) Canola oil: −0.04 (0.02) Canola Oleic: −0.02 (0.02) Canola DHA: +0.07 (0.02) Corn/Saff: −0.01 (0.02) - NS Flax/Saff: −0.04 (0.02) **All differences from baseline P<0.05 *except for Corn/Saff*** **Group differences:** **Canola DHA > Corn/Saff; Flax/Saff; Canola oil; Canola Oleic, P<0.05** **Triglycerides**, mmol/L, Mean (SEM) Canola oil: −0.14 (0.05) Canola Oleic: −0.07 (0.04) Canola DHA: -0.50 (0.04) Corn/Saff: −0.19 (0.05) Flax/Saff: −0.17 (0.04) **All differences from baseline P<0.05**	**Model adjustments:** Diet, visit, age, gender, obesity status, center **Limitations:** • Some concern about deviations from intended interventions due to compliance NR **Funding sources:** Agriculture and Agri Food Canada; Canola Council of Canada, Dow Agrosciences and Flax Council of Canada; National Center for Research Resources; NIH Grant

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
		Group differences: **Canola DHA > Corn/Saff; Flax/Saff; Canola oil; Canola Oleic P<0.05**	

McDaniel, 2013[97]
RCT crossover, U.S.
Baseline N=14 Analytic N=10 (Attrition: 29%)
 	
Participant characteristics at baseline: Healthy males ~34y with BMI ~25
 	
Summary of findings:
Participants who consumed beef or bison (12 ounces for 6 days per week for 7 weeks had no differences in total blood, LDL, or HDL cholesterol or triglycerides.
	Intervention and comparator:
	• 340 g (12 oz) beef (6 days/wk)
	• 340 g (12 oz) bison (6 days/wk)
	• Beef vs Bison roasts:
	  • SFA (% fat): 41 (4) vs 38 (3), P>0.05
	  • MUFA (% fat): 50 (2) vs 45 (4), P>0.05
	  • PUFA (% fat): 7 (2) vs 15 (3), P<0.05
	  • N-6 PUFA (% fat): 7 (2) vs 14 (3), P<0.05
	  • N-3 PUFA (% fat): 0.4 (0.2) vs 0.9 (0.1), P<0.05
	  • N-6/N-3 ratio: 17 (5) vs 16 (2), P>0.05
	
	Duration of intervention: 7 wk (washout 4 wk)
	Compliance: daily compliance checklist; participants had "excellent compliance"
	
	Dietary intake for Intervention vs Control, Mean (SD), g/day:
	SFA: Significant increase in beef but not bison, P<0.05
	MUFA: NR
	PUFA: NR
	Cholesterol: NR
	Other components of diet differed significantly: Protein intake increased with bison but not beef consumption
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 7 wk follow-up
		
		TC, mmol/L, Mean (SD)
		Relative change: Beef vs Bison: NS
		
		LDL, mmol/L, Mean (SD)
		Relative change: Beef vs Bison: NS
		
		HDL, mmol/L, Mean (SD)
		Relative change: Beef vs Bison: NS
		
		Triglycerides, mmol/L, Mean (SD)
		Relative change: Beef vs Bison: NS
			Model adjustments:
			None
			
			Limitations:
			• No information on randomization of allocation sequence
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Buffalo Foundation; NIH; Veterans Affairs

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

McKay, 2018[98]
RCT crossover, U.S.
Baseline N=26 Analytic N=26 (Attrition: 0%)
 	
Participant characteristics at baseline: Nonsmoking adults (19% female) with overweight or obesity, ~58y (males) or ~67y (females) of age
 	
Summary of findings:
Consumption of a diet rich in pecans for 4 weeks (which increase MUFA intake at the expense of SFA) did not significantly change blood lipids relative to a control diet without pecans except in some subgroups.
	Intervention and comparator:
	• Diet enriched in pecans (~15%E; 42.5 grams or 1.5 ounces daily)
	  • Sources: Pecans
	• Control: Diet resembling typical American diet
	  • Sources: NA
	
	• *All meals/snacks provided. Participants picked up meals and dropped off empty containers and unused food twice a week*
	
	Duration of intervention: 4 wk (2 wk run-in, 2 wk washout)
	Compliance: Monitored by study dietitian, NR; Confirmed via RBC FAs of primary MUFAs in pecans
	
	Estimated study diet composition for Pecan vs Control, %E:
	SFA: 9.1 vs 13.6
	MUFA: 14.8 vs 10.8
	PUFA: 8.6 vs 8.4
	Cholesterol (mg): 249 vs 256
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and 4 wk
		
		Tested between group differences in change
		
		TC, mg/dL, Mean change (SE)
		Pecan vs Control: P=NS
		When stratified by LDL cholesterol (<130mg/dL vs ≥130mg/dL):
		<130mg/dL: Pecan 4.15 vs Control 17.20, Difference -13.05, P=0.035
		≥130mg/dL: P=NS
		
		LDL, mg/dL, Mean change (SE)
		Pecan vs Control: P=NS
		When stratified by blood glucose (≤100mg/dL vs >100mg/dL):
		≤100mg/dL: P=NS
		>100mg/dL: Pecan -7.19 vs Control 8.39, Difference -15.58, P=0.006
		
		HDL, mg/dL
		Pecan vs Control: P=NS
		
		Triglycerides, mg/dL
		Pecan vs Control: P=NS
		
		Results were similar when blood lipids converted to z-scores.
			Model adjustments:
			Baseline blood lipid, period, carryover effects
			
			Limitations:
			• Potential bias due to multiple subgroups and definitions of the outcome
			
			Funding sources:
			USDA Agricultural Research Service; National Pecan Shellers Association

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Missimer, 2017[101] **RCT crossover, U.S.** Baseline N=50, Analytic N=48 (Attrition: 4%) **Participant characteristics at baseline:** Healthy participants (~50% female) aged ~23 years of age with, on average, normal BMI and blood lipid panel **Summary of findings:** *Participants had significantly higher total blood, LDL, and HDL cholesterol after intake of 2 eggs daily for 4 weeks, compared to one packet of oatmeal for breakfast.*	**Intervention and comparator:** • Eggs (2 per day): 370 mg cholesterol, 10 g fat • Oatmeal (one packet): 0 mg cholesterol, 1.5-2 g fat • *Participants instructed to eat intervention foods as first meal of the day and were allowed to add additional foods to meal; also instructed to avoid consuming whole eggs or foods containing predominantly eggs or oats.* Duration of intervention: 4 wk each diet (wash-out: 3 wk) Compliance: Monitored by self-report and bi-weekly visit to laboratory for product pickup; 2 participants dropped out due to failed compliance **Dietary intake during Egg vs Oatmeal, Mean (SD), g/d:** SFA: 27.3 (11.9) vs 21.1 (8.1), P<0.001 MUFA: 30.4 (11.6) vs 23.2 (9.6), P<0.001 PUFA: 16.6 (7.4) vs 15.7 (11.5), P=NS Cholesterol (mg/d): 546.1 (96.6) vs 173.1 (90.6), P<0.001 Other components of diet differed significantly: Total fat (higher in Egg), carbohydrate, soluble fiber, glycemic load (all lower in Egg)	**Outcomes and assessment methods**: Fasting blood lipids at baseline and end of each dietary period (4 wk) Levels at follow-up **TC**, mmol/L, Mean (SD) **Egg vs oatmeal: 4.2 (0.7) vs 4.0 (0.7), P<0.025** **LDL**, mmol/L, Mean (SD) **Egg vs oatmeal: 2.1 (0.7) vs 1.9 (0.6), P<0.025** **HDL**, mmol/L, Mean (SD) **Egg vs oatmeal: 1.71 (0.48) vs 1.62 (0.47), P<0.025** **Triglycerides**, mmol/L, Mean (SD) Egg vs oatmeal: NS	**Model adjustments:** None **Limitations:** • No information on randomization of allocation sequence • Co-interventions (fiber) differed between groups • No preregistered statistical analysis plan **Funding sources:** Esperance Family Foundation

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Morillas-Ruiz, 2014[102]
RCT crossover, Spain
Baseline N=60 Analytic N=53 (Attrition: 12%)
 	
Participant characteristics at baseline: Healthy post-menopausal, Caucasian women aged ~64y, with 73% overweight or obese, and 38% with hypercholesterolemia
 	
Summary of findings:
Total and LDL cholesterol at the end of a butter, margarine, and olive oil intervention was significantly different between groups.
	Intervention and comparator:
	• Breakfast A: containing 20 g of butter (SFA)
	  • SFA: 51.4 g
	  • MUFA: 21 g
	  • PUFA: 3 g
	  • Cholesterol: 215 mg
	• Breakfast B: containing 20 g of margarine (PUFA)
	  • SFA: 12.8 g
	  • MUFA: 15.3 g
	  • PUFA: 29.2 g
	  • Cholesterol: 0 mg
	• Breakfast C: 20 g virgin olive oil (MUFA)
	  • SFA: 14.5 g
	  • MUFA: 71 g
	  • PUFA: 10 g
	  • Cholesterol: 0 mg
	
	Duration of intervention: 4 wk (45 days for each washout period; no run-in period)
	Compliance: NR
		Outcomes and assessment methods:
		Fasting blood lipids at baseline and 4 wk
		
		TC, mg/dL, Mean (SEM) Post-intervention
		Butter: 208.21 (4.67)
		Margarine: 194.15 (3.65)
		Olive oil: 195.75 (5.19)
		P=0.050* (which groups differed NR)
		*described as being significant in the results
		
		LDL, mg/dL, Mean (SEM) Post-intervention: NS
		Butter: 120.89 (4.01)
		Margarine: 107.85 (3.10)
		Olive oil: 111.00 (4.76)
		P=0.042 (which groups differed NR)
		
		HDL cholesterol, Post-intervention: NS
		
		Triglycerides, Post-intervention: NS
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• No preregistered statistical analysis plan prior to start of study
			
			Funding sources:
			Catholic University of San Antonio

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Morton, 2019[103] **RCT crossover, U.S.** Baseline=NR Analytic N=9 (Attrition: NR) **Participant characteristics at baseline:** Overweight BMI ~29, low HDL cholesterol (mean 41 mg/dl, range 34-47), ~47 y, 33% female **Summary of findings:** *Consumption of a high unsaturated-fat (diet compared to a low-fat, high carbohydrate diet had no significant between group difference in changes to blood lipids in overweight adults with low HDL cholesterol.*	**Intervention and comparator:** • High unsat-fat (high MUFA): 40% fat (23% MUFA, 7% PUFA, 10% SFA), 45% CHO, 15% protein, 180mg cholesterol • Low fat (high carbohydrate): 20% fat (8% MUFA, 7% PUFA, 5% SFA), 65% CHO, 15% protein, 90 mg cholesterol • *Controlled feeding trial; Isocaloric diets provided by researchers* Duration of intervention: 4 wk (3 wk washout) Compliance: NR **Dietary intake for Low fat vs High fat diet**: NR	**Outcomes and assessment methods**: Fasting blood lipids: At baseline and after each feeding period. Levels at follow-up **TC,** mmol/L High fat vs low fat: NS **LDL,** mmol/L High fat vs low fat: NS **HDL,** mmol/L High fat vs low fat: NS **Triglycerides,** mmol/L High fat vs low fat: NS	**Model adjustments:** None **Limitations:** • No information provided about randomization or period effects • No data available to asses attrition rate • No information provided about diet compliance • Potential bias from missing data • No preregistered statistical analysis plan for most blood lipid outcomes **Funding sources:** NIH and the National Center for Advancing Translational Science

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Olmedilla-Alonso, 2017[105] **RCT crossover, Spain** Baseline N=30 Analytic N=30 (Attrition: 0%) **Participant characteristics at baseline:** Healthy adults (53% women) aged ~42 years, BMI of 25.1, no CVD or diabetes, borderline high total and LDL cholesterol **Summary of findings:** *No significant differences in the blood lipid concentrations of participants after the intake of semi-skimmed ewe's milk, whole ewe's milk or whole cow's milk yogurt.*	**Intervention and comparators:** • Semi-skimmed ewe´s milk yogurt (2.8% milk fat) • Whole ewe´s milk yogurt (5.8% milk fat) • Whole Cow´s milk yogurt (3% milk fat) • *Participants consumed two yogurts per day (125 g/yogurt); each type in random order* Duration of intervention: 5 wk (4 wk washout period) Compliance: 3-day dietary records from the beginning of each phase used to calculate dietary nutrient intake. No differences found in the dietary macronutrient intake in any of the study periods. **Dietary intake for ewe yogurt 2.8% fat and ewe yogurt 5.8% fat, and cow's milk yogurt, Mean (SD), g/100 g fat day:** SFA: 77.85 (2.03) vs 79.59 (1.69) vs 73.87 (2.30), P<0.05 MUFA: 19.38 (2.08) vs 17.96 (1.72) vs 23.35 (1.75), P<0.05 PUFA: 2.77 (0.40) vs 2.45 (0.43) vs 2.78 (0.60), P<0.05 Other components of diet differed: protein, fat, n6:n3, n-3, potassium, calcium, and fiber. Ewe's milk yogurt presented almost double the n-3 ALA than cow's milk and had a lower n-6:n-3 ratio.	**Outcomes and assessment methods**: Fasting blood lipids at the start and end of each period (relative percentage change by intervention period) **TC**, NS **LDL**, NS **HDL**, NS **Triglycerides**, NS No significant effects were found comparing results stratified by CVD risk (Total/HDL cholesterol index top vs low and moderate tertile, ≥5.1 for men; ≥3.5 for women)	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** MINECO (Spanish Ministry of Economy, Industry and Competitiveness); Agro Technological Institute; INIA (National Institute for Agricultural and Food Research and Technology); European Regional Development Fund

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Palacios, 2019[107]
RCT crossover, U.S.
Baseline N=54 Analytic N=33 (Attrition: 39%)
 	
Participant characteristics at baseline: Prediabetic adults (49% female) ~48y of age with overweight or obesity. Approximately 50% Caucasian, ~40% Black, and ~12% Hispanic/Latino.
 	
Summary of findings:
Consuming 3 oz of almonds per day for 6 weeks, which increased unsaturated FA intake, did not significantly affect blood lipids compared to energy-matched carbohydrate based foods.
	Intervention and comparator:
	• Raw almonds, 3.0 oz/d daily
	  • Sources: Almonds
	• Energy-matched CHO-based foods
	  • Sources: fruit and grain bars, baked potato chips, mini bagels, rice cakes, dinner rolls, pretzels, dried mango slices, pudding cups, vanilla cookie wafers
	
	Duration of intervention: 6 wk (washout ≥4 wk)
	Compliance: Study product consumption recorded in study log daily (0%, <50%, or ≥50%); Median (IQL) compliance during Almond: 100% (97.5-100) vs CHO: 98.7% (94.1-100)
	
	Dietary intake during Almond vs CHO-based foods periods, Mean (SEM):
	SFA (%E): 11.3 (0.5) vs 10.5 (0.5), P=NS
	UFA (%E): 35.3 (0.9) vs 21.7 (0.7), P<0.001
	MUFA or PUFA: NR
	Cholesterol, Median (IQL) (mg/d): 281 (211-423) vs 320 (224-464), P=NS
	Other components of diet differed significantly: Total fat, protein, dietary fiber, and magnesium (higher in Almond), CHO and sugar (lower in Almond)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and in duplicate at end of 6 wk intervention period.
		
		Comparing percentage change from baseline between groups
		
		TC, mg/dL
		Almond vs CHO-based foods: P=NS
		
		LDL, mg/dL
		Almond vs CHO-based foods: P=NS
		
		HDL, mg/dL
		Almond vs CHO-based foods: P=NS
		
		Triglycerides, mg/dL
		Almond vs CHO-based foods: P=NS
			Model adjustments:
			Baseline blood lipid value; Included when p<0.05: sequence and period.
			
			Limitations:
			• No information provided on randomization method
			• Co-interventions (protein and dietary fiber) not balanced between groups
			• Higher percentage of missing data in group who started with CHO-based foods
			• Preregistered protocol does not provide sufficient detail on analysis intentions
			
			Funding sources: Almond Board of California

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Palomaki, 2010[108] **RCT crossover, Hameenlinna Metabolic Syndrome, Finland** Baseline N=43 Analytic N=37 (Attrition: 14%) **Participant characteristics at baseline:** Men (30-65 years) with metabolic syndrome, with 21 men being diagnosed with hypertension, 19 with type 2 diabetes and 6 with coronary heart disease **Summary of findings:** *Total cholesterol and LDL cholesterol were significantly lower after participants consumed cold-pressed turnip rapeseed oil compared to butter for 6-8 weeks. HDL cholesterol and triglycerides did not differ between groups.*	**Intervention and comparator:** • Cold-pressed turnip rapeseed oil (CPTRO, 35 mL/day, no heating or frying) (n=20) • Butter (37.5 g/day, no heating or frying) (n=17) Duration of intervention: 6-8 wk (8 wk washout) Compliance: NR **Dietary intake for Intervention vs Control:** everyday diet of participants remained stable during the study	**Outcomes and assessment methods**: Fasting blood lipids after each period **TC**, mmol/L, Mean (SEM), Post-intervention **CPTRO: 4.98 (0.23)** **Butter: 5.43 (0.23)** **TC is significantly lower after CPTRO (8%) than after butter. P<0.001** **LDL**, mmol/L, Mean (SEM), Post-intervention **CPTRO: 3.00 (0.18)** **Butter: 3.35 (0.21)** **LDL cholesterol is significantly lower after CPTRO (11%) than after butter. P<0.001** **HDL**, mmol/L, Mean (SEM) CPTRO vs Butter: NS **Triglycerides**, mmol/L, Mean (SEM) CPTRO vs Butter: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization method • No preregistered statistical analysis plan **Funding sources:** Ministry of Health and Social Welfare in Finland through Medical Research Fund of Kanta-Hame Central Hospital; Hame Regional Fund under Finnish Cultural Foundation; Kankaisten Oljykasvit Ltd; Hilkka and Vaino Kiltti Foundation

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Pieters, 2015[109] **RCT crossover, Netherlands** Baseline N=36 Analytic N=32 (Attrition: 11%) **Participant characteristics at baseline:** Healthy overweight and obese adults (50% female), with mean BMI ~29, ~51y of age, no active CVD, no medication for hyperlipidemia **Summary of findings:** *In healthy overweight and obese adults, an increased intake of echium oil (which provided SDA), compared to high oleic sunflower oil, did not significantly affect blood lipid values.*	**Intervention and comparator:** • Echium oil (10g/day; provides 1.2 g stearidonic acid (SDA)) • High oleic acid sunflower oil (HOSO) (10g/day) **Fatty acid composition of Echium oil vs HOSO (% total fat):** SFA Palmitic acid: 6.7 vs 3.5 Stearic acid: 3.8 vs 3.2 MUFA Oleic acid: 15.2 vs 84.2 PUFA LA: 15.5 vs 7.4 Gamma-LA: 10.8 vs 0 ALA: 32.3 vs 0 Stearidonic acid (C18:4n-3): 12.8 vs 0 *Participants instructed to consume 5g oil, provided by researchers, at 2 meals (lunch and dinner) each day* Duration of intervention: 6 wk each diet (2 wk washout period) Compliance: Compliance, as estimated from the returned number of sachets, was 96.2% during the HOSO period and 94.4% during the Echium oil period. **Dietary intake for Intervention (EO) vs Control (HOSO), Mean (SD), %E:** SFA: NS MUFA: 13.3 (4.5) vs 15.2 (3.8); P=0.02 total PUFA: NS LA: 10.3 (3.3) vs 8 (3); P<0.01 ALA: 1.7 (0.5) vs 0.4 (0.1); P<0.01 Cholesterol: NS Protein intake was higher in the intervention arm. No other components of diet differed significantly.	**Outcomes and assessment methods**: Fasting blood lipids: Assessed at weeks 0, 3, 5 and 6 of both intervention periods. Values from weeks 5 and 6 were averaged when available. Levels after end of the two intervention periods **TC**, mmol/L, Mean (SD), Echium vs HOSO oil: NS **LDL**, mmol/L, Mean (SD), Echium vs HOSO oil: NS **HDL**, mmol/L, Mean (SD), Echium vs HOSO oil: NS **Triglycerides**, mmol/L, Mean (SD), Echium vs HOSO oil: NS	**Model adjustments:** None **Limitations:** • No information provided on randomization • No preregistered statistical analysis plan **Funding sources:** Bioriginal Europe Asia b.v.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Root, 2013[111] **RCT crossover, OmniHeart, U.S.** Baseline=191 Analytic N=164 (Attrition: 14%) **Participant characteristics at baseline:** ~53.6 y, 45% female, BMI ~30.2, 55% African American, 100% high BP or HTN, no HTN or hyperlipidemia medication, no CVD, no diabetes **Summary of findings:** *Replacement of 10% carbohydrate by unsaturated fat for 6 weeks significantly reduced blood total cholesterol and triglycerides and increased HDL cholesterol levels in healthy adults with pre- or stage 1 hypertension.*	**Intervention and comparators:** • Carbohydrate-rich diet (CHO): 58% carbohydrate, 15% protein, 27% fat, 6% SFA, 13% MUFA, 8%PUFA) • Protein-rich diet (PROT): 10% CHO replaced by protein (48% CHO, 25% protein, 27% fat, 6% SFA, 13% MUFA, 8%PUFA) • Unsaturated fat-rich diet (UNSAT): 10% CHO replaced by unsaturated fat (48% CHO, 15% protein, 37% fat, 6% SFA, 21% MUFA, 10%PUFA) • *Interventions designed to maintain weight, were low in saturated fat, cholesterol, and sodium.* • *Meals prepared in a research kitchen* Duration of intervention: 6 wk (2-4 wk washout) Compliance: 95% of trial person days, i.e. complete consumption of all study foods without any non-study foods **Dietary composition of CARBO vs PROT vs UNSAT diet, Mean**: SFA (%): 6 vs 6 vs 6 MUFA (%): 13 vs 13 vs 21 PUFA (%): 8 vs 8 vs 10 CHO (%): 58 vs 48 vs 48 Cholesterol (mg/1000kcal): 71 vs 71 vs 71 No significant difference in cholesterol, fiber, alcohol and sodium.	**Outcomes and assessment methods**: Fasting blood lipids: At baseline and after each feeding period. **TC,** mmol/L, change from baseline, Mean (SD) **UNSAT: 4.86 (0.91)** **vs CHO: 4.97 (0.88), P<0.043** **vs PROT: 4.73 (0.83), P=0.001** **HDL,** mmol/L, change from baseline, Mean (SD) **UNSAT: 1.29 (0.39)** **vs CHO: 1.26 (0.36), P=0.041** **vs PROT: 1.23 (0.34), P<0.001** **Triglycerides,** mmol/L, change from baseline, Mean (SD) **UNSAT: 1.13 (0.65, 1.92)** **vs CHO: 1.24 (0.73, 2.12), P<0.001** vs PROT: P=NS	**Model adjustments:** None **Limitations:** • Attrition >10% **Funding sources:** NIH/NHLBI

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Sawrey-Kubicek, 2019[115] **RCT crossover, U.S.** Baseline N=23 Analytic N=20 (Attrition: 13%) **Participant characteristics at baseline:** Overweight/obese postmenopausal women aged 48 to 70 years with HDL >50 mg/dL **Summary of findings:** *Consuming whole eggs, which increased dietary cholesterol intake, compared to yolk-free eggs daily for 4 weeks did not significantly change total blood, LDL, HDL cholesterol, and triglycerides.*	**Intervention and comparator:** • Liquid whole egg (100 g = equivalent to 2 whole eggs) • Yolk-free eggs (100 g = equivalent to 2 egg whites) • *Liquid whole egg and yolk-free eggs consumed as part of daily frozen breakfast meals* Duration of intervention: 4 wk each diet (2 wk run-in; 4wk washout) Compliance: 3-day diet records and food containers; Compliance was 98% **Dietary intake for Intervention vs Control, Mean (SD), g/day:** SFA: NS between groups MUFA: NS between groups PUFA: NS between groups Cholesterol: Whole egg: 498.9 (59.7) vs 126.6 (53.8), P<0.001 Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 4 wk follow-up *Change from pre- to post-intervention* **TC**, mg/dL, Mean (SD) Whole egg vs yolk-free eggs: NS **LDL**, mg/dL, Mean (SD) Whole egg vs yolk-free eggs: NS **HDL**, mg/dL, Mean (SD) Whole egg vs yolk-free eggs: NS **Triglycerides**, mg/dL, Mean (SD) Whole egg vs yolk-free eggs: NS	**Model adjustments:** None **Limitations:** • No information on potential impact of missing data • No preregistered statistical analysis plan **Funding sources:** Egg Nutrition Center

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Stonehouse, 2019[118]
RCT crossover, Australia
Baseline N=62 Analytic N=38 (Attrition: 39%)
 	
Participant characteristics at baseline: Healthy young adults ~30 y, BMI~23, blood pressure and lipid profile in the normal range.
 	
Summary of findings:
Consumption of palm olein and cocoa butter compared to olive oil for 4 weeks as part of an isocaloric diets resulted in no significant between group differences in changes to total, LDL and HDL cholesterol among young adults.
	Intervention and comparators:
	• Palm olein (PO) (IV64) (high in saturated fatty acids primarily in the sn-1 and sn-3 positions)
	  • SFA 39%, MUFA 46%, PUFA 13%
	• Cocoa butter (CB) (high in saturated fatty acids primarily in the sn-1 and sn-3 positions)
	  • SFA 64%, MUFA 33%, PUFA 3%
	• Olive oil, extra virgin (OO) (high in MUFA)
	  • SFA 20%, MUFA 65%, PUFA 15%
	
	• *Food provided by researchers. Diets isocaloric: 30-35%E from fat (20% derived from test oils (~44g fat/d)), ~18%E from protein and ~48%E from carbohydrate.*
	• *Study compared oils with unsaturated fatty acids primarily in the sn-2 position. Oils provided in frozen meals and snacks*
	
	Duration of intervention: 4 wk each diet (2- wk run-in, 2-wk washout period) during which the PO (IV72) diet was used)
	Compliance: Monitored via intake checklists and weekly online surveys. Mean compliance for completers were CB 97%, OO 99%, PO IV64 98%
	
	Dietary intake for CB vs OO vs PO Diet, mmol/l, Mean (95% CI): NR
		Outcomes and assessment methods:
		Fasting blood lipids assessed at baseline at the end of the intervention
		
		Change in lipid values from baseline
		
		TC, mmol/l, Marginal means (95%CI)
		Between group differences: P=0.14,
		
		LDL, mmol/l, Marginal means (95%CI)
		CB: 0.00 (−0.12, 0.12)
		OO: −0.05 (−0.17, 0.08)
		PO: 0.07 (−0.01, 0.14)
		Between group differences: P=0.05
		
		HDL, mmol/l, Marginal means (95%CI)
		Between group differences: P=0.31
		
		Triglycerides, mmol/l, Marginal means (95%CI)
		Between group differences: P=0.07
			Model adjustments:
			Weight change, baseline levels
			
			Limitations:
			• Potential missing data bias due to not statistically accounting for missing data
			
			Funding sources: Malaysian Palm Oil Board

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Sun, 2018[119]
RCT crossover, China
Baseline N=120 Analytic N=100 (Attrition: 17%)
 	
Participant characteristics at baseline: Healthy adults (53% female) ~40y, BMI~22, no CVD, diabetes, normal blood lipid levels
 	
Summary of findings:
Consumption of a diet with ~20%E from palm olein vs 20%E from olive oil resulted in no significant between group differences in changes to total, LDL-, HDL cholesterol and triglycerides in a healthy Chinese population
	Intervention and comparator:
	• Palm olein (PO) (48g/d)
	  • Palmitic acid: 28 g/100 g, Oleic acid: 49 g/100 g, LA: 14 g/100 g, ALA: 0.21 g/100 g, AA: 0.23 g/100 g
	• Olive oil, extra virgin (EVOO) (48g/d)
	  • Palmitic acid: 10 g/100 g, Oleic acid: 77 g/100 g, LA: 4 g/100 g, ALA: 0.55 g/100 g, AA: 0.34 g/100 g
	
	• *Baseline isocaloric diet (only variation oil content) in accordance with Chinese Dietary Reference Intakes*
	• *All meals provided by researchers at the factory canteen*
	• *%E from fat ~30% (80 g)*
	
	Duration of intervention: 5 wk each test diet (2- wk run-in, 2- wk washout period during which the PO (IV72) diet was used)
	Compliance: assessed via weighted food record; all participants consumed ~48g of each oil
	
	Dietary intake for PO vs OO Diet, mmol/l, Mean
	SFA: NR
	MUFA: NR
	PUFA: NR
	No significant differences in the dietary intake of energy, and macronutrients were observed
		Outcomes and assessment methods:
		Fasting blood lipids assessed at the beginning and end of the run-in period and at the end of each intervention
		
		Change in lipid values from baseline; between group differences
		
		TC, mmol/l, Mean (SD)
		PO vs EVOO: NS
		
		LDL, mmol/l, Mean (SD)
		PO vs EVOO: NS
		
		HDL, mmol/l, Mean (SD)
		PO vs EVOO: NS
		
		Triglycerides, mmol/l, Mean (SD)
		PO vs EVOO: NS
			Model adjustments:
			None
			
			Limitations:
			• Potential missing data bias due to not statistically accounting for missing data
			• No preregistered statistical analysis plan (plan retrospective)
			
			Funding sources:
			Malaysian Palm Oil Board, the Fundamental Research Funds for the Center Universities

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Teng, 2017[121] **RCT crossover, Malaysia** Baseline N=54 Analytic N=47 (Attrition: 13%) **Participant characteristics at baseline:** Abdominally obese participants (~75% female) aged ~33, BMI ~29, without a history of CVD, diabetes or dyslipidemia. **Summary of findings:** *Consumption of a high SFA diet for 6 weeks significantly increased total cholesterol and LDL, compared to a diet high in MUFA. Consumption of a high SFA diet for 6 weeks significantly increased HDL cholesterol, compared to replacement of 7%E of SFA with refined carbohydrates. There were no significant differences in triglycerides between groups.*	**Intervention and comparator diets:** • SFA: 32% total fat (45 g of palm olein and sunflower oil blend); Overall diet: 19.7 g SFA, 20.6 g MUFA, 9.7 g PUFA • Carb: Replacement of 7%E SFA with refined carbohydrate (rose syrup, honey and barley drinks); Overall diet: 1.5 g SFA, 13.5 g MUFA, 5.0 g PUFA from 34 g high oleic sunflower oil blended with sunflower oil • MUFA: Replacement of SFA with ~7%E MUFA (45 g high oleic sunflower oil blended with sunflower oil); Overall diet: 3.7 g SFA, 36.9 g MUFA, 9.1 g PUFA • *All food provided by researchers* • *All participants received isocaloric 2000 kcal/d diets* Duration of intervention: 6 wk eat diet; no wash-out reported Compliance: Attendance and meal intake monitored by nutritionist; compliance (full meal intake) was 97% or higher for all groups **Dietary intake during intervention:** NR	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 5 and 6 wk after each dietary treatment Blood lipid levels at 6 wk **TC**, mmol/L, Mean (95% CI) **SFA: 4.89 (4.68, 5.09)** Carb: 4.79 (4.58, 4.99) **MUFA: 4.71 (4.48, 4.94)** **SFA vs MUFA: P<0.05** SFA vs Carb: NS MUFA vs Carb: NR **LDL**, mmol/L, Mean (95% CI) **SFA: 3.05 (2.89, 3.21)** Carb: 3.00 (2.84, 3.17) **MUFA: 2.89 (2.71, 3.10)** **SFA vs MUFA: P<0.05** SFA vs Carb: NS MUFA vs Carb: NR **HDL**, mmol/L, Mean (95% CI) **SFA : 1.23 (1.17, 1.29)** **Carb: 1.18 (1.13, 1.24)** MUFA: 1.21 (1.14, 1.28) SFA vs MUFA: NS **SFA vs Carb: P<0.05** MUFA vs Carb: NR **Triglycerides**, mmol/L, Mean (95% CI) SFA vs MUFA: NS SFA vs Carb: NS MUFA vs Carb: NR	**Model adjustments:** None **Limitations:** • No information on whether missing data was different between groups • No preregistered statistical analysis plan **Funding sources:** Malaysian Palm Oil Board and Malaysian government

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Teng, 2010[122] **RCT crossover, Malaysia** Baseline N=43, Analytic N=41 (Attrition: 5%) **Participant characteristics at baseline:** *Healthy, normolipidemic subjects, 80% female, mean age 29y, BMI 22, without CVD* **Summary of findings:** *A diet high in high oleic palm olein (lower in SFA and higher in MUFA and PUFA) consumed over a 5 week period, significantly reduced blood total and LDL cholesterol and triglycerides and increased HDL cholesterol compared to a diet high in unhydrogenated palm stearin in normal weight, normolipidemic adults.*	**Intervention and comparator:** • High oleic palm olein (HOPO diet: 54% 18:1n-9, 20% 16:0) • Unhydrogenated palm stearin (PST diet: 25% 18:1n-9, 62% 16:0) • *All meals provided by researchers; 30-35% fat, 15% protein, 50-55% CHO* • *Participants consumed ~54g (accounts for 20-25%E from fat) of test oil incorporated into one cooked meal per day* **Fatty acid composition of HOPO vs PST (%E):** SFA: 10.8 vs 16.4 MUFA: 15.3 vs 10.7 Oleic: 15.3 vs 10.7 PUFA: 8.6 vs 3.8 18:2: 5.8 vs 3.6 18:3: 2.6 vs 0.2 Duration of intervention: 5 wk each diet (1 wk washout) Compliance: >90% compliance (attendance to the dinner hall) **Nutrient Composition of HOPO, and PST diets, Mean (SD):** SFA (%E): 10.8 (0.1), 16.4 (0.1) MUFA (%E): 15.3 (0.1); 10.7 (0.2) PUFA (%E): 8.6 (0.0), 3.8 (0.1) No differences observed in macronutrients.	**Outcomes and assessment methods**: Fasting blood lipids measured before and at week 4 and 5 (mean of week 4 and 5 reported) Comparing endpoint values between groups **TC**, mmol/L, Mean (SD) HOPO diet: 4.48 (0.04) PST: diet: 4.66 (0.04) **Between group: P<0.05** **LDL**, mmol/L, Mean (SD) HOPO diet: 2.69 (0.05) PST: diet: 2.95 (0.05) **Between group: P<0.05** **HDL**, mmol/L, Mean (SD) HOPO diet: 1.63 (0.03) PST: diet: 1.55 (0.03) **Between group: P<0.05** **Triglycerides**, mmol/L, Mean (SD) HOPO diet: 0.83 (0.01) PST: diet: 0.88 (0.01) **Between group: P<0.05**	**Model adjustments:** Baseline value **Limitations:** • No information provided on randomization method • Washout period (7 days) may be insufficient to prevent carry-over effects • No preregistered statistical analysis plan **Funding sources:** Malaysian Palm Oil Board

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Tindall, 2019[124]
RCT crossover, U.S.
Baseline N=45 Analytic N=36 (Attrition: 20%)
 	
Participant characteristics at baseline: Adults ~43y of age with overweight or obesity. All with elevated LDL cholesterol and/or elevated BP.
 	
Summary of findings:
In adults with overweight/obesity and elevated LDL cholesterol and/or BP, no significant differences in blood lipids were detected after consumption of a walnut-enriched diet (which increased PUFA/ALA and decreased MUFA) for 6 weeks compared to a walnut-free diet with matched FA profile or an oleic-acid enriched diet that replaced ALA with oleic acid.
	Intervention and comparators:
	• Diet with walnuts as 18%E (57-99g/d)
	  • Sources: walnuts
	• Diet without walnuts but with matched FA profile to walnut diet
	  • Sources: NA
	• Diet without walnuts that replaced 83% ALA with oleic acid
	
	• *All diets isocaloric weight maintenance diets; same macronutrient profile; all food provided by the study*
	
	Duration of intervention: 6 wk each diet (2 wk run in; washout, Mean=22.8 days, range: 1-164 days)
	Compliance: Assessed via daily food logs and monitoring participant daily body weight logs; 91% (median)
	
	Nutrient composition for Walnut vs Walnut-free FA matched vs Oleic acid replace ALA diets, Mean, %E:
	SFA: 7 vs 7 vs 7
	MUFA: 9 vs 9 vs 12
	PUFA: 16 vs 16 vs 14
	ALA: 2.7 vs 2.6 vs 0.4
	Cholesterol (mg/d): 117 vs 169 vs 163
	Other components of diet differed significantly: Fiber (higher in walnut diet)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline (end of run-in) and 6 wk
		
		Levels at 6 wk
		
		TC, mg/dL
		Walnut vs Walnut-free FA matched vs Oleic acid replace ALA: P=NS
		
		LDL, mg/dL
		Walnut vs Walnut-free FA matched vs Oleic acid replace ALA: P=NS
		
		HDL, mg/dL
		Walnut vs Walnut-free FA matched vs Oleic acid replace ALA: P=NS
		
		Triglycerides, mg/dL
		Walnut vs Walnut-free FA matched vs Oleic acid replace ALA: P=NS
			Model adjustments:
			Baseline blood lipid; Tested but P=NS: sex, randomization sequence
			
			Limitations:
			• Study not blinded
			
			Funding sources:
			California Walnut Commission; Pennsylvania State University (PSU) Clinical and Translational Research Institute; PSU Clinical and Translational Science Award; NIH National Center for Advancing Translational Sciences

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Van Meijl, 2011[128]
RCT crossover, Netherlands
Baseline N=40 Analytic N=35 (Attrition: 13%)
 	
Participant characteristics at baseline: Overweight or obese healthy men (n=10) and women (n=30), ~49.5y, with mean BMI of 32, CVD free, stable weight
 	
Summary of findings:
Intake of low fat dairy products compared to a carbohydrate-rich diet consumed over 8 weeks resulted in a significant decrease in HDL cholesterol and no significant changes in blood total and LDL cholesterol and triglycerides.
	Intervention and comparator:
	• Low-fat dairy products (n=35)
	  • Sources: 500 mL low-fat milk and 150 g low-fat yogurt
	• Carbohydrate-rich control products (n=35)
	  • Sources: 600 mL fruit juice and 3 fruit biscuits
	
	Duration of intervention: 8 wk (2 wk washout period)
	Compliance: Number of products returned reflected 100% compliance; mean daily intake of 500 mL milk and 150 g yogurt, or 601 mL fruit juice and 43 g fruit biscuits; 1 subject excluded due to non-compliance.
	
	Dietary intake for Intervention vs Control, Mean (SD):
	SFA (%E): 12.8 (2.1) vs 10.7 (2.1), P<0.05
	MUFA (%E): 10.3 (1.9) vs 9.2 (1.9), P<0.05
	PUFA (%E): 6.6 (1.1) vs 6.6 (1.2), P>0.05
	Cholesterol (mg/MJ): 23.3 (5.6) vs 19.7 (4.5), P<0.05
	TransFA (%E): 0.9 (0.3) vs 0.8 (0.3), P<0.05
	Other components of diet differed: carbohydrate, fiber, protein, fat, and calcium.
		Outcomes and assessment methods:
		Fasting blood lipids at weeks 0, 4, 7, and 8.
		Difference in change
		
		TC, NS
		
		LDL, NS
		
		HDL, mmol/L, Mean
		Between group: % Change (95% CI)
		Dairy vs Control: -2.7,(-0.07, 0.01), P=0.021
		(HDL was significantly higher in control than after dairy)
		
		Triglycerides, NS
			Model adjustments:
			None
			
			Limitations:
			• No information provided on randomization method
			• Attrition >10%
			• No preregistered statistical analysis plan
			
			Funding sources:
			Dutch Dairy Association

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Wang, 2015[131] **RCT crossover, U.S.** Baseline N=45 Analytic N=45 (Attrition: 17%) **Participant characteristics at baseline:** Predominantly Caucasian and non-Hispanic, aged ~45 years, with overweight or obese, free of CVD or diabetes **Summary of findings:** *All 3 diets significantly decreased LDL cholesterol and total cholesterol vs baseline, however, the reduction in LDL cholesterol and total cholesterol by the avocado diet was significantly greater than the low-fat and moderate-fat diets. The low-fat diet (higher in CHO) significantly increased triglycerides compared to the moderate-fat and avocado diets which both significantly decreased triglycerides.*	**Intervention and comparators:** • LF: Lower-fat diet (n=43) – replacing 6-7%E from SFA with CHO per day (from grains); 24%E total fat, 7% SFA, 11% MUFA, 6% PUFA • MF: Moderate-fat diet (n=42) – replacing 6-7%E from SFA per day with MUFA using high oleic oils (e.g., sunflower oil and canola oil), 34%E total fat, 6% SFA, 17% MUFA, 9% PUFA • AV: Avocado (n=43) – replacing 6-7%E from SFA with one Hass avocado per day (~13g MUFA), 34%E total fat, 6% SFA, 17% MUFA, 9% PUFA • *All food provided by researchers* Duration of intervention: 5 wk each diet (2 wk run-in; 2 wk washout) Compliance: self-reported monitoring; compliance was 90% (# of days participants consumed all study foods and no non-study foods) **Dietary intake for Intervention vs Control:** diets in the moderate fat and avocado diets were 90% similar.	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 5 wk follow-up **TC**, mg/dL, Mean (SEM) Change from baseline (199.9 (4.8)): **LF: 190.7 (5.1)** **MF: 188.7 (4.4)** **AV: 182.2 (4.3)** **P=0.005** LF vs MF: NS; **LF vs AV: P<0.05; MF vs AV: P<0.05** **LDL**, mg/dL, Mean (SEM) Change from baseline (128.1 (3.9)): **LF: 120.5 (4.2)** **MF: 119.0 (3.7)** **AV: 113.7 (3.4)** **P=0.005** LF vs MF: NS; **LF vs AV: P<0.05; MF vs AV: P<0.05** **HDL**, mg/dL, Mean (SEM) Change from baseline (48.7 (1.8)): **LF: 44.8 (1.5)** **MF: 47.2 (1.5)** **AV: 46.9 (1.6)** **P=0.02** **LF vs MF: P<0.05; LF vs AV: P<0.05**; MF vs AV: NS **Triglycerides**, mg/dL, Mean (SEM) Change from baseline (114.0 (5.9)): **LF: 134.3 (9.8)** **MF: 111.1 (5.8)** **AV: 108.6 (7.2)** **P=0.0005** **LF vs MF: P<0.05; LF vs AV: P<0.05**; MF vs AV: NS	**Model adjustments:** Diet sequence, period and diet period interaction as fixed effect **Limitations:** • None **Funding sources:** Hass Avocado Board; National Center for Research Board

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
NRCT			
Adams, 2010[40] **NRCT crossover, U.S.** Baseline N=10 Analytic N=10 (Attrition: 0%) **Participant characteristics at baseline:** Mildly hypercholesterolemic men (university faculty and staff) ~49y with BMI ~27 **Summary of findings:** *Among mildly hypercholesterolemic overweight men, HDL cholesterol was lower and triglycerides was higher after consuming five high SFA, high trans-fatty acid hamburger patties for 5 weeks compared to the same amount of a high MUFA, low trans-fatty acid hamburger patty. No differences were detected for LDL cholesterol.*	**Intervention and comparator:** • 1st: High SFA, high *trans*-fatty acids hamburger patties (114 g or ~4 oz each x 5/wk): pasture-fed cattle (40 g total fat) • 2nd: High MUFA, low *trans*-fatty acids hamburger (114 g or ~4 oz each x 5/wk): cattle fed grain-based diets (40 g total fat) **Types of fat in intervention (high SFA) vs control (high MUFA), Mean (SE), g/114 g patty:** SFA: 16.7 (0.6) vs 14.3 (0.2), P≤0.05 MUFA: 17.1 (0.6) vs 20.2 (0.2), P≤0.01 PUFA: 0.97 (0.03) vs 0.97 (0.06), P=NS *Trans*-FA: 1.72 (0.03) vs 1.24 (0.05), P≤0.001 Duration of intervention: 5 wk (3 wk washout) Compliance: Monitored with 3-day diet record and weekly contact with study personnel; Compliance NR **Dietary intake for Intervention (high SFA) vs Control (high MUFA) during intervention, Mean (SD), g/d:** Total fat: 132.3 (13.7) vs 129.2 (14.6), P≤0.01 SFA: 45.0 (4.6) vs 42.7 (4.5), P≤0.05 MUFA: 48.4 (6.6) vs 50.6 (7.2), P≤0.05 Oleic acid: 43.2 (6.4) vs 44.7 (7.0), P≤0.05 PUFA: 13.8 (2.9) vs 13.9 (3.2), P=NS MUFA:SFA: 1.06 (0.07) vs 1.18 (0.08), P≤0.05 Other components of diet differed significantly: Total energy intake (Higher during High SFA period)	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 5 wk follow-up Comparing levels after 5 wk of intervention vs control **LDL**, mmol/L, Mean (SE) High SFA vs High MUFA: NS **HDL**, mmol/L, Mean (SE) **High SFA: 0.88 (0.06)** **High MUFA: 1.06 (0.05)** **P≤0.05** **Triglycerides**, mmol/L, Mean (SE) **High SFA: 3.90 (1.21)** **High MUFA: 1.72 (0.43)** **P≤0.05**	**Model adjustments:** None **Limitations:** • Not all key confounders adjusted for • No information on compliance • No preregistered statistical analysis plan **Funding sources:** YamaBeef Inc., Mabank, TX, U.S.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Sari, 2010[114]
NRCT (crossover), Turkey
Baseline N=33 Analytic N=32 (Attrition: 3%)
 	
Participant characteristics at baseline: Nonsmoking, normolipidemic men ~22y of age in vocational police education school.
 	
Summary of findings:
In young adult men, consumption of pistachios as part of a Mediterranean diet for 4 weeks (which decreased SFA and PUFA intake, but increased MUFA intake) was associated with significantly decreased total blood and LDL cholesterol and triglycerides compared to a Mediterranean diet without pistachios. No association with HDL cholesterol was detected.
	Intervention and comparator diets:
	• Mediterranean diet with pistachios (~20%E)
	  • Sources: roasted, unsalted pistachios
	• Control: Mediterranean diet without pistachios
	  • Sources: NA
	
	Duration of intervention: 4 wk (no washout period reported)
	Compliance: Assessed via weighing leftover food; NR
	
	Dietary intake for Pistachio vs Control, Mean (SD), %E:
	SFA: 4.8 (1.4) vs 5.9 (1.1), P=0.02
	MUFA: 20.2 (2.3) vs 13.3 (1.6), P<0.001
	PUFA: 7.1 (1.0) vs 14.2 (1.3), P<0.001
	Cholesterol: NR
	Other components of diet differed significantly: Fiber (higher in pistachio)
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at baseline and 4 wk
		
		Difference in change
		
		TC, mg/dL, Mean (SD)
		Baseline: 199.6 (41.8)
		Control: 190.7 (30.1)
		Pistachios: 149.4 (26.5)
		P<0.001
		
		LDL, mg/dL, Mean (SD)
		Baseline: 142.0 (37.4)
		Control: 124.5 (24.5)
		Pistachios: 95.0 (23.2)
		P<0.001
		
		HDL, mg/dL, Mean (SD)
		Pistachios vs Control: P=NS
		
		Triglycerides, mg/dL, Mean (SD)
		Baseline: 91.2 (39.7)
		Control: 112.1 (45.5)
		Pistachios: 91.1 (38.1)
		P=0.008
			Model adjustments:
			None
			
			Limitations:
			• Confounding not addressed
			• Co-interventions (dietary fiber) not balanced between groups
			• No preregistered statistical analysis plan
			
			Funding sources:
			Pistachio Investigation Group of the Gaziantep Chamber of Commerce

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations

Sofi, 2010[116]
NRCT crossover, Italy
Baseline N=10, Analytic N=10 (Attrition: 0%)
 	
Participant characteristics at baseline: Adults ~54y (Median) of age, BMI ~25 with no vascular or inflammatory disease
 	
Summary of findings:
In participants self-selecting their diet, consumption of cheese lower in SFA, and higher in MUFA and PUFA, for 10 weeks did not change fasting blood lipids compared to consumption of cheese higher in SFA and lower in MUFA and PUFA.
	Intervention and comparator diets:
	• Pecorino cheese, 200g/wk (~7 oz)
	  • Sources: sheep's cheese
	• Control cheese, 200g/wk (~7 oz)
	  • Sources: cow's cheese
	
	Duration of intervention: 10 wk (washout: 10 wk)
	Compliance: Monitored via food records and 24 hour recalls; Cheese was consumed "as indicated"
	
	FA content for Pecorino cheese vs Control cheese, g/100 lipids:
	***See paper for detailed description of FAs in cheeses
	SFA: ~48 vs ~64
	MUFA: ~20 vs ~18.8
	PUFA: ~3.5 vs ~2.8
	Cholesterol: NR
	Other components of diet differed significantly: None
		Outcomes and assessment methods:
		Fasting blood lipids: Measured at beginning and end of 10wk period
		
		TC, mmol/L, Mean (SD)
		Pecorino vs Control: P=0.8
		
		LDL, mmol/L, Mean (SD)
		Experimental vs Control: P=0.7
		
		HDL, mmol/L, Mean (SD)
		Experimental vs Control: P=0.4
		
		Triglycerides, mmol/L, Mean (SD)
		Experimental vs Control: P=0.7
			Model adjustments:
			Age and sex
			
			Limitations:
			• Not all key confounders accounted for
			• All participants completed study interventions in the same order
			• No preregistered statistical analysis plan
			
			Funding sources:
			FISR project by the Ministry of Agricultural and Forestry Policies and from the Ministry of University and Research; Ente Cassa de Risparmio di Firenze, Italy.

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Sofi, 2013[117] **NRCT crossover, Italy** Baseline N=NR Analytic N=20 (Attrition: NR) **Participant characteristics at baseline:** Participants ~53 years (40% female) not taking fish supplements with BMI ~27 **Summary of findings:** *Among participants who consumed fish fed with 100% fishmeal first, followed by fish fed 50% plant protein and 50% fishmeal, there were no significant differences in total blood, LDL, HDL cholesterol or triglycerides.* *Among participants who consumed fish fed with 50% plant protein and 50% fishmeal first, followed by fish fed with 100% fishmeal, total blood cholesterol was significantly higher after consuming fish fed 50% plant protein and 50% fishmeal, compared to after consuming fish fed 100% fishmeals. There were no significant differences in LDL and HDL cholesterol or triglycerides.*	**Intervention and comparator:** • Fishmeal: Gilthead sea bream fed with 100% fishmeal for 460 days (630 grams or ~22 ounces/wk): n-6/n-3 ratio: 0.42, 2.07 EPA+DHA/100 grams • Plant protein: Gilthead sea bream fed with 50% fishmeal and 50% plant protein sources for 460 days (soybean meal, corn gluten meal, pea protein isolate) (630 grams or ~22 ounces/wk): n-6/n-3 ratio: 0.84, 1.82 EPA+DHA/100 grams • *Participants instructed to consume 4 servings (630 g) of fish per* wk *and maintain regular eating pattern* **Fatty acid composition of filets of fish fed fishmeal vs plant protein, %E:** SFA: 25.8 vs 23.4, P<0.01 MUFA: 29.9 vs 28.8, P<0.05 n-6 PUFA: 12.3 vs 21.1, P<0.01 n-3 PUFA: 29.5 vs 25.1, P<0.01 n-6:n-3 ratio: 0.42 vs 0.84, P<0.01 Duration of intervention: 10 wk each diet Compliance: None **Dietary intake for Intervention (FM) vs Control (PP), Mean (SD), g/wk:** SFA: 15.6 (0.8) vs 13.8 (0.6) g, P<0.05 MUFA: 19.3 (1.0) vs 15.9 (0.7) , P<0.05 LA: 13.8 (0.6) vs 6.0 (0.2), P<0.01 n6/n3 ratio: 0.48 vs 0.91, P=NR n-3 PUFA: 16.7 (0.8) vs 15.7 (0.7) , P<0.05 n-6 PUFA: 14.1 (0.7) vs 6.6 (0.3) , P<0.01 EPA+DHA: 12.5 vs 12.1 (similar between groups) EPA: 4.2 (0.2) vs 4.6 (0.2), P<0.05 Other components of diet differed significantly: None	**Outcomes and assessment methods**: Fasting blood lipids at baseline and 10 wk follow-up after each diet Stratified by crossover order: Group A (n=10): 1st Fishmeal, 2nd plant protein **TC**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS **LDL**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS **HDL**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS **Triglycerides**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS Group B (n=10): 1st Plant protein, 2nd fishmeal **TC**, mg/dL, Mean (95% CI) **Fishmeal: 204 (165, 254)** **Plant protein: 216 (176, 266)** **P=0.009** **LDL**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS **HDL**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS **Triglycerides**, mg/dL, Mean (95% CI) Fishmeal vs plant protein: NS	**Model adjustments:** Age, gender, smoking habit **Limitations:** • Not all key confounders accounted for • No information on compliance • No preregistered statistical analysis plan **Funding sources:** Italian Ministry of Education; Universities and Research, the Ministry of Agricultural, Food and Forestry Policies, Ministry of Environment; Ministry of Economic Development

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
Thompson, 2012[123] **NRCT parallel, CHOICE, U.S.** Baseline N=259 (in trial registry), Analytic N=142 (Attrition: All: ~45%; Control 9.4%, High fat 12.9%, Low fat 11.3%) **Participant characteristics at baseline:** Women ~55y who completed chemotherapy, radiation, and surgical treatment for breast cancer and were considered cancer free and a BMI between 25 and 34.9 **Summary of findings:** *Women who completed breast cancer treatment and followed an energy restricted low fat (high carbohydrate) diet had a significantly greater reduction in total and LDL cholesterol and significantly less of a reduction in triglycerides compared to women who followed an energy restricted high fat (low carbohydrate) diet over a 6 month period. No difference in HDL cholesterol was found between groups.*	**Intervention and comparators:** • Energy restricted High fat/Low carbohydrate diet: 46%E from fat, 32%E from CHO, 22% protein, n=48 • Energy restricted Low fat/High carbohydrate diet: 24%E from fat, 62%E from CHO, 20% protein, n=50 • No diet intervention (n=44), those who were not interested in the weight-loss arms • *Energy restricted diets (deficit of 3500kcal/wk) provided by researchers and distributed 3 times/week* • *Both groups lost weight from baseline* **Diet composition for Low CHO/High fat vs High CHO/Low Fat, Mean (SD):** Total fat: 64 (3) vs 24 (2) SFA (g): 11 (2) vs 5 (2) MUFA (g): 21 (3) vs 5 (1) PUFA (g): 9 (2) vs 5 (1) Cholesterol (mg): 244 (131) vs 120 (85) Carbohydrate (g): 100 (4) vs 193 (10) Protein (g): 68 (4) vs 62 (6) Fiber (g): 17 (4) vs 26 (5) Duration of intervention: up to 6 months Compliance: NR **Dietary intake for Intervention diets: NR**	**Outcomes and assessment methods**: Fasting blood lipids: Assessed at baseline and at approximately one month intervals Change from baseline to 6 months **TC,** mg/dL, Mean (SD) High fat vs low fat: P=0.07 Change from baseline: Control: 0.10 (0.47) **vs Low-fat, low weight-loss: -1.56 (0.56), P≤0.05** **vs Low-fat, high weight-loss: -3.23 (0.65), P≤0.05** vs High fat, low weight-loss: NS **vs High fat, high weight-loss: -2.65 (0.59), P≤0.05** **LDL,** mg/dL, Mean (SD) High fat vs low fat: P=0.13 Change from baseline: Control: 0.20 (0.40) vs Low-fat, low weight-loss: NS **vs Low-fat, high weight-loss: -2.30 (0.63), P≤0.05** vs High fat, low weight-loss: NS **vs High fat, high weight-loss: -1.42 (0.57), P≤0.05** **HDL,** mg/dL, Mean (SD) High fat vs low fat: P=0.08 Change from baseline: Control: 0.20 (0.15) **vs Low-fat, low weight-loss: 0.41 (0.17), P≤0.05** vs Low-fat, high weight-loss: NS **vs High fat, low weight-loss: 0.69 (0.19), P≤0.05** **vs High fat, high weight-loss: 0.60 (0.18), P≤0.05**	**Model adjustments:** None **Limitations:** • Energy restricted diet • Study arm assignment was based upon subject preference • >10% attrition • Not all key sources of confounding were addressed • Dietary compliance was not reported • No preregistered statistical analysis plan **Funding sources:** National Cancer Institute

Study and Population Characteristics	Intervention, Comparator, Dietary intake	Outcomes & Results†	Model adjustments & Study Limitations
		Triglycerides, mg/dL, Mean (SD) Baseline, Last follow-up: High fat: 138 (8.9), 97 (6.7) Low fat: 114 (8.7), 100 (6.6) **Low fat vs high fat: P=0.01** Change from baseline: Control: -0.16 (0.62) vs Low-fat, low weight-loss: NS **vs Low-fat, high weight-loss: -2.58 (0.68), P≤0.05** **vs High fat, low weight-loss: -2.44 (0.66), P≤0.05** **vs High fat, high weight-loss: -4.97 (0.62), P≤0.05**	

* Abbreviations: ANOVA – analysis of variance, CHO – carbohydrates, CI – confidence interval, HDL – HDL cholesterol, IQR – interquartile range, kcal – kilocalories, LDL – LDL cholesterol, NR – not reported, NS – non significant, %E – percent energy, PCOS – polycystic ovary syndrome, PRO – protein, SD – standard deviation, SE – standard error, SEM – standard error of the mean, TC – total cholesterol, UFA – unsaturated fatty acids, wk – week(s), y – year(s)

† Statistically significant results bolded.

Table 6. Risk of bias for randomized controlled trials examining types of dietary fat consumed by adults and cardiovascular disease intermediate outcomes (blood lipids)[*,†]

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Abbaspour, 2019,[38] RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Abdullah, 2015,[39] Crossover RCT	Low	Low	Low	Low	Low
Akrami, 2018,[41] RCT	Some Concerns	Some Concerns	Some Concerns	Low	Some Concerns
Alphonse, 2017,[42] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Andraski, 2019,[43] Crossover RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Annuzzi, 2014,[44] RCT	Low	Low	Low	Low	Some Concerns
Baer, 2019,[45] Crossover RCT	Low	High	Low	Low	Low
Barbour, 2015,[46] Crossover RCT	Low	Low	Low	Low	Low
Baxheinrich, 2012,[47] RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Beavers, 2010,[48] RCT	Some Concerns	Low	Low	Low	Some Concerns
Bergeron, 2019,[49] Crossover RCT	Low	Low	Some Concerns	Low	Some Concerns
Bergeron, 2019,[49] RCT	Low	Low	High	Low	Some Concerns
Bjermo, 2012,[50] RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Bladbjerg, 2011,[51] RCT	Some Concerns	Some Concerns	Some Concerns	Low	Some Concerns
Blesso, 2013,[52] RCT	Some Concerns	Low	Low	Low	Some Concerns
Bos, 2010,[53] RCT	Low	Some Concerns	Low	Low	Low
Bowen, 2019,[54] Crossover RCT	Low	Some Concerns	Some Concerns	Low	Some Concerns
Brassard, 2017,[55] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Burns-Whitmore, 2014,[56] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Cheng, 2019,[57] Crossover RCT	Low	Low	Low	Low	Some Concerns

[*] A detailed description of the methodology used for assessing risk of bias is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

[†] Possible ratings of low, some concerns, or high determined using the "Cochrane Risk-of-bias 2.0" (RoB 2.0) (August 2016 version)" (Higgins JPT, Sterne JAC, Savović J, Page MJ, Hróbjartsson A, Boutron I, Reeves B, Eldridge S. A revised tool for assessing risk of bias in randomized trials In: Chandler J, McKenzie J, Boutron I, Welch V (editors). Cochrane Methods. *Cochrane Database of Systematic Reviews* 2016, Issue 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.)

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Chinwong, 2017,[58] Crossover RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Chiu, 2014,[59] RCT	Some Concerns	Low	Low	Low	Some Concerns
Choi, 2018,[60] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Clayton, 2015,[61] RCT	Some Concerns	Some Concerns	Some Concerns	Low	Some Concerns
Dawczynski, 2010,[62] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
de Souza, 2018,[63] RCT	Low	Low	Low	Low	Some Concerns
Dhillon, 2018,[64] RCT	Low	Low	Low	Low	Some Concerns
Dias, 2017,[65] RCT	Low	Low	Some Concerns	Low	Some Concerns
Drouin-Chartier, 2015,[66] Crossover RCT	Some Concerns	Low	Low	Low	Low
Egert, 2010,[67] RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Engel, 2015,[68] Crossover RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Faghihnia, 2010,[69] Crossover RCT	Some Concerns	High	Some Concerns	Low	Some Concerns
Farajbakhsh, 2019,[70] RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Gagliardi, 2010,[71] RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Gilmore, 2011,[72] Crossover RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Grieger, 2014,[73] RCT	Some Concerns	Low	Low	Low	Some Concerns
Hagen, 2016,[74] RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Hallund, 2010,[75] RCT	Some Concerns	Low	Low	Low	Some Concerns
Harris, 2017,[76] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Hyde, 2019,[77] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Iggman, 2014,[78] RCT	Low	Low	Low	Low	Some Concerns
Intorre, 2011,[79] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Isherwood, 2010,[80] Crossover RCT	Low	Low	Low	Low	Some Concerns
Jaakkola, 2017,[81] RCT	Low	Low	Some Concerns	Low	Some Concerns
Jebb, 2010,[82] RCT	Low	Low	Some Concerns	Low	Some Concerns
Jones, 2014,[83] Crossover RCT	Low	Low	Some Concerns	Low	Some Concerns
Kalgaonkar, 2011,[84] RCT	Some Concerns	Low	High	Low	Some Concerns
Karupaiah, 2016,[85] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Katz, 2012,[86] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Kawakami, 2015,[87] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Khaw, 2018,[88] RCT	Low	Low	Low	Low	Some Concerns

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Klempel, 2013,[89] RCT	Some Concerns	Low	Low	Low	Some Concerns
Kontogianni, 2013,[90] Crossover RCT	Some Concerns	Low	High	Low	Some Concerns
Kovell, 2019,[91] Crossover RCT	Low	Low	Low	Low	Some Concerns
Kruse, 2015,[92] RCT	Low	Low	Low	Low	Some Concerns
Lim, 2010,[93] RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Liu, 2018,[94] Crossover RCT	Low	Some Concerns	Low	Low	Low
Lucci, 2016,[95] RCT	Low	Some Concerns	Low	Low	Some Concerns
Lv, 2018,[96] RCT	Some Concerns	Low	Low	Low	Some Concerns
McDaniel, 2013,[97] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
McKay, 2018,[98] Crossover RCT	Low	Low	Low	Low	Some Concerns
Michielsen, 2019,[99] RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Miller, 2016,[100] RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Missimer, 2017,[101] Crossover RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns
Morilla-Ruiz, 2014,[102] Crossover RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Morton, 2019,[103] Crossover RCT	Some Concerns	Some Concerns	Some Concerns	Low	Some Concerns
Ng, 2018,[104] RCT	Some Concerns	Low	Low	Low	Some Concerns
Olmedilla-Alonso, 2017,[105] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Ooi, 2012,[106] RCT	Some Concerns	Low	Low	Low	Some Concerns
Palacios, 2019,[107] Crossover RCT	Some Concerns	Some Concerns	High	Low	Some Concerns
Palomaki, 2010,[108] Crossover RCT	Some Concerns	Some Concerns	Some Concerns	Low	Some Concerns
Pieters, 2015,[109] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Raziani, 2016,[110] RCT	Low	Low	Low	Low	Low
Root, 2013, Crossover RCT	Low	Low	Some Concerns	Low	Some Concerns
Rozati, 2015,[111] RCT	Some Concerns	Low	Low	Low	Some Concerns
Rueda, 2013,[113] RCT	Some Concerns	Some Concerns	Some Concerns	Low	Some Concerns
Sawrey-Kubicek, 2019,[115] Crossover RCT	Low	Low	Some Concerns	Low	Some Concerns
Sofi, 2013,[117] Crossover RCT	Some Concerns	High	Some Concerns	Low	Some Concerns
Stonehouse, 2019,[118] Crossover RCT	Low	Low	Some Concerns	Low	Low
Sun, 2018,[119] Crossover RCT	Low	Low	Some Concerns	Low	Some Concerns
Tapsell, 2010,[120] RCT	Low	Some Concerns	Low	Low	Some Concerns
Teng, 2010,[122] Crossover RCT	Some Concerns	Some Concerns	Low	Low	Some Concerns

	Randomization	Deviations from intended interventions	Missing outcome data	Outcome measurement	Selection of the reported result
Teng, 2017,[121] Crossover RCT	Low	Low	Some Concerns	Low	Some Concerns
Tindall, 2019,[124] Crossover RCT	Low	Some Concerns	Low	Low	Low
Utzschneider, 2013,[125] RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Vafeiadou, 2015,[126] RCT	Low	Low	Low	Low	Some Concerns
van der Made, 2014,[127] RCT	Some Concerns	Low	Low	Low	Some Concerns
van Meijl, 2011,[128] Crossover RCT	Some Concerns	Low	Low	Low	Some Concerns
Varady, 2011,[129] RCT	Low	Low	Low	Low	Some Concerns
Veum, 2017,[130] RCT	Low	High	Low	Low	Some Concerns
Wang, 2015,[131] Crossover RCT	Low	Low	Low	Low	Low
Werner, 2013,[132] RCT	Some Concerns	Low	Some Concerns	Low	Some Concerns
Young, 2017,[133] RCT	Low	Low	Low	Low	Some Concerns
Yubero-Serrano, 2015,[134] RCT	Low	Low	Low	Low	Some Concerns

Table 7. Risk of bias for non-randomized controlled trials examining types of dietary fat consumed by adults and cardiovascular disease intermediate outcomes (blood lipids)*

	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Outcome measurement	Selection of the reported result
Adams, 2010,[40] Crossover NRCT	Serious	Low	Low	Low	Low	Low	Moderate
Sari, 2010,[114] NRCT	Serious	Low	Low	Moderate	Low	Low	Moderate
Sofi, 2010,[116] NRCT	Serious	Low	Low	Low	Low	Low	Moderate
Thompson, 2012,[123] NRCT	Serious	Low	Low	Moderate	Moderate	Low	Moderate

* Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool" (Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JPT

Table 8. Evidence from prospective cohort studies examining types of dietary fat consumed by adults and cardiovascular disease endpoint outcomes*

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Samieri, 2011[203]
PCS, 3C (Three-City) Study, France
Baseline N=9,294 Analytic N=7,625 (Attrition: 18%)
 	
Participant characteristics at baseline:
• 100% without stroke
• Age: Mean: 73.8y (SD=5.3)
• Sex (female): 62%
• Race/ethnicity: NR
• SES: Education: None or primary 25.5%, Secondary 35.9%, High school 20.2%, University 18.4%
• Anthropometry: BMI, Mean: 25.7 (SD=4.0)
 	
Fat intake at baseline: NR
 	
Blood lipids and BP at baseline, Mean (SD):
• TC: 5.83 (0.98) mmol/L
• HDL: 1.62 (0.40) mmol/L
• LDL: 3.64 (0.86) mmol/L
• SBP: 146.3 (21.6) mmHg
 	
Summary of findings:
Intensive use of olive oil in both cooking and dressing was significantly associated with lower incidence of stroke compared to no use of olive oil.
	Exposures:
	• Olive oil (categorical)
	  • No use (n=1,738): 0g (ref)
	  • Moderate use (n=3,052): cooking or dressing
	  • Intensive use (n=2,835): Both cooking and dressing
	
	Assessment method and timing:
	• Self-administered FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 6y (Median 5.25 y) of follow-up
	• Stroke (nonfatal ischemic or hemorrhagic): follow-up, medical data including emergency medical service, hospitalization reports, neuroimaging reports, and interview with patient's physician or family
	• Stroke: 148 cases
		Stroke, HR (95% CI)
		Olive oil:
		No use (ref) vs:
		Moderate use: NS
		Intensive use: 0.60 (0.38, 0.96), P=0.03*
		In unadjusted data, **higher olive oil use was associated with lower risk of ischemic stroke (P-trend=0.02)** but not hemorrhagic stroke (P-trend NS**).**
		*Similar findings when only controlled for age, sex, education, center, omega-6 rich oils
			Key confounders NOT accounted for: Race/ethnicity, family history of CVD or diabetes
			Key confounders accounted for: Sex, age, SES, TEI, alcohol intake, physical activity, smoking
			Additional model adjustments: Center, consumption of fish, meat, pulses, raw vegetables, raw fruits, cooked fruits and vegetables, cereals, regular use of n-3 rich oils, n-6 rich oils, butter, goose or duck fat, SBP, antihypertensive therapy, diabetes, history of CVD, atrial fibrillation, BMI, triglyceridemia, hypercholesterolemia
			Limitations:
			• Not all key confounders adjusted for
			• FFQ was not validated
			• Missing data may be unbalanced between exposure groups
			• No preregistered statistical analysis plan
			Funding sources: Institut National de la Sante et de la Recherche Medicale; Institut de Sante Publique et Developpement of the Victor Segalen Bordeaux 2 University, and sanofi-aventis; Foundation pour la Recherche Medicale; Caisse Nationale Maladie des Travailleurs Salaries, Direction Generale de la Sante, Mutuelle Generale de L'Education Nationale, Institut de la Longeviet; Regional Governments of Aquitaine and Bourgogne; Foundation de France and Ministry of Research – INSERM Programme "Cohortes et Collections de Donnees Biologiques"; ANR

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Simila, 2013[205]
PCS, ATBC (Alpha-Tocopherol, Beta-Carotene) Cancer Prevention Study, Finland
Baseline N=29,133 Analytic N=21,955 (Attrition: 25%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: Mean~57y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI: Mean~26
 	
Fat intake at baseline, Mean:
• SFAs: ~17%E
• MUFA: ~11%E
• PUFA: ~11%E
• *Trans* fat: ~1%E
 	
Blood lipids and BP at baseline, Mean:
• TC: ~6 mmol/L
• HDL: ~1.14 mmol/L
• SBP: Mean~140 mmHg
• DBP: Mean~88 mmHg
 	
Summary of findings:
Replacement of MUFAs with carbohydrates was significantly associated with a higher risk of CHD. Replacement of SFAs or PUFAs with carbohydrates was not associated with risk of CHD.
	Exposures:
	• Replacement of 2% energy from SFAs, MUFAs and PUFAs (continuous) with 2% energy from:
	  • Total carbohydrates
	  • Low-GI carbohydrates
	  • Medium-GI carbohydrates
	  • High-GI carbohydrates
	
	Assessment method and timing:
	• Self-administered, validated 276-item FFQ to assess diet over previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 19y of follow-up
	• Incident coronary heart disease (CHD; nonfatal MI or CHD death): National Hospital Discharge Register, National Register of Causes of Death
	• CHD: 4,379 cases
	• Nonfatal MI: 2,377 cases
	• CHD deaths: 2,002 cases
		Incident CHD, relative risk (RR) (95% CI)
		*Replacement of SFAs with:**
		Total CHO: NS
		Low-GI CHO: NS
		Medium-GI CHO: NS
		High-GI CHO: NS
		*Replacement of MUFAs with:**
		Total CHO: 1.08 (1.01, 1.16)
		Low-GI CHO: 1.09 (1.02, 1.16)
		Medium-GI CHO: NS
		High-GI CHO: 1.08 (1.01, 1.15)
		*Replacement of PUFAs with:**
		Total CHO: NS
		Low-GI CHO: NS
		Medium-GI CHO: NS
		High-GI CHO: NS
		*Analyses without blood lipids and BP resulted in minor changes in risk estimates.
			Key confounders NOT accounted for:
			Race/ethnicity, SES, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Intervention group, BMI, serum total cholesterol and HDL cholesterol, BP, fat subgroups (in each model, the nutrient to be replaced was left out and the model was adjusted for non-substitutive nutrients), protein, Mg, and K
			
			Limitations:
			• Not all key confounders adjusted for
			• Potential selection bias due to excluding 100% smokers and diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			U.S. Public Health Service contracts from National Cancer Institute; Academy of Finland, Juho Vainio Foundation; Finnish Foundation for Cardiovascular Research

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Kouli, 2019[177]
PCS, ATTICA, Greece
Baseline N=3042 Analytic N=2020 (Attrition: 34%)
 	
Participant characteristics at baseline:
• No existing CVD at baseline
• Type 2 diabetes (%): 7
• Age: Mean=45y
• Sex (female): 50%
• Race/ethnicity: 100% Caucasian
• SES: Education, Mean school years: 12
• Anthropometry: BMI, Mean=26
 	
Fat intake at baseline:
• SFA (%E): 10
• MUFA (%E): 23
• MUFA/SFA ratio intake: 1.7
• Trans FA (%E): 0.59
• Olive oil intake: NR
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia (%): 39
• Hypertension (%): 30
 	
Summary of findings:
Exclusive use of olive oil and daily use of olive oil along with other additive fats was associated with statistically significant reduced risk of major cardiovascular disease over approximately 8.4 years among a middle-aged Mediterranean population.
	Exposures:
	• Olive oil intake at baseline (categorical)
	  • No use: 10.5% (n=212)
	  • Mixed use (daily use of olive oil with other additive fats or exclusive use): 89.5% (n=1808)
	  • Exclusive use in daily cooking 1.1% (n=20)
	
	Diet assessment method and timing:
	• Validated semi-quantitative FFQ, plus self-reported intake of additional foods and liquids including oils used in cooking (assessed average intake over 12mo)
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 8.41y of follow-up
	• Incidence of CVD event (fatal and non-fatal) ascertained by medical record review
	  • CVD events (myocardial infarction or stroke): 317 cases (198 men, 119 women)
		Major cardiovascular event, HR (95% CI)
		Olive oil intake
		No use vs mixed use: 0.91 (0.45, 1.83), P< 0.05*
		No use vs exclusive use: 0.07 (0.01, 0.66), P<0.05*
		
		***Association was not altered when adherence to Mediterranean diet and omega-3 fatty acids were included in the model.
			Key confounders NOT accounted for:
			TEI, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, race/ethnicity, SES (education), smoking, alcohol intake, physical activity
			Additional model adjustments:
			BMI, prevalence of diabetes, hypertension and hypercholesterolemia, metabolic syndrome
			
			Limitations:
			• Not all key confounders accounted for
			• No analyses conducted to address risk of bias from missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			Coca-Cola SA; Hellenic Cardiology Society; the Hellenic Atherosclerosis Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Owen, 2016[192] **PCS, AusDiab (Australian Diabetes, Obesity and Lifestyle Study), Australia** Baseline N= 11,247, Analytic N~11,217 (Attrition: 0.3%) **Participant characteristics at baseline:** • Type 2 diabetes (%): 7.4 • Age: ~53y • Sex (female): 55% • Race/ethnicity: NR • SES: Education: ~17% Bachelor degree/post grad, ~12% associate diploma, ~30% trade/technician, ~40% secondary school • Anthropometry: BMI, Mean=27 **Fat intake at baseline, Median:** • n-3 PUFA (EPA+DPA+DHA) (g/d): Median: Women=0.26; Men=0.33 • DHA (g/d): Median: Women =0.16; Men=0.20 • EPA (g/d) Median: Women =0.07; Men=0.09 • n-6 PUFA (g/d): Mean: Women=8.97; Men=12.03 **Blood lipids and BP at baseline:** NR **Summary of findings:** *Dietary n-3 and n-6 polyunsaturated fat intake was not associated with CVD mortality over 12y follow-up among Australian adults.*	**Exposures:** • n-3 PUFA (EPA+DHA) intake (quintiles, g/d), (90 cases) • N-6 PUFA intake (quintiles, g/d), (54 cases) Diet assessment method and timing: • 121 item semi-quantitative FFQ (validated) • Administered at baseline **Outcomes and assessment methods**: • Assessed during median 12.6y of follow-up • CVD mortality ascertained via linkage to the National Death Index registry • CVD mortality: 277 cases	**CVD mortality,** HR (95% CI) ***n-3 PUFA (quintiles)*** Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS P>0.05 ***n-6 PUFA (quintiles)*** Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS P>0.05	**Key confounders NOT accounted for:** Race/ethnicity; alcohol intake **Key confounders accounted for:** Age, sex, SES (education), TEI, smoking, physical activity, family history of CVD **Additional model adjustments:** Diabetes **Limitations:** • Not all key confounders accounted for • Analysis did not adjust for baseline differences in co-exposures (types of fat) • No preregistered statistical analysis plan **Funding sources:** Aus. National Health and Medical Research Council; Aus. Government Dept. of Health and Ageing; Abbott Australasia Pty Ltd; Alphapharm Pty Ltd; Amgen Australia; AstraZeneca; Bristol-Myers Squibb; City Health Centre-Diabetes Service-Canberra; Dept. of Health and Community Services Northern Terr., Department of Health (and Human Services) Tasmania, NSW, WA, SA, Victoria; Diabetes Australia, Diabetes Australia Northern Territory; Eli Lilly Australia, Estate of the Late Edward Wilson; GlaxoSmithKline; Jack Brockhoff Foundation; Janssen-Cilag; Kidney Health Australia, Marian & FH Flack Trust; Menzies Research Institute; Merck Sharp & Dohme; Novartis Pharmaceuticals, Novo Nordisk Pharmaceuticals; Pfizer Pty Ltd; Pratt Foundation; Queensland Health; Roche Diagnostics Australia; Royal Prince Alfred Hospital, Sydney; Sanofi Aventis, sanofi-synthelabo and the Victorian Govt's OIS Program.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Atkinson, 2011[139] **PCS, CaPS (Caerphilly Prospective Study), U.K.** Baseline N=2,960, Analytic N=2,710 (Attrition: 9%) **Participant characteristics at baseline:** • Age: Mean=53.3y • Ischemic heart disease (%): 30.3 • Type 2 diabetes (%): 2 • Sex (female): 0% • Race/ethnicity: NR • SES: 67% Employed in manual occupations • Anthropometry: Mean BMI: 26.2 **Fat intake at baseline:** NR **Blood lipids and BP at baseline, Mean:** • TC (mmol/L): 5.894 • SBP (mmHg): 142.7 • DBP (mmHg): 88.8 **Summary of findings:** *Dietary intake of saturated and unsaturated fat was not associated with risk of stroke during 18 year follow-up in middle-aged men from the U.K.*	**Exposures:** • Saturated fat intake, most recent (quintiles, g) • Unsaturated fat intake, most recent (quintiles, g) Diet assessment method and timing: • Semi-quantitative FFQ, (differed slightly between study phases) • Administered at baseline, 5 and 10y after baseline • Analysis presented based upon most recent intakes; analysis also conducted on baseline and all diet phases preceding stroke (intake levels not sig different) **Outcomes and assessment methods**: • Assessed during median 18y of follow-up • Risk of stroke (fatal and non-fatal) ascertained via medical and death records and self- or close relative-report • Risk of stroke: 225 cases (209 ischaemic and 19 haemorrhagic)	**Risk of stroke,** HR (95% CI) ***Saturated fat (quintiles)*** Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P=0.67 ***Unsaturated fat (quintiles)*** Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P=0.13	**Key confounders NOT accounted for:** Race/ethnicity, physical activity, family history of CVD or diabetes **Key confounders accounted for:** Age, sex, SES, TEI, smoking, alcohol intake **Additional model adjustments:** Marital status, vitamin C intake, vegetable fiber intake, BP, cholesterol, BMI, fasting glucose, diabetes, atrial fibrillation **Limitations:** • Not all key confounders accounted for and no adjustment made for time-varying confounding • Analyses did not account for co-exposures (types of fat) • Potential bias in classification of exposures due to not validated FFQ • No preregistered statistical analysis plan **Funding sources:** NHS R&D Program on Cardiovascular Disease and Stroke

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Lemaitre, 2012[180]
PCS, CHS (Cardiovascular Health Study), U.S.
Baseline N=5,888, Analytic N=4,432 (Attrition: 25%)
 	
Participant characteristics at baseline:
• No CVD
• Diabetes: Mean~22%
• Age: Median~72y
• Sex (female): 63.9%
• Race/ethnicity: 87% Caucasian
• SES: ~75% > high school
• Anthropometry: BMI, Mean~26
 	
Fat intake at baseline, Mean:
ALA (% total fat): 2.3
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Dietary ALA was not associated with incident congestive heart failure in older adults during 12y follow-up.
	Exposures:
	• ALA intake (quartiles, % total fat), Median, range
	  • Q1 0.09, 0.05-0.11
	  • Q2 0.13, 0.11-0.14
	  • Q3 0.16, 0.14-0.18
	  • Q4 0.22, 0.18-0.47
	
	Diet assessment method and timing:
	• Picture-sort FFQ (validated) at baseline and 131-item semi quantitative FFQ ~5y later
	• Administered at baseline by trained staff
	
	Outcomes and assessment methods:
	• Assessed during 12y of follow-up
	• Congestive heart failure (CHF) assessed via annual medical exams and phone contact for 10y and phone contact every 6mo thereafter
	  • Total CHF: 1,072
	  • Nonvalvular CHF: 696
		ALA
		Total congestive heart failure, HR (95% CI),
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.97
		Nonvalvular congestive heart failure, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.59
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, SES (education), race/ethnicity, TEI, smoking, alcohol intake, physical activity
			Additional model adjustments:
			Enrollment site, BMI, WC
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (types of fat)
			• No preregistered statistical analysis plan
			
			Funding sources:
			NHLBI, National Institute of Neurological Disorders and Stroke; National Institute on Aging

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Fretts, 2014[159]
PCS, CHS, U.S.
Baseline N=5,565 Analytic N=2,583 (Attrition: 54%)
 	
Participant characteristics at baseline:
• No CVD
• Diabetes: Mean~9.5%
• Age: Median=73y, IQR: 71.0 - 98.0y
• Sex (female): 63.9%
• Race/ethnicity: 90% Caucasian
• SES: ~37% > high school
• Anthropometry: BMI, Mean~26.5
 	
Fat intake at baseline, Mean:
• SFA (%E): ~10
• ALA: see exposure section
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Dietary ALA was not associated with the risk of total CVD mortality, total CHD mortality, risk of incident CHD or stroke in older adults during 12y follow-up.
	Exposures:
	• ALA intake (quintiles, % total fat), Median, range
	  • Q1 1.33, 0.39-1.45
	  • Q2 1.56, 1.45-1.65
	  • Q3 1.76, 1.65-1.87
	  • Q4 2.0, 1.87-2.17
	  • Q5 2.44, 2.17-4.88
	
	Diet assessment method and timing:
	• 131-item semi quantitative FFQ (validated)
	• Administered at baseline by trained staff
	
	Outcomes and assessment methods:
	• Assessed during 12y of follow-up
	• Mortality, CHD and stroke assessed via medical records, laboratory/diagnostic reports, death certificates and/or interviews with next of kin.
	  • CVD mortality: 429 cases
	  • CHD mortality: 280 cases
	  • Incident CHD: 378 cases
	  • Incident stroke: 356 cases
	  • Ischaemic stroke: 278 cases
	  • Haemorrhagic stroke: 56 cases
		ALA
		CVD mortality, HR (95% CI),
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P-trend=0.92
		CHD mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P-trend=0.54
		Total CHD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P-trend=0.75
		Incident stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P-trend=0.80
		Ischaemic stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P-trend=0.29
		Haemorrhagic stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P-trend=0.16
			Key confounders NOT accounted for:
			Physical activity, family history of CVD or diabetes
			Key confounders accounted for:
			Age, sex, SES (education), race/ethnicity, TEI, smoking, alcohol intake
			Additional model adjustments:
			Enrollment site, BMI, diabetes, treated hypertension
			
			Limitations:
			• Not all key confounders accounted for
			• It is unclear whether those excluded for incomplete dietary data differed from responders
			• Analyses did not account for SFA as a co-exposure
			• No preregistered statistical analysis plan
			
			Funding sources:
			NHLBI, NIA

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Okada, 2019[190]
PCS, CIRCS (Circulatory Risk in Communities Study), Japan
Baseline N=3289, Analytic N=2292 (Attrition: 30%)
 	
Participant characteristics at baseline:
• Adults 40-59y of age without history of MI, or stroke at baseline
• Type 2 diabetes: Men~6%; Women ~2%
• Age: Mean~49y
• Sex (female): 48%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI, Mean~23.4
 	
Fat intake at baseline from the breakfast meal, Mean:
• SFA (g/d): 2.6 g (men and women)
• MUFA (g/d): 1.6 g (men and women)
• PUFA (g/d): 2.6 g
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
SFA and MUFA intake at breakfast by men, but not women, was significantly associated with reduced incidence of intracerebral hemorrhage during 25 years of follow-up. PUFA intake at breakfast was not significantly associated with incidence of intracerebral hemorrhage in men or women during 25 years of follow-up.
	Exposures:
	• SFA, MUFA, PUFA intake at breakfast in men (women's intake NR)
	• SFA (quartiles; g), Median (range):
	  • Q1: 0.5 (0.0–0.8)
	  • Q2: 1.2 (0.8–1.9)
	  • Q3: 2.5 (1.9–4.0)
	  • Q4: 6.0 (4.0–22.1)
	• MUFA (quintiles; g), Median (range):
	  • Q1: 0.4 (0.0–0.9)
	  • Q2: 1.7 (0.9–2.4)
	  • Q3: 3.2 (2.4–4.5)
	  • Q4: 6.4 (4.5–19.6)
	• PUFA (quintiles; g), Median (range):
	  • Q1: 0.7 (0.0–1.3)
	  • Q2: 1.7 (1.3–2.2)
	  • Q3: 2.8 (2.2–3.6)
	  • Q4: 5.0 (3.6–18.5)
	
	Assessment method and timing:
	• 24-hour recall
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during median 24.6y of follow-up
	• Intracerebral hemorrhage: Obtained through death certificates, from public health nurses, local physicians, volunteers, insurance claims, and an annual cardiovascular risk survey.
	  • Intracerebral hemorrhage: 230 cases
		Intracerebral hemorrhage, HR (95% CI)
		
		SFA
		Men
		Q1 (ref) vs Q2: 1.19 (0.58–2.43)
		Q1 (ref) vs Q3: 0.44 (0.17–1.18)
		Q1 (ref) vs Q4: 0.22 (0.06–0.79)
		P=0.008
		Women:
		Data NR, NS
		
		MUFA
		Men
		Q1 (ref) vs Q2, Q3: All NS
		Q1 vs Q4: 0.21 (0.05-0.86)
		P-trend: 0.06
		Women: data NR, NS
		
		PUFA
		Men
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.43 (men),
		Women: data NR: NS
			Key confounders NOT accounted for:
			Race/ethnicity, SES, physical activity family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, TEI, smoking, alcohol intake
			
			Additional model adjustments:
			Community, nutrient intakes from other meals, and also protein, saturated fat and carbohydrate intakes from breakfast, BMI, serum triglycerides, TC, SBP, use on antihypertensive medication and diabetes
			
			Limitations:
			• Not all key confounders accounted for
			• Dietary data not validated and only pertained to intake during breakfast
			• No preregistered statistical analysis plan
			
			Funding sources:
			Japan Society for the Promotion of Science

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Jakobsen, 2010[170]
PCS, DDCH (Danish Diet, Cancer and Health), Denmark
Baseline N=57,053 Analytic N=53,644 (Attrition: 4%)
 	
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer, MI, or diabetes mellitus
• Age: Median=56y, 80% central range (51-63)
• Sex (female): ~53%
• Race/ethnicity: NR
• SES: >10y of education, 21%
• Anthropometry: BMI, Median=25, 80% central range (21-31)
 	
Fat intake at baseline, Median (80% central range):
• SFA (%E): 14 (11-18)
• MUFA (%E): 12 (10-15)
• PUFA (%E): 6 (4-8)
 	
Blood lipids and BP at baseline:
• Hypertension: 15%
 	
Summary of findings:
Replacing SFA intake with high-glycemic index CHO intake at ~56y of age was significantly associated with higher risk of incident MI during ~12.0y of follow-up in men alone, and men and women combined; the association was not significant in women. Replacing SFA intake with low- or medium-glycemic index CHO or total CHO was not significantly associated with incident MI.
	Exposures:
	• Replacement of SFA with CHO (continuous; per 5% increase in CHO, 5% decrease in SFA)
	• Replacement of SFA with CHO of differing glycemic index (GI) values (per 5% increase in CHO, 5% decrease in SFA)
	  • Low-GI CHO (first tertile)
	  • Medium GI CHO (second tertile)
	  • High GI CHO (third tertile)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~12.0y of follow-up
	• Incident MI (fatal and nonfatal): Obtained via linkage with central Danish registries
	  • Men: 1406 cases
	  • Women: 537 cases
		Replacement of SFA with CHO
		Incident MI, HR (95% CI)
		All: 1.04 (0.92, 1.17)
		Men: 1.05 (0.92, 1.21)
		Women: 1.02 (0.82, 1.28)
		
		Replacement of SFA with Low-GI CHO
		Incident MI, HR (95% CI)
		All: 0.88 (0.72, 1.07)
		Men: 0.83 (0.65, 1.04)
		Women: 1.17 (0.80, 1.71)
		
		Replacement of SFA with Medium-GI CHO
		Incident MI, HR (95% CI)
		All: 0.98 (0.80, 1.21)
		Men: 1.08 (0.84, 1.38)
		Women: 0.80 (0.54, 1.18)
		
		Replacement of SFA with High-GI CHO
		Incident MI, HR (95% CI)
		All: 1.33 (1.08, 1.64)
		Men: 1.34 (1.04, 1.71)
		Women: 1.10 (0.75, 1.63)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education level), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI; history of hypertension, intake of glycemic CHO, proteins, MUFA, and PUFA (all %E).
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			European Commission 6th Framework Programme; Danish Council for Strategic Research

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Joensen, 2010[171]
PCS, DDCH (Danish Diet, Cancer and Health), Denmark
Baseline N=57,053 Analytic N=53,803 (Attrition: 6%)
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer or acute coronary syndrome (ACS)
• Age: Median~56y
• Sex (female): ~54%
• Race/ethnicity: NR
• SES: <8y of education, 33%
• Anthropometry: BMI >25, 64.7% of men and 48.2% of women
Fat intake at baseline, Median (IQR):
• n-3 PUFA (g/d), men: 0.70 (0.47, 1.00), women: 0.57 (0.38, 0.83)
• EPA (g/d), men: 0.18 (0.11, 0.27), women: 0.15 (0.09, 0.23)
• DHA (g/d), men: 0.43 (0.29, 0.63), women: 0.36 (0.24, 0.52)
• DPA (g/d), men: 0.08 (0.06, 0.10), women: 0.06 (0.04, 0.08)
Baseline blood lipids & BP, Median (IQR):
• TC (mmol/L), men: 5.9 (5.2, 6.7), women: 6.2 (5.4, 7.0)
• SBP (mmHg), men: 140 (128, 154), women: 136 (122, 151)
Summary of findings:
In men, marine n-3 PUFA intake at ~56y of age was not significantly associated with risk of acute coronary syndrome during ~7.6y of follow-up, although risk tended to be lower with higher intakes. Except one comparison that showed higher risk when comparing Q4 of EPA intake to Q1, marine n-3 PUFA intake in women at ~56y of age was not associated with ACS.
	Exposures:
	• Marine n-3 PUFA (quintiles; g/d)
	  • Q1 (ref; Men: 0-0.39, Women: 0-0.38)
	  • Q2 (Men: 0.39-0.58, Women: 0.38-0.57)
	  • Q3 (Men: 0.58-0.79, Women: 0.57-0.76)
	  • Q4 (Men: 0.79-1.08, Women: 0.76-1.02)
	  • Q5 (Men >1.08, Women >1.02)
	• EPA (quintiles; g/d)
	  • Q1 (ref; Men: 0-0.09, Women: 0-0.08)
	  • Q2 (Men: 0.09-0.14, Women: 0.08-0.13)
	  • Q3 (Men: 0.14-0.20, Women: 0.13-0.19)
	  • Q4 (Men: 0.20-0.28, Women: 0.19-0.24)
	  • Q5 (Men >0.28, Women >0.24)
	• DPA (quintiles; g/d)
	  • Q1 (ref; Men: 0-0.05, Women: 0-0.04)
	  • Q2 (Men: 0.05-0.07, Women: 0.04-0.06)
	  • Q3 (Men: 0.07-0.09, Women: 0.06-0.07)
	  • Q4 (Men: 0.09-0.11, Women: 0.07-0.09)
	  • Q5 (Men >0.11, Women >0.09)
	• DHA (quintiles; g/d)
	  • Q1 (ref; Men: 0-0.23, Women: 0-0.20)
	  • Q2 (Men: 0.23-0.35, Women: 0.20-0.32)
	  • Q3 (Men: 0.35-0.48, Women: 0.32-0.43)
	  • Q4 (Men: 0.48-0.65; Women: 0.43-0.59)
	  • Q5 (Men: >0.65, Women >0.59)
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~7.6y of follow-up
	• Incident acute coronary syndrome (ACS): Obtained via linkage with central Danish registries; Included unstable angina pectoris, non-fatal MI, and fatal MI
	  • Men: 852 cases
	  • Women: 272 cases
		Marine n-3 (EPA+DPA+DHA) PUFA
		ACS, HR (95% CI)
		Men:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		
		EPA
		ACS, HR (95% CI)
		Men:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Women:
		Q1 (ref) vs Q2: 0.92 (0.62, 1.36)
		Q1 (ref) vs Q3: 1.11 (0.75, 1.66)
		Q1 (ref) vs Q4: 1.57 (1.04, 2.38)
		Q1 (ref) vs Q5: 0.93 (0.60, 1.42)
		
		DPA
		ACS, HR (95% CI)
		Men:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		
		DHA
		ACS, HR (95% CI)
		Men:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
			Key confounders NOT accounted for:
			Race/ethnicity, SES, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education level), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, history of diabetes mellitus, SBP, total cholesterol, intake of fruit, vegetables, SFA, MUFA, and n-6 PUFA
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			NR

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Bork, 2016[148]
PCS, DDCH (Danish Diet, Cancer and Health), Denmark
Baseline N=57,053 Analytic N=53,901 (Attrition: 7%)
 	
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer or MI
• Age: Median~56y
• Sex (female): 52%
• Race/ethnicity: NR
• SES: Education, ~33% ≤7y, ~46% 8-10y, ~21% >10y
• Anthropometry: BMI ≥25, 64.7% of men, 48.0% of women
 	
Fat intake at baseline, Median (2.5th, 97.5th percentiles):
• ALA (g/d), Men: 2.1 (1.1, 3.6)
• ALA (g/d), Women: 1.5 (0.9, 2.7)
• LA (g/d), Men: 12.5 (7.0, 21.6)
• LA (g/d), Women: 9.6 (5.3, 17.4)
• Marine n-3 FA (g/d), Men: 0.7 (0.2, 1.8)
• Marine omega-3 FA (g/d), Women: 0.6 (0.1, 1.5)
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: ~6.8%
• Hypertension: ~15.9%
 	
Summary of findings:
In men and women, ALA intake at ~56y of age was not associated with incident MI during ~17y of follow-up.
	Exposures:
	• ALA (continuous; energy adjusted g/d)
	• ALA (quintiles; energy adjusted g/d)
	  • Q1 (ref; Men <1.67, Women <1.24)
	  • Q2 (Men 1.67-1.94, Women 1.24-1.43)
	  • Q3 (Men1.94-2.19, Women 1.43-1.62)
	  • Q4 (Men 2.19-2.54, Women 1.62-1.88)
	  • Q5 (Men ≥2.54, Women ≥1.88)
	• ALA x LA interaction (quintiles; energy adjusted g/d)
	• ALA x marine omega-3 FA interaction (quintiles; energy adjusted g/d)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~17y of follow-up
	• Incident MI (fatal and nonfatal): Obtained via linkage with Danish nationwide registers
	  • Total: 2124 cases in men, 854 cases in women
	  • Fatal: 417 cases in men
		Incident MI (total), HR (95% CI)
		Men:
		ALA (continuous)
		Data NR, P=0.838
		ALA (quintiles)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.299
		ALA x LA interaction (quintiles)
		P-interaction=0.355
		ALA x marine omega-3 FA interaction (quintiles)
		P-interaction=0.576
		Women:
		ALA (continuous)
		Data NR, P=0.308
		ALA (quintiles)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.746
		ALA x LA interaction (quintiles)
		P-interaction=0.703
		ALA x marine omega-3 FA interaction (quintiles)
		P-interaction=0.572
		
		Incident MI (fatal), (95% CI)
		Men:
		ALA (continuous)
		Data NR, P=0.328
		ALA (quintiles)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.401
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (length of education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, WC, fiber intake, glycaemic load, MUFA intake, PUFA intake, LA intake, SFA intake, marine-long chain omega-3 FA intake; In women: menopausal status, hormone replacement therapy.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			NR

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Gammelmark, 2016[160]
PCS, DDCH (Danish Diet, Cancer and Health), Denmark
Baseline N=57,053 Analytic N=54,904 (Attrition: 4%)
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer, MI, or cardiac arrest
• Age: Median~56y
• Sex (female): ~53%
• Race/ethnicity: NR
• SES: Education, ~33% Basic school, ~46% Higher education (1-3y), ~21% Higher education (>3y)
• Anthropometry: BMI, Median~25
Fat intake at baseline, Median (5th-95th percentiles):
• Marine n-3 PUFA (mg/d)
  • Men: 692.2 (313.7-1370.1)
  • Women: 569.2 (248.8-1148.3)
• EPA (mg/d)
  • Men: 177.3 (68.7-379.1)
  • Women: 147.5 (56.1-321.7)
• DPA (mg/d)
  • Men: 82.0 (47.3-134.5)
  • Women: 61.8 (33.7-105.1)
• DHA (mg/d)
  • Men: 430.7 (189.2-866.1)
  • Women: 358.3 (151.7-726.9)
Blood lipids and BP at baseline:
• Hypercholesterolemia: ~7%
• Hypertension: ~16%
Summary of findings:
In men and women, total marine n-3 PUFA intake, or EPA, DPA, and DHA intake, at ~56y of age, was not significantly associated with incident MI during ~17.0y of follow-up.
	Exposures:
	• Total marine n-3 PUFA (quintiles; mg/d)
	  • Q1 (ref; Men 0-421, Women 0-341)
	  • Q2 (Men >421-602, Women >341-491)
	  • Q3 (Men >602-793, Women >491-656)
	  • Q4 (Men >793-1083, Women >656-904)
	  • Q5 (Men >1083, Women >904)
	• EPA (quintiles; mg/d)
	  • Q1 (ref; Men 0-99, Women 0-82)
	  • Q2 (Men >99-151, Women >82-125)
	  • Q3 (Men >151-207, Women >125-173)
	  • Q4 (Men >207-294, Women >173-247)
	  • Q5 (Men >294, Women >247)
	• DPA (quintiles; mg/d)
	  • Q1 (ref; Men 0-58, Women 0-42)
	  • Q2 (Men >58-74, Women >42-56)
	  • Q3 (Men >74-91, Women >56-69)
	  • Q4 (Men >91-113, Women >69-88)
	  • Q5 (Men >113, Women >88)
	• DHA (quintiles; mg/d)
	  • Q1 (ref; Men >257, Women 0-211)
	  • Q2 (Men >257-373, Women >211-307)
	  • Q3 (Men >373-496, Women >307-413)
	  • Q4 (Men >496-683, Women >413-573)
	  • Q5 (Men >683, Women >573)
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	Outcomes and assessment methods:
	• Assessed during ~17.0y of follow-up
	• Incident MI (fatal and nonfatal): Obtained via linkage with Danish National Patient Registry and/or Danish Causes of Death Registry
	  • Total: 2136 cases in men, 892 cases in women
	  • Fatal: 424 cases in men, 156 cases in women
		Total marine n-3 (EPA+DPA+DHA) PUFA
		Incident MI (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.49
		Women: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.56
		Incident MI (fatal), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.58
		Women: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.22
		
		EPA
		Incident MI (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.69
		Women: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.73
		
		DPA
		Incident MI (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.74
		Women: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.46
		
		DHA
		Incident MI (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.44
		Women: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P-trend=0.49
		
		Analyses adjusted for diabetes mellitus, hypertension, and hypercholesterolemia instead of dietary covariates obtained similar results. See Gammelmark, 2016 for details.
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education level), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			WC (adjusted for BMI), total intake of SFA, MUFA and PUFA (excluding n-3 PUFA), dietary fiber.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			The Danish Heart Foundation; the Hertha Christensen Foundation; the Danish Cancer Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Veno, 2017[212]
PCS, DDCH (Danish Diet, Cancer and Health), Denmark
Baseline N=57,053 Analytic N=55,338 (Attrition: 3%)
 	
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer or stroke
• Age: Median=56.1y, 5th-95th percentiles (50.7-64.2y)
• Sex (female): 52.4%
• Race/ethnicity: NR
• SES: Education, 32.8% ≤7y, 46.1% 8-10y, 21.1% >10y
• Anthropometry: BMI, Median=25.5, 5th-95th percentiles (20.5-33.3)
 	
Fat intake at baseline, Median (5th-95th percentiles):
• LA (g/d): 10.7 (5.2-20.6)
• SFA (g/d): 31.1 (15.8-55.3)
• MUFA (g/d): 27.2 (14.4-48.6)
• Marine n-3 PUFA (g/d): 0.6 (0.2-1.5)
Blood lipids and BP at baseline:
• Hypercholesterolemia: 7.3% (Unknown=42.4%)
• Hypertension: 16.0% (Unknown=13.1%)
 	
Summary of findings:
In men and women, LA intake at ~56y of age, modeled to replace SFA, MUFA, or Glycemic CHO intake, was not significantly associated with total ischemic stroke or any ischemic stroke subtypes during ~13.5y of follow-up except for risk of small vessel occlusion with was lower when LA intake replaced MUFA intake.
	Exposures:
	• LA (continuous; per 5%E increase) replacing:
	  • SFA (per 5%E decrease)
	  • MUFA (per 5%E decrease)
	  • Glycemic CHO (per 5%E decrease)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Ischemic stroke and subtypes: Obtained via linkage with Danish National Patient Register, validated by physician
	  • Total: 1879 cases
	  • Large artery atherosclerosis: 319 cases
	  • Small vessel occlusion: 844 cases
	  • Cardioembolism: 102 cases
	  • Strokes of other etiology: 98 cases
	  • Undetermined etiology: 516 cases
		LA replacing SFA
		Total ischemic stroke, HR (95% CI)
		0.98 (0.83, 1.16)
		Ischemic stroke subtypes, HR (95% CI)
		Large artery atherosclerosis: P=NS
		Cardioembolism: P=NS
		Small vessel occlusion: P=NS
		Stroke of other etiology: P=NS
		Stroke of undetermined etiology: P=NS
		Noncardioembolic stroke: P=NS
		
		LA replacing MUFA
		Total ischemic stroke, HR (95% CI)
		0.80 (0.63, 1.02)
		Ischemic stroke subtypes, HR (95% CI)
		Large artery atherosclerosis: P=NS
		Cardioembolism: P=NS
		Small vessel occlusion: 0.67 (0.46, 0.96)
		Stroke of other etiology: P=NS
		Stroke of undetermined etiology: P=NS
		Noncardioembolic stroke: P=NS
		
		LA replacing Glycemic CHO
		Total ischemic stroke, HR (95% CI)
		0.92 (0.78, 1.09)
		Ischemic stroke subtypes, HR (95% CI)
		Large artery atherosclerosis: P=NS
		Cardioembolism: P=NS
		Small vessel occlusion: P=NS
		Stroke of other etiology: P=NS
		Stroke of undetermined etiology: P=NS
		Noncardioembolic stroke: P=NS
		
		Analyses that did not adjust for lifestyle factors, but did adjust for hypertension, hypercholesterolemia, diabetes mellitus, atrial fibrillation/atrial flutter, were similar in direction but achieved statistical significance for total ischemic stroke (LA replacing SFA), small vessel occlusion (LA replacing MUFA or Glycemic CHO), and noncardioembolic stroke (LA replacing SFA, MUFA, or Glycemic CHO). See Veno, 2017 for details.
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (length of education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			WC (adjusted for BMI).
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			The Danish Heart Foundation; The Danish Cancer Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Bork, 2018[149]
PCS, Danish Diet, Cancer and Health, Denmark
Baseline N=57,053 Analytic N=55,018 (Attrition: 4%)
 	
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer or stroke
• Age: Median~56y
• Sex (female): 52%
• Race/ethnicity: NR
• SES: Education, ~33% ≤7y, ~46% 8-10y, ~21% >10y
• Anthropometry: WC adjusted for BMI, ~88.9 cm
 	
Fat intake at baseline, Median (2.5th, 97.5th percentiles):
• ALA (g/d): 1.8 (0.9, 3.3)
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: 7.3%
• Hypertension: 16.0%
 	
Summary of findings:
In men and women, ALA intake at ~56y of age was not associated with ischemic stroke during ~13.5y of follow-up.
	Exposures:
	• ALA (continuous; energy adjusted g/d)
	• ALA (quintiles; energy adjusted g/d)
	  • Q1 (ref; ≤1.35)
	  • Q2 (1.36-1.62)
	  • Q3 (1.63-1.90)
	  • Q4 (1.91-2.26)
	  • Q5 (≥2.27)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Ischemic stroke and subtypes: Obtained via linkage with Danish National Patient Register, validated by physician
	  • Total: 1859 cases
	  • Large artery atherosclerosis: 316
	  • Small vessel occlusion: 835
	  • Cardioembolism: 102
	  • Stroke of other etiology: 98 cases
	  • Stroke of undetermined etiology: 508 cases
		Total ischemic stroke, HR (95% CI)
		ALA (continuous)
		Data NR, P=0.431
		ALA (quintiles)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.333
		
		Similar NS results seen in analyses that assessed risk of different ischemic stroke subtypes (large artery atherosclerosis, small-vessel occlusion, cardio-embolism, stroke of other etiology, stroke of undetermined etiology). See Bork, 2018 for more details.
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (length of education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			WC (adjusted for BMI), fiber intake, glycaemic load, MUFA intake, PUFA intake, SFA intake, LA intake, marine omega-3 FA intake.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			The Danish Heart Foundation; The Danish Cancer Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Veno, 2019[211]
PCS, Danish Diet, Cancer and Health, Denmark
Baseline N=57,053 Analytic N=55,338 (Attrition: 3%)
 	
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer or stroke
• Age: Median=56.1y, 5th-95th percentiles (50.7-64.2y)
• Sex (female): 52.4%
• Race/ethnicity: NR
• SES: Education, 32.9% ≤7y, 46.1% 8-10y, 21.1% >10y
• Anthropometry: Median=25.5, 5th-95th percentiles (20.5-33.3)
 	
Fat intake at baseline: NR
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: 7.4% (Unknown=42.4%)
• Hypertension: 16.0% (Unknown=13.4%)
 	
Summary of findings:
In men and women, marine n-3 PUFA intake at ~56y of age was not associated with total ischemic stroke during ~13.5y of follow-up, except for higher intakes of DPA, which were associated with higher risk of total ischemic stroke. Higher intakes of total marine n-3 PUFA, EPA, and DHA were associated with lower risk of ischemic stroke due to large artery atherosclerosis and higher risk of ischemic stroke due to cardioembolism. Higher intakes of DPA were associated with higher risk of ischemic stroke due to cardioembolism.
	Exposures:
	• Total marine n-3 PUFA (quartiles; energy adjusted g/d)
	• EPA (quartiles; energy adjusted g/d)
	• DPA (quartiles; energy adjusted g/d)
	• DHA (quartiles; energy adjusted g/d)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Ischemic stroke and subtypes: Obtained via linkage with Danish National Patient Register, validated by physician
	  • Total: 1879 cases
	  • Large artery atherosclerosis: 319 cases
	  • Cardioembolism: 102 cases
	  • Small vessel occlusion: 844 cases
	  • Stroke of other cause: 98 cases
	  • Stroke of undetermined cause: 516 cases
		Total marine n-3 PUFA
		Total ischemic stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.458
		Large artery atherosclerosis, HR (95% CI)
		Q1 (ref) vs Q2: 0.97 (0.72, 1.30)
		Q1 (ref) vs Q3: 0.88 (0.65, 1.19)
		Q1 (ref) vs Q4: 0.69 (0.50, 0.95)
		P-trend=0.020
		Cardioembolism, HR (95% CI)
		Q1 (ref) vs Q2: 1.36 (0.69, 2.66)
		Q1 (ref) vs Q3: 1.49 (0.78, 2.88)
		Q1 (ref) vs Q4: 2.50 (1.38, 4.53)
		P-trend=0.001
		Small vessel occlusion, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.518
		
		EPA
		Total ischemic stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.732
		Large artery atherosclerosis, HR (95% CI)
		Q1 (ref) vs Q2: 0.86 (0.64, 1.16)
		Q1 (ref) vs Q3: 0.82 (0.60, 1.11)
		Q1 (ref) vs Q4: 0.66 (0.48, 0.91)
		P-trend=0.012
		Cardioembolism, HR (95% CI)
		Q1 (ref) vs Q2: 1.17 (0.58, 2.35)
		Q1 (ref) vs Q3: 2.34 (1.27, 4.30)
		Q1 (ref) vs Q4: 2.02 (1.09, 3.73)
		P-trend=0.005
		Small vessel occlusion, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.647
		
		Results of analyses for other subtypes (stroke of other cause, stroke of undetermined cause) were NS for all exposures. See Veno, 2019 for more details.
		
		(Continued on next page)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (length of education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			WC (adjusted for BMI).
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			The Danish Heart Foundation; The Danish Cancer Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Veno, 2019 (CONTINUED)
PCS, Danish Diet, Cancer and Health, Denmark
Baseline N=57,053 Analytic N=55,338 (Attrition: 3%)
 	
Participant characteristics at baseline:
• Native Danish citizens aged 50-64y without prior diagnosis of cancer or stroke
• Age: Median=56.1y, 5th-95th percentiles (50.7-64.2y)
• Sex (female): 52.4%
• Race/ethnicity: NR
• SES: Education, 32.9% ≤7y, 46.1% 8-10y, 21.1% >10y
• Anthropometry: Median=25.5, 5th-95th percentiles (20.5-33.3)
 	
Fat intake at baseline: NR
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: 7.4% (Unknown=42.4%)
• Hypertension: 16.0% (Unknown=13.4%)
 	
Summary of findings:
In men and women, marine n-3 PUFA intake at ~56y of age was not associated with total ischemic stroke during ~13.5y of follow-up, except for higher intakes of DPA, which were associated with higher risk of total ischemic stroke. Higher intakes of total marine n-3 PUFA, EPA, and DHA were associated with lower risk of ischemic stroke due to large artery atherosclerosis and higher risk of ischemic stroke due to cardioembolism. Higher intakes of DPA were associated with higher risk of ischemic stroke due to cardioembolism.
	Exposures:
	• Total marine n-3 PUFA (quartiles; energy adjusted g/d)
	• EPA (quartiles; energy adjusted g/d)
	• DPA (quartiles; energy adjusted g/d)
	• DHA (quartiles; energy adjusted g/d)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 192-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Ischemic stroke and subtypes: Obtained via linkage with Danish National Patient Register, validated by physician
	  • Total: 1879 cases
	  • Large artery atherosclerosis: 319 cases
	  • Cardioembolism: 102 cases
	  • Small vessel occlusion: 844 cases
	  • Stroke of other cause: 98 cases
	  • Stroke of undetermined cause: 516 cases
		DPA
		Total ischemic stroke, HR (95% CI)
		Q1 (ref) vs Q2: 1.10 (0.96, 1.26)
		Q1 (ref) vs Q3: 1.10 (0.96, 1.26)
		Q1 (ref) vs Q4: 1.16 (1.02, 1.33)
		P-trend=0.033
		Large artery atherosclerosis, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.353
		Cardioembolism, HR (95% CI)
		Q1 (ref) vs Q2: 0.80 (0.41, 1.56)
		Q1 (ref) vs Q3: 1.14 (0.63, 2.08)
		Q1 (ref) vs Q4: 1.68 (0.96, 2.91)
		P-trend=0.020
		Small vessel occlusion, HR (95% CI)
		Q1 (ref) vs Q2: 1.27 (1.04, 1.55)
		Q1 (ref) vs Q3: 1.21 (0.99, 1.48)
		Q1 (ref) vs Q4: 1.19 (0.98, 1.46)
		P-trend=0.179
		
		DHA
		Total ischemic stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.513
		Large artery atherosclerosis, HR (95% CI)
		Q1 (ref) vs Q2: 0.90 (0.67, 1.22)
		Q1 (ref) vs Q3: 0.86 (0.63, 1.16)
		Q1 (ref) vs Q4: 0.72 (0.53, 0.99)
		P-trend=0.043
		Cardioembolism, HR (95% CI)
		Q1 (ref) vs Q2: 0.97 (0.50, 1.89)
		Q1 (ref) vs Q3: 1.27 (0.68, 2.36)
		Q1 (ref) vs Q4: 2.12 (1.21, 3.69)
		P-trend=0.002
		Small vessel occlusion, HR (95% CI)
		Q1 (ref) vs Q2: 1.26 (1.04, 1.54)
		Q1 (ref) vs Q3: 1.17 (0.96, 1.43)
		Q1 (ref) vs Q4: 1.13 (0.93, 1.38)
		P-trend=0.411
		
		Results of analyses for other subtypes (stroke of other cause, stroke of undetermined cause) were NS for all exposures. See Veno, 2019 for more details.
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (length of education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			WC (adjusted for BMI).
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			The Danish Heart Foundation; The Danish Cancer Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Praagman, 2019[198]
PCS, DDCH (Danish Diet, Cancer and Health; EPIC-Denmark) and EPIC-Norfolk, Denmark and U.K.
Baseline N=82,692 Analytic N=75,425 (Attrition: 9%)
 	
Participant characteristics at baseline:
• Participants without history of cancer, CVD or MI
• Age: Mean~58 y
• Sex (female): ~54%
• Race/ethnicity: NR
• SES: EPIC-Norfolk: Educational level: None ~36%, Degree ~13%; EPIC-Denmark: 7y or less: ~33%, 8-10y ~46%, >10y ~21%
• Anthropometry: BMI, Mean~26.2
 	
Fat intake at baseline, Mean (SD):
• SFAs: Norfolk: 13.3%E (3.5); Denmark: 12.5%E (2.6)
• MUFAs: Norfolk: ~9.3%; Denmark: ~11.0%E
• PUFAs: Norfolk: ~5.8%E; Denmark: ~5.4%E
• Cholesterol: Norfolk: ~277 mg; Denmark: ~443mg
 	
Blood lipids and BP at baseline, Mean:
• TC: Norfolk: ~6.2 mmol/L
• HDL: Norfolk: ~1.4 mmol/L
• LDL: Norfolk: ~4.0 mmol/L
• Triglycerides: Norfolk: ~1.8 mmol/L
• SBP: Norfolk: ~135 mmHg; Denmark: ~140 mmHg
• DBP: ~83 mmHg
	Exposures:
	• SFAs (quintiles)
	• Sum of C4:0-C10:0 (Median intake for Norfolk and Denmark, respectively)
	  • Q1: 0.3; 0.6
	  • Q2: 0.5; 0.95
	  • Q3: 0.7; 1.23
	  • Q4: 1.0; 1.54
	  • Q5: 1.6; 2.05
	• Sum of C12:0-C18:0 (Median intake for Norfolk and Denmark, respectively)
	  • Q1: 8.4; 9.3
	  • Q2: 10.5; 10.5
	  • Q3: 11.9; 12.5
	  • Q4: 13.5; 13.7
	  • Q5: 16.2; 15.4
	• Specific sources of SFAs (continuous, per 1%E) from (Median):
	  • Total dairy (Norfolk: 3.7%E; Denmark: 4.1%E)
	  • Meat (Norfolk: 1.6%E; Denmark: 3.2%E)
	  • Cakes & cookies (Norfolk: 1.5%E)
	  • Cheese (Norfolk: 1.1%E)
	  • Soft fats (Norfolk: 0.8%E)
	  • Hard fats (Norfolk: 0.04%E)
	• Replacement of 1%E/d of SFAs (continuous) with 1%E of:
	  • CisMUFA
	  • CisPUFA
	  • Starch carbohydrates
	  • Plant protein
	Assessment method and timing:
	• Self-administered, validated FFQ to assess intake in the previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
		Incident MI, HR (95% CI)
		*Sum of C4:0-C10:0**
		Norfolk: Q1 vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Denmark: Q1 vs Q2, Q5: NS
		Q1 vs Q3: 0.87 (0.75, 1.00), P<0.05
		Q1 vs Q4: 0.81 (0.69, 0.94), P<0.05
		P-trend: NS
		Pooled
		Q1 vs Q2, Q3, Q5: NS
		Q1 vs Q4: 0.82 (0.72, 0.93)
		
		*Sum of C12:0-C18:0**
		Norfolk: Q1 vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Denmark: Q1 vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Pooled: Q1 vs Q2, Q3, Q4, Q5: All NS
		*Additional adjustment for hypercholesterolemia and menopausal status did not change results
		
		Specific sources of SFAs from:
		Norfolk:
		Total dairy (not incl butter): NS
		Meat: NS
		Cakes & cookies: NS
		Cheese: NS
		Soft fats: NS
		Hard fats: NS
		Denmark:
		Total dairy: NS
		Meat: 1.08 (1.04, 1.12), P<0.05
		
		Replacement of sum C12:0-C18:0 with:
		Norfolk:
		cisMUFA: NS
		cisPUFA: NS
		Starch carbohydrates: NS
		Plant protein: NS
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Sex, age, SES (education level), TEI, alcohol intake, physical activity, smoking, family history of CVD (EPIC-Norfolk only)
			
			Additional model adjustments:
			BMI, hypertension, use of post-menopausal hormones, sum of other SFAs, intake of protein and PUFA
			EPIC-Norfolk only: aspirin use, multivitamin use, and trans-fatty acids
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Cancer Research U.K.; Medical Research Council; MRC; Danish Cancer Society

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Summary of findings: *In Denmark, higher intake of SFAs from meat was significantly associated with higher risk of MI incidence; higher intake of SFAs (C4:0-C10:0) was significantly associated with lower risk of MI. Additionally, replacing 1%E of SFA (C12:0-C18:0) with 1%E plant protein was significantly associated with lower risk of MI.*	• Assessed during 18.8y (Norfolk) and 13.6y (Denmark) of follow-up • Incidence myocardial infarction: death certification at United Kingdom Office of National Statistics, The Danish National Patient Register, The Danish Register of Causes of Death, Norfolk Health Authority database, Danish National Patient Register • MI cases: 1,204 in Norfolk, 2,260 in Denmark	Denmark: cisMUFA: NS cisPUFA: NS Starch carbohydrates: NS **Plant protein: 0.87 (0.82, 0.94)**	

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Strom, 2012[208]
PCS, Danish National Birth Cohort, Denmark
Baseline N=53,981, Analytic N=48,627 (Attrition: ~10%)
 	
Participant characteristics at baseline:
• Pregnant women at ~25 weeks gestation without preeclampsia or gestational diabetes
• Age: Mean=29.9y (range: 15.7-46.9y)
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Education, 24% ≤10y school, 51% high school, 25% unknown; Occupation, 39% white collar, 19% skilled, 21% unskilled, 12% student, 10% unemployed
• Anthropometry: Pre-pregnant BMI, 4% <18.5, 69% ≥18.5-25.0, 19% ≥25.0-30.0, 7% ≥30.0
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
Among women interviewed when pregnant, higher intake of long chain n-3 PUFA at ~30y of age was associated with lower risk of incident cerebrovascular disease and ischemic heart disease during ~8y of follow-up.
	Exposures:
	• Marine long chain n-3 PUFA (lowest intake and quintiles; energy-adjusted g/d), Median:
	  • Lowest 3% (n=1446): 0.06
	  • Q1 (n=9227): 0.13
	  • Q2 (n=9521): 0.21
	  • Q3 (n=9517): 0.31
	  • Q4 (n=9509): 0.45
	  • Q5 (ref; n=9407): 0.73
	
	Assessment method and timing:
	• Self-administered, validated, semi-quantitative >360-item FFQ representing intake during previous 1mo (n-3 PUFA quantified based on estimated fish intake)
	• Assessed at baseline (~25wk gestation)
	
	Outcomes and assessment methods:
	• Assessed during ~8y (range: 6-12y) of follow-up
	• Incident CVD: Obtained via linkage with Danish National Patient Registry; Included cerebrovascular diseases and ischemic heart diseases
	  • Cerebrovascular disease: 146 cases
	  • Ischemic heart disease: 103 cases
	  • Note: (328 cases of hypertensive disease, not an included outcome)
		Marine long chain n-3 PUFA
		Incident Cerebrovascular Disease, HR (95% CI)
		Q5 (ref) vs Lowest 3%: 2.34 (1.10, 4.99)
		Q5 (ref) vs Q1, Q2, Q3, or Q4: Data NR
		Incident Ischemic Heart Disease, HR (95% CI)
		Q5 (ref) vs Lowest 3%: 3.80 (1.53, 9.42)
		Q5 (ref) vs Q1, Q2, Q3, or Q4: Data NR
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education, occupation), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Prepregnant BMI, cohabitant status, parity, SFA intake, fiber intake, *trans*-FA intake
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of women with preeclampsia or gestational diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			Faroese Research Council; Fisheries Research Fund of the Faroe Islands; EU Sixth Framework Programme Integrated Research Project SEAFOOD-plus; EU Sixth Framework Programme EARNEST; Nordic Working Group on Fishery Research

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Bendinelli, 2011[143]
PCS, EPIC-Italy, Italy
Baseline N=32,578 Analytic N=29,689 (Attrition: 9%)
 	
Participant characteristics at baseline:
• 100% without prevalent stroke or myocardial infarction
• Age: Mean: 50.0 (SE=7.9), range 35-74
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Education: None/elementary school ~29%, Secondary/professional school ~34%, High school ~23%, University degree ~14%
• Anthropometry: BMI~25.7
 	
Fat intake at baseline, Mean:
• Olive oil: 24.7 (SE=13.0) g/d
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Olive oil intake was significantly associated with lower risk of CHD incidence; this was no longer significant among post-menopausal women only.
	Exposures:
	• Olive oil (continuous, per 10 g; categorical in quartile)
	  • Q1 (ref): ≤15.9g
	  • Q2: ≤22.5g
	  • Q3: ≤31.2g
	  • Q4: >31.2g
	
	Assessment method and timing:
	• Self-administered, validated semi-quantitative FFQ to assess usual food intake in previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 7.85 y of follow-up
	• Incident CHD (fatal and nonfatal events of myocardial infarction, coronary revascularization, or both); unspecified cardiac event: Death certificates from Mortality Registries, hospital discharge files
	• Nonfatal MI: 144 events
	• Fatal MI with hospitalization: 3
	• Fatal MI without hospitalization: 9
	• Coronary revascularizations: 27 events
	• Unspecified cardiac event: 1 event
		Incident CHD, HR (95% CI)
		Olive oil:
		Q1 (ref) vs Q2, Q3: All NS
		Q1 (ref) vs Q4: 0.56 (0.31, 0.99)
		P-trend=0.04
		Continuous:
		Olive oil: NS
		Post-menopausal women only:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.04
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (educational level), TEI excluding alcohol, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Body height, body weight, WC, hypertension, menopausal status, total meat consumption
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants who were being treated for hyperlipidemia and diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			Compagnia di San Paolo; Associazione Italiana per la Ricerca sul Cancro; Programma Integrato Oncologia, Regione Toscana, Ministero della Salute

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Pala, 2019[193]
PCS, EPIC-Italy, Italy
Baseline N=47,745 Analytic N=45,009 (Attrition: 6%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: Mean: 50.1 (SEM=0.037)
• Sex (female): NR
• Race/ethnicity: NR
• SES: Relative index of inequality: 0.50 (SEM=0.001)
• Anthropometry: BMI, Mean: 26.0 (SEM=0.019)
 	
Fat intake at baseline, Mean (SEM):
• SFA: 31.0 (0.054)
• MUFA: 41.7 (0.067)
• PUFA: 10.6 (0.020)
• Butter: 1.7 (0.014)
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Butter intake was not significantly associated with CVD mortality.
	Exposures:
	• Butter (categorical)
	  • 1: 0g (ref)
	  • 2: >0 to ≤1.4g/d
	  • 3: >1.4 to 100.1g/d
	
	Assessment method and timing:
	• Self-administered, validated FFQ to assess usual food intake in previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 14.9 y of follow-up
	• CVD mortality: mortality databases
	• CVD mortality: 104 cases (0 intake), 223 cases (>0-1.4g), 132 cases (>1.4-100.1g)
		CVD mortality
		Butter:
		Intake category 1 vs 2, 3: All NS
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES, TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Center, weight, height, waist-to-hip ratio, intake of sugar, Italian Mediterranean Index
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Associazione Italiana per la Ricerca sul Cancro

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Goede, 2010[153]
PCS, EPIC-Netherlands (MORGEN), Netherlands
Baseline N=22,654 Analytic N=21,342 (Attrition: 6%)
 	
Participant characteristics at baseline:
• 100% without prevalent MI or stroke
• Age: Mean: 42.1 y (SD=11.2)
• Sex (female): 55%
• Race/ethnicity: Dutch ethnicity: ~97%
• SES: Education: University or higher vocation training ~22%
• Anthropometry: BMI ~25
 	
Fat intake at baseline, Mean:
• EPA+DHA: 114 (62-195) mg/d
• SFA: ~14.4%E
• PUFA: ~6.8%E
 	
Blood lipids and BP at baseline, Mean:
• TC: ~5.3 mmol/L
• HDL: ~1.4 mmol/L
• SBP: ~120 mmHg
• DBP: ~76 mmHg
 	
Summary of findings:
Higher EPA+DHA intake compared to lower EPA+DHA intake was significantly associated with lower fatal CHD and MI incidence, but not non-fatal MI incidence in Dutch adults, aged 20-65 years.
	Exposures:
	• EPA+DHA (categorical in quartiles)
	  • Q1 (ref, n=5336): Median=40 mg/d
	  • Q2 (n=5335): Median=84 mg
	  • Q3 (n=5335): Median=151 mg
	  • Q4 (n=5336): Median=234 mg
	Assessment method and timing:
	• Self-administered, validated 178-item FFQ to assess usual intake in the previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 11.3 y (range 9-14 y) of follow-up
	• CHD (fatal), MI (fatal or nonfatal): registries, including Statistics Netherlands, hospital admission data
	• CHD: 82 cases
	• Fatal MI: 64 cases
	• Nonfatal MI: 252 cases
		Fatal CHD, HR (95% CI)
		EPA+DHA
		Q1 vs Q2, Q3: All NS
		Q1 vs Q4: 0.51 (0.27-0.94)
		P-trend=0.05
		Fatal MI, HR (95% CI)
		EPA+DHA
		Q1 vs Q2, Q3: All NS
		Q1 vs Q4: 0.38 (0.19, 0.77)
		P-trend=0.01
		Incident Non-fatal MI, HR (95% CI)
		EPA+DHA
		Q1 vs Q2, Q3, Q4: All NS
		P-trend=0.18
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, alcohol intake, physical activity, smoking, family history of CHD
			
			Additional model adjustments:
			BMI, vitamin or mineral supplement use, use of drugs for hypertension or hypercholesterolemia, fruit consumption, vegetable consumption, saturated fat intake
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Ministry of Health, Welfare and Sport of the Netherlands (The Hague); National Institute for Public Health and the Environment (Biilthoven, The Netherlands)

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Goede, 2011[155]
PCS, EPIC-Netherlands (MORGEN), Netherlands
Baseline N=22,654 Analytic N=20,069 (Attrition: 11%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: Mean: 41.5 (SD=11.1)
• Sex (female): 65%
• Race/ethnicity: NR
• SES: High educational level (higher vocational education and university), ~25%
• Anthropometry: BMI, Mean~24.8
 	
Fat intake at baseline, Mean (SD):
• SFA: ~37 g/d; ~14%E
• Cis-MUFA: ~31 g/d; ~12%E
• PUFA: ~17 g/d; ~7%E
• ALA: ~1.4 g/d; ~0.5%E
 	
Blood lipids and BP at baseline:
• TC: ~5.3 mmol/L
• HDL: ~1.4 mmol/L
• SBP: ~120 mmHg
• DBP: ~76 mmHg
 	
Summary of findings:
ALA intake, especially ALA from salad dressing, was significantly associated with lower odds of total stroke and ischemic stroke. ALA intake, regardless of source, was not associated with risk of CHD. ALA intake from other sources than salad dressing was not associated with total stroke and ischemic stroke.
	Exposures:
	• ALA (n=19,896; quintiles, g/d)
	• Total ALA, Median (ALA from salad dressing; ALA from all sources except salad dressing)
	  • Q1 (ref): 1.0 g/d (0.1 g/d; 0.7 g/d)
	  • Q2: 1.2 g/d (0.2 g/d; 0.9 g/d)
	  • Q3: 1.3 g/d (0.3 g/d; 1.0 g/d)
	  • Q4: 1.5 g/d (0.5 g/d; 1.1 g/d)
	  • Q5: 1.9 g/d (0.7 g/d; 1.4 g/d)
	• ALA from salad dressing
	• ALA from other sources than salad dressing
	
	Assessment method and timing:
	• Self-administered, validated 178-item FFQ to assess usual food intake in previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 12.2 y of follow-up
	• Incident CHD and stroke: Dutch Center for Health Care Information, hospital discharge diagnoses by National Medical Registry
	  • CHD: 280 cases
	  • Ischemic cerebrovascular accident: 80 cases
	  • Transient ischemic attacks: 59 cases
	  • Hemorrhagic stroke: 47 cases
	  • Unspecified stroke: 35 cases
		Incident CHD, HR (95% CI)
		ALA intake:
		Q1 vs Q2, Q3, Q4, Q5: All NS
		ALA intake from salad dressing:
		Q1 vs Q2, Q3, Q4, Q5: All NS
		ALA intake from other sources than salad dressing: Q1 vs Q2, Q3, Q4, Q5: All NS
		Incident Total stroke, HR (95% CI)
		ALA intake:
		Q1 vs Q2: 0.65 (0.43, 0.97)
		Q1 vs Q3: 0.49 (0.31, 0.76)
		Q1 vs Q4: 0.53 (0.34, 0.83)
		Q5: NS
		ALA intake from salad dressing:
		Q1 vs Q2: NS
		Q1 vs Q3: 0.45 (0.29, 0.72)
		Q1 vs Q4: 0.44 (0.27,0.72)
		Q1 vs **Q5: 0.57 (0.34, 0.96)**
		ALA intake from other sources than salad dressing: Q1 vs Q2, Q3, Q4, Q5: All NS
		Incident Ischemic Stroke, HR (95% CI)
		ALA intake:
		Q1 vs Q2: NS
		Q1 vs Q3: 0.45 (0.26, 0.79)
		Q1 vs Q4: 0.56 (0.32, 0.97)
		Q1 vs Q5: NS
		ALA intake from salad dressing:
		Q1 vs Q2: NS
		Q1 vs Q3: 0.50 (0.29, 0.86)
		Q1 vs Q4: 0.47 (0.26, 0.86)
		Q1 vs Q5: NS
		ALA intake from other sources than salad dressing: Q1 vs Q2, Q3, Q4, Q5: All NS
		Adjustment for plasma cholesterol or SBP did not change results. Associations in subgroups (age and gender) did not differ.
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Sex, age, SES (educational level), TEI, alcohol intake, physical activity, smoking, family history of myocardial infarction
			
			Additional model adjustments:
			BMI, intake of vitamin C, beta-carotene, fiber, saturated fatty acids, trans fatty acids, PUFA other than ALA, raw vegetables (only salad dressing and ALA from other sources than salad dressing)
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants on lipid or BP medication or with diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			Alpro Foundation, Belgium; Ministry of Health; Welfare and Spot of The Netherlands; National Institute for Public Health, Environment, Bilthoven, The Netherlands; Europe Against Cancer Program of the European Union

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Goede, 2012[154]
PCS, EPIC-Netherlands (MORGEN), Netherlands
Baseline N=22,654 Analytic N=20,069 (Attrition: 11%)
 	
Participant characteristics at baseline:
• 100% without prevalent MI or stroke
• Age: Mean: 41.5 y (SD=11.1)
• Sex (female): 55%
• Race/ethnicity: Dutch ethnicity: ~97%, previously reported
• SES: Highly educated (University or higher vocation training) ~25%
• Anthropometry: BMI ~25
 	
Fat intake at baseline, Mean (SD):
• LA: 13.9 g/d (5.9)
• PUFA intake: LA was 79% of total PUFA intake
 	
Blood lipids and BP at baseline, Mean:
• TC: ~5.3 mmol/L
• HDL: ~1.4 mmol/L
• SBP: ~120 mmHg
• DBP: ~76 mmHg
 	
Summary of findings:
LA was not significantly associated with CHD incidence in Dutch adults ages 20-65 years.
	Exposures:
	• LA (categorical in quintiles; continuous per 2%E)
	  • Q1 (ref, n=4013): Median=3.7%E
	  • Q2 (n=4014): Median=4.7%E
	  • Q3 (n=4014): Median=5.4%E
	  • Q4 (n=4014): Median=6.2%E
	  • Q5 (n=4014): Median=7.7%E
	Assessment method and timing:
	• Self-administered, validated 178-item FFQ to assess usual intake in the previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during median of 10.5 y (range 8-13 y) of follow-up
	• CHD (fatal CHD, fatal and non-fatal cardiac arrest, nonfatal MI): registries, including Statistics Netherlands, national hospital discharge register
	  • CHD: 280 total cases
		Incident CHD, HR (95% CI)
		LA
		Q1 vs Q2, Q3, Q4, Q5: All NS
		Continuous: NS
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, alcohol intake, physical activity (subgroup), smoking, family history of MI
			
			Additional model adjustments:
			BMI, dietary fiber, protein, SFA, cis-MUFA, *trans* fatty acids, PUFA other than LA
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants on lipid modifying drugs, antihypertension drugs and diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			Product Board for Margarine, Fats and Oils, Rijswijk, The Netherlands; Wageningen University

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Praagman, 2016[196]
PCS, EPIC-Netherlands (MORGEN and Prospect), Netherlands
Baseline N=40,011 Analytic N=35,597 (Attrition: 11%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: Mean~49.3 y
• Sex (female): ~75%
• Race/ethnicity: NR
• SES: High educational level, ~20%
• Anthropometry: BMI, Mean~25.7
 	
Fat intake at baseline, Mean:
• Total SFAs: ~34 g/d; Median~14.9%E
• Total PUFAs: ~6.8 %E
• *cis* MUFAs: ~9.6%E
 	
Blood lipids, BP at baseline, Mean:
• TC: ~5.7 mmol/L
• HDL: ~1.4 mmol/L
• SBP: Mean~126 mmHg
• DBP: Mean~78 mmHg
 	
Summary of findings:
Higher SFA intake at ~49y of age was significantly associated with a lower risk of IHD during ~12.2y of follow-up. Higher intake of SFAs from butter, cheese, milk and milk products were significantly associated with lower risk of IHD. Other foods were not significantly associated with risk of IHD. Replacement of 5%E of SFAs with CHO, cis-MUFAs, PUFAs, protein and animal protein was significantly associated with greater risk of IHD.
	Exposures:
	• Total SFAs (continuous; per 5% energy)
	• SFAs (continuous) from:
	  • Butter (per 1.42% energy)
	  • Cheese (per 1.95% energy)
	  • Milk & milk products (per 1.45% energy)
	  • Meat (per 1.44% energy)
	  • Cakes (per 0.83% energy)
	  • Snacks (per 0.40% energy)
	  • Hard, solid fats (per 1.25% energy)
	  • Soft, liquid fats (per 0.50% energy)
	  • Other (per 1.06% energy)
	• Replacement of 5% energy from SFAs (continuous) with 5% energy from:
	  • CHO
	  • CHO with low GI
	  • CHO with medium GI
	  • CHO with high GI
	  • cis MUFAs
	  • PUFAs
	  • Protein
	  • Animal protein
	  • Vegetable protein
	
	Assessment method and timing:
	• Self-administered, validated 79-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 12.2 y of follow-up
	• Incident ischemic heart disease (IHD; fatal & nonfatal): morbidity data from Dutch Center for Health Care Information hospital discharge diagnoses
	  • Total: 1807 cases (158 fatal)
		Incident IHD, HR (95% CI)
		Total SFAs: 0.83 (0.74, 0.93)*
		SFAs from:
		Butter: 0.94 (0.90, 0.99)
		Cheese: 0.91 (0.86, 0.97)
		Milk & milk products: 0.92 (0.86, 0.97)
		Meat: 1.00 (0.95, 1.06)
		Cakes: 0.96 (0.91, 1.02)
		Snacks: 1.03 (0.97, 1.10)
		Hard, solid fats: 0.97 (0.91, 1.02)
		Soft, liquid fats: 0.99 (0.95, 1.04)
		Other: 0.94 (0.88, 1.01)
		Replacement of SFAs with:
		CHO: 1.23 (1.09, 1.40)
		CHO with low GI: 1.14 (0.91, 1.43)
		CHO with medium GI: 1.35 (1.05, 1.73)
		CHO with high GI: 1.27 (1.03, 1.56)
		cis MUFAs: 1.30 (1.02, 1.65)
		PUFAs: 1.35 (1.14, 1.61)
		Protein: 1.29 (1.08, 1.54)
		Animal protein: 1.37 (1.14, 1.65)
		Vegetable protein: 0.81 (0.57, 1.17)
		
		*Results similar when adjusted for TC:HDL ratio or SBP. See Praagman, 2016 for details.
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (educational level), TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			BMI, WC, energy-adjusted intakes of cholesterol, fiber, and vitamin C, *trans* fat, vegetable protein, animal protein. SFA from sources: total CHO, *cis* MUFAs, PUFAs
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			"Europe Against Cancer" Programme of the European Commission; Dutch Ministry of Health, Welfare and Sports; Netherlands Organization for Health Research and Development; World Cancer Research Fund

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Vissers, 2019[215]
PCS, EPIC-Netherlands (MORGEN and Prospect), Netherlands
Baseline N=40,011 Analytic N=35,767 (Attrition: 11%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: Mean~49.2 y
• Sex (female): ~75%
• Race/ethnicity: NR
• SES: High educational level (higher vocational education & university), ~20%
• Anthropometry: BMI, Mean~25.7
 	
Fat intake at baseline, Mean (SD):
• SFAs: 34.4 (12.4) g/d, 14.6 (2.5) %E/d
• Dairy:
  • SFAs: 17.9 (9.5) g/d, 7.7 (3.5) %E/d
  • MUFAs: ~2.3 g/d
  • PUFA: ~0.2 g/d
• Meat:
  • SFAs:15.3 (3.5) g/d, 6.5 (3.5) %E/d
  • MUFAs: ~3.0 g/d
  • PUFAs: ~0.7 g/d
• Cholesterol: ~218 mg/d
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Replacement of SFAs from dairy with SFAs from meat was significantly associated with greater risk of CHD. Increase in SFAs, MUFAs, and PUFAs from meat was significantly associated with a greater incidence of CHD. Increase in SFAs and MUFAs from dairy was associated with a lower incidence of CHD when controlling for energy from protein.
	Exposures:
	• Replacement of dairy-derived SFA, MUFA, and PUFA (1%E) with meat-derived SFA, MUFA, and PUFA (1%E), respectively (continuous)
	• SFA from meat (per 1%E)
	• SFA from dairy (per 1%E)
	• MUFA from meat (per 1%E)
	• MUFA from dairy (per 1%E)
	• PUFA from meat (per 1%E)
	• PUFA from dairy (per 1%E)
	
	Assessment method and timing:
	• Self-administered, validated 79-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 12.2 y of follow-up
	• Incident coronary heart disease (CHD; fatal & nonfatal): Dutch Center for Health Care Information, hospital discharge diagnoses by National Medical Registry
		Incident CHD, HR (95% CI)
		Replacement of SFAs from dairy with:
		SFAs from meat: 1.08 (1.04, 1.13)
		Replacement of MUFAs from dairy with:
		MUFAs from meat: NS
		Replacement of PUFAs from dairy with:
		PUFAs from meat: NS
		
		Continuous:
		SFAs from meat: 1.06 (1.03, 1.10)*
		SFAs from meat: 1.07 (1.04, 1.11)**
		MUFAs from meat: 1.05 (1.03, 1.08)*
		MUFAs from meat: 1.06 (1.03, 1.09)**
		PUFAs from meat: 1.17 (1.07, 1.28)*
		PUFAs from meat: 1.18 (1.07, 1.30)**
		SFAs from dairy: 0.97 (0.95, 0.99)*
		SFAs from dairy: NS**
		MUFAs from dairy: 0.94 (0.91, 0.99)*
		MUFAs from dairy: NS**
		PUFAs from dairy: NS*
		PUFAs from dairy: NS**
		*Adjusted with protein (%E)
		**Adjusted with carbohydrate (%E)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (educational level), TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			WC, energy-adjusted intakes of cholesterol and fiber, intake of protein, carbohydrates and all fatty acids except dairy-derived FA from the substitution of interest, protein or carbohydrate (for non-replacement analyses)
			
			Limitations:
			• Not all key confounders accounted for
			• Potential missing data bias for not statistically accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			"Europe Against Cancer" Programme of the European Commission; Dutch Ministry of Public Health, Welfare and Sports; Netherlands Cancer Registry; LK Research Funds; Dutch Prevention Funds, Dutch ZON; World Cancer Research Fund

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Buckland, 2012[150]
PCS, EPIC-Spain, Spain
Baseline N=41,438 Analytic N=40,622 (Attrition: 2%)
 	
Participant characteristics at baseline:
• Participants were not all free of disease
• Age: Mean~48 y
• Sex (female): ~62%
• Race/ethnicity: NR
• SES: Education: None ~39%, Primary ~39%, Technical/professional ~8.2%, Secondary ~6.5%, University ~11.5%, Unspecified ~4.7%
• Anthropometry: BMI: <25 ~22%, 25-30: ~48%, ≥30 ~30%
 	
Fat intake at baseline, Mean (SD):
• Olive oil: 20.1 (13.1) g/day per 2000 kcal
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Highest quartiles of olive oil consumption compared to non-consumers was associated with reduced risk of CVD-related mortality.
	Exposures:
	• Olive oil (continuous, 10 g/d per 2000 kcal; categorical in quartile, g/2000 kcal/d)
	  • Non-consumers (ref)
	  • Quartile 1: <14.8g
	  • Quartile 2: 14.8 - <21.7g
	  • Quartile 3: 21.7 - <29.4g
	  • Quartile 4: ≥29.4g
	
	Assessment method and timing:
	• Interview-administered, validated dietary history questionnaire to assess usual food intake in previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 10.4 (SD=1.3) y of follow-up
	• CVD deaths: follow-up, EPIC-Spain database, Spanish National Statistics Institute
		CVD deaths, HR (95% CI)
		Olive oil:
		Non-consumers (ref) vs:
		Q1: NS
		Q2: NS
		Q3: 0.71 (0.52, 0.98)
		Q4: 0.56 (0.40, 0.79)
		P-trend<0.001
		Continuous:
		Olive oil: 0.87 (0.80, 0.94)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (educational level), TEI excluding alcohol, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Center, BMI, WC, fruit, vegetables, dairy, meat
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Spanish Ministry of Health; Spanish Regional Governments of Andalusia, Asturias, Basque Country, Murcia and Navarra; Catalan Institute of Oncology

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Buckland, 2012a[151] **PCS, EPIC-Spain, Spain** Baseline N=41,438 Analytic N=40,142 (Attrition: 3%) **Participant characteristics at baseline:** • 100% without prevalent CHD • Age: Mean~48 y • Sex (female): ~62% • Race/ethnicity: NR • SES: Education: None ~39%, Primary ~39%, Technical/professional ~8.2%, Secondary ~6.5%, University ~11.5%, Unspecified ~4.7% • Anthropometry: BMI: <25 ~22%, ≥25 ~78% **Fat intake at baseline, Mean:** • SFAs: ~26.4g • MUFA: ~37.4g • PUFA: ~13.7g • Olive oil: 20.1g/d per 2000 kcal **Blood lipids and BP at baseline:** NR **Summary of findings:** *Olive oil intake was not significantly associated with risk of CHD.*	**Exposures:** • Olive oil (continuous, 10 g/d per 2000 kcal; categorical in quartile) ○ Q1 (ref): <10.0g ○ Q2: 10.0 - <20.1g ○ Q3: 20.1 - <28.9g ○ Q4: ≥28.9g Assessment method and timing: • Interview-administered, validated dietary history questionnaire to assess usual food intake in previous 12mo • Assessed at baseline **Outcomes and assessment methods**: • Assessed during mean of 10.4 (SD=1.3) y of follow-up • Incident coronary heart disease (CHD; fatal & nonfatal): self-reported questionnaires, hospital discharge databases, population-based myocardial infarction registries, and regional and national mortality registries	**Incident CHD,** HR (95% CI) *Olive oil:* Quartile 1 (ref) vs Q2, Q3, Q4, All NS P-trend: P=0.20 *Continuous:* Olive oil: NS Ordinary olive oil: NS Virgin olive oil: NS Results did not change when participants with improbable dietary values were excluded Results did not change among subjects with hyperlipidemia, hypertension, and diabetes at recruitment	**Key confounders NOT accounted for:** Race/ethnicity, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, SES (educational level), TEI excluding alcohol, alcohol intake, physical activity, smoking **Additional model adjustments:** BMI, WC, hyperlipidemia, hypertension and diabetes, Mediterranean diet score (excluding olive oil and alcohol) **Limitations:** • Not all key confounders accounted for • No preregistered statistical analysis plan **Funding sources:** Spanish Ministry of Health; Spanish Regional Governments of Andalusia, Asturias, Basque Country, Murcia and Navarra; Catalan Institute of Oncology

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Amiano, 2014[138]
PCS, EPIC-Spain, Spain
Baseline N=41,438 Analytic N=41,091 (Attrition: 1%)
 	
Participant characteristics at baseline:
• 100% without prevalent CHD
• Age: Mean: 49.2y, SD=8.0
• Sex (female): ~62%
• Race/ethnicity: NR
• SES: Education: None 30.4%, Primary ~38.7%, Technical/professional 8.2%, Secondary 6.5%, University 11.5%, Unspecified 4.7%
• Anthropometry: BMI: underweight 0.7%, normal weight 21.5%, overweight 47.8%, obese 30.1%
 	
Fat intake at baseline, Mean (SD):
• SFAs (g/d): 26.6 (12.4)
• MUFA (g/d): 37.5 (15.7)
• PUFA (g/d: 13.8 (7.7)
• Total n-3 PUFA (g/d): 1.4 (0.7)
• EPA (g/d): 0.2 (0.2)
• DHA (g/d): 0.4 (0.3)
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Total n-3 fatty acid, EPA or DHA intake were not significantly associated with risk of CHD.
	Exposures:
	• Total n-3 PUFA (g/d)
	  • Q1: (ref; Men ≤1.19, Women ≤0.85)
	  • Q2: (Men 1.20-1.57, Women 0.86-1.12)
	  • Q3: (Men 1.58-2.04, Women 1.13-1.47)
	  • Q4: (Men ≥2.05, Women ≥1.48)
	• EPA (g/d)
	  • Q1: (ref; Men ≤0.08, Women ≤0.05)
	  • Q2: (Men 0.09-0.17, Women 0.06-0.10)
	  • Q3: (Men 0.18-0.33, Women 0.11-0.21)
	  • Q4: (Men ≥0.34, Women ≥0.22)
	• DHA (g/d)
	  • Q1: (ref; Men ≤0.19g, Women ≤0.12g)
	  • Q2: (Men 0.20-0.35g, Women 0.13-0.22g)
	  • Q3: (Men 0.36-0.61g, Women 0.23-0.40g)
	  • Q4: (Men ≥0.62g, Women ≥0.41g)
	Assessment method and timing:
	• Interview-administered, validated dietary history questionnaire to assess usual food intake in previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 10.4 y of follow-up
	• Incident coronary heart disease (CHD; fatal & nonfatal): telephone 3y follow-up, hospital discharge databases, population-based myocardial infarction registries, and regional and national mortality registries
		Incident CHD, HR (95% CI)
		Total n-3 PUFA:
		Men:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.20
		Women:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.76
		
		EPA:
		Men:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.57
		Women:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.57
		
		DHA:
		Men:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.50
		Women:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend=0.82
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (educational level), TEI excluding alcohol, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Center, weight, height, waist/hip ratio, BMI, total fat, SFA, PUFA, MUFA, total protein, total carbohydrates, fruit, vegetables, meat, dairy products, vitamin C, vitamin E, use of antithrombotic and antihemorrhagic agents, CVD drugs, salicylic acid and derivatives, use of hormone replacement therapy, high BP, hyperlipidemia, and diabetes
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Spanish Ministry of Health; CIBERESP; European Commission; participating Regional Governments and International Agency for Research on Cancer

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Lin, 2018[184]
PCS, FOS (Framingham Offspring Study), U.S.
Baseline N=4,064 Analytic N=993 (Attrition: 76%)
 	
Participant characteristics at baseline:
• 100% either impaired fasting glucose or type 2 diabetes
• 100% without prevalent CVD
• Age: Mean: ~52.7
• Sex (female): ~40%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: WC: ~38 inches
 	
Fat intake at baseline, Mean (SD):
• SFAs (%E*): Low cholesterol tertile: 19.0 (7.2), Moderate cholesterol tertile: 25.6 (8.6); High cholesterol tertile: 33.1 (11.2)
*May be mislabeled and may be g/d
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Men in the highest tertile of dietary cholesterol intake had significantly lower risk of CVD compared to the lowest tertile.
	Exposures:
	• Dietary cholesterol (mg)
	  • Low (n=330): (ref; Men 71.0-225.0, Women 58.7-164.2)
	  • Moderate (n=332): (Men 225.1-324.5, Women 164.3-241.2)
	  • High (n=331): (Men 324.6-1033.3, Women 241.3-582.4)
	Assessment method and timing:
	• 3-d diet records
	• Assessed at baseline (from 1984 to 1995)
	
	Outcomes and assessment methods:
	• Assessed during 20 y of follow-up
	• Incident cardiovascular disease (CVD; fatal & nonfatal myocardial infarction, coronary heart disease, stroke): follow-up
	  • CVD events: 210 cases (150 in men, 60 in women)
		Incident CVD, HR (95% CI)
		Dietary cholesterol:
		Low (ref) vs moderate: NS
		Low (ref) vs high: 0.61 (0.41, 0.90)
		Men:
		Low (ref) vs moderate: NS
		Low (ref) vs high: 0.57 (0.36, 0.91)
		Women:
		Low (ref) vs moderate: NS
		Low (ref) vs high: NS
			Key confounders NOT accounted for: Race/ethnicity, SES, TEI, alcohol intake, physical activity, family history of CVD or diabetes
			
			Key confounders accounted for: Sex, age, smoking
			
			Additional model adjustments: WC, % of energy from SFA and carbohydrates, and use of lipid-lowering medication
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants with type 2 diabetes or impaired fasting glucose
			• Potential classification of exposures bias due to undefined midpoint for exposure
			• Potential bias due to departures from intended exposures due to not controlling for other types of fats
			• Potential missing data bias due to high attrition rate of those who did not complete food diaries
			• No information on outcome assessment
			• No preregistered statistical analysis plan
			
			Funding sources: National Heart, Lung and Blood Institute's Framingham Heart Study; Multidisciplinary Training Program in Cardiovascular Epidemiology; American Egg Board/Egg Nutrition Center

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
O'Neil, 2015[191] **PCS, GOS (Geelong Osteoporosis Study), Australia** Baseline N=1,540 Analytic N=1,363 (Attrition: 11%) **Participant characteristics at baseline:** • 100% without prevalent CVD • Age: Mean: ~56 y • Sex (female): NR • Race/ethnicity: NR • SES: NR • Anthropometry: WC: ~102 cm; Height: ~176 cm **Fat intake at baseline, Mean:** • SFAs: ~36.6g • MUFAs: ~31.9g • PUFAs: ~14.2g **BP at baseline, Mean:** • SBP: ~146 mmHg • DBP: ~93 mmHg **Summary of findings:** *Higher intake of SFA was not associated with odds of CVD incidence.*	**Exposures:** • SFA Assessment method and timing: • Self-administered, 74-item FFQ to assess usual intake in the previous 12mo • Assessed at baseline **Outcomes and assessment methods**: • Assessed during 5 y of follow-up • Incident cardiovascular disease (CVD; cardiac death, non-fatal myocardial infarction, coronary intervention or percutaneous coronary intervention, coronary artery bypass grafting, amputation or transient ischaemic attack, ischaemic or haemorrhagic stroke): hospital medical records at Barwon Health • CVD: 76 events	**Incident CVD,** OR (95% CI) SFA: 1.74 (0.92, 3.26)	**Key confounders NOT accounted for:** Race/ethnicity, SES, TEI, alcohol intake, physical activity, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, smoking **Additional model adjustments:** WC, % of energy from SFA and carbohydrates, and use of lipid-lowering medication **Limitations:** • Not all key confounders accounted for • Potential bias in classification of exposure due to FFQ not being validated • Analyses did not account for co-exposure (other types of fats) • No preregistered statistical analysis plan **Funding sources:** National Health and Medical Research Council; Cancer Training Branch of the National Cancer Institute

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Vedtofte, 2011[210]
PCS, GPS (Glostrup Population Studies), Denmark
Baseline N=3,427 Analytic N=3,277 (Attrition: 4%)
 	
Participant characteristics at baseline:
• 100% without prevalent IHD
• Age: Mean: ~50.6
• Sex (female): 50%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI~24
 	
Fat intake at baseline, Median:
• ALA: Women 1.2g/d, Men 1.6g/d
• n-3 long chain PUFA (EPA+DHA): Women 0.28 g/d; Men 0.38 g/d
• LA: Women 8.38 g/d; Men 10.9 g/d
 	
BP at baseline, Mean:
• SBP: ~123 mmHg
 	
Summary of findings:
High n-3 long chain PUFA intake compared to low n-3 long chain PUFA intake was significantly associated with lower IHD incidence. ALA and LA intake was not significantly associated with IHD incidence.
	Exposures:
	• ALA (g/d, Median)
	  • Low (ref; Women 0.81 g/d, Men 1.09 g/d)
	  • Medium (Women 1.24 g/d, Men 1.61 g/d)
	  • High (Women 1.83 g/d, Men 2.27 g/d)
	• n-3 long chain PUFA
	• LA
	Assessment method and timing:
	• Self-administered, validated 7-d weighed food record
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during median of 23.3 y of follow-up
	• Incident Ischemic Heart Disease (IHD): hospital medical records at Barwon Health
	  • IHD: 471 cases
		Incident IHD, HR (95% CI)
		ALA
		Women: Low (ref) vs medium, high: All NS; P-trend: NS
		Men: Low (ref) vs medium, high: All NS; P-trend: NS
		n-3 long chain PUFA
		Women: Low (ref) vs medium: NS
		Low (ref) vs high: 0.62 (0.40, 0.97)
		P-trend=0.04
		Men: Low (ref) vs medium, high: All NS; P-trend: NS
		LA
		Women: Low (ref) vs medium, high: All NS; P-trend: NS
		Men: Low (ref) vs medium, high: All NS; P-trend: NS
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, alcohol intake, physical activity, smoking, family history of acute MI
			
			Additional model adjustments:
			BMI, SBP, other PUFAs as appropriate (i.e., n-3 LC-PUFA and LA in analyses of ALA; ALA and LA in analyses of n-3 long chain PUFA; ALA and n-3 long chain PUFA in analyses of LA)
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Danish Council for Strategic Research

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Stefler, 2017[207] **PCS, HAPIEE (Health Alcohol and Psychosocial Factors in Eastern Europe), Poland, Russia, and Czech Republic** Baseline N=28,945 Analytic N=19,333 (Attrition: 33%) **Participant characteristics at baseline:** • 100% without prevalent CVD or diabetes • Age: ~57 y • Sex (female): 55% • Race/ethnicity: Czech (~30%), Polish (~33%), Russian (~37%) • SES: Education: Primary or less ~10%, University ~26% • Anthropometry: BMI ~27 **Fat intake at baseline:** • Olive Oil usage during cooking (1 point for used for cooking): Males: 16.4%, Females 15.1% **Blood lipids and BP at baseline, Mean:** • TC: ~6.0 mmol/L • Arterial pressure: ~105 mmHg • Hypertension: ~46% • Hypercholesterolemia: ~76% **Summary of findings:** *Olive oil usage was not significantly associated with CVD, CHD and stroke mortality.*	**Exposures:** • Olive oil (dichotomous; 1=used olive oil for cooking, 0=not used for cooking) Assessment method and timing: • Self-administered, semi-quantitative, validated FFQ (136-148 food items) • Assessed at baseline **Outcomes and assessment methods**: • Assessed during a median of 7 y of follow-up • CVD, CHD and stroke mortality: regional or national death registers	**Mortality** *Olive oil usage:* CVD: NS CHD: NS Stroke: NS	**Key confounders NOT accounted for:** family history of CVD or diabetes **Key confounders accounted for:** Sex, age, race/ethnicity (cohort by country), SES (education), TEI, alcohol intake, physical activity, smoking **Additional model adjustments:** Cohort, marital status, vitamin supplement intake **Limitations:** • Not all key confounders accounted for • Potential selection bias due to excluding participants with diabetes • Potential bias due to classification of exposures due to exposure not being clearly defined • No preregistered statistical analysis plan **Funding sources:** Wellcome Trust; U.S. National Institute of Aging; MacArthur Foundation Initiative on Social Upheaval and Health; Russian Scientific Foundation; British Heart Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Houston, 2011[168]
PCS, Health ABC (Healthy, Aging and Body Composition), U.S.
Baseline N=3,075 Analytic N=1,941 (Attrition: 37%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: Mean: 74.5 y
• Sex (female): 56%
• Race/ethnicity: 37.8% Black
• SES: Education: <High school education ~22%
• Anthropometry: BMI ~27
 	
Fat intake at baseline, Mean:
• SFA (%E): ~9.6%
• MUFA (%E): ~12.3%
• PUFA (%E): ~8.9%
• Cholesterol (mg/1000kcal): ~110
 	
Blood lipids at baseline, Mean:
• TC: ~5.4 mmol/L
 	
Summary of findings:
SFA, MUFA, PUFA, and cholesterol intake were not significantly associated with CVD incidence.
	Exposures:
	• SFA (categorical in tertiles, %E)
	  • Tertile 1 (ref): Median=7.2%E
	  • Tertile 2: Median=9.6%E
	  • Tertile 3: Median=11.9%E
	• MUFA (categorical in tertiles, %E)
	  • Tertile 1 (ref): Median=9.4%E
	  • Tertile 2: Median=12.2%E
	  • Tertile 3: Median=15.2%E
	• PUFA (categorical in tertiles, %E)
	  • Tertile 1 (ref): Median=6.3%E
	  • Tertile 2: Median=8.7%E
	  • Tertile 3: Median=11.4%E
	• Cholesterol (categorical in tertiles, mg/1000 kcal)
	  • Tertile 1 (ref): Median=67.3 mg/1000 kcal
	  • Tertile 2: Median=100.7 mg/1000 kcal
	  • Tertile 3: Median=147.2 mg/1000 kcal
	
	Assessment method and timing:
	• Interviewer-administered, semi-quantitative, validated 108-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 9 y of follow-up
	• Incident CVD (confirmed myocardial infarction, coronary death or stroke): in-person clinic exams, phone interviews, medical records
	  • CVD events: 203 cases
		CVD incidence, HR (95% CI)
		SFA:
		CVD: T1 vs T2, T3, All NS; P-trend: NS
		MUFA:
		CVD: T1 vs T2, T3, All NS; P-trend: NS
		PUFA:
		CVD: T1 vs T2, T3, All NS; P-trend: NS
		Cholesterol:
		CVD: T1 vs T2, T3, All NS; P-trend: NS
		
		CVD incidence, HR (95% CI)
		Dietary Cholesterol intake:
		Participants with Type 2 Diabetes:
		T1 vs T2: NS
		T1 vs T3: 3.66 (1.09, 12.29)
		P-trend=0.04
		Participants without diabetes:
		T1 vs T2, T3, All NS; P-trend: NS
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Field center, BMI, protein intake, fiber intake, multivitamin use, supplemental vitamin E use, statin use, aspirin use, oral estrogen use (women only), prevalent diabetes or hypertension, other types of fats (e.g., SFA analyses controlled for MUFA, PUFA, *trans* fat, and cholesterol)
			
			Limitations:
			• Not all key confounders accounted for
			• Potential bias in classification of exposures due to not validated FFQ
			• Potential missing data bias due to not statistically accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			Intramural Research Program of the NIH, National Institute on Aging; National Institute of Aging; Wake Forest University Claude D. Pepper Older Americans Independence Center; American Egg Board/Egg Nutrition Center

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Yamagishi, 2010[222]
PCS, JACC, Japan
Baseline N=110,792, Analytic N=58,453 (Attrition: 47%)
 	
Participant characteristics at baseline:
• Men and women 40-79y of age without history of heart disease, stroke, or cancer at baseline
• Age: Mean~56y
• Sex (female): 60.6%
• Race/ethnicity: NR
• SES: College or higher education, ~18% men, ~11% women
• Anthropometry: BMI, Mean~23
 	
Fat intake at baseline:
• SFA: See "Exposures" in next column
• MUFA (g/d): Mean~9.5
• PUFA (g/d): Mean~7.9
 	
Blood lipids and BP at baseline:
• History of hypertension: ~21%
 	
Summary of findings:
In men and women, higher intakes of SFA at ~56y of age was significantly associated lower risk of total stroke mortality, in particular lower risk of intraparenchymal hemorrhage and ischemic stroke mortality, during ~14.1y of follow-up. SFA intake was not associated with IHD, MI, cardiac arrest, or heart failure mortality. Replacement of SFA with PUFA was associated with higher risk of total stroke mortality; replacement of SFA with MUFA or CHO was not associated with total stroke mortality.
	Exposures:
	• SFA (quintiles; energy adjusted g/d)
	  • Q1 (ref): 2.5 to <11.0
	  • Q2: 11.0 to <13.4
	  • Q3: 13.4 to <15.4
	  • Q4: 15.4 to <17.9
	  • Q5: 17.9 to 40.0
	• Replacement of SFA (continuous; per 1%E substituted) with:
	  • MUFA
	  • PUFA
	  • CHO
	
	Assessment method and timing:
	• 33-item FFQ; SFA values divided by underestimation factor (63.3%) derived from comparison with dietary records in subsample (mostly women)
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~14.1y of follow-up
	• CVD Mortality: Obtained through death certificates from public health centers
	  • Total CVD Mortality: 2,142
	  • Total Stroke Mortality: 976 cases
	  • Intraparenchymal Hemorrhage Mortality: 224 cases
	  • Subarachnoid Hemorrhage Mortality: 153 cases
	  • Ischemic Stroke Mortality: 321 cases
	  • Ischemic Heart Disease (IHD) Mortality: 420 cases
	  • MI Mortality: 330 cases
	  • Cardiac Arrest Mortality: 107 cases
	Heart Failure Mortality: 309 cases
		SFA
		Total CVD Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.89 (0.78, 1.02)
		Q1 (ref) vs Q3: 0.89 (0.77, 1.03)
		Q1 (ref) vs Q4: 0.89 (0.77, 1.04)
		Q1 (ref) vs Q5: 0.82 (0.69, 0.97)
		P-trend: 0.05
		Total Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.90 (0.74, 1.09)
		Q1 (ref) vs Q3: 0.89 (0.72, 1.10)
		Q1 (ref) vs Q4: 0.80 (0.64, 1.00)
		Q1 (ref) vs Q5: 0.69 (0.53, 0.89)
		P-trend: 0.004
		Intraparenchymal Hemorrhage Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.87 (0.58, 1.29)
		Q1 (ref) vs Q3: 0.89 (0.58, 1.36)
		Q1 (ref) vs Q4: 0.90 (0.57, 1.42)
		Q1 (ref) vs Q5: 0.48 (0.27, 0.85)
		P-trend: 0.03
		Subarachnoid Hemorrhage Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 1.77 (1.08, 2.89)
		Q1 (ref) vs Q3: 1.12 (0.64, 1.98)
		Q1 (ref) vs Q4: 1.22 (0.68, 2.20)
		Q1 (ref) vs Q5: 0.91 (0.46, 1.80)
		P-trend: 0.47
		Ischemic Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.74 (0.53, 1.04)
		Q1 (ref) vs Q3: 0.79 (0.55, 1.14)
		Q1 (ref) vs Q4: 0.63 (0.42, 0.93)
		Q1 (ref) vs Q5: 0.58 (0.37, 0.90)
		P-trend: 0.01
		
		(Continued on next page)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			History of hypertension and diabetes, smoking status, BMI, mental stress, intake of cholesterol, n-3 and n-6 PUFA, vegetables and fruit.
			
			Limitations:
			• Not all key confounders accounted for
			• FFQ was not validated
			• No information on whether those excluded for incomplete dietary data differed from responders
			• No preregistered statistical analysis plan
			
			Funding sources:
			Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan and Tokyo

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Yamagishi, 2010 (CONTINUED)
PCS, JACC, Japan
Baseline N=110,792, Analytic N=58,453 (Attrition: 47%)
 	
Participant characteristics at baseline:
• Men and women 40-79y of age without history of heart disease, stroke, or cancer at baseline
• Age: Mean~56y
• Sex (female): 60.6%
• Race/ethnicity: NR
• SES: College or higher education, ~18% men, ~11% women
• Anthropometry: BMI, Mean~23
 	
Fat intake at baseline:
• SFA: See "Exposures" in next column
• MUFA (g/d): Mean~9.5
• PUFA (g/d): Mean~7.9
 	
Blood lipids and BP at baseline:
• History of hypertension: ~21%
 	
Summary of findings:
In men and women, higher intakes of SFA at ~56y of age was significantly associated lower risk of total stroke mortality, in particular lower risk of intraparenchymal hemorrhage and ischemic stroke mortality, during ~14.1y of follow-up. SFA intake was not associated with IHD, MI, cardiac arrest, or heart failure mortality. Replacement of SFA with PUFA was associated with higher risk of total stroke mortality; replacement of SFA with MUFA or CHO was not associated with total stroke mortality.
	Exposures:
	• SFA (quintiles; energy adjusted g/d)
	  • Q1 (ref): 2.5 to <11.0
	  • Q2: 11.0 to <13.4
	  • Q3: 13.4 to <15.4
	  • Q4: 15.4 to <17.9
	  • Q5: 17.9 to 40.0
	• Replacement of SFA (continuous; per 1%E substituted) with:
	  • MUFA
	  • PUFA
	  • CHO
	
	Assessment method and timing:
	• 33-item FFQ; SFA values divided by underestimation factor (63.3%) derived from comparison with dietary records in subsample (mostly women)
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~14.1y of follow-up
	• CVD Mortality: Obtained through death certificates from public health centers
	  • Total CVD Mortality: 2,142
	  • Total Stroke Mortality: 976 cases
	  • Intraparenchymal Hemorrhage Mortality: 224 cases
	  • Subarachnoid Hemorrhage Mortality: 153 cases
	  • Ischemic Stroke Mortality: 321 cases
	  • Ischemic Heart Disease (IHD) Mortality: 420 cases
	  • MI Mortality: 330 cases
	  • Cardiac Arrest Mortality: 107 cases
	  • Heart Failure Mortality: 309 cases
		SFA
		IHD Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.86
		MI Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.40
		Cardiac Arrest Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.11
		Heart Failure Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.83
		
		Replacement of SFA
		Total Stroke Mortality, HR (95% CI)
		With MUFA: 1.06 (0.89, 1.27)
		With PUFA: 1.19 (1.09, 1.30)
		With CHO: 1.05 (0.98, 1.13)
		IHD Mortality, HR (95% CI)
		With MUFA: 0.95 (0.74, 1.23)
		With PUFA: 1.02 (0.89, 1.16)
		With CHO: 1.00 (0.91, 1.11)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			History of hypertension and diabetes, smoking status, BMI, mental stress, intake of cholesterol, n-3 and n-6 PUFA, vegetables and fruit.
			
			Limitations:
			• Not all key confounders accounted for
			• FFQ was not validated
			• No information on whether those excluded for incomplete dietary data differed from responders
			• No preregistered statistical analysis plan
			
			Funding sources:
			Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan and Tokyo

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Wakai, 2014[216]
PCS, JACC, Japan
Baseline N=86,401, Analytic N=58,672 (Attrition: 32%)
 	
Participant characteristics at baseline:
• Men and women 40-79y of age without history of MI, stroke, or cancer at baseline
• Age: Mean~56y
• Sex (female): 60.6%
• Race/ethnicity: NR
• SES: College or higher education, ~19% men, ~11% women
• Anthropometry: BMI, Mean~23
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
In men, higher intake of PUFA, particularly n-6 PUFA, and a higher PUFA:SFA intake ratio at ~56y of age was significantly associated with CVD mortality during ~19.3y of follow-up; no significant association between these variables and CVD mortality was detected in women. In both men and women, intake of SFA, MUFA, and n-3 PUFA at ~56y of age was not associated with CVD mortality, except for the comparison between the 4th and 1st quartile of intake for SFA.
	Exposures:
	• SFA (quintiles; %E), Medians:
	  • Q1: 3 (men), 3.7 (women)
	  • Q2: 4.1 (men), 5.2 (women)
	  • Q3: 4.9 (men), 6.3 (women)
	  • Q4: 5.8 (men), 7.1 (women)
	  • Q5: 7.3 (men), 8.6 (women)
	• MUFA (quintiles; %E), Medians:
	  • Q1: 3.3 (men), 4.2 (women)
	  • Q2: 4.3 (men), 5.4 (women)
	  • Q3: 5.0 (men), 6.2 (women)
	  • Q4: 5.9 (men), 7.1 (women)
	  • Q5: 7.4 (men), 8.6 (women)
	• PUFA (quintiles; %E), Medians:
	  • Q1: 2.6 (men), 3.2 (women)
	  • Q2: 3.3 (men), 4.0 (women)
	  • Q3: 3.7 (men), 4.4 (women)
	  • Q4: 4.2 (men), 4.8 (women)
	  • Q5: 5.0 (men), 5.5 (women)
	• n-3 PUFA (quintiles; %E), Medians:
	  • Q1: 0.5 (men), 0.6 (women)
	  • Q2: 0.6 (men), 0.8 (women)
	  • Q3: 0.8 (men), 0.9 (women)
	  • Q4: 0.9 (men), 1.1 (women)
	  • Q5: 1.2 (men), 1.3 (women)
	• n-6 PUFA (quintiles; %E), Medians:
	  • Q1: 2.1 (men), 2.6 (women)
	  • Q2: 2.7 (men), 3.3 (women)
	  • Q3: 3.2 (men), 3.8 (women)
	  • Q4: 3.7 (men), 4.3 (women)
	  • Q5: 4.5 (men), 5.0 (women)
	• PUFA:SFA ratio (quintiles), Medians:
	  • Q1: 0.49 (men), 0.48 (women)
	  • Q2: 0.64 (men), 0.61 (women)
	  • Q3: 0.76 (men), 0.71 (women)
	  • Q4: 0.91 (men), 0.85 (women)
	  • Q5: 1.17 (men), 1.12 (women)
	Assessment method and timing:
		CVD Mortality, HR (95% CI)
		SFA
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.30
		Women:
		Q1 (ref) vs Q2: 0.97 (0.84, 1.11)
		Q1 (ref) vs Q3: 1.07 (0.92, 1.23)
		Q1 (ref) vs Q4: 0.85 (0.72, 0.99)
		Q1 (ref) vs Q5: 0.99 (0.84, 1.16)
		P-trend: 0.46
		MUFA
		Men and Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.74 (men), 0.32 (women)
		PUFA
		Men:
		Q1 (ref) vs Q2: 1.02 (0.85, 1.22)
		Q1 (ref) vs Q3: 1.06 (0.89, 1.26)
		Q1 (ref) vs Q4: 1.10 (0.92, 1.31)
		Q1 (ref) vs Q5: 1.18 (0.99, 1.41)
		P-trend: 0.044
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.59
		n-3 PUFA
		Men and Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.36 (men), 0.36 (women)
		n-6 PUFA
		Men:
		Q1 (ref) vs Q2: 0.96 (0.80, 1.15)
		Q1 (ref) vs Q3: 1.14 (0.96, 1.37)
		Q1 (ref) vs Q4: 1.23 (1.03, 1.47)
		Q1 (ref) vs Q5: 1.18 (0.98, 1.42)
		P-trend: 0.015
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.92
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Area, BMI, sleep duration, consumption of vegetables and fruit.
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (other FAs)
			• No information on whether those excluded for incomplete dietary data differed from responders
			• No preregistered statistical analysis plan
			
			Funding sources:
			Grants-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan and Tokyo

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
	• 33-item FFQ • Assessed at baseline **Outcomes and assessment methods**: • Assessed during ~19.3y of follow-up • CVD Mortality: Obtained through death certificates from public health centers; Includes CVD, stroke, and CHD mortality. • Total: 3,393 cases	**PUFA:SFA Ratio** Men: **Q1 (ref) vs Q2: 1.38 (1.15, 1.66)** **Q1 (ref) vs Q3: 1.29 (1.07, 1.55)** **Q1 (ref) vs Q4: 1.38 (1.15, 1.66)** **Q1 (ref) vs Q5: 1.39 (1.16, 1.66)** **P-trend: 0.011** Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend: 0.48	

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Yamagishi, 2013[221]
PCS, JPHC, Japan
Baseline N=92,905, Analytic N=81,932 (Attrition: 12%)
 	
Participant characteristics at baseline:
• No history of CVD or cancer
• Type 2 diabetes (%): ~3.3
• Age: Mean=56.7
• Sex (female): 53.5%
• Race/ethnicity: NR
• SES: ~7% non-employed
• Anthropometry: BMI, Mean~23.6
 	
Fat intake at baseline:
• SFA (g/d): Median=16.3
• MUFA (g/d): Mean~22
 	
Blood lipids and BP at baseline, Mean:
• TC (mg/dL): ~207
• SBP (mmHg): ~130
• DBP (mmHg): ~78
• Hypertension (%): ~19
 	
Summary of findings:
Dietary saturated fat intake was inversely, statistically associated with incidence rates of total stroke, and total CVD, and positively associated with incidence rates of myocardial infarction (in men, not women) during 11y follow-up. No significant association was seen between saturated fat intake and incidence rates of ischemic stroke and sudden cardiac death over the same period.
	Exposures:
	• SFA intake (quintiles, g), Median
	  • Q1 9.6
	  • Q2 13.4
	  • Q3 16.3
	  • Q4 19.4
	  • Q5 24.9
	
	Diet assessment method and timing:
	• 138-item FFQ (validated)
	• Administered at ~5y after baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 11.1y (median=9.9y) of follow-up
	• Total CVD ascertained by record linkage to medical and death registers.
	  • Total stroke: 3192 cases
	  • Ischemic stroke: 1939 cases
	  • Myocardial infarction: 610 cases
	  • Sudden cardiac death: 116 cases
		SFA
		Total stroke, HR (95% CI)
		Q1 (ref) vs Q2: 0.98 (0.88–1.10)
		Q1 (ref) vs Q3: 0.90 (0.79–1.03)
		Q1 (ref) vs Q4: 0.83 (0.71–0.97)
		Q1 (ref) vs Q5: 0.77 (0.65–0.93)
		P=0.002
		Ischemic stroke, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4 or Q5: All NS
		P=0.08
		Myocardial infarction, HR (95% CI)
		Q1 (ref) vs Q2: 0.90 (0.68–1.18)
		Q1 (ref) vs Q3: 1.24 (0.92–1.67)
		Q1 (ref) vs Q4: 1.24 (0.88–1.75)
		Q1 (ref) vs Q5: 1.39 (0.93–2.08)
		P=0.046
		Sudden cardiac death, HR (95% CI)
		Q1 (ref) vs Q2: 0.53 (0.30–0.93)
		Q1 (ref) vs Q3: 0.29 (0.14–0.60)
		Q1 (ref) vs Q4: 0.42 (0.19–0.92)
		Q1 (ref) vs Q5: 0.39 (0.15–0.99)
		P=0.06
		Total CVD, HR (95% CI)
		Q1 (ref) vs Q2: 0.94 (0.85–1.05))
		Q1 (ref) vs Q3: 0.91 (0.81–1.03)
		Q1 (ref) vs Q4: 0.86 (0.75–0.98)
		Q1 (ref) vs Q5: 0.82 (0.69–0.96)
		P=0.01
		
		Secondary analysis by sex indicated the positive association between SFA intake and incidence of myocardial infarction was significant in men but not in women.
			Key confounders NOT accounted for:
			Race/ethnicity, SES, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, TEI, smoking, alcohol intake, physical activity
			
			Additional model adjustments:
			Cohort, perceived mental stress, energy-adjusted intakes of carbohydrates, protein, cholesterol, vegetables, fruit and calcium
			
			Limitations:
			• Not all key confounders accounted for and assessment occurred 5y prior to dietary intake assessment
			• Analyses did not account for co-exposures (e.g. MUFA, PUFA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Ministry of Health, Labour and Welfare of Japan; Ministry of Education, Culture, Sports, Science, and Technology of Japan.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Virtanen, 2014[213]
PCS, KIHD (Kuopio Ischaemic Heart Disease Risk Factor Study), Finland
Baseline N=2,682, Analytic N=1,981 (Attrition: 62%)
 	
Participant characteristics at baseline:
• Men, aged 42-60 years with no history of stroke or coronary artery disease
• Age: Mean=52y, SD=5.3
• Sex (female): 0%
• Race/ethnicity: NR
• SES: Education (years): Mean=9, SD=3.6
• Anthropometry: BMI, Mean= 26.7, SD=3.5
 	
Fat intake at baseline, Mean (SD):
• SFAs (%E): 18.0 (4.1)
• MUFAs (%E): 11.0 (2.2)
• PUFAs (%E): 4.6 (1.5
• n-3 PUFA (%E): 0.7 (0.3)
 	
Blood lipids and BP at baseline, Mean (SD):
• LDL (mmol/L): 4.00 (0.99)
• HDL (mmol/L): 1.31 (0.29)
• Triglycerides (mmol/L): 1.25 (0.74)
• Hypertension: 56%
 	
Summary of findings:
Increased intake of polyunsaturated fat is associated with fatal, but not non-fatal CHD and an isocaloric replacement of saturated fat or carbohydrate with polyunsaturated fat is associated with reduced risk of fatal and non-fatal CHD in middle-aged and older men from eastern Finland. An isocaloric substitution of SFA with monounsaturated fat increased CHD risk. No association was found between saturated fat and fatal and non-fatal CHD.
	Exposures:
	• Type dietary fat: yearly updated totals
	• SFA (quintiles; Range, %E)
	  • Q1 (ref; < 15.2)
	  • Q2 (15.2-17.7)
	  • Q3 (17.8-20.6)
	  • Q4 (>20.6)
	• MUFA (quintiles; Range, %E)
	  • Q1 (ref; < 9.4)
	  • Q2 (9.4-10.8)
	  • Q3 (10.9-12.3)
	  • Q4 (>12.3)
	• PUFA (quintiles; Range, %E)
	  • Q1 (ref; < 3.4)
	  • Q2 (3.4-4.3)
	  • Q3 (4.3-5.4)
	  • Q4 (> 5.4)
	• Isocaloric replacement (1%E) of SFA and CHO with MUFA, PUFA and CHO (continuous, median intake for each quintile)
	
	Diet assessment method and timing:
	• 4-d guided food diary followed by a check for completeness by a nutritionist (with the participant).
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 21.4y of follow-up
	• Fatal and non-fatal CHD events ascertained by record linkage to hospital discharge registries and Finland's death register.
	  • Fatal CHD events: 183
	  • Non-fatal CHD events: 382
		SFA
		Fatal CHD, HR (95% CI)
		Q1 (ref) vs Q2,Q3, or Q4: All NS
		P-trend=0.68
		Non-Fatal CHD, HR (95% CI)
		Q1 (ref) vs Q2,Q3, or Q4: All NS
		P-trend=0.66
		MUFA
		Fatal CHD, HR (95% CI)
		Q1 (ref) vs Q2,Q3, or Q4: All NS
		P-trend=0.07
		Non-Fatal CHD, HR (95% CI)
		Q1 (ref) vs Q2,Q3, or Q4: All NS
		P-trend=0.21
		PUFA
		Fatal CHD, HR (95% CI),
		Q1 (ref) vs Q2: 0.67 (0.44–1.03)
		Q1 (ref) vs Q3: 0.53 (0.31–0.90)
		Q1 (ref) vs Q4: 0.46 (0.24–0.90)
		P-trend=0.03
		Non-Fatal CHD, HR (95% CI)
		Q1 (ref) vs Q2,Q3, or Q4: All NS
		P-trend=0.93
		Replacement of SFA (1%E)
		Fatal CHD, HR (95% CI),
		With MUFA: Data NR, P<0.05
		With PUFA: Data NR, P<0.05
		Non-Fatal CHD, HR (95% CI),
		With MUFA: Data NR, P<0.05
		With PUFA: Data NR, P<0.05
		Replacement of CHO (1%E)
		Fatal CHD, HR (95% CI),
		With SFA: Data NR, P>0.05 (no interaction by low vs high GI CHO)
		With MUFA: Data NR, P<0.05
		With PUFA: Data NR, P<0.05
		Non-Fatal CHD, HR (95% CI),
		With SFA: Data NR, P>0.05 (no interaction by low vs high GI CHO)
		With MUFA: Data NR, P<0.05
		With PUFA: Data NR, P>0.05
			Key confounders NOT accounted for:
			Race/ethnicity
			Key confounders accounted for:
			Age, sex, SES (education, income), TEI, smoking, alcohol intake, physical activity, family history of CHD
			Additional model adjustments:
			Examination year, BMI, diabetes, hypertension, intake of fiber, %E protein, %E from remaining fatty acids (MUFA, PUFA, SFA, trans-FA)
			
			Limitations:
			• Not all key confounders accounted for
			• Potential bias in classification of exposures due to use of non-validated FFQ
			• No preregistered statistical analysis plan
			
			Funding sources:
			University of Eastern Finland.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Virtanen, 2016[214]
PCS, KIHD (Kuopio Ischaemic Heart Disease Risk Factor Study), Finland
Baseline N=2,682, Analytic N=1,032 (Attrition: 62%)
 	
Participant characteristics at baseline:
• Men, aged 42-60 years with no history of stroke or coronary artery disease
• Type 2 diabetes: ~5%
• Age: Mean~52y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: Education: Mean~9y
• Anthropometry: BMI, Mean~26.50
 	
Fat intake at baseline, Mean (SD):
• Cholesterol (mg/d): 398 (147)
 	
BP at baseline:
• Hypertension: ~55%
 	
Summary of findings:
Cholesterol intake was not significantly associated with fatal and non-fatal CHD in middle-aged and older men from eastern Finland.
	Exposures:
	• Cholesterol intake (tertiles, mg/d)
	  • Q1 (ref; < 321)
	  • Q2 (321-438)
	  • Q3 (>438)
	
	Diet assessment method and timing:
	• 4-d guided food diary followed by a check for completeness by a nutritionist with the participant.
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 20.8y, SD=6.5y of follow-up
	• Fatal and non-fatal CHD events ascertained by record linkage to hospital discharge registries and Finland's death register.
	  • CHD events: 230
		Incident CHD, HR (95% CI)
		Cholesterol intake
		Q1 (ref) vs Q2, or Q3: All NS
		P-trend=0.96
			Key confounders NOT accounted for:
			Race/ethnicity
			Key confounders accounted for:
			Age, sex, SES (education, income), TEI, smoking, alcohol intake, physical activity, family history of CHD
			Additional model adjustments:
			Examination year, BMI, diabetes, hypertension, intake of fruits, berries, and vegetables, fiber, PUFA, and SFA
			
			Limitations:
			• Not all key confounders accounted for
			• Potential bias in classification of exposures due to use of non-validated FFQ
			• No preregistered statistical analysis plan
			
			Funding sources:
			University of Eastern Finland.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Koskinen, 2018[176]
PCS, KIHD (Kuopio Ischemic Heart Disease Risk Factor Study), Finland
Baseline N=2,682, Analytic N=1,981 (Attrition: 26%), Butter analysis N=495
 	
Participant characteristics at baseline:
• Men, aged 42-60 years without CHD
• Type 2 diabetes: ~5%
• Age: Mean~52y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: Education: Mean~9y
• Anthropometry: BMI, Mean~26.5
 	
Fat intake at baseline, Mean (SD):
• Butter intake (g/d): 33 (27)
• PUFA (E%): ~4.6
• MUFA (E%): ~11.8
• SFA (E%): ~18
 	
Blood lipids and BP at baseline, Mean:
• LDL (mmol/L): ~4.0
• HDL (mmol/L): ~1.3
• Triglycerides (mmol/L): ~1.26
• Hypertension: ~5%
 	
Summary of findings:
Butter intake was not significantly associated with fatal and non-fatal CHD events in middle-aged and older men from eastern Finland.
	Exposures:
	• Butter intake (including butter from spreads and recipes) (quartiles, median intake, g/d)
	  • Q1: 4
	  • Q2: 20
	  • Q3: 37
	  • Q4: 63
	• Butter intake (continuous, g/d)
	
	Diet assessment method and timing:
	• 4-d guided food diary followed by a check for completeness by a nutritionist (with the participant)
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 20.1y, SD=7.2y of follow-up
	• Fatal and non-fatal CHD events ascertained by record linkage to hospital discharge registries and Finland's death register.
	  • CHD events: 472 CHD cases
		Incident CHD at 21.1y, HR (95% CI)
		Butter intake
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.55
		
		Incident CHD at 11y, HR (95% CI)
		Butter intake (continuous)
		0.99 (95% CI 0.57, 1.72; P-trend=0·85)
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Age, sex, SES (education, income), TEI, smoking, alcohol intake, physical activity, family history of CVD
			
			Additional model adjustments:
			Examination year, BMI, use of hypertensive medication, energy adjusted intake of PUFA, intakes of fruits, berries, vegetables, and fiber, presence of diabetes, presence of hypertension
			Limitations:
			• Not all key confounders accounted for
			• Potential bias in classification of exposures due to use of non-validated FFQ
			• No preregistered statistical analysis plan
			
			Funding sources:
			Finnish Foundation for Cardiovascular Research; Otto A. Malm Foundation; Olvi Foundation; Yrjö Jahnsson Foundation; and North Savo Regional Fund.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Abdollahi, 2019[135]
PCS, KIHD (Kuopio Ischaemic Heart Disease Risk Factor Study), Finland
Baseline N=2,682, Analytic N=1,950 (Attrition: 27%)
 	
Participant characteristics at baseline:
• Men, ages 42-60 y with no history of stroke or coronary artery disease
• Family history of CHD: ~47%
• Family history of stroke: ~20%
• Type 2 diabetes: ~5%
• Age: Mean~52y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: Education: Mean~9y
• Anthropometry: BMI, Mean~26.50
 	
Fat intake at baseline, Mean (SD):
• Cholesterol (mg/d): 408 (150)
 	
Blood lipids and BP at baseline, Mean:
• TC (mmol/L): ~5.9
• LDL (mmol/L): ~4.0
• Hypertension: ~55%
 	
Summary of findings:
Cholesterol intake was not significantly associated with stroke risk in middle-aged and older men from eastern Finland.
	Exposures:
	• Cholesterol intake (continuous, 100mg/d)
	• Cholesterol intake (quartiles, mg/d)
	  • Q1 (ref; < 333)
	  • Q2 (333-387)
	  • Q3 (388-459)
	  • Q4 (>459)
	
	Diet assessment method and timing:
	• 4-d guided food diary followed by a check for completeness by a nutritionist (with the participant).
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 21.2y, SD=7.2y of follow-up
	• Incident stroke events ascertained through FINMONICA (Finnish Monitoring Trends and Determinants in Cardiovascular Diseases) stroke register and by record linkage to hospital discharge registries, Finland's stroke register and Finland's death register.
	  • Any stroke: 217 cases
	  • Ischemic stroke: 166 cases
	  • Hemorrhagic stroke: 55 cases
		Total stroke, HR (95% CI)
		Cholesterol intake (quartiles)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.42
		Cholesterol intake (continuous)
		0.98 (95% CI: 0.86, 1.12)
		
		Ischemic stroke, HR (95% CI)
		Cholesterol intake (quartiles)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.32
		Cholesterol intake (continuous)
		0.97 (95% CI:0.83, 1.13)
		
		Hemorrhagic stroke, HR (95% CI)
		Cholesterol intake (quartiles)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend=0.75
		Cholesterol intake (continuous)
		0.94 (95% CI: 0.71, 1.23)
		
		Similar results were found at the 10y follow-up point.
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, SES (education, income), TEI, smoking, alcohol intake, physical activity,
			
			Additional model adjustments:
			Examination year, BMI, use of hypertensive medication, intake of fruits, berries, and vegetables (g/d)
			
			Limitations:
			• Not all key confounders accounted for
			• Potential bias in classification of exposures due to use of non-validated FFQ
			• No preregistered statistical analysis plan
			
			Funding sources:
			University of Eastern Finland.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zhong, 2019[224]
PCS, LRPP (Lifetime Risk Pooling Project: ARIC, CARDIA, FHS, FOS, FHS, MESA), U.S.
Baseline N=34,497, Analytic N=29,615 (Attrition: 14%)
 	
Participant characteristics at baseline:
• No history of CVD
• Use lipid lowering medication: 5.9%
• Use hypertensive medication: 27.5%
• Age: Mean=51.6y
• Sex (female): 55.1%
• Race/ethnicity: 62.1% White, 31.1% Black, 4.4% Hispanic, 2.4% Chinese
• SES: Education: 54.7% Some college or more
• Anthropometry: Mean BMI: 27.6
 	
Fat intake at baseline:
• Cholesterol (mg/d): Median=241, IQR=164-350, Mean=285
 	
Blood lipids and BP at baseline, Mean:
• TC (mg/dL): 203.4
• SBP (mmHg): 121.6
 	
Summary of findings:
Among adults pooled from 6 U.S. prospective cohort studies, with a median follow-up of 17.5 years, higher consumption of dietary cholesterol was significantly associated with higher risk of incident CVD, incident stroke and CVD mortality, but was not associated with incident CHD or heart failure.
	Exposures:
	• Dietary cholesterol intake, (continuous, per 300mg/d)
	
	Diet assessment method and timing:
	• Five of 6 cohorts used validated 66 to 158-item FFQs and one cohort (CARDIA) used a validated 700-item diet history.
	• Administered at baseline within each cohort
	• Standardized protocol used to harmonize data
	
	Outcomes and assessment methods:
	• Assessed during median 17.5y of follow-up
	• Risk of incident CVD from coronary heart disease, stroke, and heart failure, and other CVD causes ascertained via medical and death records.
	  • Incident CVD events: 5400 cases
	  • CHD events (fatal and non-fatal): 2088 cases
	  • Stroke (fatal and non-fatal): 1302 cases
	  • Heart failure (fatal and non-fatal): 1897 cases
	  • Other CVD deaths: 113 cases
		Cholesterol
		All subjects
		Incident CVD, HR (95% CI)
		Per 300mg/d: 1.14 (1.06, 1.23), P<0.01
		Incident CHD, HR (95% CI)
		Per 300mg/d: 1.12 (1.00, 1.26), P>0.05
		Incident Stroke, HR (95% CI)
		Per 300mg/d: 1.24 (1.07-1.44) P<0.05
		Incident Heart Failure, HR (95% CI)
		Per 300mg/d: 1.11 (0.98-1.27), P>0.05
		Incident CVD mortality, HR (95% CI)
		Per 300mg/d: 1.22 (1.07, 1.40), P<0.05
		
		Subgroup analyses among subjects eating a high -SFA diet (≥138%E) (yes/no) and among subjects eating a low-SFA diet (<7%E) (yes/no) indicated no significant interaction. See Zhong, 2019 for details.
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, race/ethnicity, SES, physical activity, TEI, smoking, alcohol intake
			Additional model adjustments:
			Hormone replacement therapy, BMI, diabetes status, SBP, use of antihypertensive medications, (HDL) cholesterol, non-HDL cholesterol, and use of lipid-lowering medications
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			NHLBI; Northwestern University Feinberg School of Medicine.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Sonestedt, 2011[206]
PCS, MDCC (Malmo Diet and Cancer Cohort, Sweden)
Baseline N=28,098, Analytic N=26,445 (Attrition: 6%)
 	
Participant characteristics at baseline:
• Men and women without history of MI, stroke, or diabetes at baseline.
• Age: ~57y
• Sex (female): 62%
• Race/ethnicity: NR
• SES: Education, ~41% Elementary, ~27% Primary/Secondary, ~9% Upper secondary, ~9% Further education without degree, ~14% University degree
• Anthropometry: BMI, ~25.2
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline, Mean:
• LDL (mmol/L): ~4.1
• HDL (mmol/L): ~1.3
• Triglycerides (mmol/L): ~1.1
• SBP (mmHg): ~139
• DBP (mmHg): ~85
 	
Summary of findings:
In men and women, butter intake at ~57y of age was not significantly associated with incident CVD during ~12y of follow-up.
	Exposures:
	• Butter (non-consumers and tertiles of consumers; energy adjusted g/d)
	  • C1 (ref): No intake
	  • C2: Men, Mean=8; Women, Mean=5
	  • C3: Men, Mean=31; Women, Mean=18
	  • C4: Men, Mean=61; Women, Mean=41
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~12y of follow-up
	• Incident CVD: Obtained via linkage with Swedish Hospital Discharge Register, Cause-of-death Register, and STROMA (local stroke register in Malmo)
	  • Total: 2520 cases
	  • Coronary event (fatal or non-fatal MI or death due to IHD): 1344 cases
	  • Stroke: 1176 cases
		Incident CVD (total), HR (95% CI)
		C1 (ref) vs C2, C3, or C4: All NS
		P-trend=0.16
		
		Incident Coronary Event, HR (95% CI)
		C1 (ref) vs C2, C3, or C4: All NS
		P-trend=0.24
		
		Incident Stroke, HR (95% CI)
		C1 (ref) vs C2, C3, or C4: All NS
		P-trend=0.60
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection; Incident CVD (total): intake of vegetables, fruit and berries, fish and shellfish, meat, coffee, and whole grains.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Lund University Diabetes Center; Swedish Medical Research Council; Swedish Heart and Lung Foundation; Region Skane; Skane University Hospital Foundation; Albert Pahlsson Research Foundation; Crafoord Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Wallstrom, 2012[217]
PCS, MDCC (Malmo Diet and Cancer Cohort), Sweden
Baseline N=28,098, Analytic N=20,674 (Attrition: 26%)
 	
Participant characteristics at baseline:
• Men and women without history of MI, stroke, or diabetes at baseline.
• Age: Mean~58y
• Sex (female): 61%
• Race/ethnicity: NR
• SES: Education, ~42% ≤7y, ~26% 8-9y, ~9% 10-12y, ~23% >12y
• Anthropometry: BMI, ~1% <18.5, ~48% 18.5-24.99, ~39% 25.0-29.99, ~12% ≥30
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
BP at baseline, Mean:
• SBP (mmHg): ~141
• DBP (mmHg): ~86
 	
Summary of findings:
In men and women, consumption of MUFA, total PUFA, n-3 PUFA, long-chain n-3 PUFA, and n-6 PUFA at ~58y of age was not associated with incident ischemic CVD (total, coronary event, or stroke) during ~13.5y of follow-up. Higher SFA intake in women was significantly associated with lower risk of coronary events; however, no significant association was detected for total ischemic CVD or stroke in women or any ischemic CVD outcome in men.
	Exposures (medians):
	• SFA (quintiles; %E)
	  • Q1 (Men, 13; Women, 12.9), Q2 (Men, 15.2; Women, 15.1), Q3 (Men, 16.8; Women, 16.7), Q4 (Men, 18.9; Women, 18.6), Q5 (Men, 22.7; Women, 22.1)
	• MUFA (quintiles; %E)
	  • Q1 (Men, 13.0; Women, 11.0), Q2 (Men, 11.4; Women, 12.5), Q3 (Men, 13.1; Women, 13.6), Q4 (Men, 14.2; Women, 14.6), Q5 (Men, 15.3; Women, 16.1)
	• *PUFA, n-6 PUFA, n-3 PUFA and long chain n-3 PUFA reported on next pages.*
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Incident Total Ischemic CVD: Obtained via linkage with National Patient Register, National Cause of Death Register, and Stroke Register in Malmo; Included MI (fatal and nonfatal), death from chronic ischemic heart disease, cerebral infarction, or non-specific stroke
	  • Total: 1089 cases in men, 687 cases in women
	  • Coronary event (MI or death from chronic ischemic heart disease): 688 cases in men, 333 cases in women
	  • Ischemic stroke: 401 cases in men, 354 cases in women
		SFA
		Incident Ischemic CVD (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.32
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.22
		Incident Coronary Event, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.12
		Women:
		Q1 (ref) vs Q2: 0.68 (0.48, 0.95)
		Q1 (ref) vs Q3: 0.68 (0.48, 0.96)
		Q1 (ref) vs Q4: 0.60 (0.41, 0.86)
		Q1 (ref) vs Q5: 0.67 (0.46, 0.97)
		P-trend=0.037
		Incident Ischemic Stroke, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.69
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.75
		
		MUFA
		Incident Ischemic CVD (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.64
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.94
		Incident Coronary Event, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.27
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.99
		Incident Ischemic Stroke, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.47
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.90
		
		(Continued below)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection, BMI, SBP, antihypertensive treatment, antihyperlipidemic treatment, energy adjusted dietary fiber
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish governmental funds for clinical research (ALF); Heart-Lung Foundation; Region Skane; Research funds of Skane University Hospital; Ernhold Lundstrom Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Wallstrom, 2012 (CONTINUED)
PCS, MDCC (Malmo Diet and Cancer Cohort), Sweden
Baseline N=28,098, Analytic N=20,674 (Attrition: 26%)
 	
Participant characteristics at baseline:
• Men and women without history of MI, stroke, or diabetes at baseline.
• Age: Mean~58y
• Sex (female): 61%
• Race/ethnicity: NR
• SES: Education, ~42% ≤7y, ~26% 8-9y, ~9% 10-12y, ~23% >12y
• Anthropometry: BMI, ~1% <18.5, ~48% 18.5-24.99, ~39% 25.0-29.99, ~12% ≥30
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
BP at baseline, Mean:
• SBP (mmHg): ~141
• DBP (mmHg): ~86
 	
Summary of findings:
In men and women, consumption of MUFA, total PUFA, n-3 PUFA, long-chain n-3 PUFA, and n-6 PUFA at ~58y of age was not associated with incident ischemic CVD (total, coronary event, or stroke) during ~13.5y of follow-up. Higher SFA intake in women was significantly associated with lower risk of coronary events; however, no significant association was detected for total ischemic CVD or stroke in women or any ischemic CVD outcome in men.
	Exposures (medians):
	• PUFA (quintiles; %E)
	  • Q1 (Men, 4.5; Women, 4.3), Q2 (Men, 5.5; Women, 5.1), Q3 (Men, 6.2; Women, 5.8), Q4 (Men, 7.1; Women, 6.6), Q5: Men, 8.5; Women, 8.0)
	• n-6 PUFA (quintiles; %E)
	  • Q1 (Men, 3.5; Women, 3.3), Q2 (Men, 4.3; Women, 4.0), Q3 (Men, 5.0; Women, 4.7), Q4 (Men, 5.8; Women, 5.4), Q5 (Men, 7.1; Women, 6.7)
	• *SFA and MUFA reported on previous page. n-3 PUFA and long chain n-3 PUFA reported on next page.*
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Incident Total Ischemic CVD: Obtained via linkage with National Patient Register, National Cause of Death Register, and Stroke Register in Malmo; Included MI (fatal and nonfatal), death from chronic ischemic heart disease, cerebral infarction, or non-specific stroke
	  • Total: 1089 cases in men, 687 cases in women
	  • Coronary event: 688 cases in men, 333 cases in women
	  • Ischemic stroke: 401 cases in men, 354 cases in women
		PUFA
		Incident Ischemic CVD (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.98
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.91
		Incident Coronary Event, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.88
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.32
		Incident Ischemic Stroke, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.82
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.42
		
		n-6 PUFA
		Incident Ischemic CVD (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.62
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.75
		Incident Coronary Event, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.96
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.55
		Incident Ischemic Stroke, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.46
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS P-trend=0.32
		
		(Continued below)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection, BMI, SBP, antihypertensive treatment, antihyperlipidemic treatment, energy adjusted dietary fiber
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish governmental funds for clinical research (ALF); Heart-Lung Foundation; Region Skane; Research funds of Skane University Hospital; Ernhold Lundstrom Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Wallstrom, 2012 (CONTINUED)
PCS, Malmo Diet and Cancer Cohort, Sweden
Baseline N=28,098, Analytic N=20,674 (Attrition: 26%)
 	
Participant characteristics at baseline:
• Men and women without history of MI, stroke, or diabetes at baseline.
• Age: Mean~58y
• Sex (female): 61%
• Race/ethnicity: NR
• SES: Education, ~42% ≤7y, ~26% 8-9y, ~9% 10-12y, ~23% >12y
• Anthropometry: BMI, ~1% <18.5, ~48% 18.5-24.99, ~39% 25.0-29.99, ~12% ≥30
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
BP at baseline, Mean:
• SBP (mmHg): ~141
• DBP (mmHg): ~86
 	
Summary of findings:
In men and women, consumption of MUFA, total PUFA, n-3 PUFA, long-chain n-3 PUFA, and n-6 PUFA at ~58y of age was not associated with incident ischemic CVD (total, coronary event, or stroke) during ~13.5y of follow-up. Higher SFA intake in women was significantly associated with lower risk of coronary events; however, no significant association was detected for total ischemic CVD or stroke in women or any ischemic CVD outcome in men.
	Exposures (medians):
	• n-3 PUFA (quintiles; %E)
	  • Q1 (Men, 0.70; Women, 0.67), Q2 (Men, 0.86; Women, 0.82), Q3 (Men, 0.99; Women, 0.94), Q4 (Men, 1.14; Women, 1.08), Q5 (Men, 1.40; Women, 1.34)
	• Long chain n-3 PUFA (quintiles; %E)
	  • Q1 (Men, 0.08; Women, 0.07), Q2 (Men, 0.13; Women, 0.12), Q3 (Men, 0.19; Women, 0.18), Q4 (Men, 0.30; Women, 0.27), Q5 (Men, 0.53; Women, 0.49)
	• *SFA, MUFA, PUFA, n-6 PUFA reported on previous pages*
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~13.5y of follow-up
	• Incident Total Ischemic CVD: Obtained via linkage with National Patient Register, National Cause of Death Register, and Stroke Register in Malmo; Included MI (fatal and nonfatal), death from chronic ischemic heart disease, cerebral infarction, or non-specific stroke
	  • Total: 1089 cases in men, 687 cases in women
	  • Coronary event: 688 cases in men, 333 cases in women
	  • Ischemic stroke: 401 cases in men, 354 cases in women
		n-3 PUFA
		Incident Ischemic CVD (total), HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.92
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.50
		Incident Coronary Event, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.82
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.14
		Incident Ischemic Stroke, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.91
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.63
		
		Long chain n-3 PUFA
		Incident Ischemic CVD (total), HR (95% CI)
		Men:
		Q1 (ref) vs Q2: 1.24 (1.02, 1.51)
		Q1 (ref) vs Q3: 1.22 (1.00, 1.48)
		Q1 (ref) vs Q4: 1.09 (0.89, 1.33)
		Q1 (ref) vs Q5: 1.03 (0.84, 1.26)
		P-trend=0.59
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.25
		Incident Coronary Event, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.57
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.31
		Incident Ischemic Stroke, HR (95% CI)
		Men: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.89
		Women: Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.53
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection, BMI, SBP, antihypertensive treatment, antihyperlipidemic treatment, energy adjusted dietary fiber
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish governmental funds for clinical research (ALF); Heart-Lung Foundation; Region Skane; Research funds of Skane University Hospital; Ernhold Lundstrom Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Hlebowicz, 2013[167]
PCS, MDCC (Malmo Diet and Cancer Cohort), Sweden
Baseline N=28,098 Analytic N=17,126 (Attrition: 39%)
 	
Participant characteristics at baseline:
• Men and women without history of MI, stroke, or diabetes at baseline.
• Age: ~58y
• Sex (female): 59%
• Race/ethnicity: NR
• SES: Education, ~40% <9y, ~27% 9y, ~18% High school degree, ~15% University/college degree
• Anthropometry: WC, Men~93cm, Women~77cm
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
BP at baseline:
• SBP (mmHg): ~140
• DBP (mmHg): ~85
 	
Summary of findings:
In men and women, adherence to SFA or PUFA intake recommendations at ~58y of age was not associated with risk of incident CVD events through 16y of follow-up.
	Exposures:
	• SFA (dichotomized; adherence to recommended intake of ≤14%E)
	  • Non-adherence (ref; n~5719 men, n~8434 women): ≥14%E
	  • Adherence (n~1221 men, n~1752): ≤14%E
	• PUFA (dichotomized; adherence to recommended intake of 5-10%E)
	  • Non-adherence (ref; n~1464 men, n~2842 women): <5%E or >10%E
	  • Adherence (n~5476 men, n~7344): 5-10%E
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed up to 16y of follow-up
	• Incident CVD: Obtained via linkage with Swedish Hospital Discharge Register, National Myocardial Infarction Register, Stroke Register of Malmo (STROMA), and National Cause of Death Register; Included fatal and nonfatal MI, fatal and nonfatal ischemic or non-specific stroke, death attributable to ischemic heart disease.
	  • Total events: 1797 cases (1093 in men, 703 in women)
		SFA
		Incident CVD, HR (95% CI)
		Men:
		Non-adherence (ref) vs Adherence: NS
		Women:
		Non-adherence (ref) vs Adherence: NS
		
		PUFA
		Incident CVD, HR (95% CI)
		Men:
		Non-adherence (ref) vs Adherence: NS
		Women:
		Non-adherence (ref) vs Adherence: NS
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection, WC, PUFA or SFA (as applicable), fish and shellfish, dietary fiber, fruit and vegetables, sucrose.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Heart-Lung Foundation; Swedish Research Council; Swedish Government funds for clinical research (ALF); Foundations for Research at Skane University Hospital Malmo; Ernhold Lundstrom's Foundation; Funds by Region Skane

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Hellstrand, 2014[165]
PCS, MDCC (Malmo Diet and Cancer Cohort), Sweden
Baseline N=28,098 Analytic N=24,032 (Attrition: 14%)
 	
Participant characteristics at baseline:
• Men and women without history of MI, stroke, or diabetes at baseline.
• Age: ~58y
• Sex (female): 62%
• Race/ethnicity: NR
• SES: Education, ~41% Elementary, ~27% Primary and secondary, ~9% Upper secondary, ~9% Additional education without a degree, ~14% University degree
• Anthropometry: BMI, Mean~25.7
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
In men and women, n-3 and n-6 PUFA intake at ~58y of age was not associated with risk of incident CVD events during ~14y of follow-up except for some comparisons between intake quintiles for total n-6 PUFA and LA. However, the test of trend was non-significant.
	Exposures (medians):
	• Total n-3 PUFA (continuous & quintiles; %E)
	  • Q1 (0.68), Q2 (0.83), Q3 (0.96), Q4 (1.10), Q5 (1.37)
	• ALA (quintiles; %E)
	  • Q1 (0.52), Q2 (0.63), Q3 (0.72), Q4 (0.82), Q5 (0.99)
	• Long-chain n-3 PUFA [EPA, DHA, DPA] (quintiles; %E)
	  • Q1 (0.07), Q2 (0.13), Q3 (0.19), Q4 (0.30), Q5 (0.53)
	• Total n-6 PUFA (quintiles; %E)
	  • Q1 (3.32), Q2 (4.11), Q3 (4.79), Q4 (5.55), Q5 (6.86)
	• LA (quintiles; %E)
	  • Q1 (3.26), Q2 (4.05), Q3 (4.73), Q4 (5.49), Q5 (6.80)
	• ALA:LA Ratio (quintiles)
	  • Q1 (0.12), Q2 (0.14), Q3 (0.15), Q4 (0.17), Q5 (0.21)
	• n-3:n-6 PUFA Ratio (quintiles)
	  • Q1 (0.14), Q2 (0.17), Q3 (0.19), Q4 (0.23), Q5 (0.30)
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~14y of follow-up
	• Incident CVD: Obtained via linkage with Swedish Hospital Discharge Register, National Cause-of-Death Register, and local stroke register in Malmo (STROMA); Included coronary events (fatal/nonfatal MI, death due to ischemic heart disease) and ischemic stroke
	  • Total: 2648 cases (1539 men, 1109 women)
		Total n-3 PUFA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Per 1%E: P=NS
		
		ALA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Per 1%E: P=NS
		
		Long-chain n-3 PUFA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Per 1%E: P=NS
		
		Total n-6 PUFA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 1.15 (1.02, 1.30)
		Q1 (ref) vs Q3: 1.09 (0.96, 1.23)
		Q1 (ref) vs Q4: 0.99 (0.87, 1.12)
		Q1 (ref) vs Q5: 1.16 (1.03, 1.31)
		Per 1%E: 1.01 (0.99, 1.04)
		
		LA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 1.15 (1.02, 1.30)
		Q1 (ref) vs Q3: 1.08 (0.96, 1.22)
		Q1 (ref) vs Q4: 0.99 (0.88, 1.13)
		Q1 (ref) vs Q5: 1.16 (1.02, 1.30)
		Per 1%E: 1.01 (0.99, 1.04)
		
		ALA:LA Ratio
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Per 1%E: P=NS
		
		n-3:n-6 PUFA Ratio
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		Per 1%E: P=NS
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection, BMI.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• FFQ had low validity for long-chain n-3 PUFAs
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Heart-Lung Foundation; Swedish Research Council; Swedish Government funds for clinical research (ALF); Foundations for Research at Skane University Hospital Malmo; Ernhold Lundstrom's Foundation; Funds by Region Skane

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Kulezic, 2019[178]
PCS, MDCC (Malmo Diet and Cancer Cohort), Sweden
Baseline N=28,098 Analytic N=26,010 (Attrition: 7%)
 	
Participant characteristics at baseline:
• Men and women without history of PAD, CVD, abdominal aortic aneurysm, or diabetes at baseline.
• Age: ~58y
• Sex (female): 62%
• Race/ethnicity: NR
• SES: Education, ~41% <9y, ~26% Elementary school, ~9% Upper secondary, ~9% University without a degree, ~15% University degree
• Anthropometry: BMI, Mean~25.6
 	
Fat intake at baseline, Mean:
• SFA: ~16%E
• PUFA: ~6%E
 	
Blood lipids and BP at baseline:
• Hypertension: ~76%
 	
Summary of findings:
In men and women, adherence to SFA or PUFA intake recommendations at ~58y of age was not associated with risk of incident peripheral artery disease.
	Exposures:
	• SFA (dichotomized; adherence to recommended intake of ≤14%E)
	  • Non-adherence (ref; 18,559): ≥14%E
	  • Adherence (n=7,451): ≤14%E
	• PUFA (dichotomized; adherence to recommended intake of 5-10%E)
	  • Non-adherence (ref; n=8,160): <5%E or >10%E
	  • Adherence (n=17,850): 5-10%E
	
	Assessment method and timing:
	• Validated 168-item FFQ assessing intake over past year and seven-d menu book
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~21.7y of follow-up
	• Incident PAD: Obtained via linkage with Cause of Death Register and Inpatient and Outpatient Registers; Included first diagnosis or surgical procedures for peripheral artery disease (PAD)
	  • Total: 1122 cases
		SFA
		Incident PAD, HR (95% CI)
		Non-adherence (ref) vs Adherence: NS
		
		PUFA
		Incident PAD, HR (95% CI)
		Non-adherence (ref) vs Adherence: NS
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Diet assessment method, season of data collection, SFA or PUFA (as applicable), fish and shellfish, fiber, fruit and vegetables, sucrose.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• No preregistered statistical analysis plan
			
			Funding sources:
			NR

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Oliveira Otto, 2012[156]
PCS, MESA (Multi-Ethnic Study of Atherosclerosis), U.S.
Baseline N=6,814 Analytic N=5,209 (Attrition: 24%)
Participant characteristics at baseline:
• Men and women 45-84y of age without CVD or type 2 diabetes at baseline
• Age: ~62y
• Sex (female): ~52%
• Race/ethnicity: ~44% White, ~24% African American, ~20% Hispanic, ~12% Chinese
• SES: ~84% ≥12y of formal education
• Anthropometry: BMI, ~27.9
Fat intake at baseline:
• Total SFA (g/d): ~18.4
• Dairy SFA (g/d): ~6.2
• Meat SFA (g/d): ~3.0
• Butter SFA (g/d): ~0.7
• Plant SFA (g/d0: ~0.9
• Mixed sources SFA (g/d): ~4.5
Blood lipids and BP at baseline, Mean:
• LDL (mg/dL): ~118
• HDL (mg/dL): ~52
• SBP (mmHg): ~126
• DBP (mmHg): ~72
Summary of findings:
In men and women, higher intake of total SFA and dairy SFA at ~62y of age was significantly associated with lower risk of incident total CVD and CHD over 10y of follow-up. Higher intake of meat SFA was significantly associated was higher risk of total CVD and CHD. Replacement of meat SFA with dairy SFA was significantly associated with lower risk of total CVD and CHD. Intake of butter, plant, and mixed sources of SFA was not significantly associated with total CVD and CHD.
	Exposures:
	• Total SFA (continuous; per 5g/d or per 5%E)
	• Dairy SFA (continuous; per 5g/d or per 5%E)
	• Meat SFA (continuous; per 5g/d or per 5%E)
	• Butter SFA (continuous; per 5g/d or per 5%E)
	• Plant SFA (continuous; per 5g/d or per 5%E)
	
	Assessment method and timing:
	• Modified, Block 120-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed through 10y of follow-up
	• Incident CVD: Obtained through cohort examinations, follow-up calls, medical record abstractions, or obituaries (reviewed by medical endpoints committee); CVD included CHD events (MI, cardiac arrest, definite/probable angina, CHD death), stroke, stroke death, or other CVD/atherosclerotic death
	  • Total CVD: 316 cases
	  • CHD events: 231 cases
		Total SFA
		Incident CVD, HR (95% CI)
		Per 5g/d: 0.86 (0.75, 0.97), P=0.02
		Per 5%E: 0.71 (0.56, 0.89), P<0.01
		Incident CHD Events, HR (95% CI)
		Per 5g/d: 0.86 (0.74, 1.00), P=0.05
		Per 5%E: 0.73 (0.56, 0.96), P=0.02
		Dairy SFA
		Incident CVD, HR (95% CI)
		Per 5g/d: 0.79 (0.68, 0.92), P<0.01
		Per 5%E: 0.62 (0.47, 0.82), P<0.01
		Incident CHD Events, HR (95% CI)
		Per 5g/d: 0.84 (0.71, 0.99), P=0.03
		Per 5%E: 0.71 (0.52, 0.98), P=0.03
		Meat SFA
		Incident CVD, HR (95% CI)
		Per 5g/d: 1.26 (1.02, 1.54), P=0.03
		Per 5%E: 1.48 (0.98, 2.23), P=0.06
		Incident CHD Events, HR (95% CI)
		Per 5g/d: 1.29 (1.03, 1.62), P=0.03
		Per 5%E: 1.57 (0.98, 2.51), P=0.06
		Processed meat SFA: Both NS
		Unprocessed meat SFA:
		Per 5g/d: 1.51 (1.12, 2.05), P<0.01
		Per 5%E: 2.22 (1.20, 4.08), P=0.01
		Butter SFA
		Incident CVD, HR (95% CI)
		Per 5g/d: 0.87 (0.66, 1.15), P=0.33
		Per 5%E: 0.83 (0.50, 1.37), P=0.47
		Incident CHD Events, HR (95% CI)
		Per 5g/d: 0.79 (0.55, 1.12), P=0.18
		Per 5%E: 0.67 (0.35, 1.27), P=0.20
		Plant SFA
		Incident CVD, HR (95% CI)
		Per 5g/d: 1.00 (0.50, 2.01), P=0.99
		Per 5%E: 0.62 (0.18, 2.11), P=0.44
		Incident CHD Events, HR (95% CI)
		Per 5g/d: 1.00 (0.44, 2.25), P=0.99
		Per 5%E: 2.09 (0.19, 23.04), P=0.63
		
		(Continued below)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Study center, BMI, dietary supplement use, use of cholesterol-lowering medication, fruit and vegetable intake, energy adjusted intake of dietary fiber, vitamin E, *trans* fat, and PUFA
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• No preregistered statistical analysis plan
			
			Funding sources:
			University of Texas Health Innovation for Cancer Prevention Research Postdoctoral Fellowship; University of Texas School of Public Health – Cancer Prevention and Research Institute of Texas; NIDDK; NHLBI.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Oliveira Otto, 2012 (CONTINUED)
PCS, MESA (Multi-Ethnic Study of Atherosclerosis), U.S.
Baseline N=6,814 Analytic N=5,209 (Attrition: 24%)
Participant characteristics at baseline:
• Men and women 45-84y of age without CVD or type 2 diabetes at baseline
• Age: ~62y
• Sex (female): ~52%
• Race/ethnicity: ~44% White, ~24% African American, ~20% Hispanic, ~12% Chinese
• SES: ~84% ≥12y of formal education
• Anthropometry: BMI, ~27.9
Fat intake at baseline:
• Total SFA (g/d): ~18.4
• Dairy SFA (g/d): ~6.2
• Meat SFA (g/d): ~3.0
• Butter SFA (g/d): ~0.7
• Plant SFA (g/d): ~0.9
• Mixed sources SFA (g/d): ~4.5
Blood lipids and BP at baseline, Mean:
• LDL (mg/dL): ~118
• HDL (mg/dL): ~52
• SBP (mmHg): ~126
• DBP (mmHg): ~72
Summary of findings:
In men and women, higher intake of total SFA and dairy SFA at ~62y of age was significantly associated with lower risk of incident total CVD and CHD over 10y of follow-up. Higher intake of meat SFA was significantly associated was higher risk of total CVD and CHD. Replacement of meat SFA with dairy SFA was significantly associated with lower risk of total CVD and CHD. Intake of butter, plant, and mixed sources of SFA was not significantly associated with total CVD and CHD.
	Exposures:
	• Mixed sources of SFA (continuous; per 5g/d or per 5%E)
	• Replacement of SFA from different sources (continuous; per 2%E)
	  • Replacing Meat SFA with Dairy, Butter, or Plant SFA
	  • Replacing Dairy SFA with Butter or Plant SFA
	  • Replacing Butter SFA with Plant SFA
	
	Assessment method and timing:
	• Modified, Block 120-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed through 10y of follow-up
	• Incident CVD: Obtained through cohort examinations, follow-up calls, medical record abstractions, or obituaries (reviewed by medical endpoints committee); CVD included CHD events (MI, cardiac arrest, definite/probable angina, CHD death), stroke, stroke death, or other CVD/atherosclerotic death
	  • Total CVD: 316 cases
	  • CHD events: 231 cases
		Mixed source of SFA
		Incident CVD, HR (95% CI)
		Per 5g/d: 1.01 (0.77, 1.32), P=0.96
		Per 5%E: 0.83 (0.51, 1.36), P=0.51
		Incident CHD Events, HR (95% CI)
		Per 5g/d: 0.90 (0.65, 1.24), P=0.47
		Per 5%E: 0.68 (0.38, 1.24), P=0.19
		Replacement of Meat SFA (per 2%E)
		Incident CVD, HR (95% CI)
		With Dairy SFA: 0.75 (0.63, 0.91)
		With Butter SFA: 0.81 (0.64, 1.03)
		With Plant SFA: 0.63 (0.38, 1.03)
		Incident CHD Events, HR (95% CI)
		With Dairy SFA: 0.76 (0.61, 0.94)
		With Butter SFA: 0.71 (0.53, 0.95)
		With Plant SFA: 0.62 (0.35, 1.11)
		
		Replacement of Dairy SFA (per 2%E)
		Incident CVD, HR (95% CI)
		With Butter SFA: 1.08 (0.88, 1.33)
		With Plant SFA: 0.83 (0.52, 1.33)
		Incident CHD Events, HR (95% CI)
		With Butter SFA: 0.94 (0.72, 1.22)
		With Plant SFA: 0.82 (0.48, 1.42)
		
		Replacement of Butter SFA (per 2%E)
		Incident CVD, HR (95% CI)
		With Plant SFA: 0.77 (0.48, 1.25)
		Incident CHD Events, HR (95% CI)
		With Plant SFA: 0.88 (0.50, 1.55)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Study center, BMI, dietary supplement use, use of cholesterol-lowering medication, fruit and vegetable intake, energy adjusted intake of dietary fiber, viatmin E, *trans* fat, and PUFA
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes at baseline
			• No preregistered statistical analysis plan
			
			Funding sources:
			University of Texas Health Innovation for Cancer Prevention Research Postdoctoral Fellowship; University of Texas School of Public Health – Cancer Prevention and Research Institute of Texas; NIDDK; NHLBI.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Oliveira Otto, 2013[157]
PCS, MESA (Multi-Ethnic Study of Atherosclerosis), U.S.
Baseline N=2,880 (random subset of total 6,814 participants) Analytic N=2,372 (Attrition: 18%)
 	
Participant characteristics at baseline:
• Men and women 45-84y of age without CVD at baseline
• Age: Mean=61.5y, SD=10.2y
• Sex (female): 53.2%
• Race/ethnicity: ~25% White, ~25% African American, ~25% Hispanic, ~25% Chinese
• SES: 60.3% with some college degree
• Anthropometry: BMI, Mean=27.9, SD=5.5
 	
Fat intake at baseline:
• ALA (g/d): 1.0 (0.6)
• LA (g/d): 9.0 (6.3)
• AA (g/d): 0.12 (0.08)
• EPA (mg/d): 45 (50)
• DPA (mg/d): 20 (20)
• DHA (mg/d): 82 (73)
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
In men and women, higher intakes of EPA, DPA, and DHA at ~62y of age were significantly associated with lower risk of total incident CVD and CHD through 10y of follow-up. When modeled continuously, intake of ALA, LA, and AA were not significantly associated with total incident CVD and CHD. However, those in the 2nd quartile of intake for LA and AA+LA had a significantly lower risk of incident CVD and CHD compared to the 1st quartile of intake.
	Exposures:
	• EPA (continuous; per 1-IQR unit [80mg/d])
	• EPA (quartiles; mg/d), Medians (Q1 (10), Q2 (20), Q3 (40), Q4 (90))
	• DPA (continuous; per 1-IQR unit [35mg/d])
	• DPA (quartiles; mg/d), Medians (Q1 (4), Q2 (10), Q3 (19), Q4 (39))
	• DHA (continuous; per 1-IQR unit [130mg/d])
	• DHA (quartiles; mg/d), Medians (Q1 (20), Q2 (50), Q3 (80), Q4 (150))
	• EPA+DPA+DHA (continuous; per 1-IQR unit [240mg/d])
	• EPA+DPA+DHA (quartiles; mg/d), Medians (Q1 (40), Q2 (80), Q3 (140), Q4 (280))
	• ALA (continuous; per 1-IQR unit [1200mg/d])
	• ALA (quartiles; mg/d), Medians (Q1 (390), Q2 (690), Q3 (1020), Q4 (1610))
	• LA (continuous; per 1-IQR unit [11100mg/d])
	• LA (quartiles; mg/d), Medians (Q1 (3870), Q2 (6230), Q3 (9220), Q4 (14980))
	• AA (continuous; per 1-IQR unit [160mg/d])
	• AA (quartiles; mg/d), Medians (Q1 (40), Q2 (80), Q3 (120), Q4 (200))
	• LA+AA (continuous; per 1-IQR unit [11200mg/d])
	• LA+AA (quartiles; mg/d), Medians (Q1 (4000), Q2 (6300), Q3 (9400), Q4 (15200))
	Outcomes and assessment methods:
	• Assessed through 10y of follow-up
	• Incident CVD: Obtained through cohort examinations, follow-up calls, medical record abstractions, or obituaries (reviewed by medical endpoints committee); CVD included CHD events (MI, cardiac arrest, definite/ probable angina, CHD death), stroke, stroke death, or other CVD/atherosclerotic death
	  • Total CVD: 189 cases
	  • CHD events: 161 cases
		EPA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 0.94 (0.62, 1.42)
		Q1 (ref) vs Q3: 0.65 (0.42, 1.03)
		Q1 (ref) vs Q4: 0.60 (0.37, 0.98)
		P-trend: 0.03; Continuous: 0.67 (0.46, 0.97)
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.06**;** Continuous: P=NS
		
		DPA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 1.10 (0.74, 1.63)
		Q1 (ref) vs Q3: 0.67 (0.42, 1.07)
		Q1 (ref) vs Q4: 0.59 (0.35, 0.97)
		P-trend: 0.02; Continuous: 0.70 (0.48, 1.02)
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2: 1.19 (0.76, 1.86)
		Q1 (ref) vs Q3: 0.74 (0.50, 1.26)
		Q1 (ref) vs Q4: 0.54 (0.29, 0.99)
		P-trend: 0.02; Continuous: 0.65 (0.41, 1.03)
		
		DHA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 0.98 (0.64, 1.49)
		Q1 (ref) vs Q3: 0.92 (0.59, 1.44)
		Q1 (ref) vs Q4: 0.60 (0.35, 1.02)
		P-trend: 0.048: Continuous: 0.66 (0.44, 1.00)
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.09**;** Continuous: P=NS
		
		EPA+DPA+DHA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 1.16 (0.77, 1.75)
		Q1 (ref) vs Q3: 0.81 (0.52, 1.28)
		Q1 (ref) vs Q4: 0.64 (0.38, 1.09)
		P-trend: 0.05**; Continuous: 0.66 (0.44, 0.98)**
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.08**;** Continuous: NR
		
		(Continued below)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Study center, BMI, prevalent diabetes, weekly dietary supplement use, hypertensive medication use, fruits and vegetables, processed and unprocessed meat, fiber, vitamin E, SFA, *trans*-fat
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Harvard-Bunge Fellowship Program in Nutrition and Health; NHLBI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

de Oliveira Otto, 2013 (CONTINUED)
PCS, MESA (Multi-Ethnic Study of Atherosclerosis), U.S.
Baseline N=2,880 (random subset of total 6,814 participants) Analytic N=2,372 (Attrition: 18%)
 	
Participant characteristics at baseline:
• Men and women 45-84y of age without CVD at baseline
• Age: Mean=61.5y, SD=10.2y
• Sex (female): 53.2%
• Race/ethnicity: ~25% White, ~25% African American, ~25% Hispanic, ~25% Chinese
• SES: 60.3% with some college degree
• Anthropometry: BMI, Mean=27.9, SD=5.5
 	
Fat intake at baseline:
• ALA (g/d): 1.0 (0.6)
• LA (g/d): 9.0 (6.3)
• AA (g/d): 0.12 (0.08)
• EPA (mg/d): 45 (50)
• DPA (mg/d): 20 (20)
• DHA (mg/d): 82 (73)
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
In men and women, higher intakes of EPA, DPA, and DHA at ~62y of age were significantly associated with lower risk of total incident CVD and CHD through 10y of follow-up. When modeled continuously, intake of ALA, LA, and AA were not significantly associated with total incident CVD and CHD. However, those in the 2nd quartile of intake for LA and AA+LA had a significantly lower risk of incident CVD and CHD compared to the 1st quartile of intake.
	Exposures:
	• EPA (continuous; per 1-IQR unit [80mg/d])
	• EPA (quartiles; mg/d), Medians (Q1 (10), Q2 (20), Q3 (40), Q4 (90))
	• DPA (continuous; per 1-IQR unit [35mg/d])
	• DPA (quartiles; mg/d), Medians (Q1 (4), Q2 (10), Q3 (19), Q4 (39))
	• DHA (continuous; per 1-IQR unit [130mg/d])
	• DHA (quartiles; mg/d), Medians (Q1 (20), Q2 (50), Q3 (80), Q4 (150))
	• EPA+DPA+DHA (continuous; per 1-IQR unit [240mg/d])
	• EPA+DPA+DHA (quartiles; mg/d), Medians (Q1 (40), Q2 (80), Q3 (140), Q4 (280))
	• ALA (continuous; per 1-IQR unit [1200mg/d])
	• ALA (quartiles; mg/d), Medians (Q1 (390), Q2 (690), Q3 (1020), Q4 (1610))
	• LA (continuous; per 1-IQR unit [11100mg/d])
	• LA (quartiles; mg/d), Medians (Q1 (3870), Q2 (6230), Q3 (9220), Q4 (14980))
	• AA (continuous; per 1-IQR unit [160mg/d])
	• AA (quartiles; mg/d), Medians (Q1 (40), Q2 (80), Q3 (120), Q4 (200))
	• LA+AA (continuous; per 1-IQR unit [11200mg/d])
	• LA+AA (quartiles; mg/d), Medians (Q1 (4000), Q2 (6300), Q3 (9400), Q4 (15200))
	Outcomes and assessment methods:
	• Assessed through 10y of follow-up
	• Incident CVD: Obtained through cohort examinations, follow-up calls, medical record abstractions, or obituaries (reviewed by medical endpoints committee); CVD included CHD events (MI, cardiac arrest, definite/ probable angina, CHD death), stroke, stroke death, or other CVD/atherosclerotic death
	  • Total CVD: 189 cases
	  • CHD events: 161 cases
		ALA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.20**;** Continuous: P=NS
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.24**;** Continuous: P=NS
		
		LA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 0.47 (0.28, 0.78)
		Q1 (ref) vs Q3: 0.87 (0.54, 1.41)
		Q1 (ref) vs Q4: 0.74 (0.38, 1.43)
		P-trend: 0.81**;** Continuous: 0.83 (0.55, 1.25)
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2: 0.45 (0.25, 0.80)
		Q1 (ref) vs Q3: 0.79 (0.45, 1.37)
		Q1 (ref) vs Q4: 0.71 (0.33, 1.51)
		P-trend: 0.73**;** Continuous: 1.20 (0.60, 2.40)
		
		AA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.34
		Continuous: P=NS
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4: All NS
		P-trend: 0.45**:** Continuous: P=NS
		
		AA+LA
		Incident CVD, HR (95% CI)
		Q1 (ref) vs Q2: 0.49 (0.30, 0.81)
		Q1 (ref) vs Q3: 0.87 (0.54, 1.41)
		Q1 (ref) vs Q4: 0.74 (0.38, 1.44)
		P-trend: 0.77**:** Continuous: 1.14 (0.63, 2.05)
		Incident CHD Events, HR (95% CI)
		Q1 (ref) vs Q2: 0.48 (0.27, 0.85)
		Q1 (ref) vs Q3: 0.79 (0.45, 1.38)
		Q1 (ref) vs Q4: 0.72 (0.33, 1.53)
		P-trend: 0.71**:** Continuous: 1.20 (0.60, 2.41)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Study center, BMI, prevalent diabetes, weekly dietary supplement use, hypertensive medication use, fruits and vegetables, processed and unprocessed meat, fiber, vitamin E, SFA, *trans*-fat
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (other types of FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Harvard-Bunge Fellowship Program in Nutrition and Health; NHLBI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Ricci, 2018[201]
PCS, NHANES (National Health and Nutrition Examination Survey), U.S.
Baseline N=40,870 Analytic N=18,372 (Attrition: 55%)
 	
Participant characteristics at baseline:
• No CVD, diabetes and cancer
• Age: Median=60.2y
• Sex (female): 48.2%
• Race/ethnicity: 21% Black, 53.8% white, 25% other
• SES: 14% University degree
• Anthropometry: BMI, Median=27
 	
Fat intake at baseline, Median:
• SFAs (%E): 10.8
• PUFAs (%E): 6.3
• MUFA (%E): 12.1
• Cholesterol (mg/1000kcal): Men 183.6±53.2, Women: 200.6±59.0
 	
Blood lipids and BP at baseline, Mean:
• SBP (mmHg): 130.1
• DBP (mmHg): 71.3
 	
Summary of findings:
In U.S. adults, higher saturated fat consumption was associated with increased risk of CVD mortality; high intake of polyunsaturated fat was associated with reduced CVD mortality risk; and there was no association between monounsaturated intake and CVD mortality during approximately 6 year follow-up. Substitution of saturated fat intake with polyunsaturated fat led to beneficial CVD mortality reduction during 6-year follow-up.
	Exposures:
	• SFA intake (tertiles, %E), Median Q1-Q3
	  • Q1-Q3: 8·3, 12·4
	  • T1: 7.1%
	  • T2: 10.5%
	  • T3: 14.5%
	• MUFA intake (tertiles, %E),
	  • T1: 8.4%
	  • T2: 12.0%
	  • T3: 15.9%
	• PUFA intake (tertiles, %E),
	  • T1: 4.4%
	  • T2: 6.7%
	  • T3: 10.2%
	• Iso-caloric substitution of SFA with MUFA and PUFA (continuous, per 10%E)
	
	Diet assessment method and timing:
	• NHANES 1990 – 2002: 24-h dietary recall and dietary post interview
	• NHANES 2001 -2010: 2d recall and post recall
	• Post recall: 3-10 d from the first dietary evaluation
	• Administered at baseline by trained staff
	
	Outcomes and assessment methods:
	• Assessed during mean 6.1y of follow-up
	• CVD mortality risk assessed via link to U.S. death registry
	  • CVD mortality: 267
		CVD deaths, HR (95% CI)
		SFA (tertiles)
		T1 (ref) vs T2: 1.08 (1.03, 1.12)
		T1 (ref) vs T3: 1.12 (1.06, 1.17)
		P for trend< 0.0002
		MUFA (tertiles)
		T1 (ref), T2 or T3: All NS
		P-trend=0.37
		PUFA (tertiles)
		T1 (ref) vs T2: 1.01 (0.97, 1.05)
		T1 (ref) vs T3: 0.93 (0.89, 0.97)
		P for trend< 0.002
		
		Replacement of 10% SFA, HR (95% CI)
		MUFA: 0.97 (0.93, 1.01), P<0.0621
		PUFA: 0.92 (0.90, 0.95), P<0.05
		Replacement of 10% MUFA, HR (95% CI)
		SFA: 1.03 (0.99, 1.07), NS
		PUFA: 0.95 (0.91, 0.99), P<0.05
		Replacement of 10% PUFA, HR (95% CI)
		SFA: 1.08 (1.06, 1.11), P<0.05
		MUFA: 1.05 (1.10, 1.10), P<0.05)
			Key confounders NOT accounted for:
			Age, sex, TEI, family history of CVD or diabetes
			
			Key confounders accounted for:
			SES (education), ethnicity, alcohol intake, smoking, physical activity
			
			Additional model adjustments:
			BMI, BP, fiber intake
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants with diabetes
			• Unlikely that analyses removed risk of bias due to missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			No funding received

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zhuang, 2019[225]
PCS, NHANES (National Health and Nutrition Examination Survey), U.S.
Baseline N=45,082 Analytic N=36,032 (Attrition: 20%)
 	
Participant characteristics at baseline:
• Men and women ≥20y of age without CVD or cancer at baseline.
• Age: ~44y
• Sex (female): ~51%
• Race/ethnicity: ~43% non-Hispanic Caucasian, ~24% non-Hispanic Black, ~25% Hispanic, ~8% other
• SES: Greater than high school education ~40%
• Anthropometry: BMI, ~27
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• History of Hypertension: ~36%
 	
Summary of findings:
In men and women, higher marine long chain n-3 PUFA intake at ~44y of age was significantly associated with lower risk of total vascular mortality, heart disease mortality, and stroke mortality during ~9.1y of follow-up. Higher AA intake was significantly associated with lower total vascular mortality and heart disease mortality. Total n-3 PUFA, ALA (except at the highest quartile of intake), total n-6 PUFA, and LA intake, as well as the n-6:n-3 PUFA intake ratio was not significantly associated with vascular mortality.
	• Total n-3 PUFA (quartiles; g/d)
	  • Q1: 0-0.78, Q2: 0.78-1.25, Q3: 1.25-1.97, Q4: ≥1.97
	• Marine long chain n-3 PUFA (quartiles; mg/d)
	  • Q1: 0, Q2: 0-33.0, Q3: 33.0-100.0, Q4: ≥100.0
	• ALA (quartiles; g/d)
	  • Q1: 0-0.70, Q2: 0.70-1.15, Q3: 1.15-1.80, Q4: ≥1.80
	• Total n-6 PUFA (quartiles; g/d)
	  • Q1: 0-7.55, Q2: 7.55-12.50, Q3: 12.50-19.34, Q4: ≥19.34
	• LA (quartiles; g/d)
	  • Q1: 0-7.43, Q2: 7.43-12.32, Q3: 12.32-19.17, Q4: ≥19.17
	• AA (quartiles; mg/d)
	  • Q1: 0-55.0, Q2: 55.0-100.0, Q3: 100.0-200.0, Q4: ≥200.0
	• n-6:n-3 PUFA ratio (quartiles)
	  • Q1: ≤8, Q2: 8-10, Q3: 10-12, Q4: ≥12
	
	Assessment method and timing:
	• One, 24-hr dietary recall administered by trained interviewers
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~9.1y of follow-up
	• Vascular Mortality: Measured via probabilistic record linkage with National Death Index
	  • Total Vascular Mortality: 1,299 cases
	  • Heart Disease Mortality: 978 cases
	  • Stroke Mortality: 321 cases
		Total n-3 PUFA
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.32
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.42
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.61
		
		Marine long chain n-3 PUFA
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.55 (0.41, 0.75)
		Q1 (ref) vs Q3: 0.65 (0.53, 0.81)
		Q1 (ref) vs Q4: 0.77 (0.61, 0.98)
		P-trend: 0.002
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.56 (0.41, 0.78)
		Q1 (ref) vs Q3: 0.66 (0.52, 0.84)
		Q1 (ref) vs Q4: 0.73 (0.53, 1.00)
		P-trend: 0.01
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.53 (0.29, 0.98)
		Q1 (ref) vs Q3: 0.61 (0.38, 0.99)
		Q1 (ref) vs Q4: 0.93 (0.57, 1.52)
		P-trend: 0.34
		
		ALA
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.42
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.79
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.97 (0.63, 1.51)
		Q1 (ref) vs Q3: 1.00 (0.67, 1.47)
		Q1 (ref) vs Q4: 0.54 (0.30, 0.98)
		P-trend: 0.13
		
		(Continued below)
			Key confounders NOT accounted for:
			None
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			Marital status, BMI, history of hypertension, history of diabetes, intake of vegetables, fruits, red meat, and SFA
			
			Limitations:
			• Only one, 24-hr recall used to assess diet
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Natural Science Foundation of China; Chinese Institute of Nutrition DSM Research Fund

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zhuang, 2019 (CONTINUED)
PCS, NHANES (National Health and Nutrition Examination Survey), U.S.
Baseline N=45,082 Analytic N=36,032 (Attrition: 20%)
 	
Participant characteristics at baseline:
• Men and women ≥20y of age without CVD or cancer at baseline.
• Age: ~44y
• Sex (female): ~51%
• Race/ethnicity: ~43% non-Hispanic Caucasian, ~24% non-Hispanic Black, ~25% Hispanic, ~8% other
• SES: Greater than high school education ~40%
• Anthropometry: BMI, ~27
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
BP at baseline:
• History of Hypertension: ~36%
 	
Summary of findings:
In men and women, higher marine long chain n-3 PUFA intake at ~44y of age was significantly associated with lower risk of total vascular mortality, heart disease mortality, and stroke mortality during ~9.1y of follow-up. Higher AA intake was significantly associated with lower total vascular mortality and heart disease mortality. Total n-3 PUFA, ALA (except at the highest quartile of intake), total n-6 PUFA, and LA intake, as well as the n-6:n-3 PUFA intake ratio was not significantly associated with vascular mortality.
	• Total n-3 PUFA (quartiles; g/d)
	  • Q1: 0-0.78, Q2: 0.78-1.25, Q3: 1.25-1.97, Q4: ≥1.97
	• Marine long chain n-3 PUFA (quartiles; mg/d)
	  • Q1: 0, Q2: 0-33.0, Q3: 33.0-100.0, Q4: ≥100.0
	• ALA (quartiles; g/d)
	  • Q1: 0-0.70, Q2: 0.70-1.15, Q3: 1.15-1.80, Q4: ≥1.80
	• Total n-6 PUFA (quartiles; g/d)
	  • Q1: 0-7.55, Q2: 7.55-12.50, Q3: 12.50-19.34, Q4: ≥19.34
	• LA (quartiles; g/d)
	  • Q1: 0-7.43, Q2: 7.43-12.32, Q3: 12.32-19.17, Q4: ≥19.17
	• AA (quartiles; mg/d)
	  • Q1: 0-55.0, Q2: 55.0-100.0, Q3: 100.0-200.0, Q4: ≥200.0
	• n-6:n-3 PUFA ratio (quartiles)
	  • Q1: ≤8, Q2: 8-10, Q3: 10-12, Q4: ≥12
	
	Assessment method and timing:
	• One, 24-hr dietary recall administered by trained interviewers
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~9.1y of follow-up
	• Vascular Mortality: Measured via probabilistic record linkage with National Death Index
	  • Total Vascular Mortality: 1,299 cases
	  • Heart Disease Mortality: 978 cases
	  • Stroke Mortality: 321 cases
		Total n-6 PUFA
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS P-trend: 0.48
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.61
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.57
		
		LA
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.49
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.59
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.65
		
		AA
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.90 (0.71, 1.15)
		Q1 (ref) vs Q3: 0.71 (0.57, 0.88)
		Q1 (ref) vs Q4: 0.81 (0.63, 1.05)
		P-trend: 0.01
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.87 (0.64, 1.18)
		Q1 (ref) vs Q3: 0.67 (0.53, 0.84)
		Q1 (ref) vs Q4: 0.80 (0.58, 1.11)
		P-trend: 0.02
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.54
		
		n-6:n-3 PUFA Ratio
		Vascular Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.87
		Heart Disease Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.90
		Stroke Mortality, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: NS, P-trend: 0.39
			Key confounders NOT accounted for:
			None
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			Marital status, BMI, history of hypertension, history of diabetes, intake of vegetables, fruits, red meat, and SFA
			
			Limitations:
			• Only one, 24-hr recall used to assess diet
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Natural Science Foundation of China; Chinese Institute of Nutrition DSM Research Fund

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Chiuve, 2012[152] **PCS, NHS (Nurse's Health Study), U.S.** Baseline N=121,700 Analytic N=91,981 (Attrition: 24%) **Participant characteristics at baseline:** • Age (Mean): 47 y (SD=7) • Sex (female): 100% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI ~24.4 **Fat intake at baseline:** NR **Blood lipids and BP at baseline:** • Hypertension: ~17% • Hypercholesterolemia: ~6% **Summary of findings:** *Higher SFA intake was significantly associated with greater risk of sudden cardiac death. Total PUFA, total n-3 PUFA, ALA, marine n-3 fats (EPA+DHA), n-6 PUFA and LA were associated with lower risk of sudden cardiac death. There were no associations with MUFA and sudden cardiac death. Replacement of carbohydrate with PUFAs, but not SFAs, was significantly associated with lower risk of sudden cardiac death.*	**Exposures:** • SFA (quintile; continuous, per 5% of total fat), Median (% total fat) (Q1 (ref) 32.8, Q2 35.7, Q3 38.0, Q4 40.3, Q5 43.9) • MUFA (quintile), Median (% total fat) (Q1 (ref) 35.9, Q2 37.8, Q3 39.2, Q4 40.8, Q5 43.7) • PUFA (quintile; continuous, per 5% of total fat), Median (% of total fat) (Q1 (ref) 10.5, Q2 13.6, Q3 15.8, Q4 17.8, Q5 20.7) • Total n-6 PUFA (quintile) Median (% total fat) (Q1 (ref) 8.2, Q2 11.4, Q3 13.6, Q4 15.6, Q5 18.6) • LA (quintile), Median (% total fat) (Q1 (ref) 7.8, Q2 11.0, Q3 13.2, Q4 15.2, Q5 17.9) • AA (quintile), Median (% total fat) (Q1 (ref) 0.15, Q2 0.19, Q3 0.22, Q4 0.26, Q5 0.33) • Total n-3 PUFAs (quintile), Median (%E) (Q1 (ref) 1.24, Q2 1.45, Q3 1.66, Q4 1.93, Q5 2.41) • ALA (quintile), Median (% total fat) (Q1 (ref) 1.14, Q2 1.31, Q3 1.46, Q4 1.64, Q5 2.10) • Marine n-3 fats (EPA + DHA) (quintile), Median (% total fat) (Q1 (ref) 0.05, Q2 0.10, Q3 0.17, Q4 0.27, Q5 0.51) • Isocaloric replacement of carbohydrate with SFA, total PUFAs, n-3 PUFAs or n-6 PUFAs Assessment method and timing: • Average of self-administered, validated 61-item FFQ ; expanded to 116-items in 1984 • Assessed at baseline and every 4 years **Outcomes and assessment methods**: • Assessed during 30 y of follow-up • Incident sudden cardiac death (SCD; includes acute coronary thrombosis, severe coronary artery disease without myocardial necrosis): reports from next of kin, National Death Index, death certificates, medical records • SCD: 385 cases	**Incident SCD**, RR (95% CI) SFA **Continuous: 1.11 (1.01, 1.23)** Q1 (ref) vs Q2, Q3, Q4: All NS **Q1 (ref) vs Q5: 1.44 (1.04, 1.98)** **P linear trend=0.01** MUFA Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P linear trend=0.29 PUFA **Continuous: 0.79 (0.69, 0.90)** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.54 (0.39, 0.74)** **Q1 (ref) vs Q4: 0.56 (0.40, 0.78)** **Q1 (ref) vs Q5: 0.57 (0.41, 0.78)** **P-trend: linear <0.001, non-linear <0.001** Total n-3 PUFA Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.67 (0.50, 0.91)** **Q1 (ref) vs Q4: 0.45 (0.32, 0.64)** **Q1 (ref) vs Q5: 0.49 (0.35, 0.69)** **P-trend: linear <0.001, non-linear <0.001** ALA Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.74 (0.55, 0.99)** **Q1 (ref) vs Q4: 0.53 (0.38, 0.74)** **Q1 (ref) vs Q5: 0.38 (0.25, 0.59)** **P linear trend<0.001** Marine n-3 fats (EPA+DHA) **Q1 (ref) vs Q2: 0.72 (0.54, 0.96)** **Q1 (ref) vs Q3: 0.63 (0.46, 0.86)** **Q1 (ref) vs Q4: 0.56 (0.40, 0.77)** **Q1 (ref) vs Q5: 0.50 (0.35, 0.70)** **P linear trend<0.001** n-6 PUFA Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.63 (0.46, 0.86)** **Q1 (ref) vs Q4: 0.54 (0.39, 0.76)** **Q1 (ref) vs Q5: 0.61 (0.44, 0.85)** **P-trend: linear <0.001, non-linear <0.001** ***(Continued below)***	**Key confounders NOT accounted for:** Sex, race/ethnicity, SES **Key confounders accounted for:** Age, TEI, alcohol intake, physical activity, smoking, family history of MI **Additional model adjustments:** Percent of energy from remaining fatty acids (replacement analyses only), Percent of energy from total fat, BMI, menopausal status, hormone therapy, aspirin use, use of multivitamins, use of vitamin E supplements, history of diabetes, hypertension, hypercholesterolemia, coronary heart disease and cancer at baseline **Limitations:** • Not all key confounders accounted for • Bias due to missing data due to not accounting for missing data • No preregistered statistical analysis plan **Funding sources:** American Heart Association, NIH

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Chiuve, 2012 (CONTINUED) **PCS, NHS (Nurse's Health Study), U.S.** Baseline N=121,700 Analytic N=91,981 (Attrition: 24%) **Participant characteristics at baseline:** • Age (Mean): 47 y (SD=7) • Sex (female): 100% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI ~24.4 **Fat intake at baseline:** NR **Blood lipids and BP at baseline:** • Hypertension: ~17% • Hypercholesterolemia: ~6% **Summary of findings:** *Higher SFA intake was significantly associated with greater risk of sudden cardiac death. Total PUFA, total n-3 PUFA, ALA, marine n-3 fats (EPA+DHA), n-6 PUFA and LA were associated with lower risk of sudden cardiac death. There were no associations with MUFA and sudden cardiac death. Replacement of carbohydrate with PUFAs, but not SFAs, was significantly associated with lower risk of sudden cardiac death.*	**Exposures:** • SFA (quintile; continuous, per 5% of total fat), Median (% total fat) (Q1 (ref) 32.8, Q2 35.7, Q3 38.0, Q4 40.3, Q5 43.9) • MUFA (quintile), Median (% total fat) (Q1 (ref) 35.9, Q2 37.8, Q3 39.2, Q4 40.8, Q5 43.7) • PUFA (quintile; continuous, per 5% of total fat), Median (% of total fat) (Q1 (ref) 10.5, Q2 13.6, Q3 15.8, Q4 17.8, Q5 20.7) • Total n-6 PUFA (quintile) Median (% total fat) (Q1 (ref) 8.2, Q2 11.4, Q3 13.6, Q4 15.6, Q5 18.6) • LA (quintile), Median (% total fat) (Q1 (ref) 7.8, Q2 11.0, Q3 13.2, Q4 15.2, Q5 17.9) • AA (quintile), Median (% total fat) (Q1 (ref) 0.15, Q2 0.19, Q3 0.22, Q4 0.26, Q5 0.33) • Total n-3 PUFAs (quintile), Median (%E) (Q1 (ref) 1.24, Q2 1.45, Q3 1.66, Q4 1.93, Q5 2.41) • ALA (quintile), Median (% total fat) (Q1 (ref) 1.14, Q2 1.31, Q3 1.46, Q4 1.64, Q5 2.10) • Marine n-3 fats (EPA + DHA) (quintile), Median (% total fat) (Q1 (ref) 0.05, Q2 0.10, Q3 0.17, Q4 0.27, Q5 0.51) • Isocaloric replacement of carbohydrate with SFA, total PUFAs, n-3 PUFAs or n-6 PUFAs Assessment method and timing: • Average of self-administered, validated 61-item FFQ ; expanded to 116-items in 1984 • Assessed at baseline and every 4 years **Outcomes and assessment methods**: • Assessed during 30 y of follow-up • Incident sudden cardiac death (SCD; includes acute coronary thrombosis, severe coronary artery disease without myocardial necrosis): reports from next of kin, National Death Index, death certificates, medical records • SCD: 385 cases	LA Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.67 (0.49, 0.91)** **Q1 (ref) vs Q4: 0.60 (0.43, 0.83)** **Q1 (ref) vs Q5: 0.53 (0.38, 0.75)** **P-trend: linear <0.001, non-linear <0.001** AA Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P linear trend: NS ***Replacement of carbohydrate with:*** SFA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS P linear trend: NS Total PUFAs: Q1 (ref) vs Q2: NS **Q3: 0.58 (0.42, 0.81)** **Q4: 0.56 (0.39, 0.79)** **Q5: 0.49 (0.33, 0.71)** **P linear trend<0.001** Total n-3 PUFAs: Q1 (ref) vs Q2, Q3, Q4: All NS **Q5: 0.59 (0.40, 0.88)** **P linear trend=0.01** Total n-6 PUFAs: Q1 (ref) vs Q2: NS **Q3: 0.68 (0.48, 0.97)** Q4: NS **Q5: 0.63 (0.41, 0.96)** **P linear trend=0.02**	**Key confounders NOT accounted for:** Sex, race/ethnicity, SES **Key confounders accounted for:** Age, TEI, alcohol intake, physical activity, smoking, family history of MI **Additional model adjustments:** Percent of energy from remaining fatty acids (replacement analyses only), Percent of energy from total fat, BMI, menopausal status, hormone therapy, aspirin use, use of multivitamins, use of vitamin E supplements, history of diabetes, hypertension, hypercholesterolemia, coronary heart disease and cancer at baseline **Limitations:** • Not all key confounders accounted for • Bias due to missing data due to not accounting for missing data • No preregistered statistical analysis plan **Funding sources:** American Heart Association, NIH

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Li, 2015[183]
PCS, NHS (Nurse's Health Study) and HPFS (Health Professionals Follow-Up Study), U.S.
Baseline N=173,230 Analytic N=127,536 (Attrition: 26%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD, diabetes or cancer
• Age: Women: ~46.5y, Men: ~53.2y
• Sex (female): ~66%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI ~24.8
 	
Fat intake at baseline, Mean:
• MUFA: Women ~13.7%E, Men ~11.8%E
• PUFA: Women ~5.1%E, Men ~5.9 %E
 	
Blood lipids and BP at baseline, Mean:
• TC (mg/dL): Women ~293, Men ~291
• Hypercholesterolemia: Women:~5%; Men: ~11%
• Hypertension: Women:~16%; Men: ~20%
 	
Summary of findings:
Higher PUFA intake, compared to lower PUFA intake, was significantly associated with lower incidence of coronary heart disease. SFA and MUFA was not significantly associated with incidence of coronary heart disease.
	Exposures:
	• SFA (categorical, %E), Median (%E)
	  • Q1 (ref; Men 7.4, Women 9.6)
	  • Q2 (Men 9.2, Women 11.3)
	  • Q3 (Men 10.4, Women 12.6)
	  • Q4 (Men 11.6, Women 14.1)
	  • Q5 (Men 13.6, Women 16.9)
	• MUFA (categorical, %E), Median (%E)
	  • Q1 (ref; Men 9.0, Women 10.4)
	  • Q2 (Men 10.9, Women 12.1)
	  • Q3 (Men 12.1, Women 13.4)
	  • Q4 (Men 13.3, Women 14.8)
	  • Q5 (Men 15.1, Women 17.3)
	• PUFA (categorical, %E), Median (%E)
	  • Q1 (ref; Men 4.4, Women 3.9)
	  • Q2 (Men 5.2, Women 4.9)
	  • Q3 (Men 5.8, Women 5.6)
	  • Q4 (Men 6.4, Women 6.3)
	  • Q5 (Men 7.5, Women 7.4)
	Assessment method and timing:
	• Average of self-administered, validated FFQ
	• Assessed at baseline and every 2 to 4 years thereafter
	
	Outcomes and assessment methods:
	• Assessed during 24 (HPFS) and 30 (NHS) y of follow-up
	• Incident total coronary heart disease (CHD; nonfatal MI, fatal CHD): medical records, phone interview or letter (classified as probable), reports from next of kin, U.S. postal system, certificates from vital statistics departments and National Death Index, autopsy
	  • Nonfatal MI: 4,931 cases
	  • CHD deaths: 2,736 cases
		Incident CHD, HR (95% CI)
		SFA
		Men:
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=0.16
		Women:
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=0.73
		
		MUFA
		Men:
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=0.33
		Women:
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=0.22
		
		PUFA
		Men:
		Q1 (ref) vs Q2, Q3, Q4: All NS
		Q1 (ref) vs Q5: 0.83 (0.74, 0.94)
		P-trend=0.001
		Women:
		Q1 (ref) vs Q2: NS
		Q1 (ref) vs Q3: 0.78 (0.70, 0.88)
		Q1 (ref) vs Q4: 0.88 (0.78, 0.99)
		Q1 (ref) vs Q5: 0.76 (0.67, 0.87)
		P-trend=0.0003
			Key confounders NOT accounted for:
			SES
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, TEI, alcohol intake, physical activity, smoking, family history of MI and diabetes
			
			Additional model adjustments:
			Energy contribution from protein, cholesterol intake, BMI, use of vitamins and aspirin, presence of baseline hypertension and hypercholesterolemia, dietary intake of fruits and vegetables
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants with diabetes
			• Analyses did not account for co-exposure (other types of fats)
			• Potential risk of bias due to missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Institutes of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Wang, 2016[218] **PCS, NHS (Nurse's Health Study) and HPFS (Health Professionals Follow-up Study), U.S.** Baseline N=143,997 (NHS, n=92,468; HPFS, n=51,529) Analytic N=126,233 (NHS, n=83,349; HPFS, n=42,884) (Attrition: 12%) **Participant characteristics at baseline:** • 100% without prevalent CVD, diabetes or cancer • Age: NHS: ~46y; HPFS: ~53y • Sex (female): 66% (NHS 100%, HPFS 0%) • Race/ethnicity: NR • SES: NR • Anthropometry: BMI NHS ~24, HPFS: ~25 **Fat intake at baseline, Mean:** • SFA: Women ~12%E, Men ~10%E • MUFA: Women ~13%E, Men ~12%E • PUFA: Women ~6%E, Men ~6E • Cholesterol: Women ~300 mg/d, Men ~295 mg/d **Blood lipids and BP at baseline:** • Hypercholesterolemia: Women ~6%; Men ~11% • Hypertension: Women ~16%; Men ~20% **Summary of findings:** *Higher intake of SFAs and marine n-3 fats (DHA+EPA) were significantly associated with higher incidence of CVD. Higher intakes of unsaturated fatty acids, MUFAs, PUFAs, and replacement of total carbohydrate with unsaturated fatty acids, and PUFA were significantly associated with lower incidence of CVD. Replacement of total carbohydrates with MUFA was significantly associated with lower incidence of CVD in women only.*	**Exposures:** • SFA (quintiles), Median (%E) (NHS: Q1 8.2, Q2 10.2, Q3 11.8, Q4 13.5, Q5 16.5; HPFS: Q1 7.1 Q2 9.0, Q3 10.2, Q4 11.5, Q5 13.5,) • UFA (quintiles), Median (%E) (NHS: Q1 14.2, Q2 16.8, Q3 18.7, Q4 20.6, Q5 23.8; HPFS: Q1 13.7, Q2 16.3, Q3 18.0, Q4 19.7, Q5 22.3) • MUFA (quintiles), Median (%E) (NHS: Q1 9.4, Q2 11.4, Q3 12.8, Q4 14.4, Q5 17.2; HPFS: Q1 8.9, Q2 10.8, Q3 12.1, Q4 13.3, Q5 15.3) • PUFA (quintiles), Median (%E) (NHS: Q1 4.2, Q2 5.0, Q3 5.6, Q4 6.3, Q5 7.5; HPFS: Q1 4.4, Q2 5.2, Q3 5.8, Q4 6.5, Q5 7.7) • *n-6 PUFA, n-3 PUFA, and replacement presented on following 2 pages* Assessment method and timing: • Average of self-administered, validated, semi-quantitative FFQ • Assessed at baseline and every 2-4 years thereafter **Outcomes and assessment methods**: • Assessed during 26 (HPFS) and 32 (NHS) y of follow-up • Cardiovascular disease (CVD) mortality: National Death Index, reports from family members or postal authorities, death certificates and medical records	**CVD mortality,** HR (95% CI) **SFA** **NHS: P-trend=0.02** **Q1 (ref) vs Q2: 1.15 (1.04, 1.26)** **Q1 (ref) vs Q3: 1.17 (1.04, 1.31)** **Q1 (ref) vs Q4: 1.18 (1.03, 1.34)** **Q1 (ref) vs Q5: 1.21 (1.03, 1.41)** **HPFS:** P-trend=NS Q1 (ref) vs Q2, Q3, Q4, Q5: NS, **UFA** **NHS: P-trend<0.001** **Q1 (ref) vs Q2: 0.91 (0.83, 1.00)** **Q1 (ref) vs Q3: 0.84 (0.75, 0.93)** **Q1 (ref) vs Q4: 0.76 (0.67, 0.85)** **Q1 (ref) vs Q5: 0.68 (0.60, 0.78)** **HPFS: P-trend=0.002** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.86 (0.77, 0.96)** **Q1 (ref) vs Q4: 0.87 (0.77, 0.98)** **Q1 (ref) vs Q5: 0.83 (0.73, 0.94)** **MUFA** **NHS: P-trend=0.001** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.88 (0.78, 0.99)** **Q1 (ref) vs Q4: 0.82 (0.72, 0.95)** **Q1 (ref) vs Q5: 0.79 (0.67, 0.94)** **HPFS:** P-trend=NS Q1 (ref) vs Q2, Q3, Q4, Q5: NS, **PUFA** **NHS: P-trend<0.001** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.89 (0.80, 0.98)** **Q1 (ref) vs Q4: 0.85 (0.76, 0.94)** **Q1 (ref) vs Q5: 0.80 (0.71, 0.89)** **HPFS: P-trend<0.001** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.88 (0.79, 0.98)** **Q1 (ref) vs Q4: 0.80 (0.72, 0.90)** **Q1 (ref) vs Q5: 0.83 (0.74, 0.94)** ***(Continued on next page)***	**Key confounders NOT accounted for:** None **Key confounders accounted for:** Sex, age, race/ethnicity, SES, TEI, alcohol intake, physical activity, smoking, family history of MI and diabetes **Additional model adjustments:** BMI, multivitamin use, vitamin E supplement use, current aspirin use, family history of cancer, history of hypertension, history of hypercholesterolemia, dietary cholesterol and percentage of energy intake from dietary proteins, menopausal status and hormone use in women, % of energy intake from remaining fatty acids **Limitations:** • Potential selection bias due to excluding participants with diabetes • No preregistered statistical analysis plan **Funding sources:** National Institutes of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Wang, 2016 (CONTINUED) **PCS, NHS (Nurse's Health Study) and HPFS (Health Professionals Follow-up Study), U.S.** Baseline N=143,997 (NHS, n=92,468; HPFS, n=51,529) Analytic N=126,233 (NHS, n=83,349; HPFS, n=42,884) (Attrition: 12%) **Participant characteristics at baseline:** • 100% without prevalent CVD, diabetes or cancer • Age: NHS: ~46y; HPFS: ~53y • Sex (female): 66% (NHS 100%, HPFS 0%) • Race/ethnicity: NR • SES: NR • Anthropometry: BMI NHS ~24, HPFS: ~25 **Fat intake at baseline, Mean:** • SFA: Women ~12%E, Men ~10%E • MUFA: Women ~13%E, Men ~12%E • PUFA: Women ~6%E, Men ~6E • Cholesterol: Women ~300 mg/d, Men ~295 mg/d **Blood lipids and BP at baseline:** • Hypercholesterolemia: Women ~6%; Men ~11% • Hypertension: Women ~16%; Men ~20% **Summary of findings:** *Higher intake of SFAs and marine n-3 fats (DHA+EPA) were significantly associated with higher incidence of CVD. Higher intakes of unsaturated fatty acids, MUFAs, PUFAs, and replacement of total carbohydrate with unsaturated fatty acids, and PUFA were significantly associated with lower incidence of CVD. Replacement of total carbohydrates with MUFA was significantly associated with lower incidence of CVD in women only.*	**Exposures:** • Total n-6 PUFAs (quintiles), Median (%E) (NHS: Q1 3.4, Q2 4.3, Q3 4.9, Q4 5.5, Q5 6.7; HPFS: Q1 3.7, Q2 4.5, Q3 5.1, Q4 5.8, Q5 6.9) • LA (quintiles), Median (%E) (NHS: Q1 3.3, Q2 4.2, Q3 4.8, Q4 5.4, Q5 6.5; HPFS: Q1 3.6, Q2 4.4, Q3 5.0, Q4 5.6, Q5 6.7) • AA (quintiles), Median (%E) (NHS: Q1 0.05, Q2 0.06, Q3 0.07, Q4 0.09, Q5 0.11; HPFS: Q1 0.05, Q2 0.06, Q3 0.07, Q4 0.09, Q5 0.11) • Total n-3 PUFAs (quintiles), Median (%E) (NHS: Q1 0.48, Q2 0.57, Q3 0.63, Q4 0.72, Q5 0.88; HPFS: Q1 0.46, Q2 0.57, Q3 0.65, Q4 0.75, Q5 0.94) • ALA (quintiles), Median (%E) (NHS: Q1 0.41, Q2 0.48, Q3 0.53, Q4 0.59, Q5 0.70; HPFS: Q1 0.38, Q2 0.45, Q3 0.50, Q4 0.56, Q5 0.68) • Marine n-3 fats (DHA+EPA, includes fish, chicken or turkey, shrimp, lobster, scallops) (quintiles), Median (%E) (NHS: Q1 0.03, Q2 0.05, Q3 0.08, Q4 0.12, Q5 0.21; HPFS: Q1 0.04, Q2 0.08, Q3 0.12, Q4 0.18, Q5 0.31) • *Replacement presented on following page.* Assessment method and timing: • Average of self-administered, validated, semi-quantitative FFQ • Assessed at baseline and every 2-4 years thereafter **Outcomes and assessment methods**: • Assessed during 26 (HPFS) and 32 (NHS) y of follow-up • Cardiovascular disease (CVD) mortality: National Death Index, reports from family members or postal authorities, death certificates and medical records	**CVD mortality,** HR (95% CI) **Total n-6 PUFAs** **NHS: P-trend=0.02** **Q1 (ref) vs Q2: 0.88 (0.80, 0.98)** **Q1 (ref) vs Q3: 0.88 (0.79, 0.98)** **Q1 (ref) vs Q4: 0.82 (0.73, 0.92)** **Q1 (ref) vs Q5: 0.84 (0.74, 0.96)** **HPFS: P-trend<0.001** **Q1 (ref) vs Q2: 0.90 (0.81, 0.99)** **Q1 (ref) vs Q3: 0.84 (0.75, 0.94)** **Q1 (ref) vs Q4: 0.80 (0.71, 0.91)** **Q1 (ref) vs Q5: 0.78 (0.68, 0.89)** **LA** **NHS: P-trend=0.002** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.87 (0.78, 0.97)** **Q1 (ref) vs Q4: 0.85 (0.75, 0.95)** **Q1 (ref) vs Q5: 0.81 (0.71, 0.93)** **HPFS: P-trend<0.001** Q1 (ref) vs Q2: NS **Q1 (ref) vs Q3: 0.86 (0.77, 0.95)** **Q1 (ref) vs Q4: 0.78 (0.69, 0.87)** **Q1 (ref) vs Q5: 0.75 (0.66, 0.86)** **AA** **NHS and HPFS:** P-trend=NS Q1 (ref) vs Q2, Q3, Q4, Q5: NS **Total n-3 PUFAs** **NHS and HPFS:** P-trend=NS Q1 (ref) vs Q2, Q3, Q4, Q5: NS **ALA** **NHS:** P-trend=NS **Q1 (ref) vs Q2: 0.89 (0.81, 0.99)** Q1 (ref) vs Q3, Q4, Q5: All NS **HPFS:** P-trend=NS Q1 (ref) vs Q2, Q3, Q4, Q5: NS **Marine n-3 fats (DHA+EPA)** **NHS:** P-trend=NS Q1 (ref) vs Q2, Q3, Q4, Q5: NS **HPFS: P-trend=0.01** Q1 (ref) vs Q2, Q3: All NS **Q1 (ref) vs Q4: 1.15 (1.03, 1.28)** **Q1 (ref) vs Q5: 1.16 (1.03, 1.30)** ***(Continued on next page)***	**Key confounders NOT accounted for:** None **Key confounders accounted for:** Sex, age, race/ethnicity, SES, TEI, alcohol intake, physical activity, smoking, family history of MI and diabetes **Additional model adjustments:** BMI, multivitamin use, vitamin E supplement use, current aspirin use, family history of cancer, history of hypertension, history of hypercholesterolemia, dietary cholesterol and percentage of energy intake from dietary proteins, menopausal status and hormone use in women, % of energy intake from remaining fatty acids **Limitations:** • Potential selection bias due to excluding participants with diabetes • No preregistered statistical analysis plan **Funding sources:** National Institutes of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Wang, 2016 (CONTINUED)
PCS, NHS (Nurse's Health Study) and HPFS (Health Professionals Follow-up Study), U.S.
Baseline N=143,997 (NHS, n=92,468; HPFS, n=51,529) Analytic N=126,233 (NHS, n=83,349; HPFS, n=42,884) (Attrition: 12%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD, diabetes or cancer
• Age: NHS: ~46 y; HPFS: ~53 y
• Sex (female): 66% (NHS 100%, HPFS 0%)
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI NHS ~24, HPFS: ~25
Fat intake at baseline, Mean:
• SFA: Women ~12%E, Men ~10%E
• MUFA: Women ~13%E, Men ~12%E
• PUFA: Women ~6%E, Men ~6E
• Cholesterol: Women ~300 mg/d, Men ~295 mg/d
Blood lipids and BP at baseline:
• Hypercholesterolemia: Women ~6%; Men ~11%
• Hypertension: Women ~16%; Men ~20%
Summary of findings:
Higher intake of SFAs and marine n-3 fats (DHA+EPA) were significantly associated with higher incidence of CVD. Higher intakes of unsaturated fatty acids, MUFAs, PUFAs, and replacement of total carbohydrate with unsaturated fatty acids, and PUFA were significantly associated with lower incidence of CVD. Replacement of total carbohydrates with MUFA was significantly associated with lower incidence of CVD in women only.
	Exposures:
	• Isocaloric replacement of total carbohydrate with:
	  • SFA (5%E)
	  • UFA (5%E)
	  • MUFA (5%E)
	  • PUFA (5%E)
	  • Total n-6 PUFA (2%E)
	  • LA (2%E)
	  • Total n-3 PUFA (0.3%E)
	  • AA (0.3%E)
	  • ALA (0.3%E)
	  • Marine n-3 fats (0.3%E)
	• *SFA, UFA, MUFA, PUFA, n-6 PUFA, and n-3 PUFA presented on previous pages.*
	
	Assessment method and timing:
	• Average of self-administered, validated, semi-quantitative FFQ
	• Assessed at baseline and every 2-4 years thereafter
	
	Outcomes and assessment methods:
	• Assessed during 26 (HPFS) and 32 (NHS) y of follow-up
	• Cardiovascular disease (CVD) mortality: National Death Index, reports from family members or postal authorities, death certificates and medical records
		CVD mortality, HR (95% CI)
		Isocaloric replacement of total carbohydrate with:
		NHS:
		SFA: 1.11 (1.02, 1.22)
		UFA: 0.82 (0.76, 0.87)
		MUFA: 0.84 (0.75, 0.93)
		PUFA: 0.72 (0.62, 0.85)
		Total n-6 PUFAs: 0.91 (0.84, 0.98)
		LA: 0.88 (0.81, 0.96)
		AA: NS
		Total n-3 PUFAs: NS
		ALA: NS
		Marine n-3 fats (DHA+EPA): NS
		HPFS:
		SFA: NS
		UFA: 0.90 (0.84, 0.96)
		MUFA: NS
		PUFA: 0.73 (0.61, 0.87)
		Total n-6 PUFAs: 0.86 (0.79, 0.93)
		LA: 0.82 (0.75, 0.89)
		AA: NS
		Total n-3 PUFAs: NS
		ALA: NS
		Marine n-3 fats (DHA+EPA): 1.16 (1.04, 1.31)
			Key confounders NOT accounted for:
			None
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES, TEI, alcohol intake, physical activity, smoking, family history of MI and diabetes
			
			Additional model adjustments:
			BMI, multivitamin use, vitamin E supplement use, current aspirin use, family history of cancer, history of hypertension, history of hypercholesterolemia, dietary cholesterol and percentage of energy intake from dietary proteins, menopausal status and hormone use in women, % of energy intake from remaining fatty acids
			
			Limitations:
			• Potential selection bias due to excluding participants with diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Institutes of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zong, 2016[228]
PCS, NHS (Nurse's Health Study) and HPFS (Health Professionals Follow-up Study), U.S.
Baseline N=173,229 Analytic N=115,782 (Attrition: 33%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD, diabetes or cancer
• Age: Women 30-55y Men: 40-75y
• Sex (female): NHS: 100%, HPFS: 0%
• Race/ethnicity: ~97% white
• SES: NR ("homogeneous … socioeconomic status")
• Anthropometry: BMI ~25
 	
Fat intake at baseline, Mean:
• SFAs: 12:0, 14:0, 16:0, 18:0 accounted for 8.8-10.7%E
• MUFAs: ~12%E
• PUFAs: ~6.3%E
• *Trans* fat: Women ~2.0%E, Men ~1.3%E
 	
Blood lipids and BP at baseline:
• Hypertension: women ~20%; men ~20%
• Hypercholesterolemia: women ~7%; men ~10%
 	
Summary of findings:
Higher intake of SFA (sum of C12:0-C18:0) was significantly associated with higher incidence of coronary heart disease in men and women. This was not significant with shorter-chain SFA (sum of C4:0-C10:0). Isocaloric replacement of 12:0-18:0 SFA by PUFA, whole-grains, and plant proteins was significantly associated with a reduced risk of CHD.
	Exposures:
	• SFA (sum of C4:0-C10:0) (quintile, %E), Median (%E)
	  • Q1 (ref; Women 0.30, Men 0.21)
	  • Q2 (Women 0.41, Men 0.32)
	  • Q3 (Women 0.50, Men 0.41)
	  • Q4 (Women 0.61, Men 0.52)
	  • Q5 (Women 0.82, Men 0.73)
	• SFA (sum of C12:0-C18:0) (quintile, %E), Median (%E)
	  • Q1 (ref; Women 7.58, Men 6.71)
	  • Q2 (Women 9.00, Men 8.42)
	  • Q3 (Women 9.96, Men 9.57)
	  • Q4 (Women 10.98, Men 10.72)
	  • Q5 (Women 12.64, Men 12.49)
	• Replacement of SFA (1%E) with:
	  • PUFA
	  • MUFA
	  • Whole-grain carbohydrate
	  • Plant protein
	Assessment method and timing:
	• Average of self-administered, validated FFQ
	• Assessed at baseline and every 2 to 4 years thereafter
	
	Outcomes and assessment methods:
	• Assessed during Mean of 25.8 (NHS) and 21.2 (HPFS) y of follow-up
	• Incident total coronary heart disease (CHD; nonfatal MI, fatal CHD): medical records, phone interview or letter (classified as probable), reports from next of kin, U.S. postal system, certificates from vital statistics departments and National Death Index, autopsy
	  • Nonfatal MI: 4,348 cases
	  • CHD deaths: 2,687 cases
		Incident CHD, HR (95% CI)
		SFA (4:0-10:0)
		NHS (women):
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		HPFS (men):
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		
		SFA (12:0-18:0)
		NHS (women):
		Q1 (ref) vs
		Q2, Q3: All NS
		Q4: 1.14 (1.01, 1.28)
		Q5: 1.17 (1.04, 1.31)
		P=0.01
		HPFS (men):
		Q1 (ref) vs
		Q2, Q3: All NS
		Q4: 1.20 (1.08, 1.32)
		Q5: 1.19 (1.08, 1.32)
		P-trend<0.001
		Replacement of SFA (C12:0-C18:0) with:*
		NHS (women):
		PUFA: 0.89 (0.84, 0.95), <0.001
		MUFA: NS
		Whole-grain carbohydrate: 0.94 (0.89, 0.99), P=0.03
		Plant protein: NS
		HPFS (men):
		PUFA: 0.95 (0.91, 0.99), P=0.02
		MUFA: NS
		Whole-grain carbohydrate: 0.96 (0.92, 1.00), P=0.04
		Plant protein: 0.93 (0.89, 0.98), P=0.01
		*Similar results were found when excluding participants with probable fatal CHD
			Key confounders NOT accounted for:
			SES
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, TEI, alcohol intake, physical activity, smoking, family history of MI
			
			Additional model adjustments:
			Menopausal status and postmenopausal hormone use (women), current aspirin use, multivitamin use, baseline hypertension, baseline hypercholesterolemia, BMI
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants with diabetes
			• Analyses did not account for co-exposure (other types of fats)
			• No preregistered statistical analysis plan
			
			Funding sources:
			NIH, NHLBI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zong, 2018[227]
NHS (Nurse's Health Study) and HPFS (Health Professionals Follow-up Study), U.S.
Baseline N=173,229 (NHS, N=121,700; HPFS, N=51,529) Analytic N=93,384 (NHS, N=63,442; HPFS: n=29,942) (Attrition: 46%)
 	
Participant characteristics at baseline:
• 100% without prevalent CHD, cancer or diabetes
• Age: Women: ~68y, Men: ~67y
• Sex (female): NHS: 100%, HPFS: 0%
• Race/ethnicity: NHS: ~98% White, HPFS: ~96% White
• SES: NR
• Anthropometry: BMI: NHS:~26, HPFS:~24
Fat intake at baseline, Mean (SD):
• SFAs (%E): NHS: ~10, HPFS: ~10
• MUFAs from plants (%E): NHS: 5.8, HPFS: 6.3
• MUFAs from animals (%E): NHS: 5.4, HPFS: 5.5
• PUFAs (%E):NHS: ~6, HPFS: ~6
• *Trans* fat (%E): NHS: ~1.4, HPFS: ~1.5
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Higher intake of total MUFAs was associated with lower incidence of CHD when comparing the lowest to second lowest quintiles of intake in men only. MUFAs from plants were not associated with incidence of CHD. MUFAs from animal sources was associated with higher incidence of CHD in women and men. Significantly lower CHD risk was observed when SFAs or refined carbohydrates were replaecd by MUFAs from plant sources but not MUFAs from animal sources.
	Exposures:
	• Total MUFAs (%e, quintile), Median (Q1: NHS 8.7, HPFS: 8.8; Q2: NHS 10.5, HPFS: 10.8; Q3: NHS 11.7, HPFS: 12.1; Q4: NHS 13.0, HPFS: 13.3; Q5: NHS 14.9, HPFS: 15.3)
	• Total MUFAs from plants (vegetable cooking oils, breads and cereals, fruit, vegetables, legumes, nuts, seeds) (%e, quintile), Median (Q1: NHS 3.7, HPFS: 4.0; Q2: NHS 4.9, HPFS: 5.2; Q3: NHS 5.8, HPFS: 6.1; Q4: NHS 6.8, HPFS: 7.1; Q5: NHS 8.6, HPFS: 8.8)
	• Total MUFAs from animals (animal fats for cooking, dairy products, eggs, poultry, processed and unprocessed red meats, fish) (%e, quintile), Median (Q1: NHS 3.4, HPFS: 3.2; Q2: NHS 4.5, HPFS: 4.5; Q3: NHS 5.3, HPFS: 5.4; Q4: NHS 6.1, HPFS: 6.4; Q5: NHS 7.5, HPFS: 8.0)
	• Replacement of SFAs (%5E) with:
	  • MUFAs from plants or animals
	• Replacement of MUFAs from animals (5%E) with:
	  • MUFAs from plants
	• Replacement of SFAs+MUFAs from animals (5%E) with:
	  • MUFAs from plants
	• Replacement of refined CHO (5%E) with:
	  • MUFAs from plants or animals
	Assessment method and timing:
	• Average of self-administered, validated FFQ
	• Assessed at baseline (1990) and every 2 years
	Outcomes and assessment methods:
	• Assessed during ~22 y of follow-up
	• Incident coronary heart disease (CHD; nonfatal MI, fatal CHD): medical records, follow-up questionnaires, phone interview or letter, reports from next of kin, U.S. postal authorities, National Death Index, autopsy reports
		Incident CHD, HR (95% CI)
		Total MUFAs
		NHS (women): P-trend=NS
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		HPFS: (men): P-trend=NS
		Q1 (ref) vs Q2: 0.82 (0.71, 0.94)
		Q1 (ref) vs Q3, Q4, Q5: All NS
		MUFAs from plants
		NHS (women): P-trend=0.04
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		HPFS: (men): P-trend=NS
		Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		MUFAs from animals
		NHS (women): P-trend=NS
		Q1 (ref) vs Q2: NS
		Q1 (ref) vs Q3: 1.29 (1.09, 1.51)
		Q1 (ref) vs Q4: 1.20 (1.00, 1.43)
		Q1 (ref) vs Q5: NS
		HPFS (men): P-trend=0.004
		Q1 (ref) vs Q2, Q3: NS
		Q1 (ref) vs Q4: 1.22 (1.04, 1.44)
		Q1 (ref) vs Q5: 1.26 (1.04, 1.54)
		
		Replacement of SFAs with:
		MUFAs from plants: NHS: NS; HPFS: NS
		MUFAs from animals: NHS: NS, HPFS: NS
		Replacement of MUFAs from animals with:
		MUFAs from plants:
		NHS: 0.73 (0.58, 0.92), P=0.007
		HPFS: 0.77 (0.63, 0.93), P=0.007
		Replacement of SFA+MUFAs from animals with:
		MUFAs from plants:
		NHS: 0.79 (0.68, 0.92), P=0.002
		HPFS: 0.82 (0.71, 0.94), P=0.005
		Replacement of refined carbohydrates with:
		MUFAs from plants: NHS: NS; HPFS: NS
		MUFAs from animals: NHS: NS; HPFS: NS
			Key confounders NOT accounted for:
			SES
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES, TEI, alcohol intake, physical activity, smoking, family history of MI and diabetes
			
			Additional model adjustments:
			Menopausal status and postmenopausal hormone use (NHS only), current aspirin use, multivitamin use, baseline hypertension, baseline hypercholesterolemia, BMI, intakes of fruit and vegetables, SFA intake
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to excluding participants with diabetes
			• Analyses did not account for co-exposure (other types of fats)
			• Potential missing data bias due to not accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Institutes of Health, Unilever R&D, California Walnut Commission and Metagenics; National Institute of Environmental Health Sciences

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Reedy, 2014[199]
PCS, NIH-AARP Diet and Health Study, U.S.
Baseline N=566,398 Analytic N=424,662 (Attrition: 25%)
 	
Participant characteristics at baseline:
• AARP members 50-71y of age at baseline without previous cancer or heart disease
• Age: ~62y
• Sex (female): 43%
• Race/ethnicity: ~91% White
• SES: College graduate or postgraduate, ~39%
• Anthropometry: BMI, ~26
 	
Fat intake at baseline:
• NR
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
In men, higher intake of PUFA and EPA+DHA, and a higher PUFA+MUFA:SFA and MUFA:SFA at ~62y of age was significantly associated with lower risk of CVD mortality over 15y of follow-up. In women, only EPA+DHA intake and the PUFA+MUFA:SFA intake ratio were significantly associated with lower risk of CVD mortality.
	• PUFA (continuous; per 1 point increase in AHEI-2010 component score)
	  • Criteria for minimum score: ≤2%E
	  • Criteria for maximum score: ≥10%E
	• EPA+DHA (continuous; per 1 point increase in AHEI-2010 component score)
	  • Criteria for minimum score: 0 mg/d
	  • Criteria for maximum score: 250 mg/d
	• PUFA+MUFA:SFA ratio (continuous; per 1 point increase in HEI-2010 component score)
	  • Criteria for minimum score: <1.2
	  • Criteria for maximum score: ≥2.5
	• MUFA:SFA ratio (continuous; per 1 point increase in aMED component score)
	  • Criteria for minimum score: Less than median
	  • Criteria for maximum score: Median or greater
	
	Assessment method and timing:
	• Validated, self-administered, 124-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 15y of follow-up
	• CVD Mortality: Obtained via linkage to Social Security Administration Death Master File and National Death Index Plus
	  • CVD Mortality: 23,502 cases (15,497 men, 8,005 women)
		PUFA
		Total CVD Mortality, HR (95% CI)
		Men: 0.989 (0.982, 0.996)
		Women: 0.995 (0.986, 1.005)
		
		EPA+DHA
		Total CVD Mortality, HR (95% CI)
		Men: 0.985 (0.979, 0.991)
		Women: 0.983 (0.974, 0.993)
		
		PUFA+MUFA:SFA ratio
		Total CVD Mortality, HR (95% CI)
		Men: 0.984 (0.978, 0.989)
		Women: 0.992 (0.985, 0.9996)
		
		MUFA:SFA ratio
		Total CVD Mortality, HR (95% CI)
		Men: 0.937 (0.908, 0.968)
		Women: 1.003 (0.960, 1.049)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Marital status, BMI, diabetes, hormone replacement therapy (women), modified total index score minus component of interest
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposure (other types of fats)
			• No preregistered statistical analysis plan
			
			Funding sources:
			NR

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zhang, 2018[223]
PCS, NIH-AARP Diet and Health Study, U.S.
Baseline N=567,169 Analytic N=421,309 (Attrition: 26%)
 	
Participant characteristics at baseline:
• AARP members 50-71y of age without cancer, heart disease, stroke, or end-stage renal disease, and not in "poor health" at baseline
• Age: ~62y
• Sex (female): 42.9%
• Race/ethnicity: Men, 92% White, 3% Black, 2% Hispanic, 1% Asian; Women, 89% White, 6% Black, 2% Hispanic, 1% Asian
• SES: Annual household income, Men ~$50,500, Women, ~$46,800; College graduate or postgraduate, 46% of men, 31% of women
• Anthropometry: BMI, Men ~26.6, Women ~25.6
Fat intake at baseline:
• See "Exposures" in next column
Blood lipids and BP at baseline:
• History of high cholesterol: ~28% of men, ~32% of women
• History of hypertension: ~22% of men, ~22% of women
 	
Summary of findings:
In men and women, higher intake of long chain n-3 PUFA at ~62y of age was associated with lower risk of cardiovascular disease mortality (both heart disease and stroke/cerebrovascular mortality) over ~16y of follow-up.
	Exposures:
	• Long chain n-3 PUFA (EPA, DHA, and DPA; quintiles; g/d)
	  • Q1 (ref; Men: ≤0.04, Women: ≤0.03)
	  • Q2 (Men: 0.05-0.07, Women: 0.04-0.06)
	  • Q3 (Men: 0.08-0.10, Women: 0.07-0.09)
	  • Q4 (Men: 0.11-0.17, Women: 0.10-0.15)
	  • Q5 (Men: ≥0.18, Women: ≥0.16)
	
	Assessment method and timing:
	• Validated, self-administered, semi-quantitative 124-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~16y of follow-up
	• CVD Mortality (heart disease and stroke/cerebrovascular mortality): Obtained via linkage to Social Security Administration Death Master File and National Death Index Plus
	  • Total CVD Mortality: 14,824 cases in men, 7,541 cases in women
	  • Heart Disease Mortality: 12,636 cases in men, 5,939 cases in women
	  • Stroke or Cerebrovascular Mortality: 2,188 cases in men, 1,602 cases in women
		Long chain n-3 PUFA
		Total CVD Mortality, HR (95% CI)
		Men: P-trend: <0.0001
		Q1 (ref) vs Q2: 0.92 (0.87, 0.97)
		Q1 (ref) vs Q3: 0.88 (0.83, 0.93)
		Q1 (ref) vs Q4: 0.87 (0.82, 0.92)
		Q1 (ref) vs Q5: 0.85 (0.80, 0.90)
		Women: P-trend: <0.0001
		Q1 (ref) vs Q2: 0.93 (0.86, 1.00)
		Q1 (ref) vs Q3: 0.88 (0.81, 0.95)
		Q1 (ref) vs Q4: 0.87 (0.80, 0.94)
		Q1 (ref) vs Q5: 0.82 (0.75, 0.90)
		Heart Disease Mortality, HR (95% CI)
		Men: P-trend: 0.0004
		Q1 (ref) vs Q2: 0.92 (0.87, 0.97)
		Q1 (ref) vs Q3: 0.89 (0.84, 0.94)
		Q1 (ref) vs Q4: 0.89 (0.84, 0.95)
		Q1 (ref) vs Q5: 0.90 (0.85, 0.95)
		Women: P-trend: 0.0029
		Q1 (ref) vs Q2: 0.94 (0.87, 1.01)
		Q1 (ref) vs Q3: 0.90 (0.83, 0.98)
		Q1 (ref) vs Q4: 0.91 (0.84, 0.99)
		Q1 (ref) vs Q5: 0.87 (0.80, 0.95)
		Stroke or Cerebrovascular Mortality, HR (95% CI)
		Men: P-trend: 0.0005
		Q1 (ref) vs Q2: 0.97 (0.86, 1.11)
		Q1 (ref) vs Q3: 0.92 (0.80, 1.06)
		Q1 (ref) vs Q4: 0.89 (0.77, 1.02)
		Q1 (ref) vs Q5: 0.78 (0.68, 0.90)
		Women: P-trend: 0.0029
		Q1 (ref) vs Q2: 0.94 (0.81, 1.09)
		Q1 (ref) vs Q3: 0.86 (0.73, 1.01)
		Q1 (ref) vs Q4: 0.82 (0.70, 0.97)
		Q1 (ref) vs Q5: 0.80 (0.67, 0.95)
		
		Statistically significant interactions between long chain n-3 PUFA intake and BMI (men), alcohol intake (men and women), diabetes (women), physical activity (women), red meat consumption (men and women), and **SFA intake (men; lower risk with SFA intake below median)** were detected
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, marital status, intake of red meat, SFA, vegetables and fruit, multi-vitamin use, aspirin use, history of diabetes, history of hypertension, history of high cholesterol, intake of ALA, n-6 PUFA, MUFA, and *trans*-FA; Women: hormones use.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Zhejiang Provincial Natural Science Foundation of China; National Natural Science Foundation of China; Intramural Research Program of the NIH, NCI; China National Program for Support of Top-notch Young Professionals

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zhuang, 2019a[226]
PCS, NIH-AARP Diet and Health Study, U.S.
Baseline N=567,169 Analytic N=521,120 (Attrition: 8%)
 	
Participant characteristics at baseline:
• AARP members 50-71y of age at baseline
• Age: ~63y
• Sex (female): 41.2%
• Race/ethnicity: ~91% White, ~4% Black, ~2% Hispanic, ~1% Asian;
• SES: Annual household income, ~$48,700; College graduate or postgraduate, ~39%
• Anthropometry: BMI, ~26
Fat intake at baseline:
• See "Exposures" in next column
Blood lipids and BP at baseline:
• History of hypercholesterolemia: ~26%
• History of hypertension: ~23%
 	
Summary of findings:
In men and women, higher intake of SFA at ~63y of age was associated with higher risk of CVD mortality during ~16y of follow-up when replacing CHO. Replacing SFA intake with total MUFA, plant-MUFA, total PUFA, marine n-3 PUFA, n-6 PUFA, or LA intake was associated with lower risk of CVD mortality. Replacing SFA intake with AA intake was associated with higher risk of CVD mortality. Higher intake of plant-MUFA, total PUFA, marine n-3 PUFA, total n-6 PUFA, and ALA were associated with lower risk of CVD mortality when replacing CHO. Higher intake of animal-MUFA and AA were associated with higher risk of CVD mortality when replacing CHO. The n-6/n-3 PUFA ratio was not associated with CVD mortality.
	Exposures (all continuous and quintiles:
	• SFA (%E)
	  • Q1 (≤6.89), Q2 (6.89-8.50), Q3 (8.50-9.98), Q4 (9.98-11.78), Q5 (≥11.78)
	• MUFA (%E)
	  • Q1 (≤8.73), Q2 (8.73-10.62), Q3 (10.62-12.23), Q4 (12.23-14.03), Q5 (≥14.03)
	• Animal-MUFA (%E)
	  • Q1 (≤4.19), Q2 (4.19-5.43), Q3 (5.43-6.56), Q4 (6.56-7.92), Q5 (≥7.92)
	• Plant-MUFA (%E)
	  • Q1 (≤4.19), Q2 (4.19-5.43), Q3 (5.43-6.56), Q4 (6.56-7.92), Q5 (≥7.92)
	
	• *For PUFAs, please see next page*
	
	Assessment method and timing:
	• Validated, self-administered, 124-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~16y of follow-up
	• CVD Mortality: Obtained via linkage to Social Security Administration Death Master File and National Death Index Plus
	  • CVD Mortality: 38,747 cases
		SFA (Replacing CHO)
		Total CVD Mortality, HR (95% CI)
		Continuous: 1.07 (1.05, 1.09)
		Q1 (ref) vs Q2: 1.11 (1.06, 1.15)
		Q1 (ref) vs Q3: 1.15 (1.10, 1.20)
		Q1 (ref) vs Q4: 1.23 (1.17, 1.29)
		Q1 (ref) vs Q5: 1.27 (1.21, 1.34)
		P-trend: <0.0001
		Replacement of SFA with Other FAs
		Total CVD Mortality, HR (95% CI)
		MUFA (per 5%): 0.87 (0.81, 0.94)
		P-MUFA (per 5%): 0.90 (0.84, 0.97)
		Total PUFA (per 5%): 0.85 (0.82, 0.88)
		Marine n-3 PUFA: 0.96 (0.94, 0.99)
		n-6 PUFA (per 2%): 0.94 (0.92, 0.96)
		LA: 0.94 (0.92, 0.96)
		AA: 1.15 (1.08, 1.22)
		A-MUFA (per 5%), n-3 PUFA (per 0.3%), and ALA: All NS
		MUFA (Replacing CHO)
		Total CVD Mortality, HR (95% CI)
		MUFA: Continuous: NS
		Q1 (ref) vs Q2: 0.95 (0.91, 1.00)
		Q1 (ref) vs Q3: 0.91 (0.86, 0.96)
		Q1 (ref) vs Q4: 0.92 (0.87, 0.98)
		Q1 (ref) vs Q5: 0.95 (0.88, 1.01)
		P-trend: 0.42
		Animal-MUFA: Continuous: 1.04 (1.02, 1.07)
		Q1 (ref) vs Q2: 1.02 (0.98, 1.06)
		Q1 (ref) vs Q3: 0.99 (0.94, 1.04)
		Q1 (ref) vs Q4: 1.06 (1.00, 1.11)
		Q1 (ref) vs Q5: 1.09 (1.03, 1.16)
		P-trend: 0.0015
		Plant-MUFA: Continuous: NS
		Q1 (ref) vs Q2: 0.99 (0.96, 1.03)
		Q1 (ref) vs Q3: 0.93 (0.89, 0.97)
		Q1 (ref) vs Q4: 0.94 (0.89, 0.97)Q1 (ref) vs Q5: 0.94 (0.89, 0.99)
		P-trend: 0.015
		Sensitivity analyses produced similar results. See Zhuang, 2019 for details.
		
		(Continued on next page)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education, income), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, marital status, history of hypertension, history of hypercholesterolemia, perceived health condition, history of heart disease, stroke, or diabetes mellitus, multi-vitamin use, aspirin use, hormones use (women), energy from protein, other FAs as applicable.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Key Research and Development Program; National Natural Science Foundation of China; China National Program for Support of Top-notch Young Professionals; Intramural Research Program of the NIH, NCI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Zhuang, 2019a (CONTINUED)
PCS, NIH-AARP Diet and Health Study, U.S.
Baseline N=567,169 Analytic N=521,120 (Attrition: 8%)
 	
Participant characteristics at baseline:
• AARP members 50-71y of age at baseline
• Age: ~63y
• Sex (female): 41.2%
• Race/ethnicity: ~91% White, ~4% Black, ~2% Hispanic, ~1% Asian;
• SES: Annual household income, ~$48,700; College graduate or postgraduate, ~39%
• Anthropometry: BMI, ~26
Fat intake at baseline:
• See "Exposures" in next column
Blood lipids and BP at baseline:
• History of hypercholesterolemia: ~26%
• History of hypertension: ~23%
 	
Summary of findings:
In men and women, higher intake of SFA at ~63y of age was associated with higher risk of CVD mortality during ~16y of follow-up when replacing CHO. Replacing SFA intake with total MUFA, plant-MUFA, total PUFA, marine n-3 PUFA, n-6 PUFA, or LA intake was associated with lower risk of CVD mortality. Replacing SFA intake with AA intake was associated with higher risk of CVD mortality. Higher intake of plant-MUFA, total PUFA, marine n-3 PUFA, total n-6 PUFA, and ALA were associated with lower risk of CVD mortality when replacing CHO. Higher intake of animal-MUFA and AA were associated with higher risk of CVD mortality when replacing CHO. The n-6/n-3 PUFA ratio was not associated with CVD mortality.
	Exposures (all continuous and quintiles, replacing CHO unless otherwise noted):
	• PUFA (%E)
	  • Q1 (≤5.20), Q2 (5.20-6.27), Q3 (6.27-7.29), Q4 (7.29-8.64), Q5 (≥8.64)
	• Total n-3 PUFA (%E)
	  • Q1 (≤0.54), Q2 (0.54-0.63), Q3 (0.63-0.73), Q4 (0.73-0.87), Q5 (≥0.87)
	• ALA (%E)
	  • Q1 (≤0.48), Q2 (0.48-0.58), Q3 (0.58-0.67), Q4 (0.67-0.80), Q5 (≥0.80)
	• Marine n-3 PUFA (EPA+DHA; %E)
	  • Q1 (≤0.02), Q2 (0.02-0.03), Q3 (0.03-0.05), Q4 (0.05-0.08), Q5 (≥0.08)
	• Total n-6 PUFA (%E)
	  • Q1 (≤4.57), Q2 (4.57-5.56), Q3 (5.56-6.49), Q4 (6.49-7.73), Q5 (≥7.73)
	• LA (%E)
	  • Q1 (≤4.53), Q2 (4.53-5.50), Q3 (5.50-6.44), Q4(6.44-7.67), Q5(≥7.67)
	• AA (%E)
	  • Q1 (≤0.03), Q2 (0.03-0.04), Q3 (0.04-0.05), Q4 (0.05-0.07), Q5 (≥0.07)
	• n-6/n-3 PUFA ratios
	  • Q1 (≤7.43), Q2 (7.43-8.29), Q3 (8.29-9.08), Q4 (9.08-10.14), Q5 (≥10.14)
	
	Assessment method and timing:
	• Validated, self-administered, 124-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~16y of follow-up
	• CVD Mortality: Obtained via linkage to Social Security Administration Death Master File and National Death Index Plus
	• CVD Mortality: 38,747 cases
		PUFAs (Replacing CHO)
		Total CVD Mortality, HR (95% CI)
		Total PUFA: Continuous: NS
		Q1 (ref) vs Q2: 0.97 (0.94, 1.01)
		Q1 (ref) vs Q3: 0.95 (0.92, 0.99)
		Q1 (ref) vs Q4: 0.93 (0.90, 0.97)
		Q1 (ref) vs Q5: 0.94 (0.90, 0.98)
		P-trend: 0.0074
		Total n-3 PUFA: Continuous: NS
		Q1 (ref) vs Q2, Q3, Q4, and Q5: All NS
		P-trend: 0.95
		ALA: Continuous: NS
		Q1 (ref) vs Q2, Q3, Q4, and Q5: All NS
		P-trend: 0.16
		Marine n-3 PUFA: Continuous: 0.98 (0.97, 0.99)
		Q1 (ref) vs Q2: 0.96 (0.93, 0.99)
		Q1 (ref) vs Q3: 0.96 (0.93, 0.99)
		Q1 (ref) vs Q4: 0.93 (0.90, 0.96)
		Q1 (ref) vs Q5: 0.90 (0.87, 0.94)
		P-trend: <0.0001
		Total n-6 PUFA: Continuous: NS
		Q1 (ref) vs Q2: 0.97 (0.93, 1.00)
		Q1 (ref) vs Q3: 0.94 (0.90, 0.98)
		Q1 (ref) vs Q4: 0.92 (0.88, 0.97)
		Q1 (ref) vs Q5: 0.93 (0.88, 0.98)
		P-trend: 0.0065
		LA: Continuous: NS
		Q1 (ref) vs Q2: 0.96 (0.93, 1.00)
		Q1 (ref) vs Q3: 0.93 (0.89, 0.98)
		Q1 (ref) vs Q4: 0.92 (0.87, 0.96)
		Q1 (ref) vs Q5: 0.92 (0.87, 0.98)
		P-trend: 0.0038
		AA: Continuous: 1.03 (1.02-1.05)
		Q1 (ref) vs Q2: 1.02 (0.98, 1.05)
		Q1 (ref) vs Q3: 1.03 (0.99, 1.07)
		Q1 (ref) vs Q4: 1.07 (1.03, 1.11)
		Q1 (ref) vs Q5: 1.11 (1.06, 1.16)
		P-trend: <0.0001
		n-6/n-3 PUFA ratio:
		Q1 (ref) vs Q2, Q3, Q4, and Q5: All NS
		P-trend: 0.63
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education, income), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, marital status, history of hypertension, history of hypercholesterolemia, perceived health condition, history of heart disease, stroke, or diabetes mellitus, multi-vitamin use, aspirin use, hormones use (women), energy from protein, other FAs as applicable.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Key Research and Development Program; National Natural Science Foundation of China; China National Program for Support of Top-notch Young Professionals; Intramural Research Program of the NIH, NCI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Hisamatsu, 2013[166]
PCS, NIPPON, Japan
Baseline N=4,639 Analytic N=4,348 (Attrition: 6%)
 	
Participant characteristics at baseline:
• No CVD
• Age: Mean=49.3y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI, Mean~23
 	
Fat intake at baseline, Mean:
• Marine-derived n-3 PUFA (%E): Range 0.23-0.57
• ALA (%E): ~0.64
• SFAs (%E): ~5.65
• MUFA (%E): ~7.46
• PUFAs (%E):~ 5.3
 	
Blood lipids at baseline, Mean:
• TC (mg/dL): ~186
• SBP (mmHg): ~138
• DBP (mmHg): ~83
 	
Summary of findings:
In men without J-point elevation, dietary marine–derived n3FAs intake is not associated with risk of cardiac death.
	Exposures (medians):
	• Marine-derived n-3 PUFA intake (categorical, %E), Mean (SD)
	  • %E <0.35 (n=2111), 0.23 (0.07)
	  • %E≥0.35 (n=2237), 0.57 (0.22)
	
	Diet assessment method and timing:
	• 3-d weighed food records of households (National Nutritional Survey of Japan (NNSJ)
	  • Estimated individual family member nutrient intake by dividing household intake data proportionally using average intakes by sex and age groups calculated for NNSJ80
	• Administered at baseline by trained staff
	
	Outcomes and assessment methods:
	• Assessed during 24y (mean=20.4y, SD=6.1y) of follow-up
	• Cardiac death risk assessed yearly via government registration records identifying cause of death
	  • Cardiac death: 200 cases
		Marine-derived n-3 PUFA
		Cardiac deaths, HR (95% CI),
		High marine-derived n-3 (%E≥0.35), no J-point elevation vs low marine-derived n-3 (%E <0.35), no J-point elevation:
		1.01 (0.74–1.38), P>0.05
			Key confounders NOT accounted for:
			SES, race/ethnicity, TEI, physical activity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, smoking, alcohol intake
			
			Additional model adjustments:
			BMI, medication status, SBP, serum total cholesterol, blood glucose, heart rate, left ventricular hypertrophy on electrocardiography, suspected coronary heart disease on electrocardiography, PUFA, SFA, sodium, and fiber intake
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Japanese Ministry of Health, Labor and Welfare

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Nakamura, 2013[187]
PCS, NIPPON, Japan
Baseline N=8,384 Analytic N=7,819 (Attrition: 7%)
 	
Participant characteristics at baseline:
• No CVD
• Diabetes: ~5%
• Age: Mean~55y
• Sex (female): 58%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI, Mean~23
 	
Fat intake at baseline, Mean (SD):
• SFAs (%E): Men 5.9 (1.4), women 6.5 (1.5)
• PUFAs (%E): Men: 5.6 (1.3), women, 6.1 (1.4)
• Cholesterol (mg/1000kcal): Men: 183.6 (53.2), Women: 200.6 (59.0)
 	
Blood lipids at baseline, Mean:
• TC (mg/dL): ~206
• HDL (mg/dL): ~50
 	
Summary of findings:
SFA intake was significantly positively associated with CHD mortality in women, but not in men after 14y follow-up. Polyunsaturated fat and dietary cholesterol intakes were not associated with CHD mortality in middle-aged men or women.
	Exposures:
	• SFA intake (quintiles, %E), range
	  • Q1 1.2-4.7
	  • Q2 4.7-5.5
	  • Q3 5.5-6.2
	  • Q4 6.2-7.0
	  • Q5 7.0-13.0
	• SFA intake (categorical, %E)
	  • SFA intake ≤7%E
	  • SFA intake >7%E
	• PUFA intake (quintiles, %E), Mean (SD)
	  • Q1 (Men 4.9(0.05), women 5.2(0.05))
	  • Q5 (Men 6.1(0.05), women 6.6(0.05))
	• Cholesterol intake (quintiles, mg/1000kcal)
	  • Quintiles NR
	
	Diet assessment method and timing:
	• 3-d weighed household food records National Nutritional Survey of Japan (NNSJ) 1990
	• Estimated individual family member nutrient intake by dividing household intake data from NNSJ90 proportionally using average intakes by sex and age groups calculated for NNSJ95
	• Administered at baseline by trained staff
	
	Outcomes and assessment methods:
	• Assessed during mean 13.9y, SD= 2.9 of follow-up
	• CHD mortality risk assessed yearly via local government registration records identifying cause of death
	  • Fatal CHD: 72 cases (men 42, women 30)
		CHD deaths, HR (95% CI)
		Men:
		SFA (per 1 quintile increase)
		NS, P-trend=0.46
		SFA (categorical, >7%E)
		SFA >7%E (ref) vs SFA≤7%E: NS, P-trend=0.712
		PUFA (per 1 quintile increase)
		NS, P-trend=0.64
		Dietary cholesterol (per 1 quintile increase)
		NS, P-trend=0.511
		Women:
		SFA (per 1 quintile increase)
		1.34, 95% CI 1.02-1.74, P-trend=0.034
		SFA (categorical, >7%E)
		SFA >7%E (ref) vs SFA≤7%E: 2.59, 95% CI 1.19, 5.63, P=0.016
		PUFA (per 1 quintile increase)
		NS, P-trend=0.974
		Dietary cholesterol (per 1 quintile increase)
		NS, P-trend=0.544
			Key confounders NOT accounted for:
			SES, race/ethnicity, TEI, physical activity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, smoking, alcohol intake
			
			Additional model adjustments:
			BMI, hypertension, diabetes, and dietary intake of vegetables, fruits, and fish
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Japanese Ministry of Health, Labor and Welfare

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Miyagawa, 2014[185]
PCS, NIPPON, Japan
Baseline N=10,546 Analytic N=9,190 (Attrition: 13%)
 	
Participant characteristics at baseline:
• No CVD
• Age: Mean=50.2y
• Sex (female): 56.2%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI, Mean~22.7
 	
Fat intake at baseline, Mean:
• Long chain n-3 PUFA (%E): 0.37
• SFAs (%E): ~5.9
• PUFAs (%E):~ 4.3
• Total n-3 PUFA (%E): ~1.1
 	
Blood lipids at baseline, Mean:
• TC (mg/dL): ~189
 	
Summary of findings:
In men and women, long chain n-3 polyunsaturated fat intake was inversely associated with risk of total CVD, however, no significant association was found with CHD death or fatal stroke during 24y of follow-up. Analysis stratified by age group at baseline found long chain n-3 polyunsaturated fat intake in subjects 30 to 59y inversely associated with CVD death and stroke death during 24y follow-up and no association was found with CHD deaths or in subjects greater than 60y.
	Exposures (medians):
	• Long chain n-3-PUFA intake (quartiles, g/d, Mean (SD))
	  • Q1 0.42 (0.15)
	  • Q2 0.74 (0.17)
	  • Q3 1.06 (0.25)
	  • Q4 1.72 (0.62)
	• DHA (quartiles, %E)
	  • Q1 (Men, 0.00-0.15, Women, 0.01-0.16)
	  • Q2 (Men, 0.16-0.22, Women, 0.17-0.23)
	  • Q3 (Men, 0.23-0.31, Women, 0.24-0.34)
	  • Q4 (Men, 0.32-1.39, Women, 0.35-1.45)
	
	Diet assessment method and timing:
	• 3-d weighed food records (National Nutritional Survey of Japan)
	• Administered at baseline by trained staff
	
	Outcomes and assessment methods:
	• Assessed during 24y of follow-up
	• CVD mortality risk assessed yearly via local government registration records identifying cause of death
	  • Fatal CVD: 879 cases
	  • Fatal CHD: 171 cases
	  • Fatal stroke: 417 cases
		Long chain n-3 PUFA
		CVD deaths, HR (95% CI),
		All:
		Q1 (ref) vs Q2: 0.85 (0.70, 1.03)
		Q1 (ref) vs Q3: 0.85 (0.70,1.03)
		Q1 (ref) vs Q4: 0.80 (0.66, 0.96)
		P for trend 0.038
		Age 30-59y:
		Q1 (ref) vs Q2: 0.92 (0.64,1.32)
		Q1 (ref) vs Q3: 0.75 (0.51,1.09)
		Q1 (ref) vs Q4: 0.68 (0.46, 1.00)
		P for trend 0.031
		Age >60y: Q1 (ref) vs Q2, Q3 or Q4: All NS
		P-trend=0.323
		CHD deaths, HR (95% CI)
		All, Age 30-59y, and Age >60y:
		Q1 (ref) vs Q2, Q3 or Q4: All NS
		P-trend: All >0.34
		Stroke deaths, HR (95% CI)
		All: Q1 (ref) vs Q2, Q3 or Q4: All NS
		P-trend=0.1115
		Age 30-59y:
		Q1 (ref) vs Q2: 1.10 (0.64, 1.87)
		Q1 (ref) vs Q3: 0.95 (0.55, 1.64)
		Q1 (ref) vs Q4: 0.59 (0.33, 1.08)
		P for trend 0.043
		Age >60y: Q1 (ref) vs Q2, Q3 or Q4: All NS
		P-trend=0.497
		DHA
		CVD deaths, HR (95% CI)
		Q1 (ref) vs Q2: 0.87 (0.72-1.05)
		Q1 (ref) vs Q3: 0.84 (0.69-1.01)
		Q1 (ref) vs Q4: 0.79 (0.65-0.96)
		P for trend 0.023
		CHD deaths, HR (95% CI)
		Q1 (ref) vs Q2, Q3 or Q4: All NS
		P-trend=0.261
		Stroke deaths, HR (95% CI)
		Q1 (ref) vs Q2, Q3 or Q4: All NS
		P-trend=0.121
		Analysis stratified by gender and analysis by total n-3FA, and DHA were all NS. See Miyagawa, 2013 for details.
			Key confounders NOT accounted for:
			Race/ethnicity, TEI, physical activity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, SES (residential area), smoking, alcohol intake
			
			Additional model adjustments:
			BMI, antihypertensive medication, SBP, total cholesterol, blood glucose, and dietary factors including SFA, PUFA, vegetable protein, fiber, and sodium
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Japanese Ministry of Health, Labor and Welfare

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Goldbohm, 2011[162]
PCS, NLCS (Netherlands Cohort Study), Netherlands
Baseline N=120,852 Analytic N=20,782 (Attrition: 83%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: 55-59y ~37%,60-64y ~34%,65-69y ~29%
• Sex (female): ~38%
• Race/ethnicity: NR
• SES: Education: Primary ~28%, Extended primary ~22%, Secondary (including vocational) ~36%, College/university ~14%
• Anthropometry: BMI ≤22 ~24%, 23-24 ~30%, 25-26 ~24%, ≥27 ~22%
 	
Fat intake at baseline, Mean:
• Butter: Men ~9 g/d, Women ~8 g/d
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Butter was significantly associated with higher incidence of CHD in women only. Butter was not associated with incidence of stroke for men and women.
	Exposures:
	• Butter (categorical; continuous per 10 g/d)
	  • Category 1 (ref): 0 g/d
	  • Category 2: Men 25 g/d; Women 20 g/d
	Assessment method and timing:
	• Validated, semi-quantitative 150-item FFQ to assess usual food intake in previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 10 y of follow-up
	• Incident ischemic heart disease (IHD; fatal & nonfatal), stroke: Dutch Central Bureau of Genealogy and the Dutch Central Bureau of Statistics
	  • IHD: 2689 cases
	  • Stroke: 842 cases
		Incident CHD, HR (95% CI)
		Butter
		Men:
		C1 (ref) vs C2: NS
		Continuous per 10 g/d): NS
		Women:
		C1 (ref) vs C2: NS
		Continuous per 10 g/d: 1.13 (1.02, 1.25)
		
		Incident stroke, HR (95% CI)
		Butter
		Men:
		C1 (ref) vs C2: NS
		Continuous per 10 g/d: NS
		Women:
		C1 (ref) vs C2: NS
		Continuous per 10g/d: NS
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			BMI, multivitamin use, energy-adjusted MUFA and PUFA, vegetable and fruit consumption
			
			Limitations:
			• Not all key confounders adjusted for
			• Potential bais in classification of exposures due to butter as a proxy for types of fats
			• Potential missing data bias due to unknown attrition from missing data
			• No preregistered statistical analyis plan
			
			Funding sources:
			Dutch Dairy Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Gardener, 2011[161]
PCS, NOMAS (Northern Manhattan Study), U.S.
Baseline N=3,298 Analytic N=2,568 (Attrition: 22%)
 	
Participant characteristics at baseline:
• 100% without MI and never diagnosed with Ischemic stroke
• Age: Mean: 69 y (SD=10)
• Sex (female): 64%
• Race/ethnicity: Hispanic 55%, Black 24%, White 21%
• SES: High school completion: Yes 45%, No 55%
• Anthropometry: NR
 	
Fat intake at baseline, Mean (SD):
• MUFA:SFA: 1.20 g/d (0.34)
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
MUFA:SFA ratio was not significantly associated with vascular deaths.
	Exposures:
	• MUFA:SFA (continuous, g/d)
	Assessment method and timing:
	• Interview-administered, validated FFQ (Block National Cancer Institute) to assess usual intake in the previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 9 y of follow-up
	• Vascular deaths: follow-up, medical records
	• Vascular events: 518 cases
	  • Ischemic strokes: 171
	  • MI: 133
	  • Vascular deaths: 314
		Vascular deaths, HR (95% CI)
		MUFA:SFA: NS
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (educational level), TEI excluding alcohol, alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			All Mediterranean-style diet score components (alcohol, fish, legumes, vegetables, fruit, cereal, meat, dairy)
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (PUFA)
			• Risk of missing data bias due to relatively high attrition
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Institute of Neurological Disorders and Stroke

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Wilk, 2012[219]
PCS, PHS (Physicians' Health Study), U.S.
Baseline N=19,649 Analytic N=19,097 (Attrition: 3%)
 	
Participant characteristics at baseline:
• 100% male physicians
• Age: ~66 y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI ~26
 	
Fat intake at baseline, Mean (SD):
See "Results"
 	
Blood lipids and BP at baseline:
• Hypertension: 43%
• High cholesterol: 42%
 	
Summary of findings:
Marine n-3 FAs and ALA were not associated with incidence of heart failure in male physicians.
	Exposures:
	• Marine n-3 FAs (EPA+DHA+DPA) (quintiles), Median
	  • Q1: 0.079 g/d
	  • Q3: 0.152 g/d
	  • Q5: 0.397 g/d
	• ALA (quintiles), Median
	  • Q1: 0.576 g/d
	  • Q3: 0.765 g/d
	  • Q5: 1.0 g/d
	Assessment method and timing:
	• Validated FFQs
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during 13 y of follow-up
	• Heart failure: follow-up questionnaires, self-reported diagnosis, medical records
	  • Heart failure: 703 cases
		Heart failure, HR (95% CI)
		Marine n-3 FAs:
		Q1 vs Q2, Q3, Q4, Q5: All NS
		P linear trend=NS
		ALA:
		Q1 vs Q2, Q3, Q4, Q5: All NS
		P linear trend=NS
			Key confounders NOT accounted for:
			Sex, age, race/ethnicity, SES (educational level), TEI, family history of CVD or diabetes
			
			Key confounders accounted for:
			Alcohol intake, physical activity, smoking
			
			Additional model adjustments:
			Atrial fibrillation, valvular heart disease, hypertension, BMI
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (other types of fats)
			• No preregistered statistical analysis plan
			
			Funding sources:
			NHLBI; Office of Dietary Supplements, NIH; National Cancer Institute, National Heart, Lung, and Blood Institute

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Guasch-Ferré, 2014[164]
PCS, PREDIMED, Spain
Baseline N=7,447 Analytic N=7,216 (Attrition: 3%)
 	
Participant characteristics at baseline:
• High CVD risk, but no CVD
• Type 2 diabetes: ~49%
• Age: Mean=67y
• Sex (female): 57.4%
• Race/ethnicity: NR
• SES: Education: 78% Illiterate/primary, 15% Secondary, 7% Academic/graduate
• Anthropometry: BMI, Mean~30.0
 	
Fat intake at baseline: See olive oil intake under exposures
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: ~72%
• Hypertension: ~83%
 	
Summary of findings:
Higher Baseline total olive oil consumption, was associated with a significant reduced risk of major cardiovascular events and cardiovascular mortality in an elderly Mediterranean population at high cardiovascular risk.
	Exposures:
	• Olive oil intake at baseline (tertiles, energy-adjusted,g/d)
	  • T1 (ref; mean: 21.4, SD=8.00)
	  • T2 (mean 38.8, SD=11.6)
	  • T3 (mean 56.9, SD=10.8)
	• Olive oil intake (energy adjusted continuous, per 10g/day)
	
	Diet assessment method and timing:
	• Validated 137-item semi-quantitative FFQ (3 questions related to olive oil); during face-to-face interviews, participants were asked about frequency of consumption and specific varieties
	• Administered at baseline and during yearly follow-ups
	
	Outcomes and assessment methods:
	• Assessed during median 4.8y of follow-up
	• Major CVD events and mortality ascertained by yearly questionnaires and exams, primary care physicians, medical records and linkage to the National Death Index
	  • Major cardiovascular event (composite of myocardial infarction, stroke and death from cardiovascular causes): 277 cases
	  • Cardiovascular deaths: 81 cases
		Major cardiovascular event, HR (95% CI)
		Olive oil intake (tertiles)
		T1 (ref) vs T2: 0.78 (0.58, 1.04)
		T1 (ref) vs T3: 0.65 (0.47, 0.89),
		P for trend 0.01
		Total olive oil intake (continuous)
		0.87 (0.81, 0.94)
		Cardiovascular deaths, HR (95% CI)
		Olive oil intake (tertiles)
		T1 (ref) vs T2: 0.69 (0.40, 1.18)
		T1 (ref) vs T3: 0.52 (0.29, 0.93)
		P for trend 0.04
		Olive oil intake (continuous)
		0.84 (0.73, 0.96)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, SES (education), TEI, smoking, alcohol intake, physical activity
			
			Additional model adjustments:
			Intervention group, BMI, prevalence of diabetes, hypertension and hypercholesterolemia, use of hypertensive medication, use of statins, baseline Mediterranean diet adherence
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Spanish Ministry of Health, Centre Català de la Nutrició de l'Institut d'Estudis Catalans, the Fundación Patrimonio Comunal Olivarero and Hojiblanca SA, California Walnut Commission, Borges SA, and Morella Nuts

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Guasch-Ferré, 2015[163]
PCS, PREDIMED, Spain
Baseline N=7,447 Analytic N=7,038 (Attrition: 4%)
 	
Participant characteristics at baseline:
• High CVD risk, but no CVD
• Type 2 diabetes: ~49%
• Age: Mean=67y, SD=6
• Sex (female): 57.4%
• Race/ethnicity: NR
• SES: Education: 78% Illiterate/primary, 19% Secondary, 4% Academic/graduate
• Anthropometry: BMI, Mean~30.0
 	
Fat intake at baseline, Mean (SD):
• SFA (%E): 9.9 (2.2)
• MUFA (%E): 19.6 (4.5)
• PUFA (%E): 6.2 (2.0)
• Trans FA (%E): 0.22 (0.14)
• Dietary Cholesterol (mg/d): 361.3 (123.3)
• Total fat (%E): 39.3 (6.8)
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: ~72%
• Hypertension: ~83%
 	
Summary of findings:
Higher intakes of MUFAs and PUFAs were significantly associated with a lower risk of CVD and higher intakes of SFA from pastries and processed foods were significantly associated with a higher risk of CVD in an elderly Mediterranean population with high risk of CVD.
	Exposures:
	• SFA (quintiles; %E)
	  • Q1 (ref; mean=7.0, SD=0.8)
	  • Q5 (mean=13.2, SD=1.4)
	• MUFA (quintiles; %E)
	  • Q1 (ref; mean: 13.4, SD=1.8)
	  • Q5 (mean=26.1, SD=2.4)
	• PUFA (quintiles; %E)
	  • Q1 (ref; mean: 4.0, SD=0.47)
	  • Q5 (mean 9.4, SD=1.8)
	• Isocaloric replacement of SFA with CHO, MUFA and PUFA (continuous, median intake for each quintile, %E)
	• SFA intake from different food source
	  • Vegetable (oils, nuts, vegetables, margarine)
	  • Dairy
	  • Pastry and other processed foods (cookies, donuts, bakery, sauces, pizza, other)
	  • Meat and processed-meat (sausages, hamburger, other, and eggs)
	  • Fish/seafood
	
	Diet assessment method and timing:
	• Validated 137-item semi-quantitative FFQ (3 questions related to olive oil); during face-to-face interviews, participants were asked about frequency of consumption and portion
	• Administered at baseline and during yearly follow-ups
	
	Outcomes and assessment methods:
	• Assessed during median 6y of follow-up
	• Major CVD events and mortality ascertained by yearly questionnaires and exams, primary care physicians, medical records and linkage to the National Death Index
	  • Major cardiovascular event (composite of myocardial infarction, stroke and death from cardiovascular causes): 336 cases
	  • Cardiovascular deaths: 102 cases
		Major cardiovascular event, HR (95% CI)
		SFA
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.07
		MUFA
		Q1 (ref) vs Q2: 0.88 (0.61, 1.26)
		Q1 (ref) vs Q3: 0.66 (0.44, 0.98)
		Q1 (ref) vs Q4: 0.76 (0.50, 1.16)
		Q1 (ref) vs Q5: 0.50 (0.31, 0.81)
		P for trend< 0.01
		PUFA
		Q1 (ref) vs Q2: 0.78 (0.56, 1.09)
		Q1 (ref) vs Q3: 0.72 (0.51, 1.02)
		Q1 (ref) vs Q4: 0.71 (0.51, 1.01)
		Q1 (ref) vs Q5: 0.68 (0.48, 0.96)
		P for trend= 0.04
		
		Cardiovascular deaths, HR (95% CI)
		PUFA
		Q1 (ref) vs Q5: 0.37 (0.18, 0.76)
		P for trend <0.01
		MUFA
		Q1 (ref) vs Q5: 0.78 (0.34, 0.97)
		P for trend <0.01
		SFA
		Q1 (ref) vs Q5: NS; P-trend=NR
		
		(Continued on next page)
			Key confounders NOT accounted for: Race/ethnicity
			Key confounders accounted for: Age, sex, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD
			Additional model adjustments: Intervention group, BMI, baseline diabetes, hypertension and hypercholesterolemia, use of hypertensive medication, use of oral antidiabetic agents, use of lipid-lowering drugs, updated quintiles of fiber, protein, and dietary cholesterol and other subtypes of fat
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			Funding sources: Spanish Ministry of Health, Centre Català de la Nutrició de l'Institut d'Estudis Catalans, Instituto de Salud Carlos III, Centro Nacional de Investigaciones Cardiovasculares, Fondo de Investigación Sanitaria–Fondo Europeo de Desarrollo Regional, Ministerio de Ciencia e Innovación , Fundación Mapfre 2010, Consejería de Salud de la Junta de Andalucía, Public Health Division of the Dept of Health of the Autonomous Govt of Catalonia, Generalitat Valenciana, the Regional, Government of Navarra, Fundación Patrimonio Comunal Olivarero and Hojiblanca SA, California Walnut Commission, Borges SA, and Morella Nuts SA, CIBEROBN (Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y Nutrición) and CIBERDEM -.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Guasch-Ferré, 2015 (CONTINUED)
PCS, PREDIMED, Spain
Baseline N=7,447 Analytic N=7,038 (Attrition: 4.2%)
 	
Participant characteristics at baseline:
• High CVD risk, but no CVD
• Type 2 diabetes: ~49%
• Age: Mean=67y, SD=6
• Sex (female): 57.4%
• Race/ethnicity: NR
• SES: Education: 78% Illiterate/primary, 19% Secondary, 4% Academic/graduate
• Anthropometry: BMI, Mean~30.0
 	
Fat intake at baseline, Mean (SD):
• SFA (%E): 9.9 (2.2)
• MUFA (%E): 19.6 (4.5)
• PUFA (%E): 6.2 (2.0)
• Trans FA (%E): 0.22 (0.14)
• Dietary Cholesterol (mg/d): 361.3 (123.3)
• Total fat (%E): 39.3 (6.8)
 	
Blood lipids and BP at baseline:
• Hypercholesterolemia: ~72%
• Hypertension: ~83%
 	
Summary of findings:
Higher intakes of MUFAs and PUFAs were significantly associated with a lower risk of CVD and higher intakes of SFA from pastries and processed foods were significantly associated with a higher risk of CVD in an elderly Mediterranean population with high risk of CVD.
	Exposures:
	• SFA (quintiles; %E)
	  • Q1 (ref; mean=7.0, SD=0.8)
	  • Q5 (mean=13.2, SD=1.4)
	• PUFA (quintiles; %E)
	  • Q1 (ref; mean: 4.0, SD=0.47)
	  • Q5 (mean 9.4, SD=1.8)
	• MUFA (quintiles; %E)
	  • Q1 (ref; mean: 13.4, SD=1.8)
	  • Q5 (mean=26.1, SD=2.4)
	• Isocaloric replacement of SFA with CHO, MUFA and PUFA (continuous, median intake for each quintile, %E)
	• SFA intake from different food source
	  • Vegetable (oils, nuts, vegetables, margarine)
	  • Dairy
	  • Pastry and other processed foods (cookies, donuts, bakery, sauces, pizza, other)
	  • Meat and processed-meat (sausages, hamburger, other, and eggs)
	  • Fish/seafood
	
	Diet assessment method and timing:
	• Validated 137-item semi-quantitative FFQ (3 questions related to olive oil); during face-to-face interviews, participants were asked about frequency of consumption and portion
	• Administered at baseline and during yearly follow-ups
	
	Outcomes and assessment methods:
	• Assessed during median 6y of follow-up
	• Major CVD events and mortality ascertained by yearly questionnaires and exams, primary care physicians, medical records and linkage to the National Death Index
	  • Major cardiovascular event (composite of myocardial infarction, stroke and death from cardiovascular causes): 336 cases
	  • Cardiovascular deaths: 102 cases
		SFA sources
		Major cardiovascular event*, HR (95% CI)*
		Vegetable SFA
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		Q1 vs Q5: 0.53 (0.30, 0.93)
		P-trend=0.06
		Dairy SFA
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.54
		Pastry and other processed foods SFA
		Q1 (ref) vs Q2: 1.21 (0.83, 1.78)
		Q1 (ref) vs Q3: 1.09 (0.74, 1.63)
		Q1 (ref) vs Q4: 1.44 (0.99, 2.09)
		Q1 (ref) vs Q5: 1.46 (1.01, 2.13)
		P for trend= 0.04
		Meat, processed-meat and eggs SFA
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend=0.28
		Fish/seafood SFA
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		Q1 vs Q5: 0.70 (0.46, 0.99)
		P-trend=0.11
		
		Replacement
		Major cardiovascular event, HR (95% CI)
		Replacement of CHO (per 5%):
		With MUFA: 0.79 (0.68, 0.92), P<0.05
		With PUFA: 0.78 (0.59, 0.97), P<0.05
		With SFA: 1.35 (1.03, 1.77), P<0.05
		Replacement of SFA (per 5%E):
		With MUFA: **0.63 (0.43, 0.94), P<0.05**
		With PUFA: **0.67 (0.45, 0.98), P<0.05**
			Key confounders NOT accounted for: Race/ethnicity
			Key confounders accounted for: Age, sex, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD
			Additional model adjustments: Intervention group, BMI, baseline diabetes, hypertension and hypercholesterolemia, use of hypertensive medication, use of oral antidiabetic agents, use of lipid-lowering drugs, updated quintiles of fiber, protein, and dietary cholesterol and other subtypes of fat
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			Funding sources: Spanish Ministry of Health, Centre Català de la Nutrició de l'Institut d'Estudis Catalans, Instituto de Salud Carlos III, Centro Nacional de Investigaciones Cardiovasculares, Fondo de Investigación Sanitaria–Fondo Europeo de Desarrollo Regional, Ministerio de Ciencia e Innovación , Fundación Mapfre 2010, Consejería de Salud de la Junta de Andalucía, Public Health Division of the Dept of Health of the Autonomous Govt of Catalonia, Generalitat Valenciana, the Regional, Government of Navarra, Fundación Patrimonio Comunal Olivarero and Hojiblanca SA, California Walnut Commission, Borges SA, and Morella Nuts SA, CIBEROBN (Centro de Investigación Biomédica en Red de Fisiopatología de la Obesidad y Nutrición) and CIBERDEM -.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Sala-Vila, 2016[202]
PCS, PREDIMED, Spain
Baseline N=7,447 Analytic N=7202 (Attrition: 3%)
 	
Participant characteristics at baseline:
• High CVD risk, but no CVD
• Type 2 diabetes: 48.8%
• Age: Mean=67y
• Sex (female): 57.1%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI, Mean=30.0
 	
Fat intake at baseline, Mean:
• SFAs (g/d): 24.8
• MUFAs (g/d): 48.2
• PUFAs (g/d): 13.0
• ALA (g/d): 1.40
• ALA (%E): 0.06
• Cholesterol (mg/d): 361
 	
Blood lipids and BP at baseline:
• Dyslipidemia: 72.2%
• Hypertension: 82.7%
 	
Summary of findings:
In a high cardiovascular risk population, long chain n-3 polyunsaturated fat intake greater than 500mg/day had a protective effect on CVD and CHD mortality, but not on sudden cardiac death or fatal stroke. ALA intake greater than 0.7 percent energy per day had no effect on CVD and CHD mortality related outcomes.
	Exposures:
	• ALA intake (categorical, %E)
	  • ALA intake ≥0.7%E
	  • ALA intake <0.7%E
	• Long chain (LC) n-3-PUFA intake (categorical, mg/d)
	  • LCn-3 ≥500mg/d
	  • LCn-3 <500mg/d
	Diet assessment method and timing:
	• Validated 137-item semi-quantitative FFQ (8 items on seafood and 6 items regarding major ALA sources); during face-to-face interviews, participants were asked about frequency of consumption and portion
	• Administered at baseline and during yearly follow-ups.
	
	Outcomes and assessment methods:
	• Assessed during ~5.9y of follow-up
	• CVD and CHD mortality assessed yearly via contact with physicians and yearly review of medical records and linkage with the National Death Index
	  • Fatal CVD: 104 cases
	  • Fatal CHD: 55 cases
	  • Sudden cardiac death: 32 cases
	  • Fatal stroke: 25 cases
		ALA
		Fatal CVD, HR (95% CI)
		ALA intake <0.7%E (Ref) vs ALA intake ≥0.7%E: P>0.05
		Fatal CHD, HR (95% CI)
		ALA intake <0.7%E (Ref) vs ALA intake ≥0.7%E: P>0.05
		Sudden cardiac death, HR (95% CI)
		ALA intake <0.7%E (Ref) vs ALA intake ≥0.7%E: P>0.05
		Fatal stroke, HR (95% CI)
		ALA intake <0.7%E (Ref) vs ALA intake ≥0.7%E: P>0.05
		
		LCn-3PUFA
		Fatal CVD, HR (95% CI)
		LCn-3PUFA intake <500mg/d (Ref) vs LCn-3PUFA intake ≥500mg/d:
		0.614 (0.393–0.960), P=0.032
		Fatal CHD, HR (95% CI)
		LCn-3PUFA intake <500mg/d (Ref) vs LCn-3PUFA intake ≥500mg/d:
		0.537 (0.292–0.988), P=0.046
		Sudden cardiac death, HR (95% CI)
		LCn-3PUFA intake <500mg/d (Ref) vs LCn-3PUFA intake >500mg/d: P>0.05
		Fatal stroke, HR (95% CI)
		LCn-3PUFA intake <500mg/d (Ref) vs LCn-3PUFA intake ≥500mg/d: P>0.05
			Key confounders NOT accounted for:
			Race/ethnicity, SES
			
			Key confounders accounted for:
			Age, sex, TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes
			
			Additional model adjustments:
			Intervention group, BMI, history of diabetes, history of hyperlipidemia, history of hypertension, and dietary factors (fiber, vegetables, fruits, and red meat)
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (e.g. SFA, PUFA, MUFA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Instituto de Salud Carlos III (Spanish Ministry of Economy), Spanish Ministry of Science and Innovation, California Walnut Commission, Spanish Ministry of Economy and Competitiveness

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Praagman, 2016a[197]
PCS, Rotterdam Study, Netherlands
Baseline N=7,983, Analytic N=4,722 (Attrition: 40%)
 	
Participant characteristics at baseline:
• Noninstitutionalized men and women 55y or older without prevalent CVD
• Age: Mean~67y
• Sex (female): 62%
• Race/ethnicity: NR
• SES: High education level, ~9%
• Anthropometry: BMI, Mean~26.3
 	
Fat intake at baseline:
• Total SFA (quintiles; %E), Mean (SD)
  • Q1: 11.2 (1.4)
  • Q2: 13.9 (0.5)
  • Q3: 15.6 (0.5)
  • Q4: 17.5 (0.6)
  • Q5: 20.8 (1.9)
 	
Blood lipids and BP at baseline:
• HDL (mmol/L): Mean=1.4, SD=0.4
• Hypertension: 53%
 	
Summary of findings:
In men and women, intake of total SFA and SFA from different sources at ~67y of age was not significantly associated with incident CHD during ~16.3y of follow-up. Replacement of SFA with animal protein, but not other macronutrients, was significantly associated with higher risk of incident CHD.
	Exposures:
	• Total SFA (continuous; per 5%E)
	• SFA from sources:
	  • Butter (among consumers only, n=1551; continuous; per 2.8%E)
	  • Cheese (continuous; per 1.9%E)
	  • Milk (continuous; per 1.5%E)
	  • Meat (continuous; per 1.5%E)
	  • Cakes (continuous; per 1.5%E)
	  • Hard and solid fats (continuous; per 1.5%E)
	  • Soft and liquid fats (continuous; per 1.5%E)
	  • Other sources (continuous; per 1.5%E)
	• Replacement of SFA with:
	  • CHO (continuous; per 5%E)
	  • Low-GI CHO (continuous; per 5%E)
	  • Medium-GI CHO (continuous; per 5%E)
	  • High-GI CHO (continuous; per 5%E)
	  • Cis-MUFA (continuous; per 5%E)
	  • PUFA (continuous; per 5%E)
	  • Protein (continuous; per 5%E)
	  • Animal protein (continuous; per 5%E)
	  • Vegetable protein (continuous; per 5%E)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 170-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~16.3y of follow-up
	• Incident CHD: Obtained through linkage with digital municipality records and digital files from general practitioners; Incident CHD included fatal and nonfatal MI, and definite coronary mortality
	  • Total: 659 cases
		Incident CHD, HR (95% CI)
		Total SFA: 1.13 (0.94, 1.36)
		Sources:
		Butter: 1.08 (0.88, 1.31)
		Cheese: 1.03 (0.94, 1.13)
		Milk: 1.04 (0.94, 1.14)
		Meat: 1.09 (0.99, 1.20)
		Cakes: 1.02 (0.92, 1.13)
		Hard and solid fats: 1.05 (0.92, 1.19)
		Soft and liquid fats: 1.07 (0.97, 1.18)
		Other sources: 1.05 (0.96, 1.15)
		Replacement of SFA with:
		CHO: 0.90 (0.80, 1.02)
		Low-GI CHO: 0.96 (0.78, 1.19)
		Medium-GI CHO: 0.84 (0.68, 1.05)
		High-GI CHO: 0.94 (0.77, 1.14)
		cis-MUFA: 1.09 (0.98, 1.22)
		PUFA: 0.90 (0.71, 1.15)
		Protein: 1.22 (1.00, 1.49)
		Animal Protein: 1.24 (1.01, 1.51)
		Vegetable Protein: 0.88 (0.50, 1.53)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education, income), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, WC, intake of trans-fat, vegetable protein, animal protein, cholesterol, fiber, and vitamin C
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of institutionalized participants
			• No preregistered statistical analysis plan
			
			Funding sources:
			Erasmus MC University Medical Centre; Erasmus University Rotterdam; The Netherlands Organization for Scientific Research; The Netherlands Organization for Health Research and Development; Research Institute for Diseases in the Elderly; The Netherlands Genomics Initiative; The Netherlands Consortium of Healthy Ageing; Ministry of Education, Culture and Science; Ministry of Health, Welfare and Sports; European Commission (DG XII); Municipality of Rotterdam

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Kiage, 2015[173]
PCS, SCCS (Southern Community Cohort Study), U.S.
Baseline N>85,000 (did not provide exact number), Analytic N=69,559 (Attrition: ~18% or higher)
 	
Participant characteristics at baseline:
• Men and women 40-79y of age from the southern U.S. at baseline
• Age: Mean=52y, SD=9y
• Sex (female): ~60%
• Race/ethnicity: ~32% White
• SES: Education, 28% <High School, 39% High school/GED, 20% Some college, 13% Graduate; Income <$15,000/y, 55%
• Anthropometry: BMI, Mean=30, SD=8
 	
Fat intake at baseline:
• Total PUFA (quintiles; energy adjusted intake), Mean (SD)
  • Q1: 12.2 (2.5) g/d; 6.1 (1.6) %E
  • Q2: 17.0 (0.9) g/d; 7.2 (1.2) %E
  • Q3: 19.8 (0.8) g/d; 7.9 (1.0) %E
  • Q4: 22.6 (0.9) g/d; 8.6 (0.9) %E
  • Q5: 27.1 (2.8) g/d; 10.1 (1.2) %E
 	
BP at baseline:
• Hypertension: 54%
 	
Summary of findings:
In men and women not on statins, n-6 PUFA intake, but not n-3 PUFA intake, at ~52y of age was significantly associated with lower risk of CVD mortality during ~6.4y of follow-up. In men and women using statins, n-3 and n-6 PUFA intake was not significantly associated with CVD mortality.
	Exposures:
	• n-3 PUFA (quintiles; energy adjusted intake)
	• n-6 PUFA (quintiles; energy adjusted intake)
	
	Assessment method and timing:
	• Validated, 89-item FFQ; assistance from trained staff with 86% of participants
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~6.4y of follow-up
	• CVD Mortality: Obtained through linkage with Social Security Administration and the National Death Index
	  • Total CVD: 2023 cases
		n-3 PUFA
		CVD Mortality, HR (95% CI)
		Statin users (~16%)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.35
		Non-users (~84%)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.57
		
		n-6 PUFA
		CVD Mortality, HR (95% CI)
		Statin users (~16%)
		Q1 (ref) vs Q2: 0.65 (0.48, 0.89)
		Q1 (ref) vs Q3: 0.88 (0.65, 1.19)
		Q1 (ref) vs Q4: 0.77 (0.56, 1.07)
		Q1 (ref) vs Q5: 0.80 (0.57, 1.12)
		P-trend: 0.48
		Non-users (~84%)
		Q1 (ref) vs Q2: 0.83 (0.70, 0.98)
		Q1 (ref) vs Q3: 0.74 (0.61, 0.90)
		Q1 (ref) vs Q4: 0.80 (0.65, 0.98)
		Q1 (ref) vs Q5: 0.72 (0.57, 0.93)
		P-trend: 0.03
			Key confounders NOT accounted for:
			Family history of CVD or diabetes.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education, income), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			BMI, recruitment site, energy adjusted SFA, MUFA, and protein, diabetes, statin use, statin use by n-3 or n-6 PUFA interaction
			
			Limitations:
			• Not all key confounders accounted for
			• No information on selection of participants into analysis
			• No information on missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Cancer Institute; American Recovery and Reinvestment Act; PepsiCo Global Research and Development

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Koh, 2015[175]
PCS, SCHS (Singapore Chinese Health Study), Singapore
Baseline N=63,287 Analytic N=60,298 (Attrition: 5%)
 	
Participant characteristics at baseline:
• No CVD or cancer
• Age: Mean~56y
• Sex (female):~58%
• Race/ethnicity: NR
• SES: Education: ~28% more than secondary school
• Anthropometry: BMI, Mean~23
 	
Fat intake at baseline:
• See exposure section
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Higher intakes of EPA/DHA and ALA omega-3 fatty acids were associated with reduced risk of cardiovascular mortality, and coronary heart disease mortality, but not stroke mortality in a Chinese population.
	Exposures (medians):
	• Total n-3 PUFA (quartiles, g), Mean, SD
	  • Q1 0.59, 0.12
	  • Q2 0.79, 0.04
	  • Q3 0.92, 0.04
	  • Q4 1.26, 0.33
	• EPA+DHA intake (quartiles, g) Mean, SD (by quartile of total n-3 PUFA intake)
	  • Q1 0.19, 0.10
	  • Q2 0.28, 0.09
	  • Q3 0.35, 0.10
	  • Q4 0.46, 0.18
	• ALA intake (quartiles, g) Mean, SD (by quartile of total n-3 PUFA intake)
	  • Q1 0.40, 0.11
	  • Q2 0.51, 0.09
	  • Q3 0.56, 0.10
	  • Q4 0.80, 0.36
	
	Diet assessment method and timing:
	• 165-item semi-quantitative FFQ (validated) with 14 seafood items
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~15 years of follow-up
	• CVD death assessed via linkage to birth and death registry of Singapore
	  • CVD death: 4780 cases
	  • CHD death: 2697 cases
	  • Stroke death: 1298 cases
		CVD deaths, HR (95% CI),
		Total n-3 PUFA
		Q1 (ref) vs Q2: 0.88 (0.81, 0.96)
		Q1 (ref) vs Q3: 0.88 (0.80, 0.97)
		Q1 (ref) vs Q4: 0.83 (0.74, 0.92)
		P-trend 0.003
		EPA+DHA
		Q1 (ref) vs Q2: 0.96 (0.89, 1.05)
		Q1 (ref) vs Q3: 0.90 (0.82, 0.99)
		Q1 (ref) vs Q4: 0.86 (0.77, 0.96)
		P-trend 0.004
		ALA
		Q1 (ref) vs Q2: 0.94 (0.86, 1.02)
		Q1 (ref) vs Q3: 0.87 (0.79, 0.95)
		Q1 (ref) vs Q4: 0.81 (0.73, 0.90)
		P-trend ≤0.001
		CHD deaths, HR (95% CI)
		Total n-3 PUFA
		Q1 (ref) vs Q2: 0.92 (0.81, 1.03)
		Q1 (ref) vs Q3: 0.92 (0.80, 1.03)
		Q1 (ref) vs Q4: 0.85 (0.73, 0.98)
		P-trend 0.04
		EPA+DHA
		Q1 (ref) vs Q2 0.99 (0.88, 1.10)
		Q1 (ref) vs Q3: 0.97 (0.85, 1.09)
		Q1 (ref) vs Q4: 0.86 (0.74, 0.99)
		P-trend 0.02
		ALA
		Q1 (ref) vs Q2: 1.01 (0.90–1.13)
		Q1 (ref) vs Q3: 0.90 (0.79–1.01)
		Q1 (ref) vs Q4: 0.82 (0.71–0.93)
		P-trend 0.001
		Stroke deaths, HR (95% CI)
		Total n-3 PUFA
		Q1 (ref) vs Q2, Q3 or Q4: NS, P-trend=0.10
		EPA+DHA
		Q1 (ref) vs Q3: 0.82 (0.68-0.98)
		Q1 (ref) vs Q2 or Q4: NS, P-trend=0.28
		ALA
		Q1 (ref) vs Q2: 0.81 (0.68, 0.95)
		Q1 (ref) vs Q3: 0.81 (0.68, 0.97)
		Q1 (ref) vs Q4: 0.81 (0.67, 0.99)
		P-trend=0.07
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, SES (education, residential area), race/ethnicity (dialect group), smoking, alcohol intake, TEI, physical activity
			
			Additional model adjustments:
			Interview year, BMI, history of comorbidities at baseline (diabetes, hypertension, CHD, and stroke), fiber, protein, and all fat subtypes (i.e. omega-6 fatty acids, monounsaturated fat, and saturated fat)
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			U.S. National Institutes of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Neelakantan, 2018[188]
PCS, SCHS (Singapore Chinese Health Study), Singapore
Baseline N=63,257, Analytic N=57,078 (Attrition: 10%)
 	
Participant characteristics at baseline:
• Singapore Chinese men and women 45-74y of age without cancer or CVD at baseline.
• Age: ~56y
• Sex (female): ~56%
• Race/ethnicity: 100% ethnic Chinese
• SES: Higher education ~30%
• Anthropometry: BMI ~23
 	
Fat intake at baseline, Mean:
• SFA: ~9%E
• MUFA:SFA ratio: ~1
• PUFA: ~5%E
• Long-chain n-3 PUFA: ~0.3 g/d
• Cholesterol: ~180 mg/d
 	
Blood lipids and BP at baseline:
• Hypertension: ~21%
 	
Summary of findings:
In men and women, SFA intake of 10-15%E (but not >15%E) compared to 0-10%E at ~56y of age was significantly associated with lower risk of CVD mortality. Higher intake of long chain n-3 PUFA was significantly associated with lower risk of CVD mortality. Intake of PUFA and cholesterol, and the MUFA:SFA intake ratio were not associated with risk of CVD mortality.
	Exposures:
	• SFA (categorical; %E)
	  • 0-10%E (ref)
	  • 10-15%E
	  • >15%E
	• MUFA:SFA ratio (continuous)
	• PUFA (categorical; %E)
	  • 0-6%E
	  • 6-10%E (ref)
	  • >10%E
	• Long chain n-3 PUFA (continuous; g/d)
	• Cholesterol (continuous; per 100 mg/d)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 165-item FFQ assessing intake during the previous year
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~17y of follow-up
	• CVD Mortality: Obtained through linkage with nationwide registry of deaths
	  • Total: 4871 cases
		SFA
		CVD Mortality, HR (95% CI)
		0-10%E (ref) vs 10-15%E: 0.90 (0.84, 0.97)
		0-10%E (ref) vs >15%E: 0.98 (0.72, 1.33)
		
		MUFA:SFA ratio
		CVD Mortality, HR (95% CI)
		1.17 (1.00, 1.36)
		
		PUFA
		CVD Mortality, HR (95% CI)
		6-10%E (ref) vs 0-6%E: 1.00 (0.93, 1.08)
		6-10%E (ref) vs >10%E: 1.14 (0.91, 1.43)
		
		Long chain n-3 PUFA
		CVD Mortality, HR (95% CI)
		0.74 (0.58, 0.94)
		
		Cholesterol
		CVD Mortality, HR (95% CI)
		1.04 (1.00, 1.09)
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Sleep duration, dialect (hokkien or Cantonese), BMI, history of diabetes mellitus, history of hypertension, intake of dietary fiber, long-chain n-3 PUFA, cholesterol, sodium, SFA, mono- and disaccharides, PUFAs, protein.
			
			Limitations:
			• Not all key confounders accounted for
			• How categories of intake levels were selected for analysis was not reported
			• No preregistered statistical analysis plan
			
			Funding sources:
			NCI; National Medical Research Council, Singapore

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Levitan, 2010[182]
PCS, SIMPLER: SMC (Swedish Mammography Cohort), Sweden
Baseline N=39,227, Analytic N=36,234 (Attrition: 8%)
 	
Participant characteristics at baseline:
• Women without history of MI, diabetes, or cancer (other than non-melanoma skin cancer) at baseline
• Age: Mean~62y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Education, ~75% less than high school, ~8% high school, ~17% university
• Anthropometry: BMI, Mean~25
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• History of high cholesterol: ~20%
• History of hypertension: ~8%
 	
Summary of findings:
Among women, marine n-3 PUFA intake at ~62y of age was not significantly associated with incident heart failure during ~9y of follow-up.
	Exposures:
	• Marine n-3 PUFA intake (quintiles; g/d), Median (range):
	  • Q1 (ref): 0.14 (0.01-0.19)
	  • Q2: 0.23 (0.20-0.27)
	  • Q3: 0.30 (0.28-0.33)
	  • Q4: 0.38 (0.34-0.45)
	  • Q5: 0.57 (0.46-7.15)
	
	Assessment method and timing:
	• Self-administered, validated, 96-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~9y of follow-up
	• Incident heart failure (HF; hospitalization or mortality): Obtained via linkage with Swedish inpatient and cause-of-death registers
	  • Total: 651 cases (596 hospitalizations, 55 deaths)
		Marine n-3 PUFA
		Incident HF, Rate Ratio (95% CI)
		Q1 (ref) vs Q2: 0.87 (0.69, 1.11)
		Q1 (ref) vs Q3: 0.83 (0.64, 1.07)
		Q1 (ref) vs Q4: 0.88 (0.69, 1.12)
		Q1 (ref) vs Q5: 0.81 (0.63, 1.05)
		P-trend: NR
		
		Results were similar when a broader definition of HF diagnosis was utilized.
		
		When analyses were restricted to women without self-reported hypertension at baseline, no consistent associations across quintiles were detected.
			Key confounders NOT accounted for:
			Race/ethnicity.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			BMI, living alone, postmenopausal hormone use, fiber intake, sodium intake, intake of red or processed meat, self-reported history of hypertension, self-reported history of high cholesterol, intake of protein, SFA, MUFA, non-marine n-3 FA, and n-6 FA.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of women with diabetes at baseline
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council/Committee for Infrastructure and Committee for Medicine; Swedish Foundation for International Cooperation in Research and Higher Education; NHLBI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Larsson, 2012[179]
PCS, SIMPLER: SMC (Swedish Mammography Cohort), Sweden
Baseline N=39,227, Analytic N=34,670 (Attrition: 12%)
 	
Participant characteristics at baseline:
• Women 49-83y without history of stroke, coronary heart disease, or cancer at baseline
• Age: Mean~62y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: NR
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
Among women, higher intake of long chain n-3 PUFAs (EPA+DHA) at ~62y of age was significantly associated with lower risk of stroke, specifically cerebral infarctions, during ~10.4y of follow-up. Higher intake of cholesterol was significantly associated with higher risk of stroke, specifically cerebral infarctions. Intake of SFA, MUFA, ALA, and n-6 PUFAs were not significantly associated with risk of stroke.
	Exposures:
	• SFA (quintiles; g/d), Median: (Q1 (ref): 19.5; Q2: 23.8; Q3: 26.9; Q4: 30.3; Q5: 35.5)
	• MUFA (quintiles; g/d), Median: (Q1 (ref): 15.6; Q2: 18.3; Q3: 20.0; Q4: 21.7; Q5: 24.3)
	• PUFA (quintiles; g/d), Median: (Q1 (ref): 6.1; Q2: 7.1; Q3: 7.8; Q4: 8.6; Q5: 10.1)
	• ALA (quintiles; g/d), Median: (Q1 (ref): 0.9; Q2: 1.0; Q3: 1.1; Q4: 1.3; Q5: 1.5)
	• EPA+DHA (quintiles; mg/d), Median: (Q1 (ref): 131; Q2: 222; Q3: 289; Q4: 370; Q5: 559)
	• EPA+DHA (continuous; per 500 mg/d):
	• n-6 PUFA (quintiles; g/d), Median: (Q1 (ref): 4.7; Q2: 5.4; Q3: 6.0; Q4: 6.6; Q5: 8.0)
	• Cholesterol (quintiles; mg/d), Median: (Q1 (ref): 168; Q2: 204; Q3: 229; Q4: 255; Q5: 302)
	• Cholesterol (continuous; per 120 mg/d):
	
	Assessment method and timing:
	• Self-administered, validated, 96-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~10.4y of follow-up
	• Incident stroke (including subtypes): Obtained via linkage with Swedish Hospital Discharge Registry
	  • Total: 1680 cases
	  • Cerebral infarctions: 1310 cases
	  • Hemorrhagic strokes: 233 cases, including 154 intracerebral hemorrhage cases and 79 subarachnoid hemorrhage cases
	  • Unspecified stroke: 137 cases
		SFA
		Incident Total Stroke, relative risk (RR) (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.62
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.55
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.25
		MUFA
		Incident Total Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.29
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.40
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.46
		PUFA
		Incident Total Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.43
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.36
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.57
		ALA
		Incident Total Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.16
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.22
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.37
		
		(Continued below)
			Key confounders NOT accounted for:
			Race/ethnicity, TEI.
			
			Key confounders accounted for:
			Sex, age, SES (education), smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			BMI, history of hypertension, history of diabetes, aspirin use; Analyses of types of fat: cholesterol, other types of fat; Analyses of cholesterol: total fat.
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Council for Working Life and Social Research; Karolinska Institutet Research Fellow grant

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Larsson, 2012 (CONTINUED)
PCS, Swedish Mammography Cohort, Sweden
Baseline N=39,227, Analytic N=34,670 (Attrition: 12%)
 	
Participant characteristics at baseline:
• Women 49-83y without history of stroke, coronary heart disease, or cancer at baseline
• Age: Mean~62y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: NR
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
Among women, higher intake of long chain n-3 PUFAs (EPA+DHA) at ~62y of age was significantly associated with lower risk of stroke, specifically cerebral infarctions, during ~10.4y of follow-up. Higher intake of cholesterol was significantly associated with higher risk of stroke, specifically cerebral infarctions. Intake of SFA, MUFA, ALA, and n-6 PUFAs were not significantly associated with risk of stroke.
	Exposures:
	• SFA (quintiles; g/d), Median: (Q1 (ref): 19.5; Q2: 23.8; Q3: 26.9; Q4: 30.3; Q5: 35.5)
	• MUFA (quintiles; g/d), Median: (Q1 (ref): 15.6; Q2: 18.3; Q3: 20.0; Q4: 21.7; Q5: 24.3)
	• PUFA (quintiles; g/d), Median: (Q1 (ref): 6.1; Q2: 7.1; Q3: 7.8; Q4: 8.6; Q5: 10.1)
	• ALA (quintiles; g/d), Median: (Q1 (ref): 0.9; Q2: 1.0; Q3: 1.1; Q4: 1.3; Q5: 1.5)
	• EPA+DHA (quintiles; mg/d), Median: (Q1 (ref): 131; Q2: 222; Q3: 289; Q4: 370; Q5: 559)
	• EPA+DHA (continuous; per 500 mg/d):
	• n-6 PUFA (quintiles; g/d), Median: (Q1 (ref): 4.7; Q2: 5.4; Q3: 6.0; Q4: 6.6; Q5: 8.0)
	• Cholesterol (quintiles; mg/d), Median: (Q1 (ref): 168; Q2: 204; Q3: 229; Q4: 255; Q5: 302)
	• Cholesterol (continuous; per 120 mg/d):
	
	Assessment method and timing:
	• Self-administered, validated, 96-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~10.4y of follow-up
	• Incident stroke (including subtypes): Obtained via linkage with Swedish Hospital Discharge Registry
	  • Total: 1680 cases
	  • Cerebral infarctions: 1310 cases
	  • Hemorrhagic strokes: 233 cases, including 154 intracerebral hemorrhage cases and 79 subarachnoid hemorrhage cases
	  • Unspecified stroke: 137 cases
		EPA+DHA
		Incident Total Stroke, RR (95% CI)
		Q1 (ref) vs Q2: 0.93 (0.80, 1.08)
		Q1 (ref) vs Q3: 0.87 (0.74, 1.02)
		Q1 (ref) vs Q4: 0.89 (0.76, 1.05)
		Q1 (ref) vs Q5: 0.84 (0.72, 0.99)
		P-trend: 0.04
		Per 500mg/d increase: 0.86 (0.75, 0.99)
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2: 0.88 (0.74, 1.04)
		Q1 (ref) vs Q3: 0.84 (0.70, 1.01)
		Q1 (ref) vs Q4: 0.83 (0.69, 0.99)
		Q1 (ref) vs Q5: 0.83 (0.69, 0.99)
		P-trend: 0.06
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, Q5: NS, P-trend: 0.16
		
		n-6 PUFA
		Incident Total Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, Q5: NS, P-trend: 0.98
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.73
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, Q5: NS, P-trend: 0.39
		
		Cholesterol
		Incident Total Stroke, RR (95% CI)
		Q1 (ref) vs Q2: 0.91 (0.76, 1.08)
		Q1 (ref) vs Q3: 1.15 (0.97, 1.37)
		Q1 (ref) vs Q4: 1.17 (0.98, 1.39)
		Q1 (ref) vs Q5: 1.20 (1.00, 1.44)
		P-trend: 0.01
		Per 120mg/d increase: 1.15 (1.02, 1.31)
		Incident Cerebral Infarction, RR (95% CI)
		Q1 (ref) vs Q2: 0.95 (0.78, 1.15)
		Q1 (ref) vs Q3: 1.17 (0.96, 1.42)
		Q1 (ref) vs Q4: 1.19 (0.97, 1.45)
		Q1 (ref) vs Q5: 1.29 (1.05, 1.58)
		P-trend: 0.004
		Per 120mg/d increase: 1.21 (1.05, 1.39)
		Incident Hemorrhagic Stroke, RR (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, Q5: NS, P-trend: 0.77
			Key confounders NOT accounted for:
			Race/ethnicity, TEI.
			
			Key confounders accounted for:
			Sex, age, SES (education), smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			BMI, history of hypertension, history of diabetes, aspirin use; Analyses of types of fat: cholesterol, other types of fat; Analyses of cholesterol: total fat.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of women with coronary heart disease at baseline
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Council for Working Life and Social Research; Karolinska Institutet Research Fellow grant

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Levitan, 2012[181]
PCS, SIMPLER: SMC (Swedish Mammography Cohort), Sweden
Baseline N=39,227, Analytic N=36,234 (Attrition: 8%)
 	
Participant characteristics at baseline:
• Women without history of MI, diabetes, or cancer (other than non-melanoma skin cancer) at baseline
• Age: Mean~62y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Education, ~75% less than high school, ~8% high school, ~17% university
• Anthropometry: BMI, Mean~25
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• History of high cholesterol: ~8%
• History of hypertension: ~20%
 	
Summary of findings:
Among women, ALA and LA intake at ~62y of age was not significantly associated with incident heart failure during ~9y of follow-up.
	Exposures:
	• ALA (quintiles; g/d), Median (range):
	  • Q1 (ref): 0.88 (0.34-0.96)
	  • Q2: 1.03 (0.97-1.09)
	  • Q3: 1.15 (1.10-1.21)
	  • Q4: 1.28 (1.22-1.36)
	  • Q5: 1.50 (1.37-4.85)
	• LA (quintiles; g/d), Median (range):
	  • Q1 (ref): 4.6 (1.7-5.0)
	  • Q2: 5.3 (5.1-5.6)
	  • Q3: 5.9 (5.7-6.1)
	  • Q4: 6.5 (6.2-7.0)
	  • Q5: 7.8 (7.1-31.2)
	
	Assessment method and timing:
	• Self-administered, validated, 96-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~9y of follow-up
	• Incident heart failure (HF; hospitalization or mortality): Obtained via linkage with Swedish inpatient and cause-of-death registers
	  • Total: 651 cases (596 hospitalizations, 55 deaths)
		ALA
		Incident HF, Rate Ratio (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.41
		
		LA
		Incident HF, Rate Ratio (95% CI)
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.36
		
		Associations did not vary by long-chain n-3 PUFA intake (ALA, P-interaction: 0.29; LA, P-interaction: 0.54). No interaction between ALA and LA (P-interaction: 0.81).
			Key confounders NOT accounted for:
			Race/ethnicity.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			BMI, fiber consumption, Na consumption, living alone, post-menopausal hormone use, self-reported history of hypertension, self-reported history of high cholesterol.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of women with diabetes at baseline
			• Did not account for co-exposures (other FAs)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council/Committee for Infrastructure and Council/Committee for Medicine; Swedish Foundation for International Cooperation in Research and Higher Education

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Patterson, 2013[194]
PCS, SIMPLER: SMC (Swedish Mammography Cohort), Sweden
Baseline N=39,227, Analytic N=33,636 (Attrition: 14%)
 	
Participant characteristics at baseline:
• Women without history of CVD, diabetes, or cancer at baseline
• Age: Mean~61y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Postsecondary-level education, ~20%
• Anthropometry: BMI, Mean~25
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• History of high cholesterol: ~7%
• History of hypertension: ~19%
 	
Summary of findings:
Among women, butter intake at ~61y of age was not significantly associated with incident myocardial infarction during ~11.6y of follow-up.
	Exposures:
	• Butter (categorical):
	  • C1 (ref): No butter used on bread or in cooking
	  • C2: Butter used in cooking but not on bread
	  • C3: Butter used on bread but not in cooking
	  • C4: Butter used both on bread and in cooking
	
	Assessment method and timing:
	• Self-administered, validated, 96-item semi-quantitative FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~11.6y of follow-up
	• Incident MI (fatal and nonfatal): Obtained via linkage with Swedish inpatient and cause-of-death registers
	  • Total: 1392 cases (including 254 fatal cases)
		Butter
		Incident MI, HR (95% CI)
		C1 (ref) vs C2, C3, or C4: All NS
			Key confounders NOT accounted for:
			Race/ethnicity.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			Waist-to-hip ratio, diagnosis of hypertension, diagnosis of high cholesterol, aspirin usage, hormone therapy usage, intake of milk, cultured milk/yogurt, cheese, and cream/crème fraiche, intake of fruit and vegetables, intake of whole-grain foods, use of oils in cooking, use of low-fat margarine on bread.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of women with diabetes at baseline
			• Butter intake categories not based on amount consumed
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Council for Working Life and Social Research; Swedish Research Council/Infrastructure Medicine

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Bergkvist, 2014[146]
PCS, SIMPLER: SMC (Swedish Mammography Cohort), Sweden
Baseline N=39,227, Analytic N=34,591 (Attrition: 12%)
 	
Participant characteristics at baseline:
• Women without prevalent CVD or cancer at baseline
• Age: Mean~61y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Post-secondary education, ~20%
• Anthropometry: BMI, Mean~25
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• High cholesterol: ~7%
• Hypertension: ~19%
 	
Summary of findings:
Among women, higher intake of DHA and EPA, after adjusting for PCB exposure, at ~61y of age was associated with lower risk of stroke during ~12y of follow-up.
	Exposures:
	• EPA + DHA (quartiles; mg/d), Median:
	  • Q1 (ref): 148
	  • Q2: 247
	  • Q3: 335
	  • Q4: 520
	
	Assessment method and timing:
	• Self-administered, validated, 96-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~12y of follow-up
	• Incident stroke: Obtained via linkage with Swedish National Hospital Discharge and Cause of Death Registers
	  • Total: 2015 cases (1532 ischemic, 216 intracerebral hemorrhages, 94 subarachnoid hemorrhages, 173 unspecified)
		EPA + DHA
		Incident Stroke, Relative Risk (95% CI)
		Q1 (ref) vs Q2: 0.92 (0.78, 1.09)
		Q1 (ref) vs Q3: 0.89 (0.70,1.12)
		Q1 (ref) vs Q4: 0.72 (0.54, 0.96)
		P-trend: 0.014
			Key confounders NOT accounted for:
			Race/ethnicity.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			High cholesterol, history of hypertension, atrial fibrillation before baseline, use of postmenopausal hormones, use of aspirin, BMI, parity, use of fish oil supplements, consumption of fruit and vegetables, red and processed meat, and dairy products, dietary MeHg exposure, dietary PCB exposure
			
			Limitations:
			• Not all key confounders accounted for
			• Did not account for co-exposures (other FAs)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council Formas; Swedish Research Council for Health, Working Life, and Welfare (Forte); Swedish Research Council/Committee for Infrastructure

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Bergkvist, 2015[145]
PCS, SIMPLER: SMC (Swedish Mammography Cohort), Sweden
Baseline N=39,227, Analytic N=33,446 (Attrition: 15%)
 	
Participant characteristics at baseline:
• Women without prevalent CVD, diabetes, or cancer at baseline
• Age: Mean~61y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: Post-secondary education, ~20%
• Anthropometry: WC <80cm, ~32%
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• High cholesterol: ~7%
• Hypertension: ~19%
 	
Summary of findings:
Among women ~61y of age, moderate intake of DHA and EPA was significantly associated with lower risk of incident myocardial infarction (third quartile vs first quartile of intake), after adjustment for dietary PCB exposure, during ~12y of follow-up. The second and fourth quartile of DHA and EPA intake (compared to the first quartile) were not associated with incident myocardial infarction and there was not a statistically significant linear trend detected.
	Exposures:
	• EPA + DHA (quartiles; mg/d), Median:
	  • Q1 (ref): 148
	  • Q2: 247
	  • Q3: 334
	  • Q4: 518
	
	Assessment method and timing:
	• Self-administered, validated, 96-item FFQ representing intake during previous 12mo
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~12y of follow-up
	• Incident MI (fatal and nonfatal): Obtained via linkage with Swedish National Hospital Discharge and Cause of Death Registers
	  • Total: 1386 cases (276 fatal cases)
		EPA + DHA
		Incident MI, Relative Risk (95% CI)
		Q1 (ref) vs Q2: 0.90 (0.73, 1.11)
		Q1 (ref) vs Q3: 0.74 (0.56, 0.98)
		Q1 (ref) vs Q4: 0.74 (0.52, 1.06)
		P-trend: 0.21
			Key confounders NOT accounted for:
			Race/ethnicity.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			Use of postmenopausal hormones, use of aspirin, WC, weight loss >5kg within a year, parity, use of fish oil supplements, consumption of fruit and vegetables, dairy products, red and processed meat, intake of SFA, dietary MeHg exposure, dietary PCB exposure.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of women with diabetes at baseline
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council Formas; Swedish Research Council/Research Infrastructure; Swedish Council for Working Life and Social Research

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Bergkvist, 2016[144] **PCS, SIMPLER: CSM (Cohort of Swedish Men), Sweden** Baseline N=48,850 Analytic N=36,759 (Attrition: 25%) **Participant characteristics at baseline:** • 100% without prevalent CVD, diabetes or cancer • Age: ~59y • Sex (female): 0% • Race/ethnicity: NR • SES: Post-secondary education: 18% • Anthropometry: WC <102 cm: ~77% **Fat intake at baseline, Mean:** • SFA: ~41 g/d • EPA+DHA: ~0.46 g/d **Blood lipids and BP at baseline:** High cholesterol: ~8% Hypertension: ~14% **Summary of findings:** *Greater EPA+DHA intake was significantly associated with lower risk of myocardial infarction after adjusting for PCB exposure.*	**Exposures:** • EPA+DHA (continuous, g/d) Assessment method and timing: • Self-administered, validated 96-item FFQ to assess usual food intake in previous 12mo • Assessed at baseline **Outcomes and assessment methods**: • Assessed during 12 y of follow-up • Incident MI: Swedish National Hospital Discharge Register, Cause of Death Register • MI: 3,005 cases	**Incident MI**, Relative Risk (RR) (95% CI) *EPA+DHA* **0.67 (0.50, 0.90) P-trend=0.004**	**Key confounders NOT accounted for:** Sex, race/ethnicity **Key confounders accounted for:** Age, SES, TEI, physical activity, smoking, alcohol intake, family history of MI **Additional model adjustments:** Dietary PCB exposure, high cholesterol, hypertension, use of aspirin, WC, use of fish oil supplements, consumption of fruit and vegetables, dairy products and red and processed meat, dietary intake of SFA, dietary MeHg exposure **Limitations:** • Not all key confounders adjusted for • Potential selection bias due to excluding participants with diabetes • Analyses did not account for co-exposures (MUFAs, other PUFAs) • No preregistered statistical analysis plan **Funding sources:** Swedish Research Council Formas; Swedish Council for Working Life and Social Research; Swedish Research Council/Research Infrastructure

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Kippler, 2016[174]
PCS, SIMPLER: CSM (Cohort of Swedish Men), Sweden
Baseline N=48,850, Analytic N=39,948 (Attrition: 18%)
 	
Participant characteristics at baseline:
• No history of CVD or cancer
• Type 2 diabetes: ~8%
• Age: Mean~59y
• Sex (female): 0%
• Race/ethnicity: NR
• SES: ~18% University education
• Anthropometry: BMI, Mean~26
 	
Fat intake at baseline:
• EPA/DHA (g/d): Mean=0.40
• Fish oil supplements: 4.5%
• SFA (g/d): Mean~44
 	
BP at baseline:
• Hypertension: ~15%
 	
Summary of findings:
Dietary EPA-DHA intake was associated with lower risk of hemorrhagic stroke, but not ischemic stroke after adjusting for PCB exposure over 12y follow-up among middle-aged Swedish men.
	Exposures:
	• EPA/DHA intake (quartiles, mg/d), Median
	  • Q1 0.18
	  • Q2 0.34
	  • Q3 0.46
	  • Q4 0.73
	
	Diet assessment method and timing:
	• 96-item FFQ used to assess food and beverage intake during the previous 12mo (validated)
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during 12y of follow-up
	• Incident stroke events ascertained by record linkage to medical and death registers.
	  • Any stroke: 217 cases
	  • Ischemic stroke: 2286 cases
	  • Hemorrhagic stroke: 474 cases
		Ischemic stroke, HR (95% CI)
		EPA/DHA (quartiles)
		Q1 (ref) vs Q2, Q3, or Q4: All NS P=0.14
		Hemorrhagic stroke, HR (95% CI)
		EPA/DHA (quartiles)
		Q1 (ref) vs Q2: 0.84 (0.59–1.20)
		Q1 (ref) vs Q3: 0.57 (0.35–0.93)
		Q1 (ref) vs Q4: 0.42 (0.22–0.79) P<0.01
		Intracerebral hemorrhage, HR (95% CI)
		Q1 (ref) vs Q2: 0.83 (0.56–1.22)
		Q1 (ref) vs Q3: 0.56 (0.33–0.96)
		Q1 (ref) vs Q4: 0.42 (0.21–0.85) P<0.01
			Key confounders NOT accounted for:
			Race/ethnicity
			
			Key confounders accounted for:
			Age, sex, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD
			Additional model adjustments:
			Hypercholesterolemia, hypertension, atrial fibrillation, use of aspirin, BMI, use of fish oil supplements, intake of fruit and vegetables, intake of red and processed meat and dairy products, dietary intake of SFA and dietary MeHg exposure, and PCB exposure
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (other FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council Formas; the Swedish Research Council for Health, Working Life, and Welfare (Forte), and the Swedish Research Council/Committee for Infrastructure.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Akesson, 2019[137]
PCS, SIMPLER: SMC (Swedish Mammography Cohort) and CSM (Cohort of Swedish Men), Sweden
Baseline N=88,077, Analytic N=69,498 (Attrition: 21%)
 	
Participant characteristics at baseline:
• Men 45-79y of age and women 49-83y of age at baseline without previous diagnosis of cancer, CVD, or type 2 diabetes
• Age: Men~59y, Women~61y
• Sex (female): 47%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: WC >102cm (men), ~81%; WC>88cm (women), ~30%
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• High Cholesterol: ~8% men; ~7% women
• Hypertension: ~14% men; 19% women
 	
Summary of findings:
In women, higher EPA/DHA intake, after adjusting for dietary PCB exposure, at ~61y of age was significantly associated with lower risk of incident HF after 12y of follow-up. In men, EPA/DHA intake, after adjusting for dietary PCB exposure, at ~59y of age was not significantly associated with risk of incident HF after 12y of follow-up.
	Exposures:
	• EPA/DHA (quintiles; mg/d), Mean (SD)
	  • Q1: Men, 161 (81); Women, 132 (60)
	  • Q2: Men, 300 (64); Women, 224 (48)
	  • Q3: Men, 393 (64); Women, 286 (46)
	  • Q4: Men, 501 (76); Women, 370 (60)
	  • Q5: Men, 921 (59); Women, 646 (36)
	
	Assessment method and timing:
	• Validated, semi-quantitative, 96-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed up to 12y of follow-up
	• Incident HF: Obtained through linkage with Swedish National Patient Register and Swedish Cause of Death Register
	  • Men: 3128 cases
	  • Women: 2736 cases
		Incident HF, Relative Risk (95% CI)
		Men:
		Q1 (ref) vs Q2: 0.94 (NR)
		Q1 (ref) vs Q3: 0.80 (NR)
		Q1 (ref) vs Q4: 0.81 (NR)
		Q1 (ref) vs Q5: 0.82 (0.63, 1.07)
		P-trend: 0.19
		Women:
		Q1 (ref) vs Q2: 0.82 (NR)
		Q1 (ref) vs Q3: 0.79 (NR)
		Q1 (ref) vs Q4: 0.74 (NR)
		Q1 (ref) vs Q5: 0.71 (0.54, 0.93)
		P-trend: 0.035
			Key confounders NOT accounted for:
			Alcohol intake.
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			WC, weight loss >5kg within 1y, high cholesterol, history of hypertension, aspirin use, Mediterranean diet score, methylmercury intake, dietary PCB exposure.
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with type 2 diabetes
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Donat-Vargas, 2019[158]
PCS, SIMPLER: SMC (Swedish Mammography Cohort) and CSM (Cohort of Swedish Men), Sweden
Baseline N=88,077, Analytic N=69,498 (Attrition: 21%)
 	
Participant characteristics at baseline:
• Men 45-79y of age and women 49-83y of age at baseline without previous diagnosis of cancer, CVD, or type 2 diabetes
• Age: Men~59y, Women~61y
• Sex (female): 47%
• Race/ethnicity: NR
• SES: Postsecondary education, ~19%
• Anthropometry: WC >102cm (men), ~81%; WC>88cm (women), ~30%
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• High Cholesterol: ~8% men; ~7% women
• Hypertension: ~14% men; 19% women
 	
Summary of findings:
In men and women, higher intake of EPA/DHA at ~60y of age was associated with lower risk of CVD mortality during ~15.5y of follow-up.
	Exposures:
	• EPA/DHA (quintiles; mg/d), Median
	  • Q1: Men, 157; Women, 133
	  • Q2: Men, 296; Women, 223
	  • Q3: Men, 394; Women, 286
	  • Q4: Men, 497; Women, 364
	  • Q5: Men, 780; Women, 551
	
	Assessment method and timing:
	• Validated, semi-quantitative, 96-item FFQ assessing intake during the previous year
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~15.5y of follow-up
	• CVD Mortality: Obtained through linkage with Swedish Cause of Death Register
	  • Total: 6338 cases
		CVD Mortality, HR (95% CI)
		Q1 (ref) vs Q2: 0.89 (0.80, 0.99)
		Q1 (ref) vs Q3: 0.87 (0.76, 0.99)
		Q1 (ref) vs Q4: 0.82 (0.70, 0.95)
		Q1 (ref) vs Q5: 0.79 (0.66, 0.95)
		P-trend: 0.041
			Key confounders NOT accounted for:
			Race/ethnicity, alcohol intake.
			
			Key confounders accounted for:
			Sex, age, SES (education), TEI, smoking, physical activity, family history of CVD or diabetes.
			
			Additional model adjustments:
			WC, hypertension, hypercholesterolemia, weight loss >5kg within 1y, use of aspirin, Mediterranean diet, parity use of hormone replacement therapy, dietary methylmercury exposure, PCB exposure
			
			Limitations:
			• Not all key confounders accounted for
			• Potential selection bias due to exclusion of participants with diabetes
			• Analyses did not account for co-exposures (other FA)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Swedish Research Council

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Santiago, 2018[204]
PCS, SUN, Spain
Baseline N=21,678, Analytic N=19,341 (Attrition: 11%)
 	
Participant characteristics at baseline:
• No history of CVD
• Diabetes: ~1.7%
• Age: ~37.5y
• Sex (female): 43%
• Race/ethnicity: NR
• SES: Years of higher education: ~5
• Anthropometry: Mean BMI: ~23.5
 	
Fat intake at baseline, Mean:
• SFA (%E): ~12.5
• MUFA (%E): ~15.5
• PUFA (%E): ~5.3
• Cholesterol (mg): ~450
 	
BP at baseline:
• Hypertension: ~7.8%
 	
Summary of findings:
Saturated, polyunsaturated and monounsaturated fat intake and replacement of 5% saturated fat with MUFA, PUFA, carbohydrate or refined carbohydrate were not associated with CVD incidence during 10 years of follow-up.
	Exposures:
	• SFA intake (tertiles, %E SFA), Median
	  • T1 9.6
	  • T2 12.4
	  • T3 15.4
	• MUFA intake (tertiles, %E MUFA), Median
	  • T1 12.5
	  • T2 15.5
	  • T3 19.0
	• PUFA intake (tertiles, %E PUFA), Median
	  • T1 3.8
	  • T2 5.0
	  • T3 6.6
	• Replacement of SFA with MUFA, PUFA, CHO or refined CHO (per 5%E)
	
	Diet assessment method and timing:
	• Self-administered semi-quantitative 136-item FFQ (validated)
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during median 10.10y of follow-up
	• Composite of incident non-fatal acute coronary syndromes (myocardial infarction with or without ST elevation), non-fatal stroke or cardiovascular death ascertained via self-report and subsequent medical record review; deaths reported by next of kin/associates, postal authorities and National Death Record.
	  • Incident cases of CVD: 140 cases
		Incident CVD, HR (95% CI)
		SFA (tertiles)
		T1 (ref) vs T2, or T3: All NS
		P-trend: 0.356
		MUFA (tertiles)
		T1 (ref) vs T2, or T3: All NS
		P-trend: 0.805
		PUFA (tertiles)
		T1 (ref) vs T2, or T3: All NS
		P-trend: 0.13
		
		Replace SFA:
		With MUFA: 1.40 (0.75, 2.61); NS
		With PUFA: 1.30 (0.64, 2.63) NS
		With CHO: 1.23 (0.84, 1.97) NS
		With refined CHO: 1.14 (0.74, 1.78) NS.
			Key confounders NOT accounted for:
			Race/ethnicity, alcohol intake
			Key confounders accounted for:
			Age, sex, SES (education), TEI, smoking, physical activity, family history of CVD or diabetes
			Additional model adjustments:
			BMI, following special diets, weight gain in the past 5y, marital status, prevalent or previous angina pectoris or revascularization procedures, prevalent diabetes, prevalent hypertension, prevalent hypercholesterolemia, prevalent hypertriglyceridemia and prevalent depression
			
			Limitations:
			• Not all key confounders accounted for
			• Analyses did not account for co-exposures (types of fat)
			• No preregistered statistical analysis plan
			
			Funding sources:
			Spanish Ministry of Health –Instituto de Salud Carlos III and European Regional Development Fund; the Navarra Regional Government; the University of Navarra.

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Nagata, 2012[186]
PCS, Takayama Study, Japan
Baseline N=31,552, Analytic N=28,356 (Attrition: 10%)
 	
Participant characteristics at baseline:
• Adults ≥35y of age without history of MI, stroke, or cancer at baseline
• Age: Mean~54y
• Sex (female): 54%
• Race/ethnicity: NR
• SES: Years of education: ≤11y ~60%, 12-14y ~30%, ≥15y ~12% men, 4% women
• Anthropometry: BMI, Mean~22
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids and BP at baseline:
• NR
 	
Summary of findings:
In men and women intake of SFA, MUFA, PUFA, and long chain n-3 PUFA, at ~54y of age was not significantly associated with CVD mortality during ~16y of follow-up.
	Exposures:
	• SFA (quintiles; %E), Medians:
	  • Q1: 4.2 (men), 4.4 (women)
	  • Q2: 5.4 (men), 5.7 (women)
	  • Q3: 6.2 (men), 6.6 (women)
	  • Q4: 7.1 (men), 7.4 (women)
	  • Q5: 8.7 (men), 8.8 (women)
	• MUFA (quintiles; %E), Medians:
	  • Q1: 5.3 (men), 5.4 (women)
	  • Q2: 6.7 (men), 6.9 (women)
	  • Q3: 7.7 (men), 7.9 (women)
	  • Q4: 8.8 (men), 8.9 (women)
	  • Q5: 10.4 (men), 10.4 (women)
	• PUFA (quintiles; %E), Medians:
	  • Q1: 4.2 (men), 4.4 (women)
	  • Q2: 5.1 (men), 5.4 (women)
	  • Q3: 5.8 (men), 6.0 (women)
	  • Q4: 6.6 (men), 6.7 (women)
	  • Q5: 7.7 (men), 7.8 (women)
	• Long chain n-3 PUFA (quintiles; %E), Medians:
	  • Q1: 0.15 (men), 0.13 (women)
	  • Q2: 0.22 (men), 0.20 (women)
	  • Q3: 0.28 (men), 0.25 (women)
	  • Q4: 0.37 (men), 0.32 (women)
	  • Q5: 0.56 (men), 0.47 (women)
	Assessment method and timing:
	• 169-item FFQ (validated)
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during ~16y of follow-up
	• CVD mortality: Obtained through death certificates from public health centers
		CVD Mortality, HR (95% CI)
		SFA
		Men and Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.680 (men), 0.13 (women)
		
		MUFA
		Men and Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.65 (men), 0.35 (women)
		
		PUFA
		Men and women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.11 (men), 0.45 (women)
		
		Long chain n-3 PUFA
		Men and Women:
		Q1 (ref) vs Q2, Q3, Q4, or Q5: All NS
		P-trend: 0.65 (men), 0.27 (women)
			Key confounders NOT accounted for:
			Race/ethnicity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, SES (education), non-alcohol TEI, smoking, alcohol intake, physical activity
			
			Additional model adjustments:
			Height, BMI, marital status, history of diabetes and hypertension, protein intake, consumption of dietary fiber, vegetables and fruit, fat subtypes as appropriate
			
			Limitations:
			• Not all key confounders accounted for
			• Potential for selection bias due to exclusion of participants who died within the first 3y of follow-up
			• No preregistered statistical analysis plan
			
			Funding sources:
			Ministry of Education, Science, Sports and Science and Technology, Japan

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Isaksen, 2018[169]
PCS, Tromso Study, Norway
Baseline N=29,648, Analytic N=21,970 (Attrition: 26%)
 	
Participant characteristics at baseline:
• No history of VTE
• Age: ~46y
• Sex (female): 51.4%
• Race/ethnicity: NR
• SES: Education: ~37% Higher education
• Anthropometry: Mean BMI: ~25
 	
Fat intake at baseline:
• n-3PUFA (g/week): Median=11.1
 	
Blood lipids and BP at baseline, Mean:
• TC (mmol/L): ~5.8
• HDL (mmol/L): ~1.5
• Triglycerides (mmol/L): ~1.5
• SBP (mmHg): ~134
• DBP (mmHg): ~77
 	
Summary of findings:
Dietary intake of marine n-3 PUFAs ≥4.7g/week was associated with a lower risk of venous thromboembolism during 11.6 years of follow-up. There was no evidence of additional protection with increased intake above that threshold level.
	Exposures:
	• EPA+DHA intake from fish and supplements (quartiles, g/week), Range
	  • Q1 <4.7
	  • Q2 4.7-13.4
	  • Q3 13.4-29.1
	  • Q4 >29.1
	
	Diet assessment method and timing:
	• Self-administered questionnaires used to assess intake of lean and fat fish, fish spread and supplements containing n-3 PUFA
	• Administered prior to baseline
	
	Outcomes and assessment methods:
	• Assessed during median 11.60y of follow-up
	• risk of venous thromboembolism ascertained via hospital discharge, radiology procedure and autopsy registries
	  • Risk of venous thromboembolism: 541 cases
		Risk of venous thromboembolism, HR (95% CI)
		EPA+DPA+DHA from diet and supplements (quartiles)
		Q1 (ref) vs Q2: 0.74 (0.57-0.96)
		Q1 (ref) vs Q3: 0.77 (0.59-0.99)
		Q1 (ref) vs Q4: 0.78 (0.61-1)
		P=0.13
			Key confounders NOT accounted for:
			Race/ethnicity, SES, TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex
			
			Additional model adjustments:
			BMI
			
			Limitations:
			• Not all key confounders accounted for
			• Self-administered questionnaire used to assess EPA/DHA was not validated
			• Analyses did not account for co-exposures (SFA, MUFA, PUFA)
			• Potential missing data bias due to not statistically accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			Stiftelsen Kristian Gerhard Jebsen; UiT The Arctic University of Norway

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Blekkenhorst, 2015[147]
PCS, unnamed cohort, Australia
Baseline N=1,500, Analytic N=1,469 (Attrition: 2%)
 	
Participant characteristics at baseline:
• Prevalent atherosclerotic vascular disease (%): 11.9
• Type 2 diabetes: 6.1%
• Age: Mean=75.2y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: Mean BMI: 27.2
 	
Fat intake at baseline, Mean (SD):
• SFA (g/d): 25.3 (11.3)
• MUFA (g/d): 22.4 (8.7)
• PUFA (g/d): 10.8 (4.8)
 	
Blood lipids at baseline, Mean:
• TC (mmol/L): 5.9
• LDL (mmol/L): 3.7
• HDL (mmol/L): 1.4
• Triglycerides (mmol/L): 1.6
 	
Summary of findings:
Dietary intake of saturated fat was associated atherosclerotic vascular disease mortality in elderly women from Australia.
	Exposures:
	• SFA intake, (continuous, per SD)
	• SFA intake, (quartiles, g/d)
	  • Q1: < 17.39
	  • Q2: 17.39–23.40
	  • Q3: 23.41–31.28
	  • Q4: >31.28
	
	Diet assessment method and timing:
	• Self-administered, semi-quantitative 74-item FFQ (validated) assessing intake over 12mo
	• Administered at baseline
	
	Outcomes and assessment methods:
	• Assessed during median 5y of follow-up
	• Atherosclerotic vascular disease (ASVD) mortality (including ischemic heart disease; cerebrovascular disease, excluding hemorrhage; heart failure; and peripheral arterial disease) ascertained via death records
	  • Total: 134 cases
		SFA
		Atherosclerotic vascular disease mortality, HR (95% CI)
		Saturated fat (per SD, 11.26g/d)
		Per 1 SD: 1.77 (1.31, 2.37), P<0.001
		Saturated fat (quartiles)
		Q1 (ref) vs Q2: 1.28 (0.74, 2.21), P=0.37
		Q1 (ref) vs Q3: 1.35 (0.74, 2.45), P=0.327
		Q1 (ref) vs Q4: 3.07 (1.54, 6.11), P=0.001
			Key confounders NOT accounted for:
			SES, race/ethnicity, smoking, alcohol intake, family history of CVD or diabetes
			
			Key confounders accounted for:
			Age, sex, physical activity, TEI
			Additional model adjustments:
			BMI, prevalent diabetes, renal function, statin medication, prevalent ASVD, low-dose aspirin medication, antihypertensive medication
			Limitations:
			• Not all key confounders accounted for and no adjustment made for time-varying confounding
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Health and Medical Research Council; Raine Medical Research Foundation

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Bell, 2014[142]
PCS, VITAL (Vitamins and Lifestyle Study), U.S.
Baseline N=77,718, Analytic N=70,495 (Attrition: 9%)
 	
Participant characteristics at baseline:
• Age: Range 50-76y
• Sex (female): ~50%
• Race/ethnicity: >90% White
• SES: Education: >31-48% College or advanced degree, 35-42% some college/technical school, 13-27% secondary school
• Anthropometry: ~10%≥30 ~30% 25-<30
 	
Fat intake at baseline:
• Supplement intake (% subjects)
  • Low (0–4 d/week or <3 years): 5.6%
  • High (≥4 d/week for ≥3 years): 4.3%
 	
Blood lipids and BP at baseline: NR
 	
Summary of findings:
Dietary EPA and DHA intake from diet and supplements was not associated with CVD mortality or Intracerebral hemorrhage in middle aged and older Americans during 5y follow-up.
	Exposures:
	• EPA+DHA intake from diet and supplements (quartiles, g), Range
	  • Q1 (0–0.082)
	  • Q2 (0.083–0.174)
	  • Q3 (0.175–0.322)
	  • Q4 (>0.322)
	
	Diet assessment method and timing:
	• 120-item semi-quantitative FFQ with special emphasis on measurement of micronutrient fortified foods, dietary fats and dark fish
	• Self-report frequency and duration of n-3 supplement use over 10y.
	  • Intake estimate: (0.64 g/day for EPA and 0.35 g/day for DHA), multiplied by 10-y average use (days per week/7 × years/10)
	• Administered prior to baseline
	
	Outcomes and assessment methods:
	• Assessed during mean 5y of follow-up
	• CVD deaths ascertained by record linkage to Washington State death records, Social Security Death Index, next of kin or the Surveillance, Epidemiology and End Results cancer registry for western Washington.
	  • CVD death: 769 cases
		CVD death, HR (95% CI)
		EPA+DHA from diet and supplements (quartiles)
		Q1 (ref) vs Q2, Q3, or Q4: All NS P=0.799
		Ischemic heart disease mortality, HR (95% CI)
		EPA+DHA from diet and supplements (quartiles)
		Q1 (ref) vs Q2, Q3, or Q4: All NS, P=0.12
			Key confounders NOT accounted for:
			None
			
			Key confounders accounted for:
			Age, sex, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity, family history of CVD or diabetes
			Additional model adjustments:
			BMI, fruit and vegetable intake, use of nonsteroidal anti-inflammatory drugs, aspirin, cholesterol lowering drugs, cancer screening, self-reported health, morbidity score, trans fat, SFA, fruit and vegetable intake, hormone therapy, age at menopause, AA intake
			
			Limitations:
			• Analyses did not account for co-exposures (MUFA, PUFA)
			• Potential bias in classification of exposures due to use of non-validated FFQ
			• Potential missing data bias due to not statistically accounting for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			National Cancer Institute and the Office of Dietary Supplements, National Institutes of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Belin, 2011[140]
PCS, WHI-OS (Women's Health Initiative), U.S.
Baseline N=93,676 Analytic N=79,752 (Attrition: 15%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: ~64y (range: 50-79 y)
• Sex (female): 100%
• Race/ethnicity: African American ~7%
• SES: Education: ≤High school diploma/GED ~20%, Some school after high school ~37%, College graduate ~42%
• Anthropometry: BMI~26
 	
Fat intake at baseline, Mean:
• Total SFA: ~10%E
• MUFA: ~11%E
• PUFA: ~6%E
• Cholesterol: ~119 mg/day
• *Trans* FA: ~2%E
 	
Blood lipids and BP at baseline, Mean:
• HDL: ~60 mg/dL
• LDL: ~123 mg/dL
• Triglycerides: ~133 mg/dL
• SBP: ~125 mmHg
Summary of findings:
Lower dietary cholesterol intake was significantly associated with lower incidence of CVD and HF in women. No significant associations were observed with SFA and PUFA:SFA ratio with CVD and HF incidence.
	Exposures:
	• SFA (categorical; >8.78%E (ref) vs ≤8.78%E)
	• Cholesterol (categorical; >232.14 mg (ref) vs ≤232.14 mg)
	• PUFA:SFA (categorical; <0.77 (ref) vs ≥0.77
	
	Assessment method and timing:
	• Self-administered, validated 131-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 10 y of follow-up
	• Incident cardiovascular disease (CVD; nonfatal myocardial infarction, coronary heart disease death, stroke, coronary revascularization, and incident HF): Assessed by physician diagnosis and/or medical records
	  • CVD: 6,006 cases
	  • HF: 1,836 cases
		Incident CVD, HR (95% CI)
		SFA: NS
		Cholesterol: 0.89 (0.83, 0.95), P<0.001
		PUFA:SFA: NS
		Incident HF, HR (95% CI)
		SFA: NS
		Cholesterol: 0.82 (0.73, 0.92), P<0.001
		PUFA:SFA: NS
			Key confounders NOT accounted for: Family history of CVD or diabetes
			
			Key confounders accounted for: Sex, age, race/ethnicity, SES (educational level), TEI, alcohol intake, physical activity, smoking
			
			Additional model adjustments: BMI, diabetes medication, taking pills for hypertension ever, and ever taking pills for cholesterol
			
			Limitations:
			• Not all key confounders adjusted for
			• Analyses did not account for co-exposures (other types of fats)
			• No statistics to account for missing data
			• No preregistered statistical analysis plan
			
			Funding sources:
			NHLBI, NIH, U.S. Department of Health and Human Services

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Belin, 2011a[141] **PCS, WHI-OS (Women's Health Initiative), U.S.** Baseline N=93,676 Analytic N=84,493 (Attrition: 10%) **Participant characteristics at baseline:** • 100% without prevalent stroke or transient ischemic attack • Age: ~63y (range: 50-79 y) • Sex (female): 100% • Race/ethnicity: White 84%, African American 7%, Hispanic 4%, Other 5% • SES: Education: Did not complete high school 5%, high school/GED 16%, Some training after high school 36%, College graduate 43% • Anthropometry: BMI~27 **Fat intake at baseline, Median:** • SFA: ~10%E • LA: ~5.5%E • ALA: ~0.67%E • DHA+EPA: ~0.08%E • *Trans* FA: ~2%E **Blood lipids and BP at baseline, Mean:** • HDL cholesterol: ~63 mg/dL • Triglycerides: ~153 mg/dL • SBP: ~127 mmHg **Summary of findings:** *EPA+DHA intake and ALA intake were not associated with incidence of heart failure.*	**Exposures:** • EPA+DHA (quartile; Intake g/1000kcal Q1 0-0.02, Q2 0.021-0.04, Q3 0.041-0.07, Q4 0.071-0.17) • ALA (quartile; Intake g/1000kcal Q1 0.01-0.4, Q2 0.41-0.6, Q3 0.61-0.7, Q4 0.71-1.0) Assessment method and timing: • Self-administered, validated WHI FFQ • Assessed at baseline **Outcomes and assessment methods**: • Assessed during mean of 10 y of follow-up • Incident heart failure (HF): annual medical history	**Incident heart failure,** HR (95% CI) EPA+DHA: Q1 vs Q2, Q3, Q4: All NS P-trend=NS ALA: Q1 vs Q2, Q3, Q4: All NS P-trend=NS	**Key confounders NOT accounted for:** TEI, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, race/ethnicity, SES (education), alcohol intake, physical activity, smoking **Additional model adjustments:** BMI, Diabetes, hypertension, AF, MI/CABG/PTCA, time-dependent MI, intake of fiber, fruit/vegetables, SFA, TFA, ALA, and LA **Limitations:** • Not all key confounders adjusted for • No preregistered statistical analysis plan **Funding sources:** NHLBI; NIH; U.S. Department of Health and Human Services

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Yaemsiri, 2012[220] **PCS, WHI-OS (Women's Health Initiative), U.S.** Baseline N=93,676 Analytic N=87,025 (Attrition: 7%) **Participant characteristics at baseline:** • 100% without prevalent stroke or transient ischemic attack • Age: ~63y (range: 50-79 y) • Sex (female): 100% • Race/ethnicity: White 84%, African American 7%, Hispanic 4%, Other 5% • SES: Education: Did not complete high school 5%, high school/GED 16%, Some training after high school 36%, College graduate 43% • Anthropometry: BMI: Mean=27, SD=6 **Fat intake at baseline, Median:** • SFAs: ~14 g/d • MUFA: ~17 g/d • PUFA: ~9 g/d • Cholesterol: ~163 mg/d • *Trans* FA: ~2 g/day **BP at baseline, Mean (SD):** • SBP (mmHg): 126 (18) • DBP (mmHg): 75 (9) **Summary of findings:** *Higher dietary cholesterol (145 mg/day) intake, compared to 133 mg/day, was significantly associated with higher incidence of ischemic stroke, but was no longer significant when comparing higher quintiles of cholesterol intake. SFA, MUFA, and PUFA were not significantly associated with incidence of ischemic stroke.*	**Exposures:** • SFA (categorical, quintiles; Median intake (g/d) Q1 (ref) 12.9, Q2 13.4, Q3 14.5, Q4 17.0, Q5 26.1) • MUFA (categorical, quintiles; Median intake (g/d) Q1 (ref) 14.9, Q2 15.6, Q3 16.7, Q4 19.8, Q5 28.9) • PUFA (categorical, quintiles; Median intake (g/d) Q1 (ref) 8.4, Q2 8.4, Q3 9.0, Q4 10.6, Q5 16.0) • Cholesterol (categorical, quintiles; Median intake (mg/day) Q1 (ref) 133, Q2 144, Q3 163, Q4 203, Q5 311) Assessment method and timing: • Self-administered, validated WHI 122-item FFQ • Assessed at baseline and 3 y follow-up **Outcomes and assessment methods**: • Assessed during mean of ~7.6 y of follow-up • Incident ischemic stroke: annual medical history • Ischemic stroke: 1,049 cases	**Incident ischemic stroke,** HR (95% CI) SFA: NS MUFA: NS PUFA: NS Cholesterol: **Q1 (ref) vs Q2: 1.32 (1.06, 1.65)** Q1 (ref) vs Q3, Q4, Q5: All NS P-trend=NS	**Key confounders NOT accounted for:** Family history of CVD or diabetes **Key confounders accounted for:** Sex, age, race/ethnicity, SES, TEI, alcohol intake, physical activity, smoking **Additional model adjustments:** Hormone replacement therapy use, history of diabetes, aspirin use, use of antihypertensive medication, use of cholesterol-lowering medication, BMI, SBP, dietary vitamin E, fruits/vegetables, and fiber intake, history of CHD, atrial fibrillation **Limitations:** • Not all key confounders adjusted for • Analyses did not account for co-exposures (other types of fats) • No preregistered statistical analysis plan **Funding sources:** NHLBI; NIH; U.S. Department of Health and Human Services; National Institute of Neurological Disorders and Stroke; AHA

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Akbaraly, 2011[136] **PCS, Whitehall II, United Kingdom** Baseline N=10,308, Analytic N=7319 (Attrition: 29%) **Participant characteristics at baseline:** • Men and women 35-55y of age at baseline • Age: ~50y • Sex (female): ~30% • Race/ethnicity: ~92% White, ~5% South Asian, ~3% Black • SES: Occupational grade, ~15% Low, ~46% Intermediate, ~39% High • Anthropometry: BMI, ~4% <20, ~49% 20-25, ~38% 25-30, ~9% ≥30 **Fat intake at baseline, Mean (SD):** • PUFA:SFA (AHEI score): 5.2 (2.7) (score of 0 indicates least healthy dietary behavior, 10 indicates recommendations were fully met) **Blood lipids and BP at baseline:** • Dyslipidemia: ~59% • Hypertension: ~19% **Summary of findings:** *In men and women, higher intake scores on the AHEI for PUFA:SFA ratio at ~50y of age was not significantly associated with CVD mortality during ~17.7y of follow-up.*	**Exposures:** • PUFA:SFA ratio (continuous; per 1 SD increase in AHEI component score) Assessment method and timing: • Semi-quantitative, 127-item FFQ • Assessed at baseline **Outcomes and assessment methods**: • Assessed during ~17.7y of follow-up • CVD mortality: Obtained through linkage with National Health Services death and electronic patient records • Total: 141 cases (74 CHD, 28 stroke)	**PUFA:SFA ratio** **CVD Mortality,** HR (95% CI) 1.02 (0.86, 1.22), P=0.79	**Key confounders NOT accounted for:** Family history of CVD or diabetes **Key confounders accounted for:** Sex, age, race/ethnicity, SES (occupational grade), TEI, smoking, alcohol intake, physical activity. **Additional model adjustments:** Modified total AHEI score excluding PUFA:SFA ratio component, marital status, BMI, prevalent CVD, type 2 diabetes, hypertension, dyslipidemia, metabolic syndrome, inflammatory markers **Limitations:** • Not all key confounders accounted for • No indication that FFQ was validated • No information on other types of fat • Those excluded due to missing data were older, more likely to be women, and to have a lower occupational grade • No preregistered statistical analysis plan **Funding sources:** British Medical Research Council; British Heart Foundation; British Health and Safety Executive; British Department of Health; NHLBI; NIA; Agency for Health Care Policy and Research

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Rhee, 2017[200]
PCS, WHS (Women's Health Study), U.S.
Baseline N=39,876 Analytic N=38,392 (Attrition: 4%)
 	
Participant characteristics at baseline:
• 100% without prevalent CVD
• Age: ~54y
• Sex (female): 100%
• Race/ethnicity: NR
• SES: NR
• Anthropometry: BMI~26
 	
Fat intake at baseline, Mean:
• PUFA:SFA: ~0.6
 	
Blood lipids and BP at baseline:
• Hypertension: ~25%
• High cholesterol: ~29%
 	
Summary of findings:
There were no significant associations between energy-adjusted ALA and marine omega-3 fatty acids and risk of major CVD, MI, ischemic stroke, total stroke, and CVD death.
	Exposures:
	• ALA (categorical, quintiles; Median intake (%E): Q1 (ref) 0.74, Q2 0.88, Q3 0.99, Q4 1.12, Q5 1.36)
	• Marine omega-3 fatty acids (categorical, quintiles; Median intake (%E): Q1 (ref) 0.06, Q2 0.11, Q3 0.16, Q4 0.25, Q5 0.40)
	
	Assessment method and timing:
	• Self-administered, validated 131-item FFQ
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed during mean of 21 y of follow-up
	• Incident major cardiovascular disease (CVD; nonfatal myocardial infarction, nonfatal stroke, cardiovascular death): follow-up, medical records, review of autopsy reports, death certificates, medical records or next of kin or family members
	  • Major CVD event: 1,941 cases
	  • Nonfatal MI: 745 cases
	  • Ischemic stroke: 659 cases
	  • Total stroke: 987 cases
	  • Cardiovascular deaths: 501 cases
		Incident major CVD, HR (95% CI)
		ALA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Marine omega-3 FA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Incident MI, HR (95% CI)
		ALA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Marine omega-3 FA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Incident ischemic stroke, HR (95% CI)
		ALA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Marine omega-3 FA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Incident total stroke, HR (95% CI)
		ALA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Marine omega-3 FA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Incident CVD death, HR (95% CI)
		ALA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
		Marine omega-3 FA: Q1 (ref) vs Q2, Q3, Q4, Q5: All NS
		P-trend=NS
			Key confounders NOT accounted for:
			Race/ethnicity, TEI
			
			Key confounders accounted for:
			Sex, age, SES (educational level), alcohol intake, physical activity, smoking, family history of MI
			
			Additional model adjustments:
			BMI, Randomized treatment, intake of dietary fiber, fruits and vegetables, trans fat, sodium, PUFA:SFA, oral contraceptive use, use of hormones as defined under hormone replacement therapy, multivitamin use, baseline history of hypertension, high cholesterol and diabetes
			
			Limitations:
			• Not all key confounders accounted for
			• No preregistered statistical analysis plan
			
			Funding sources:
			NIH

* Abbreviations: AHEI – Alternative Healthy Eating Index, BP – blood pressure, CHO – carbohydrate, CI – confidence interval, d – day(s), DBP – diastolic blood pressure, FA – fatty acids, HDL – HDL cholesterol, HR – hazard ratio, IQR – interquartile range, LDL – LDL cholesterol, NR – not reported, NS – non significant, %E – percent energy, ref – reference group, SBP – systolic blood pressure, SD – standard deviation, SE – standard error, SEM – standard error of the mean, SES – socioeconomic status, TC – total cholesterol, TEI – total energy intake, WC – waist circumference, y – year(s)
† Statistically significant results bolded.

Table 9. Evidence from nested case-control studies examining types of dietary fat consumed by adults and cardiovascular disease endpoint outcomes*

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Juan, 2018[172] **Nested case-control, NHS and HPFS, U.S.** Baseline N=51,051 Analytic N=2,288 Subset of sample who provided blood samples: 720 CAD cases; 1568 CAD-free controls **Participant characteristics at baseline:** • 100% without prevalent CVD or cancer • Cases and controls matched on age, smoking status, fasting status at blood draw, time of blood draw • Age: NR • Sex (female): NHS: 100%; NHS: 0% • Race/ethnicity: NR • SES: NR • Anthropometry: NR **Fat intake at baseline:** See "Results" **Blood lipids and BP at baseline:** NR **Summary of findings:** *LA, ALA, DHA, EPA or AA intake at baseline did not differ between CAD cases and controls.*	**Exposures:** • LA intake (mg/day) • ALA intake (mg/day) • DHA intake (mg/day) • EPA intake (mg/day) • AA intake (mg/day) Assessment method and timing: • Self-administered, validated semi-quantitative FFQ • Assessed at baseline (at blood draw, NHS: 1986, 1990; HPFS: 1990, 1994) **Outcomes and assessment methods**: • Assessed during follow-up • Incident coronary artery disease (CAD): medical records, phone interview or letter (classified as probable), reports from next of kin, U.S. postal system, certificates from vital statistics departments and National Death Index, autopsy (previously reported) • CAD deaths: 720 cases	**Incident CAD,** Mean (SD), Cases vs Controls **NHS:** LA (mg/d): 10,812.4 (4247.4) vs 10,772.1 (3912.5), P=NS ALA (mg/d): 987.1 (402.6) vs 966.2 (384.0), P=NS DHA (mg/d): 152.5 (109.6) vs 154.5 (115.3), P=NS EPA (mg/d): 76.0 (63.3) vs 79.8 (102.8), P=NS AA (mg/d): 74.1 (29.3) vs 74.9 (29.5), P=NS **HPFS:** LA (mg/d): 11,302.2 (4,451.2) vs 11,029.8 (4175.8), P=NS ALA (mg/d): 1084.3 (424.6) vs 1062.9 (397.7), P=NS DHA (mg/d): 166.1 (136.9) vs 168.1 (145.3), P=NS EPA (mg/d): 99.0 (140.7) vs 101.6 (138.5), P=NS AA (mg/d): 81.4 (33.0) vs 79.5 (33.8), P=NS	**Key confounders NOT accounted for:** Sex, age, race/ethnicity, SES, TEI, alcohol intake, physical activity, smoking, family history of CVD or diabetes **Key confounders accounted for:** None **Additional model adjustments:** Energy contribution from protein, cholesterol intake, BMI, use of vitamins and aspirin, presence of baseline hypercholesterolemia, dietary intake of fruits and vegetables **Limitations:** • Not all key confounders accounted for • Analyses did not account for co-exposure (other types of fats) • No information on missing data • No preregistered statistical analysis plan **Funding sources:** NCI, NHLBI

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations
Pierucci, 2012[195] **NCC, ONCONUT, Italy** Baseline N=8,026 Analytic N=291 Cases: 97; Controls: 194 **Participant characteristics at baseline:** • 100% without prevalent MI and diabetes • Age: ~67 y • Sex (female): ~40% • Race/ethnicity: NR • SES: NR • Anthropometry: BMI~26 **Fat intake at baseline, Mean:** • SFA: ~19 g/d • MUFA: ~38 g/d • PUFA: ~8 g/d • Cholesterol: ~172 mg/d **BP at baseline:** • Hypertension: ~53% **Summary of findings:** *SFA, MUFA, PUFA, and cholesterol intake was not significantly associated with odds of incident MI.*	**Exposures:** • SFA (tertile) • MUFA (tertile) • PUFA (tertile) • Cholesterol (tertile) Assessment method and timing: • Self-administered, validated semi-quantitative FFQ • Assessed at baseline **Outcomes and assessment methods**: • Assessed during 5y of follow-up • Incident MI: self-reported and confirmed by family physician, discharge hospital records • Incident MI: 108 cases	**Incident MI**, OR, 95% CI *SFA:* T1 (ref) vs T2, T3: All NS, P=0.12 *MUFA:* T1 (ref) vs T2, T3: All NS, P=0.57 *PUFA:* T1 (ref) vs T2, T3: All NS, P=0.13 *Cholesterol:* T1 (ref) vs T2, T3: All NS, P=0.20	**Key confounders NOT accounted for:** SES, Race/ethnicity, alcohol intake, physical activity, family history of CVD or diabetes **Key confounders accounted for:** Sex, age, TEI, smoking **Additional model adjustments:** BMI, hypertension **Limitations:** • Not all key confounders adjusted for • Exposure was not quantified • No information on missing data • No preregistered statistical analyis plan **Funding sources:** Italian National Institute of Health

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Neelakantan, 2016[189]
NCC, SCHS (Singapore Chinese Health Study), Singapore
Baseline N=63,257, Cases N=751, Matched Controls N=1443 (From subset who provided blood samples, N=NR)
 	
Participant characteristics at baseline:
• Singapore Chinese 45-74y of age without CAD or stroke at baseline.
• Matched on age, sex, dialect group, recruitment date, blood collection date
• Age: ~59y
• Sex (female): ~35%
• Race/ethnicity: 100% ethnic Chinese
• SES: Education ≥Secondary Level ~27%
• Anthropometry: BMI ~23
 	
Fat intake at baseline, Mean (SD), Case vs Control:
• PUFA AHEI-2010 component score: 4.9 (1.8) vs 5.0 (1.8)
• Long chain (n-3) PUFA AHEI-2010 component score: 8.4 (2.5) vs 8.7 (2.2)
Blood lipids and BP at baseline, Mean (SD), Cases vs Controls:
• LDL (mmol/L): 3.3 (0.9) vs 3.2 (0.8)
• HDL (mmol/L): 1.3 (0.3) vs 1.3 (0.3)
• SBP (mmHg): 149 (24) vs 140 (22)
• DBP (mmHg): 83 (14) vs 81 (10)
 	
Summary of findings:
Higher intake scores on the AHEI-2010 for long chain (n-3) PUFA, but not total PUFA, at ~59y of age was significantly associated with lower odds of acute myocardial infarction over ~17y of follow-up.
	Exposures:
	• PUFA (continuous; per 2 point increase in AHEI-2010 component score
	  • Criteria for minimum score (0): ≤2%E
	  • Criteria for maximum score (10): ≥10%E
	• Long-chain (n-3) PUFA (continuous; per 2 point increase in AHEI-2010 component score
	  • Criteria for minimum score (0): 0 mg/d
	  • Criteria for maximum score (10): 250 mg/d
	
	Assessment method and timing:
	• Validated, semi-quantitative, 165-item FFQ assessing intake during the previous year
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed up to ~17y of follow-up
	• Incident Acute MI (fatal and nonfatal): Obtained through linkage with national Mediclaim System Hospital Discharge Database, Singapore Myocardial Infarction Registry, and Singapore Registry of Births and Deaths
	  • Total: 751 cases (288 fatal, 564 nonfatal)
		PUFA
		Total Acute MI, OR (95% CI)
		0.90 (0.81, 1.00), P=0.07
		
		Long-chain (n-3) PUFA
		Total Acute MI, OR (95% CI)
		0.85 (0.78, 0.93), P<0.001
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Father's dialect, year of birth, year of recruitment, BMI, history of diabetes, history of hypertension
			
			Limitations:
			• Not all key confounders accounted for
			• No information on whether those who did not provide blood samples (and were excluded from analyses) differed from those who provided blood samples (and were included)
			• No preregistered statistical analysis plan
			
			Funding sources:
			NCI; National Medical Research Council, Singapore

Study and Population Characteristics	Exposures, Comparators and Outcomes	Results†	Key Confounders, Study Limitations

Sun, 2016[209]
NCC, SCHS (Singapore Chinese Health Study), Singapore
Baseline N=63,257, Cases N=744, Matched Controls N=744 (From subset who provided blood samples, N=NR)
 	
Participant characteristics at baseline:
• Singapore Chinese 45-74y of age without cancer, CAD, or stroke at baseline.
• Matched on age, sex, dialect group, recruitment date, blood collection date
• Age: ~66y
• Sex (female): ~35%
• Race/ethnicity: 100% ethnic Chinese
• SES: Education ≥Secondary Level ~27%
• Anthropometry: BMI ~23
 	
Fat intake at baseline:
• See "Exposures" in next column
 	
Blood lipids, BP at baseline, Mean (SD):
• LDL (mmol/L): Cases, 3.3 (0.9); Controls, 3.2 (0.8)
• HDL (mmol/L): Cases, 1.3 (0.3); Controls, 1.4 (0.3)
• Hypertension: 46.9% cases, 36.8% controls
 	
Summary of findings:
EPA+DHA intake at ~66y of age was significantly associated with lower odds of total, fatal, and nonfatal acute myocardial infarction in this nested case-control study. ALA intake at baseline was not significantly associated with total, fatal, or nonfatal acute myocardial infarction.
	Exposures:
	• ALA (quartiles; %E), Median
	  • Q1 (ref): 0.21%E
	  • Q2: 0.27%E
	  • Q3: 0.32%E
	  • Q4: 0.41%E
	• EPA+DHA (quartiles; %E), Median
	  • Q1 (ref): 0.09%E
	  • Q2: 0.15%E
	  • Q3: 0.20%E
	  • Q4: 0.29%E
	
	Assessment method and timing:
	• Validated, semi-quantitative, 165-item FFQ assessing intake during the previous year
	• Assessed at baseline
	
	Outcomes and assessment methods:
	• Assessed up to ~17y of follow-up
	• Incident Acute MI (fatal and nonfatal): Obtained through linkage with national Mediclaim System Hospital Discharge Database, Singapore Myocardial Infarction Registry, and Singapore Registry of Births and Deaths
	  • Fatal: 289
	  • Nonfatal: 555
		ALA
		Total Acute MI, OR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend: 0.87
		Fatal Acute MI, OR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend: 0.45
		Nonfatal Acute MI, HR (95% CI)
		Q1 (ref) vs Q2, Q3, or Q4: All NS
		P-trend: 0.86
		
		EPA+DHA
		Total Acute MI, OR (95% CI)
		Q1 (ref) vs Q2: 0.64 (0.46, 0.88)
		Q1 (ref) vs Q3: 0.73 (0.53, 0.99)
		Q1 (ref) vs Q4: 0.64 (0.46, 0.89)
		P-trend: 0.03
		Fatal Acute MI, OR (95% CI)
		Q1 (ref) vs Q2: 0.67 (0.38, 1.19)
		Q1 (ref) vs Q3: 0.59 (0.35, 0.99)
		Q1 (ref) vs Q4: 0.46 (0.26, 0.80)
		P-trend: 0.006
		Nonfatal Acute MI, OR (95% CI)
		Q1 (ref) vs Q2: 0.57 (0.39, 0.83)
		Q1 (ref) vs Q3: 0.68 (0.48, 0.98)
		Q1 (ref) vs Q4: 0.66 (0.45, 0.97)
		P-trend: 0.12
			Key confounders NOT accounted for:
			Family history of CVD or diabetes
			
			Key confounders accounted for:
			Sex, age, race/ethnicity, SES (education), TEI, smoking, alcohol intake, physical activity.
			
			Additional model adjustments:
			Father's dialect, year of birth, year of recruitment, BMI, cholesterol intake, fiber intake, total fat intake, history of hypertension and diabetes
			
			Limitations:
			• Not all key confounders accounted for
			• Did not account for co-exposures (other fatty acids)
			• No information on whether those who did not provide blood samples (and were excluded from analyses) differed from those who provided blood samples (and were included)
			• No preregistered statistical analysis plan
			
			Funding sources:
			NIH; National Medical Research Council, Singapore

[*] Abbreviations: AHEI – Alternative Healthy Eating Index, BP – blood pressure, d – day(s), DBP – diastolic blood pressure, HDL – HDL cholesterol, HF – heart failure, LDL – LDL cholesterol, NR – not reported, NS – non significant, OR – odds ratio, %E – percent energy, ref – reference group, SD – standard deviation, SBP – systolic blood pressure, SES – socioeconomic status, TEI – total energy intake, y – year

[†] Statistically significant results bolded.

Table 10. Risk of bias for observational studies examining types of dietary fat consumed by adults and cardiovascular disease endpoint outcomes[*,†]

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Abdollahi, 2019,[135] PCS	Serious	Low	Moderate	Low	Low	Low	Moderate
Akbaraly, 2011,[136] PCS	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Akesson, 2019,[137] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Amiano, 2014,[138] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Atkinson, 2011,[139] PCS	Serious	Low	Moderate	Moderate	Low	Low	Moderate
Belin, 2011,[140] PCS	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Belin, 2011a,[141] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Bell, 2014,[142] PCS	Moderate	Low	Moderate	Moderate	Moderate	Low	Moderate
Bendinelli, 2011,[143] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Bergkvist, 2014,[146] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Bergkvist, 2015,[145] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Bergkvist, 2016,[144] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Blekkenhorst, 2015,[147] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Bork, 2016,[148] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Bork, 2018,[149] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Buckland, 2012,[150] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Buckland, 2012a,[151] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Chiuve, 2012,[152] PCS	Serious	Low	Low	Low	Moderate	Low	Moderate

[*] A detailed description of the methodology used for assessing risk of bias is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews and in Part C of the following reference: Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.

[†] Possible ratings of low, moderate, serious, critical, or no information determined using the "Risk of Bias for Nutrition Observational Studies" tool (RoB-NObs) (Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services*. U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.)

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
de Goede, 2010,[153] PCS	Serious	Low	Low	Low	Low	Low	Moderate
de Goede, 2011,[155] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
de Goede, 2012,[154] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
de Oliveira Otto, 2012,[156] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
de Oliveira Otto, 2013,[157] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Donat-Vargas, 2019,[158] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Fretts, 2014,[159] PCS	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Gammelmark, 2016,[160] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Gardener, 2011,[161] PCS	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Goldbohm, 2011,[162] PCS	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Guasch-Ferre, 2014,[164] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Guasch-Ferre, 2015,[163] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Hellstrand, 2014,[165] PCS	Serious	Moderate	Moderate	Moderate	Low	Low	Moderate
Hisamatsu, 2013,[166] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Hlebowicz, 2013,[167] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Houston, 2011,[168] PCS	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Isaksen, 2019,[169] PCS	Serious	Low	Moderate	Moderate	Moderate	Low	Moderate
Jakobsen, 2010,[170] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Joensen, 2010,[171] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Juan, 2018,[172] NCC	Serious	Low	Low	Moderate	No information	Low	Moderate
Kiage, 2015,[173] PCS	Serious	No information	Low	Low	No information	Low	Moderate
Kippler, 2016,[174] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Koh, 2015,[175] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Koskinen, 2018,[176] PCS	Serious	Low	Moderate	Low	Low	Low	Moderate
Kouli, 2019,[177] PCS	Serious	Low	Low	Low	Moderate	Low	Moderate
Kulezic, 2019,[178] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Larsson, 2012,[179] PCS	Serious	Low	Low	Low	Low	Low	Moderate

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Lemaitre, 2012,[180] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Levitan, 2010,[182] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Levitan, 2012,[181] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Li, 2015,[183] PCS	Serious	Moderate	Low	Moderate	Moderate	Low	Moderate
Lin, 2018,[184] PCS	Serious	Moderate	Moderate	Moderate	Moderate	No information	Moderate
Miyagawa, 2014,[185] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Nagata, 2012,[186] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Nakamura, 2013,[187] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Neelakantan, 2016,[189] NCC	Serious	Low	Low	Low	Moderate	Low	Moderate
Neelakantan, 2018,[188] PCS	Serious	Low	Moderate	Low	Low	Low	Moderate
Okada, 2019,[190] PCS	Serious	Low	Serious	Low	Low	Low	Moderate
O'Neil, 2015,[191] PCS	Serious	Low	Moderate	Moderate	Low	Low	Moderate
Owen, 2016,[192] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Pala, 2019,[193] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Patterson, 2013,[194] PCS	Serious	Moderate	Moderate	Low	Low	Low	Moderate
Pierucci, 2012,[195] NCC	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Praagman, 2016,[196] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Praagman, 2016a,[197] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Praagman, 2019,[198] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Reedy, 2014,[199] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Rhee, 2017,[200] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Ricci, 2018,[201] PCS	Serious	Moderate	Low	Low	Moderate	Low	Moderate
Sala-Vila, 2016,[202] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Samieri, 2011,[203] PCS	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Santiago, 2018,[204] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Simila, 2013,[205] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Sonestedt, 2011,[206] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate

	Confounding	Selection of participants	Classification of exposures	Deviations from intended exposures	Missing data	Outcome measurement	Selection of the reported result
Stefler, 2017,[207] PCS	Serious	Moderate	Moderate	Low	Low	Low	Moderate
Strom, 2012,[208] PCS	Serious	Moderate	Low	Low	Low	Low	Moderate
Sun, 2016,[209] NCC	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Vedtofte, 2011,[210] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Veno, 2017,[212] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Veno, 2019,[211] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Virtanen, 2014,[213] PCS	Serious	Low	Moderate	Low	Low	Low	Moderate
Virtanen, 2016,[214] PCS	Serious	Low	Moderate	Low	Low	Low	Moderate
Vissers, 2019,[215] PCS	Serious	Low	Low	Low	Moderate	Low	Moderate
Wakai, 2014,[216] PCS	Serious	Low	Low	Moderate	Moderate	Low	Moderate
Wallstrom, 2012,[217] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Wang, 2016,[218] PCS	Moderate	Moderate	Low	Low	Low	Low	Moderate
Wilk, 2012,[219] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Yaemsiri, 2012,[220] PCS	Serious	Low	Low	Moderate	Low	Low	Moderate
Yamagishi, 2010,[222] PCS	Serious	Low	Moderate	Low	Moderate	Low	Moderate
Yamagishi, 2013,[221] PCS	Serious	Low	Moderate	Low	Low	Low	Moderate
Zhang, 2018,[223] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Zhong, 2019,[224] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Zhuang, 2019,[225] PCS	Moderate	Low	Moderate	Low	Low	Low	Moderate
Zhuang, 2019a,[226] PCS	Serious	Low	Low	Low	Low	Low	Moderate
Zong, 2016,[228] PCS	Serious	Moderate	Low	Moderate	Low	Low	Moderate
Zong, 2018,[227] PCS	Serious	Moderate	Low	Moderate	Moderate	Low	Moderate

METHODOLOGY

The NESR team used its rigorous, protocol-driven methodology to support the 2020 Dietary Guidelines Advisory Committee in conducting this systematic review.

NESR's systematic review methodology involves:

- Developing a protocol,
- Searching for and selecting studies,
- Extracting data from and assessing the risk of bias of each included study,
- Synthesizing the evidence,
- Developing conclusion statements,
- Grading the evidence underlying the conclusion statements, and
- Recommending future research.

A detailed description of the methodology used in conducting this systematic review is available on the NESR website: https://nesr.usda.gov/2020-dietary-guidelines-advisory-committee-systematic-reviews, and can be found in 2020 Dietary Guidelines Advisory Committee Report, Part C: Methodology.[xii] This systematic review was peer reviewed by Federal scientists, and information about the peer review process can also be found in the Committee's Report, Part C: Methodology. Additional information about this systematic review, including a description of and rationale for any modifications made to the protocol are described in the 2020 Dietary Guidelines Advisory Committee Report, Chapter 9. Dietary Fats and Seafood.

The systematic review described in this document builds on evidence reviewed by the 2015 Dietary Guidelines Advisory Committee. Information about the 2015 Dietary Guidelines Advisory Committee's review of the evidence for the question "What is the relationship between intake of saturated fat and risk of cardiovascular disease?" can be found in their report[xiii] (see Part D. Chapter 6: Cross-Cutting Topics of Public Health Importance, page 337).

Below are details of the final protocol for the systematic review described herein, including the:

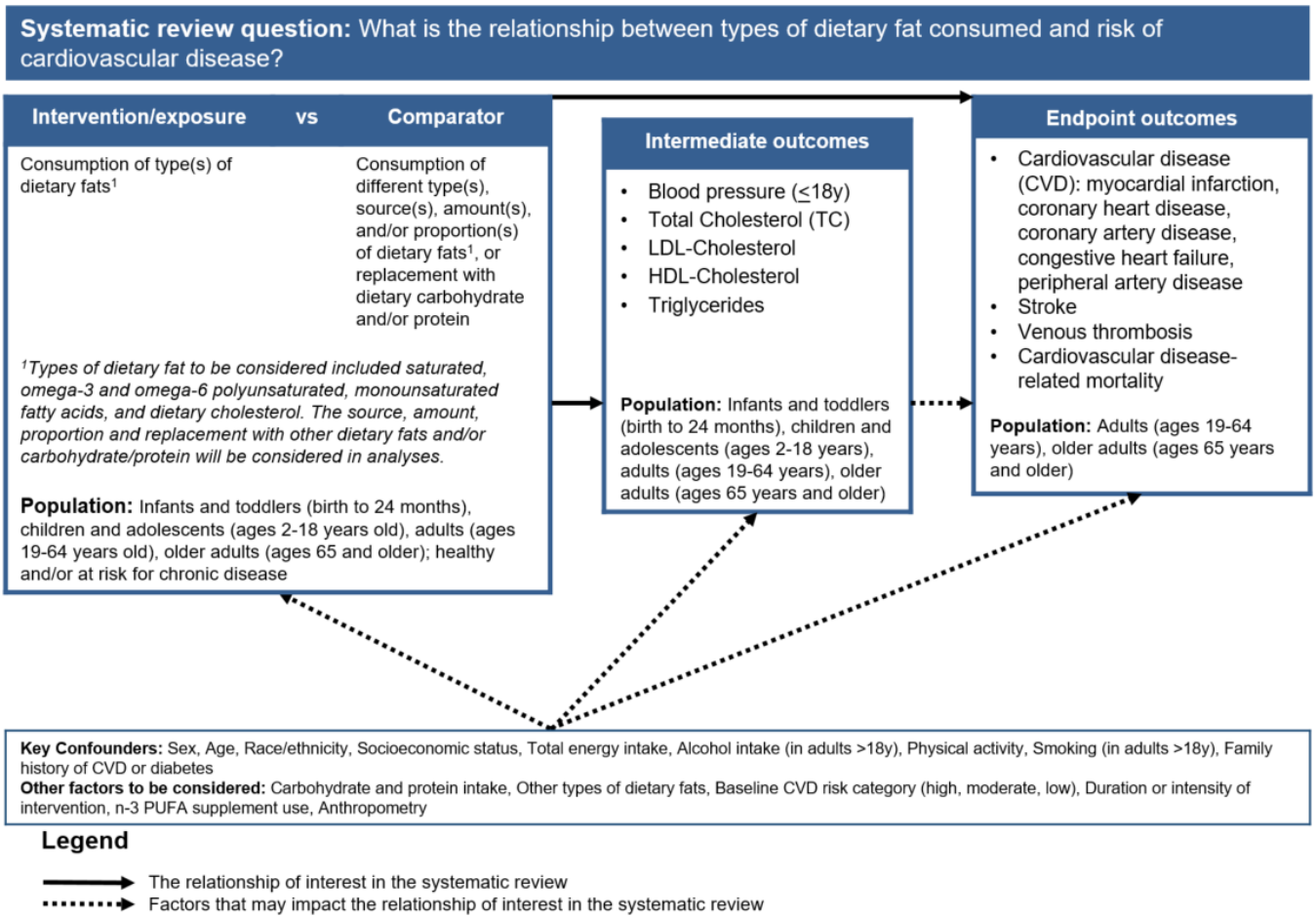
- Analytic framework
- Literature searches and screening plan
- Literature searches and screening results

[xii] Dietary Guidelines Advisory Committee. 2020. *Scientific Report of the 2020 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Agriculture and the Secretary of Health and Human Services.* U.S. Department of Agriculture, Agricultural Research Service, Washington, DC.
[xiii] Dietary Guidelines Advisory Committee. 2015. *Scientific Report of the 2015 Dietary Guidelines Advisory Committee: Advisory Report to the Secretary of Health and Human Services and the Secretary of Agriculture.* U.S. Department of Agriculture, Agricultural Research Service, Washington, D.C.

ANALYTIC FRAMEWORK

The analytic framework (**Figure 1**) illustrates the overall scope of the systematic review, including the population, the interventions and/or exposures, comparators, and outcomes of interest. It also includes definitions of key terms and identifies key confounders considered in the systematic review. The inclusion and exclusion criteria that follow provide additional information about how parts of the analytic framework were defined and operationalized for the review.

Figure 1: Analytic framework



Inclusion and exclusion criteria

This table (**Table 11**) provides the inclusion and exclusion criteria for the systematic review. The inclusion and exclusion criteria are a set of characteristics used to determine which articles identified in the literature searches were included in or excluded from the systematic review

Table 11. Inclusion and exclusion criteria

Category	Inclusion Criteria	Exclusion Criteria
Study design	• Randomized controlled trials (RCTs) • Non-randomized controlled trials (NRCTs), including quasi-experimental and controlled before-and-after studies • Prospective cohort studies • Retrospective cohort studies • Nested case-control studies	• Uncontrolled trials • Case-control studies • Cross-sectional studies • Uncontrolled before-and-after studies • Narrative reviews • Systematic reviews • Meta-analyses

Intervention/ exposure	• Consumption of type(s) of dietary fats
	  ○ Types of dietary fat to be considered included saturated, omega-3 and omega-6 polyunsaturated, monounsaturated fatty acids, and dietary cholesterol.
	  ○ The source, amount, proportion, and replacement with other dietary fats and/or carbohydrate/protein will also be considered in analyses
		• Studies that do not assess consumption of type(s) of **dietary fats** (e.g., studies that only examined biomarkers for consumption)
		• Studies that **only** assess total fat intake or overall macronutrient composition
		• Studies that **only** assess *trans* fat
		• Studies that examine food products not widely available to U.S. consumers
		• Studies that **exclusively** assess intake of fat from supplements or fish oils
		• Human milk and/or infant formula as the **only** source of dietary fat
		• Multi-component interventions that do not isolate the impact of type of fat

Category	Inclusion Criteria	Exclusion Criteria
Comparator	• Consumption of different type(s), source(s), amount(s), and/or proportion(s) of dietary fats, or replacement with dietary carbohydrates and/or protein	• No comparator
Outcomes	Intermediate Outcomes (Children: all study designs; Adults: interventions only) • Blood pressure (systolic and diastolic) (≤18y of age) • Total Cholesterol (TC) • LDL Cholesterol • HDL Cholesterol • Triglycerides Endpoint Outcomes • Cardiovascular disease (myocardial infarction, coronary heart disease, coronary artery disease, congestive heart failure, peripheral artery disease) • Stroke • Venous thrombosis • Cardiovascular disease mortality	• Studies that **only** assess post-prandial lipid levels (i.e., total, LDL, and HDL cholesterol, and/or triglycerides) • Studies that **only** assess serum lipid ratios (i.e., TC:HDL, LDL:HDL ratios) • Blood pressure in adults (>18y of age) • Intermediate outcomes in observational studies conducted in adults (>18y of age)
Study duration	• Observational studies: Any duration • RCTs and NRCTs: Interventions ≥4wk in duration	• RCTs and NRCTs: Interventions <4wk in duration
Date of publication	• January 1990 to October 2019 for articles on types of dietary fat consumed by children and adolescents and risk of cardiovascular disease. • January 2010 to October 2019 for articles on types of dietary fat consumed by adults and risk of cardiovascular disease.*	• Articles published prior to January 1990 on types of fat consumed by children and adolescents and risk of cardiovascular disease. • Articles published before 2010 on types of fat consumed by adults and risk of cardiovascular disease. • Articles published after October 2019

Category	Inclusion Criteria	Exclusion Criteria
Publication status	• Articles that have been peer-reviewed	• Articles that have not been peer-reviewed and are not published in peer-reviewed journals, including unpublished data, manuscripts, reports, abstracts, and conference proceedings
Language of publication	• Articles published in English	• Articles published in languages other than English
Country†	• Studies conducted in countries ranked as high or very high human development	• Studies conducted in countries ranked as medium or lower human development
Study participants	• Human participants (male and/or female) • Females who are pregnant and/or lactating	• Non-human subjects (e.g., animal models or in-vitro models)
Age of study participants	• Age at intervention or exposure: ○ Infants and toddlers (birth to 24 months) ○ Children and adolescents (ages 2-18 years) ○ Adults (ages 19-64 years) ○ Older adults (ages 65 years and older) • Age at intermediate outcomes: ○ Infants and toddlers ages (birth to 24 months) ○ Children and adolescents (ages 2-18 years) ○ Adults (ages 19-64 years) ○ Older adults (ages 65 years and older) • Age at endpoint outcomes: ○ Adults (ages 19-64 years) ○ Older adults (ages 65 years and older)	• Age at endpoint outcome: ○ Infants and toddlers (birth to 24 months) ○ Children and adolescents (ages 2-18 years)

Category	Inclusion Criteria	Exclusion Criteria
Health status of study participants	• Studies that enroll participants who are healthy and/or at risk for chronic disease, including those with obesity • Studies that **exclusively** enroll participants with high blood pressure or high cholesterol and are evaluating cardiovascular disease endpoint outcomes • Studies that enroll **some** participants diagnosed with cardiovascular disease endpoint outcomes. • Studies that enroll **some** participants diagnosed with a disease or hospitalized with and illness or injury • Studies that enroll infants born full-term (≥37 weeks and 0/7 days gestational age) • Studies that enroll **some** infants born preterm (gestational age <37 weeks and 0/7 days), infants with low birth weight (<2500g), and/or infants born small for gestational age	• Studies that **exclusively** enroll participants diagnosed with a disease (e.g., diabetes, renal disease), or hospitalized with an illness or injury (For this criterion, studies that exclusively enroll participants with obesity will not be excluded) • Studies that **exclusively** enroll participants with cardiovascular disease endpoint outcomes (i.e., studies that aim to treat participants who have already been diagnosed with cardiovascular disease) • Studies that **exclusively** enroll participants with high blood lipids (e.g., TC, LDL cholesterol , HDL cholesterol, or triglycerides) and are evaluating any blood lipid intermediate outcome (i.e., studies that aim to treat participants who already have high cholesterol or blood lipids)

[*] This systematic review builds upon the 2015 Dietary Guidelines Advisory Committee report that considered evidence in adults preceding January 2010.
[†] The Human Development classification was based on the Human Development Index (HDI) ranking (1) from the year the study intervention occurred or data were collected. If the study did not report the year in which the intervention occurred or data were collected, the HDI classification for the year of publication was applied. HDI values are available from 1990 to present. If a study was conducted in 2018 or 2019, the most current HDI classification was applied. If a study was conducted prior to 1990, the HDI classification from 1990 was applied. When a country was not included in the HDI ranking, the current country classification from the World Bank (2) is used instead.

1. UN Development Program. HDI 1990-2017 HDRO calculations based on data from UNDESA (2017a), UNESCO Institute for Statistics (2018), United Nations Statistics Division (2018b), World Bank (2018b), Barro and Lee (2016) and IMF (2018). Available from: http://hdr.undp.org/en/data.
2. The World Bank. World Bank country and lending groups. Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-country-and-lending-groups

Electronic databases and search terms

Listed below are the databases searched to identify all potentially relevant articles that have been published to address the systematic review question. Two search strategies were developed and implemented each in four databases (PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Embase and Cumulative Index of Nursing and Allied Health Literature (CINAHL) to conduct this systematic review.

Search strategy 1: Search strategy to capture the literature on types of dietary fats and risk of cardiovascular disease for children and adolescents from 1990-2009

PubMed

- Provider: U.S. National Library of Medicine
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 1990-December 31, 2009
- Search Terms:

#1 - "Dietary Fats"[Mesh] OR dietary fat* OR diet fat* OR dietary lipid* OR fat consumption* OR fat intake* OR "Fatty Acids"[Mesh:noexp] OR fatty acid* OR saturated fat* OR "Fatty Acids, Monounsaturated"[Mesh] OR monounsaturated fat* OR mono-unsaturated fat* OR polyunsaturated fat* OR poly-unsaturated fat* OR unsaturated fat* OR unsaturated fatty acid* OR "Fatty Acids, Omega-3"[Mesh] OR omega-3[tiab] OR N-3 fatty acid* OR "Fatty Acids, Omega-6"[Mesh] OR omega-6 OR N-6 fatty acid* OR MUFA* OR PUFA* OR "Cholesterol, Dietary"[Mesh] OR dietary cholesterol* OR alpha-linolenic acid* OR eicosapentaenoic acid* OR docosahexaenoic acid* OR linoleic acid* OR alpha-linolenic acid* OR arachidonic acid* OR "Fats, Unsaturated"[Mesh] OR milk fat*[tiab] OR "Butter"[Mesh] OR butter[tiab] OR Ghee[tiab] OR "Margarine"[Mesh] OR margarine[tiab] OR dietary oil* OR "Plant Oils"[Mesh] OR plant oil* OR "Fish Oils"[Mesh] OR fish oil* OR olive oil* OR corn oil* OR cottonseed oil* OR cotton seed oil* OR safflower oil* OR sesame oil* OR soybean oil* OR soya-bean oil* OR linseed oil* OR canola oil* OR peanut oil* OR coconut oil* OR edible oil* OR palm oil* OR fish oil* OR maize oil* OR oleic acid* OR ((fat[tiab] OR fatty[tiab]) AND (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR linolenic acid* OR "Milk"[Mesh] OR milk[tiab] OR "Infant Formula"[Mesh] OR infant formula*[tiab]))

#2 - "Cardiovascular Diseases"[Mesh:noexp] OR cardiovascular disease*[tiab] OR coronary artery disease[tiab] OR heart disease*[tiab] OR "Heart Failure"[Mesh] OR heart failure[tiab] OR "Myocardial Infarction"[Mesh] OR myocardial infarction*[tiab] OR "Myocardial Ischemia"[Mesh] OR Myocardial Ischemia*[tiab] OR "Stroke"[Mesh] OR stroke[tiab] OR angina[tiab] OR heart attack[tiab] OR "Cardiovascular System"[Mesh] OR "cardiometabolic health" OR cardiovascular health[tiab] OR "cardiac health" OR "cardiovascular biomarkers" OR "Venous Thrombosis"[Mesh] OR venous thrombosis[tiab] OR hypertension[tiab] OR high blood pressure[tiab] OR "Lipids/blood"[Mesh] OR "Cholesterol, HDL"[Mesh] OR HDL cholesterol[tiab] OR "Cholesterol, LDL"[Mesh] OR LDL cholesterol[tiab] OR total cholesterol[tiab] OR "Triglycerides"[Mesh] OR triglycerides[tiab]

#3 - "Child"[Mesh] OR child[tiab] OR children[tiab] OR youth* OR "Adolescent"[Mesh] OR adolescence[tiab] OR adolescent* OR teen[tiab] OR teens[tiab] OR teenager* OR preteen* OR pre-teen* OR pre-adolesc* OR preadolesc* OR preschool* OR "Pediatrics"[Mesh] OR pediatric* OR paediatric* OR "Infant"[Mesh] OR Infan*[tiab] OR newborn*[tiab] OR new-born*[tiab] OR perinat*[tiab] OR neonat* OR prematur* OR preterm* OR baby[tiab] OR

babies[tiab] OR toddler*[tiab] OR boy[tiab] OR boys[tiab] OR girl[tiab] OR girls[tiab] OR schoolchild* OR middle school* OR high school* OR juvenile[tiab] OR pubescent[tiab] OR pre pubescent[tiab] OR prepubescent[tiab] OR kid[tiab] OR kids[tiab] OR early childhood[tiab] OR early years[tiab] OR pre-k[tiab] OR pre-primary[tiab] OR under five*[tiab] OR young child*[tiab] OR head start[tiab] OR prekindergarten[tiab] OR pre-kindergarten[tiab]

#4 - (#1 AND #2 AND #3)

#5 - (#1 AND #2 AND #3) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti]) Filters: Publication date from 1990/01/01 to 2009/12/31; English

Cochrane Central Register of Controlled Trials (CENTRAL)

- Provider: John Wiley & Sons
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 1990-December 31, 2009
- Search Terms:

#1 - [mh "Dietary Fats"] OR [mh ^"Fatty Acids"] OR [mh "Fatty Acids, Monounsaturated"] OR [mh "Fatty Acids, Omega-3"] OR [mh "Fatty Acids, Omega-6"] OR [mh "Cholesterol, Dietary"] OR [mh "Fats, Unsaturated"] OR [mh Butter] OR [mh Margarine] OR [mh “Plant Oils”] OR [mh "Fish Oils"]

#2 - (“dietary fat*” OR “diet fat*” OR “dietary lipid*” OR “fat consumption*” OR “fat intake*” OR “fatty acid*” OR “saturated fat*” OR “monounsaturated fat*” OR “mono-unsaturated fat*” OR “polyunsaturated fat*” OR “poly-unsaturated fat*” OR “unsaturated fat*” OR “unsaturated fatty acid*” OR omega-3 OR “N-3 fatty acid*” OR omega-6 OR “N-6 fatty acid*” OR MUFA* OR PUFA* OR “dietary cholesterol*” OR “alpha-linolenic acid*” OR “eicosapentaenoic acid*” OR “docosahexaenoic acid*” OR “linoleic acid*” OR “alpha-linolenic acid*” OR “arachidonic acid*” OR “milk fat*” OR butter OR Ghee OR margarine OR “dietary oil*” OR “plant oil*” OR “fish oil*” OR “olive oil*” OR “corn oil*” OR “cottonseed oil*” OR “cotton seed oil*” OR “safflower oil*” OR “sesame oil*” OR “soybean oil*” OR “soya-bean oil*” OR “linseed oil*” OR “canola oil*” OR “peanut oil*” OR “coconut oil*” OR “edible oil*” OR “palm oil*” OR “fish oil*” OR “maize oil*” OR “oleic acid*”):ti,ab,kw

#3 - ((fat OR fatty) NEAR/6 (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR “linolenic acid*” OR [mh Milk] OR milk OR [mh "Infant Formula"] OR “infant formula*”)):ti,ab,kw

#4 - #1 OR #2 OR #3

#5 - [mh ^"Cardiovascular Diseases"] OR [mh "Heart Failure"] OR [mh "Myocardial Ischemia"] OR [mh "Myocardial Infarction"] OR [mh Stroke] OR [mh "Cardiovascular System"] OR [mh "Venous Thrombosis"] OR [mh Lipids/BL] OR [mh "Cholesterol, HDL"] OR [mh "Cholesterol, LDL"] OR [mh Triglycerides]

#6 - (“cardiovascular disease*” OR “coronary artery disease” OR “heart disease*” OR “heart failure” OR “myocardial infarction*” OR “myocardial ischemia*” OR stroke OR angina OR “heart attack” OR “cardiometabolic health” OR “cardiovascular health” OR “cardiac health” OR

“cardiovascular biomarkers” OR “venous thrombosis” OR hypertension OR “high blood pressure” OR “HDL cholesterol” OR “LDL cholesterol” OR “total cholesterol” OR triglycerides):ti,ab,kw"

#7 - #5 OR #6

#8 - [mh Child] OR [mh Adolescent] OR [mh Pediatrics] OR [mh Infant]

#9 - (Child OR children OR youth* OR adolescence OR adolescent* OR teen OR teens OR teenager* OR preteen* OR pre-teen* OR pre-adolesc* OR preadolesc* OR preschool* OR pediatric* OR paediatric* OR Infan* OR newborn* OR new-born* OR perinat* OR neonat* OR prematur* OR preterm* OR baby OR babies OR toddler* OR boy OR boys OR girl OR girls OR schoolchild* OR “middle school*” OR “high school*” OR juvenile OR pubescent OR “pre pubescent” OR prepubescent OR kid OR kids OR “early childhood” OR “early years” OR pre-k OR pre-primary OR “under five*” OR “young child*” OR “head start” OR prekindergarten OR pre-kindergarten):ti,ab,kw

#10 - #8 OR #9

#11 - #4 AND #7 AND #10" with Publication Year from 1990 to 2009, in Trials (Word variations have been searched)

Embase

- Provider: Elsevier
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 1990-December 31, 2009
- Search Terms:

#1 - 'edible oil'/exp OR 'fatty acid'/de OR 'monounsaturated fatty acid'/de OR 'omega 3 fatty acid'/de OR 'omega 6 fatty acid'/de OR 'cholesterol intake'/de OR 'unsaturated fatty acid'/exp OR 'butter'/de OR 'margarine'/de OR 'vegetable oil'/exp OR 'fish oil'/de

#2 - 'dietary fat*':ab,ti OR 'diet fat*':ab,ti OR 'dietary lipid*':ab,ti OR 'fat consumption*':ab,ti OR 'fat intake*':ab,ti OR 'fatty acid*':ab,ti OR 'saturated fat*':ab,ti OR 'monounsaturated fat*':ab,ti OR 'mono-unsaturated fat*':ab,ti OR 'polyunsaturated fat*':ab,ti OR 'poly-unsaturated fat*':ab,ti OR 'unsaturated fat*':ab,ti OR 'unsaturated fatty acid*':ab,ti OR 'omega 3':ab,ti OR 'n-3 fatty acid*':ab,ti OR 'omega 6':ab,ti OR 'n-6 fatty acid*':ab,ti OR mufa*:ab,ti OR pufa*:ab,ti OR 'dietary cholesterol*':ab,ti OR 'eicosapentaenoic acid*':ab,ti OR 'docosahexaenoic acid*':ab,ti OR 'linoleic acid*':ab,ti OR 'alpha-linolenic acid*':ab,ti OR 'arachidonic acid*':ab,ti OR 'milk fat*':ab,ti OR butter:ab,ti OR ghee:ab,ti OR margarine:ab,ti OR 'dietary oil*':ab,ti OR 'plant oil*':ab,ti OR 'olive oil*':ab,ti OR 'corn oil*':ab,ti OR 'cottonseed oil*':ab,ti OR 'cotton seed oil*':ab,ti OR 'safflower oil*':ab,ti OR 'sesame oil*':ab,ti OR 'soybean oil*':ab,ti OR 'soya-bean oil*':ab,ti OR 'linseed oil*':ab,ti OR 'canola oil*':ab,ti OR 'peanut oil*':ab,ti OR 'coconut oil*':ab,ti OR 'edible oil*':ab,ti OR 'palm oil*':ab,ti OR 'fish oil*':ab,ti OR 'maize oil*':ab,ti OR 'oleic acid*':ab,ti

#3 - ((fat OR fatty) NEAR/6 (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR 'linolenic acid*' OR milk OR 'infant formula*')):ab,ti

#4 - #1 OR #2 OR #3

#5 - 'cardiovascular disease'/de OR 'heart failure'/exp OR 'heart muscle ischemia'/exp OR 'heart infarction'/exp OR 'cerebrovascular accident'/exp OR 'cardiovascular system'/exp OR

'vein thrombosis'/exp OR 'high density lipoprotein cholesterol'/de OR 'low density lipoprotein cholesterol'/de OR 'triacylglycerol'/exp

#6 - 'cardiovascular disease*':ab,ti OR 'coronary artery disease':ab,ti OR 'heart disease*':ab,ti OR 'heart failure':ab,ti OR 'myocardial infarction*':ab,ti OR 'myocardial ischemia*':ab,ti OR stroke:ab,ti OR angina:ab,ti OR 'heart attack':ab,ti OR 'cardiometabolic health':ab,ti OR 'cardiovascular health':ab,ti OR 'cardiac health':ab,ti OR 'cardiovascular biomarkers':ab,ti OR 'venous thrombosis':ab,ti OR hypertension:ab,ti OR 'high blood pressure':ab,ti OR 'hdl cholesterol':ab,ti OR 'ldl cholesterol':ab,ti OR 'total cholesterol':ab,ti OR triglycerides:ab,ti

#7 - #5 OR #6

#8 - 'child'/exp OR 'adolescent'/exp OR 'pediatrics'/de

#9 - child:ab,ti OR children:ab,ti OR youth*:ab,ti OR adolescence:ab,ti OR adolescent*:ab,ti OR teen:ab,ti OR teens:ab,ti OR teenager*:ab,ti OR preteen*:ab,ti OR 'pre teen*':ab,ti OR 'pre adolesc*':ab,ti OR preadolesc*:ab,ti OR preschool*:ab,ti OR pediatric*:ab,ti OR paediatric*:ab,ti OR infan*:ab,ti OR newborn*:ab,ti OR 'new born*':ab,ti OR perinat*:ab,ti OR neonat*:ab,ti OR prematur*:ab,ti OR preterm*:ab,ti OR baby:ab,ti OR babies:ab,ti OR toddler*:ab,ti OR boy:ab,ti OR boys:ab,ti OR girl:ab,ti OR girls:ab,ti OR schoolchild*:ab,ti OR 'middle school*':ab,ti OR 'high school*':ab,ti OR juvenile:ab,ti OR pubescent:ab,ti OR 'pre pubescent':ab,ti OR prepubescent:ab,ti OR kid:ab,ti OR kids:ab,ti OR 'early childhood':ab,ti OR 'early years':ab,ti OR 'pre k':ab,ti OR 'pre primary':ab,ti OR 'under five*':ab,ti OR 'young child*':ab,ti OR 'head start':ab,ti OR prekindergarten:ab,ti OR 'pre kindergarten':ab,ti

#10 - #8 OR #9

#11 - #4 AND #7 AND #10 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [1990-2009]/py NOT ([conference abstract]/lim OR [conference review]/lim OR [conference paper]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

Cumulative Index of Nursing and Allied Health Literature (CINAHL Plus)

- Provider: EBSCO*host*
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 1990-December 31, 2009
- Search Terms:

#S1 - (MH "Dietary Fats+") OR (MH "Fatty Acids") OR (MH "Fatty Acids, Monounsaturated+") OR (MH "Fatty Acids, Omega-3+") OR (MH "Fatty Acids, Omega-6+") OR (MH "Cholesterol, Dietary") OR (MH "Fats, Unsaturated+") OR (MH "Butter") OR (MH "Margarine") OR (MH "Plant Oils+") OR (MH "Fish Oils+")

#S2 - “dietary fat*” OR “diet fat*” OR “dietary lipid*” OR “fat consumption*” OR “fat intake*” OR “fatty acid*” OR “saturated fat*” OR “monounsaturated fat*” OR “mono-unsaturated fat*” OR “polyunsaturated fat*” OR “poly-unsaturated fat*” OR “unsaturated fat*” OR “unsaturated fatty acid*” OR omega-3 OR “N-3 fatty acid*” OR omega-6 OR “N-6 fatty acid*” OR MUFA* OR PUFA* OR “dietary cholesterol*” OR “alpha-linolenic acid*” OR “eicosapentaenoic acid*” OR “docosahexaenoic acid*” OR “linoleic acid*” OR “alpha-linolenic acid*” OR “arachidonic acid*” OR “milk fat*” OR butter OR Ghee OR margarine OR “dietary oil*” OR “plant oil*” OR “fish oil*” OR “olive oil*” OR “corn oil*” OR “cottonseed oil*” OR “cotton seed oil*” OR “safflower oil*” OR

“sesame oil*” OR “soybean oil*” OR “soya-bean oil*” OR “linseed oil*” OR “canola oil*” OR “peanut oil*” OR “coconut oil*” OR “edible oil*” OR “palm oil*” OR “fish oil*” OR “maize oil*” OR “oleic acid*”

#S3 - ((fat OR fatty) N6 (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR “linolenic acid*” OR milk OR “infant formula*”))

#S4 - S1 OR S2 OR S3

#S5 - (MH "Cardiovascular Diseases") OR (MH "Heart Failure+") OR (MH "Myocardial Ischemia+") OR (MH "Myocardial Infarction+") OR (MH "Stroke+") OR (MH "Cardiovascular System+") OR (MH "Venous Thrombosis+") OR (MH "Lipids/BL") OR (MH "Lipoproteins, HDL Cholesterol") OR (MH "Lipoproteins, LDL Cholesterol") OR (MH "Triglycerides")

#S6 - “cardiovascular disease*” OR “coronary artery disease” OR “heart disease*” OR “heart failure” OR “myocardial infarction*” OR “myocardial ischemia*” OR stroke OR angina OR “heart attack” OR “cardiometabolic health” OR “cardiovascular health” OR “cardiac health” OR “cardiovascular biomarkers” OR “venous thrombosis” OR hypertension OR “high blood pressure” OR “HDL cholesterol” OR “LDL cholesterol” OR “total cholesterol” OR triglycerides

#S7 - S5 OR S6

#S8 - (MH "Child+") OR (MH "Adolescence+") OR (MH "Pediatrics+") OR (MH "Infant+")

#S9 - Child OR children OR youth* OR adolescence OR adolescent* OR teen OR teens OR teenager* OR preteen* OR pre-teen* OR pre-adolesc* OR preadolesc* OR preschool* OR pediatric* OR paediatric* OR Infan* OR newborn* OR new-born* OR perinat* OR neonat* OR premature* OR preterm* OR baby OR babies OR toddler* OR boy OR boys OR girl OR girls OR schoolchild* OR “middle school*” OR “high school*” OR juvenile OR pubescent OR “pre pubescent” OR prepubescent OR kid OR kids OR “early childhood” OR “early years” OR pre-k OR pre-primary OR “under five*” OR “young child*” OR “head start” OR prekindergarten OR pre-kindergarten

#S10 - S8 OR S9

#S11 - S4 AND S7 AND S10 NOT (MH "Literature Review" OR MH "Meta Analysis" OR MH "Systematic Review" OR MH "News" OR MH "Retracted Publication" OR MH "Retraction of Publication”) Limiters - Publication Year: 1990-2009; Peer Reviewed; English Language; Human

Search Strategy 2: Search strategy to capture the literature on types of dietary fats and risk of cardiovascular disease for all ages from 2010-2019

PubMed

- Provider: U.S. National Library of Medicine
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 2010- October 30, 2019
- Search Terms:

#1 - "Dietary Fats"[Mesh] OR dietary fat* OR diet fat* OR dietary lipid* OR fat consumption* OR fat intake* OR "Fatty Acids"[Mesh:noexp] OR fatty acid* OR saturated fat* OR "Fatty Acids, Monounsaturated"[Mesh] OR monounsaturated fat* OR mono-unsaturated fat* OR polyunsaturated fat* OR poly-unsaturated fat* OR unsaturated fat* OR unsaturated fatty acid*

OR "Fatty Acids, Omega-3"[Mesh] OR omega-3[tiab] OR N-3 fatty acid* OR "Fatty Acids, Omega-6"[Mesh] OR omega-6 OR N-6 fatty acid* OR MUFA* OR PUFA* OR "Cholesterol, Dietary"[Mesh] OR dietary cholesterol* OR alpha-linolenic acid* OR eicosapentaenoic acid* OR docosahexaenoic acid* OR linoleic acid* OR alpha-linolenic acid* OR arachidonic acid* OR "Fats, Unsaturated"[Mesh] OR milk fat*[tiab] OR "Butter"[Mesh] OR butter[tiab] OR Ghee[tiab] OR "Margarine"[Mesh] OR margarine[tiab] OR dietary oil* OR "Plant Oils"[Mesh] OR plant oil* OR "Fish Oils"[Mesh] OR fish oil* OR olive oil* OR corn oil* OR cottonseed oil* OR cotton seed oil* OR safflower oil* OR sesame oil* OR soybean oil* OR soya-bean oil* OR linseed oil* OR canola oil* OR peanut oil* OR coconut oil* OR edible oil* OR palm oil* OR fish oil* OR maize oil* OR oleic acid* OR ((fat[tiab] OR fatty[tiab]) AND (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR linolenic acid* OR "Milk"[Mesh] OR milk[tiab] OR "Infant Formula"[Mesh] OR infant formula*[tiab]))

#2 - "Cardiovascular Diseases"[Mesh:noexp] OR cardiovascular disease*[tiab] OR coronary artery disease[tiab] OR heart disease*[tiab] OR "Heart Failure"[Mesh] OR heart failure[tiab] OR "Myocardial Infarction"[Mesh] OR myocardial infarction*[tiab] OR "Myocardial Ischemia"[Mesh] OR Myocardial Ischemia*[tiab] OR "Stroke"[Mesh] OR stroke[tiab] OR angina[tiab] OR heart attack[tiab] OR "Cardiovascular System"[Mesh] OR "cardiometabolic health" OR cardiovascular health[tiab] OR "cardiac health" OR "cardiovascular biomarkers" OR "Venous Thrombosis"[Mesh] OR venous thrombosis[tiab] OR hypertension[tiab] OR high blood pressure[tiab] OR "Lipids/blood"[Mesh] OR "Cholesterol, HDL"[Mesh] OR HDL cholesterol[tiab] OR "Cholesterol, LDL"[Mesh] OR LDL cholesterol[tiab] OR total cholesterol[tiab] OR "Triglycerides"[Mesh] OR triglycerides[tiab]

#3 - (#1 AND #2)

#4 - (#1 AND #2) NOT ("Animals"[Mesh] NOT ("Animals"[Mesh] AND "Humans"[Mesh])) NOT (editorial[ptyp] OR comment[ptyp] OR news[ptyp] OR letter[ptyp] OR review[ptyp] OR systematic review[ptyp] OR systematic review[ti] OR meta-analysis[ptyp] OR meta-analysis[ti] OR meta-analyses[ti] OR retracted publication[ptyp] OR retraction of publication[ptyp] OR retraction of publication[tiab] OR retraction notice[ti]) Filters: Publication date from 2010/01/01 to 2019/10/30; English

Cochrane Central Register of Controlled Trials (CENTRAL)

- Provider: John Wiley & Sons
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 2010- October 30, 2019
- Search Terms:

#1 - [mh "Dietary Fats"] OR [mh ^"Fatty Acids"] OR [mh "Fatty Acids, Monounsaturated"] OR [mh "Fatty Acids, Omega-3"] OR [mh "Fatty Acids, Omega-6"] OR [mh "Cholesterol, Dietary"] OR [mh "Fats, Unsaturated"] OR [mh Butter] OR [mh Margarine] OR [mh “Plant Oils”] OR [mh "Fish Oils"]

#2 - (“dietary fat*” OR “diet fat*” OR “dietary lipid*” OR “fat consumption*” OR “fat intake*” OR “fatty acid*” OR “saturated fat*” OR “monounsaturated fat*” OR “mono-unsaturated fat*” OR “polyunsaturated fat*” OR “poly-unsaturated fat*” OR “unsaturated fat*” OR “unsaturated fatty acid*” OR omega-3 OR “N-3 fatty acid*” OR omega-6 OR “N-6 fatty acid*” OR MUFA* OR PUFA* OR “dietary cholesterol*” OR “alpha-linolenic acid*” OR “eicosapentaenoic acid*” OR “docosahexaenoic acid*” OR “linoleic acid*” OR “alpha-linolenic acid*” OR “arachidonic acid*”

OR “milk fat*” OR butter OR Ghee OR margarine OR “dietary oil*” OR “plant oil*” OR “fish oil*” OR “olive oil*” OR “corn oil*” OR “cottonseed oil*” OR “cotton seed oil*” OR “safflower oil*” OR “sesame oil*” OR “soybean oil*” OR “soya-bean oil*” OR “linseed oil*” OR “canola oil*” OR “peanut oil*” OR “coconut oil*” OR “edible oil*” OR “palm oil*” OR “fish oil*” OR “maize oil*” OR “oleic acid*”):ti,ab,kw

#3 - ((fat OR fatty) NEAR/6 (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR “linolenic acid*” OR [mh Milk] OR milk OR [mh "Infant Formula"] OR “infant formula*”)):ti,ab,kw

#4 - #1 OR #2 OR #3

#5 - [mh ^"Cardiovascular Diseases"] OR [mh "Heart Failure"] OR [mh "Myocardial Ischemia"] OR [mh "Myocardial Infarction"] OR [mh Stroke] OR [mh "Cardiovascular System"] OR [mh "Venous Thrombosis"] OR [mh Lipids/BL] OR [mh "Cholesterol, HDL"] OR [mh "Cholesterol, LDL"] OR [mh Triglycerides]

#6 - (“cardiovascular disease*” OR “coronary artery disease” OR “heart disease*” OR “heart failure” OR “myocardial infarction*” OR “myocardial ischemia*” OR stroke OR angina OR “heart attack” OR “cardiometabolic health” OR “cardiovascular health” OR “cardiac health” OR “cardiovascular biomarkers” OR “venous thrombosis” OR hypertension OR “high blood pressure” OR “HDL cholesterol” OR “LDL cholesterol” OR “total cholesterol” OR triglycerides):ti,ab,kw"

#7 - #5 OR #6

#8 - #4 AND #7" with Publication Year from 2010 to 2019, in Trials (Word variations have been searched)

Embase

- Provider: Elsevier
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 2010- October 30, 2019
- Search Terms:

#1 - 'edible oil'/exp OR 'fatty acid'/de OR 'monounsaturated fatty acid'/de OR 'omega 3 fatty acid'/de OR 'omega 6 fatty acid'/de OR 'cholesterol intake'/de OR 'unsaturated fatty acid'/exp OR 'butter'/de OR 'margarine'/de OR 'vegetable oil'/exp OR 'fish oil'/de

#2 - 'dietary fat*':ab,ti OR 'diet fat*':ab,ti OR 'dietary lipid*':ab,ti OR 'fat consumption*':ab,ti OR 'fat intake*':ab,ti OR 'fatty acid*':ab,ti OR 'saturated fat*':ab,ti OR 'monounsaturated fat*':ab,ti OR 'mono-unsaturated fat*':ab,ti OR 'polyunsaturated fat*':ab,ti OR 'poly-unsaturated fat*':ab,ti OR 'unsaturated fat*':ab,ti OR 'unsaturated fatty acid*':ab,ti OR 'omega 3':ab,ti OR 'n-3 fatty acid*':ab,ti OR 'omega 6':ab,ti OR 'n-6 fatty acid*':ab,ti OR mufa*:ab,ti OR pufa*:ab,ti OR 'dietary cholesterol*':ab,ti OR 'eicosapentaenoic acid*':ab,ti OR 'docosahexaenoic acid*':ab,ti OR 'linoleic acid*':ab,ti OR 'alpha-linolenic acid*':ab,ti OR 'arachidonic acid*':ab,ti OR 'milk fat*':ab,ti OR butter:ab,ti OR ghee:ab,ti OR margarine:ab,ti OR 'dietary oil*':ab,ti OR 'plant oil*':ab,ti OR 'olive oil*':ab,ti OR 'corn oil*':ab,ti OR 'cottonseed oil*':ab,ti OR 'cotton seed oil*':ab,ti OR 'safflower oil*':ab,ti OR 'sesame oil*':ab,ti OR 'soybean oil*':ab,ti OR 'soya-bean oil*':ab,ti OR 'linseed oil*':ab,ti OR 'canola oil*':ab,ti OR 'peanut oil*':ab,ti OR 'coconut oil*':ab,ti OR 'edible oil*':ab,ti OR 'palm oil*':ab,ti OR 'fish oil*':ab,ti OR 'maize oil*':ab,ti OR 'oleic acid*':ab,ti

#3 - ((fat OR fatty) NEAR/6 (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR 'linolenic acid*' OR milk OR 'infant formula*')):ab,ti

#4 - #1 OR #2 OR #3

#5 - 'cardiovascular disease'/de OR 'heart failure'/exp OR 'heart muscle ischemia'/exp OR 'heart infarction'/exp OR 'cerebrovascular accident'/exp OR 'cardiovascular system'/exp OR 'vein thrombosis'/exp OR 'high density lipoprotein cholesterol'/de OR 'low density lipoprotein cholesterol'/de OR 'triacylglycerol'/exp

#6 - 'cardiovascular disease*':ab,ti OR 'coronary artery disease':ab,ti OR 'heart disease*':ab,ti OR 'heart failure':ab,ti OR 'myocardial infarction*':ab,ti OR 'myocardial ischemia*':ab,ti OR stroke:ab,ti OR angina:ab,ti OR 'heart attack':ab,ti OR 'cardiometabolic health':ab,ti OR 'cardiovascular health':ab,ti OR 'cardiac health':ab,ti OR 'cardiovascular biomarkers':ab,ti OR 'venous thrombosis':ab,ti OR hypertension:ab,ti OR 'high blood pressure':ab,ti OR 'hdl cholesterol':ab,ti OR 'ldl cholesterol':ab,ti OR 'total cholesterol':ab,ti OR triglycerides:ab,ti

#7 - #5 OR #6

#8 - #4 AND #7 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim AND [english]/lim AND [2010-2019]/py NOT ([conference abstract]/lim OR [conference review]/lim OR [conference paper]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [systematic review]/lim OR [meta analysis]/lim)

Cumulative Index of Nursing and Allied Health Literature (CINAHL Plus)

- Provider: EBSCO*host*
- Date(s) Searched: October 30, 2019
- Date range searched: January 1, 2010-December 31, 2019
- Search Terms:

#S1 - (MH "Dietary Fats+") OR (MH "Fatty Acids") OR (MH "Fatty Acids, Monounsaturated+") OR (MH "Fatty Acids, Omega-3+") OR (MH "Fatty Acids, Omega-6+") OR (MH "Cholesterol, Dietary") OR (MH "Fats, Unsaturated+") OR (MH "Butter") OR (MH "Margarine") OR (MH "Plant Oils+") OR (MH "Fish Oils+")

#S2 - “dietary fat*” OR “diet fat*” OR “dietary lipid*” OR “fat consumption*” OR “fat intake*” OR “fatty acid*” OR “saturated fat*” OR “monounsaturated fat*” OR “mono-unsaturated fat*” OR “polyunsaturated fat*” OR “poly-unsaturated fat*” OR “unsaturated fat*” OR “unsaturated fatty acid*” OR omega-3 OR “N-3 fatty acid*” OR omega-6 OR “N-6 fatty acid*” OR MUFA* OR PUFA* OR “dietary cholesterol*” OR “alpha-linolenic acid*” OR “eicosapentaenoic acid*” OR “docosahexaenoic acid*” OR “linoleic acid*” OR “alpha-linolenic acid*” OR “arachidonic acid*” OR “milk fat*” OR butter OR Ghee OR margarine OR “dietary oil*” OR “plant oil*” OR “fish oil*” OR “olive oil*” OR “corn oil*” OR “cottonseed oil*” OR “cotton seed oil*” OR “safflower oil*” OR “sesame oil*” OR “soybean oil*” OR “soya-bean oil*” OR “linseed oil*” OR “canola oil*” OR “peanut oil*” OR “coconut oil*” OR “edible oil*” OR “palm oil*” OR “fish oil*” OR “maize oil*” OR “oleic acid*”

#S3 - ((fat OR fatty) N6 (saturat* OR unsatur* OR monounsatur* OR polyunsatur* OR poly-unsatur* OR “linolenic acid*” OR milk OR “infant formula*”))

#S4 - S1 OR S2 OR S3

#S5 - (MH "Cardiovascular Diseases") OR (MH "Heart Failure+") OR (MH "Myocardial Ischemia+") OR (MH "Myocardial Infarction+") OR (MH "Stroke+") OR (MH "Cardiovascular System+") OR (MH "Venous Thrombosis+") OR (MH "Lipids/BL") OR (MH "Lipoproteins, HDL Cholesterol") OR (MH "Lipoproteins, LDL Cholesterol") OR (MH "Triglycerides")

#S6 - “cardiovascular disease*” OR “coronary artery disease” OR “heart disease*” OR “heart failure” OR “myocardial infarction*” OR “myocardial ischemia*” OR stroke OR angina OR “heart attack” OR “cardiometabolic health” OR “cardiovascular health” OR “cardiac health” OR “cardiovascular biomarkers” OR “venous thrombosis” OR hypertension OR “high blood pressure” OR “HDL cholesterol” OR “LDL cholesterol” OR “total cholesterol” OR triglycerides

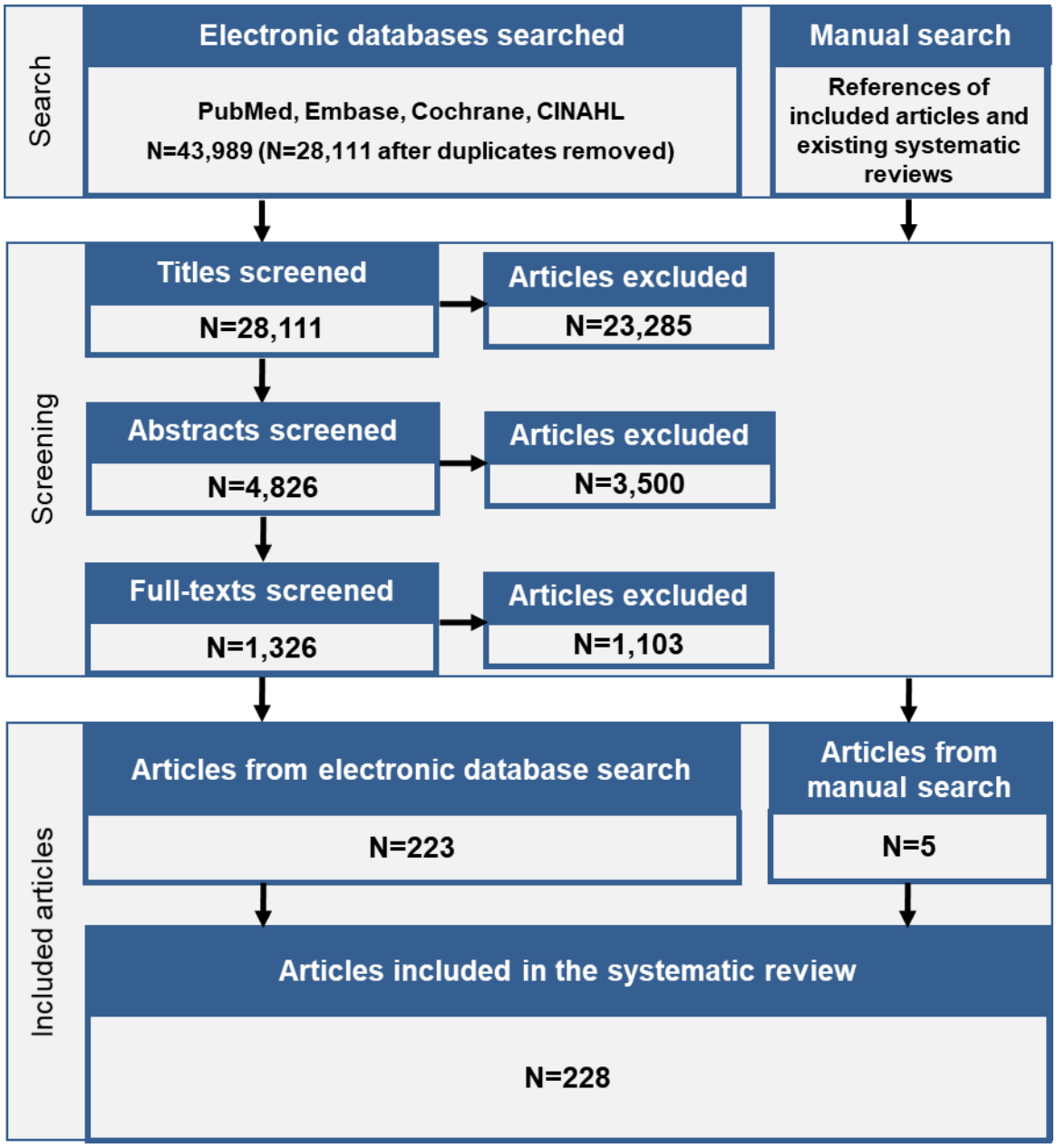
#S7 - S5 OR S6

#S8 - S4 AND S7 NOT (MH "Literature Review" OR MH "Meta Analysis" OR MH "Systematic Review" OR MH "News" OR MH "Retracted Publication" OR MH "Retraction of Publication”) Limiters - Publication Year: 2010-2019; Peer Reviewed; English Language; Human

LITERATURE SEARCHES AND SCREENING RESULTS

The flow chart (**Figure 2**) below illustrates the literature searches and screening results for articles examining the systematic review question. The results of the two literature searches, after removal of duplicates, were combined for efficiency and screened independently by two NESR analysts using a step-wise process by reviewing titles, abstracts, and full-texts to determine which articles met the inclusion criteria. Refer to **Table 12** for the rationale for exclusion for each excluded full-text article. A manual search was done to find articles that were not identified when searching the electronic databases; all manually identified articles are also screened to determine whether they meet criteria for inclusion.

Figure 2: Flow chart of literature searches and screening results*



* The flow chart depicts the combined raw search totals from the two literature searches that included 43,989 raw results, 6,048 raw results in the first search strategy and 37,941 raw results in the second search strategy (both search strategies described in the **Electronic databases and search terms** section). Search results were combined for efficiency and screened together in screening software by two analysts independently because both searches addressed the same overall systematic review question from different search date ranges.

Excluded articles

The table below (**Table 12**) lists the articles excluded after full-text screening from two literature searches, and includes columns for the categories of inclusion and exclusion criteria that studies were excluded based on. At least one reason for exclusion is provided for each article, as indicated by an "X" in one of the columns, though this may not reflect all possible reasons for exclusion. Information about articles excluded after title and abstract screening is available upon request.

Table 12. Articles excluded after full-text screening with rationale for exclusion*

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1	Aadland EK, Lavigne C, Graff IE, et al. Lean-seafood intake reduces cardiovascular lipid risk factors in healthy subjects: results from a randomized controlled trial with a crossover design. *Am J Clin Nutr*. 2015;102(3):582-92. doi:10.3945/ajcn.115.112086		X		
2	Abbott L, Gordon Schluck G, Graven L, Martorella G. Exploring the intervention effect moderators of a cardiovascular health promotion study among rural African-Americans. *Public Health Nurs*. 2018;35(2):126-134. doi:10.1111/phn.12377		X		
3	Abdullah MM, Cyr A, Lepine MC, et al. Common variants in cholesterol synthesis- and transport-related genes associate with circulating cholesterol responses to intakes of conventional dairy products in healthy individuals. *J Nutr*. 2016;146(5):1008-16. doi:10.3945/jn.115.222208		X		
4	Abellan R, Mansego ML, Martinez-Hervas S, et al. Dietary polyunsaturated fatty acids may increase plasma LDL-cholesterol and plasma cholesterol concentrations in carriers of an ABCG1 gene single nucleotide polymorphism: study in two Spanish populations. Atherosclerosis. 2011;219(2):900-6. doi:10.1016/j.atherosclerosis.2011.09.018	X			

* This table presents the combined list of articles excluded after full text screening from both searches. As stated previously, the search results from both search strategies (described in the **Electronic databases and search terms**) were combined for efficiency and screened together in screening software by two analysts independently because both searches addressed the same overall systematic review question from different search date ranges.

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
5	AbuMweis SS, Panchal SK, Jones PJH. Triacylglycerol-lowering effect of docosahexaenoic acid is not influenced by single-nucleotide polymorphisms involved in lipid metabolism in humans. *Lipids.* 2018;53(9):897-908. doi:10.1002/lipd.12096		X		
6	Abu-Saad K, Novikov I, Gimpelevitz I, et al. Micronutrient intake and adherence to DASH diet are associated with incident major adverse cardiovascular events and all-cause mortality in a bi-ethnic population. Eur Heart J. 2017;381120-. doi:10.1093/eurheartj/ehx502.P5321				Publication Status
7	AbuZaid OI, Al-Dhaif BM, Alqunais FE, Ismail MS. Impact of metabolic syndrome on nutrients intakes among Saudi females. J Pak Med Assoc. 2019;69(3):330-336.	X		X	
8	Adamsson V, Cederholm T, Vessby B, Risérus U. Influence of a healthy Nordic diet on serum fatty acid composition and associations with blood lipoproteins - results from the NORDIET study. Food Nutr Res. 2014;58. doi:10.3402/fnr.v58.24114		X		Health Status
9	Adamsson V, Reumark A, Fredriksson IB, et al. Effects of a healthy Nordic diet on cardiovascular risk factors in hypercholesterolaemic subjects: a randomized controlled trial (NORDIET). J Intern Med. 2011;269(2):150-9. doi:10.1111/j.1365-2796.2010.02290.x		X		
10	Adedeji OO, Oyakhire GK, Saeed AK, Ghamdi AI. Effectiveness of interventions to reduce coronary heart disease risk. West Afr J Med. 2011;30(3):197-201.	X	X		
11	Adeyanju M. Adolescent health status behaviors and cardiovascular disease. Adolescence. 1990. 25(97):155-69.		X		
12	Aeberli I, Spinas GA, Lehmann R, l'Allemand D, Molinari L, Zimmermann MB. Diet determines features of the metabolic syndrome in 6- to 14-year-old children. Int J Vitam Nutr Res. 2009. 79(1):14-23. doi:10.1024/0300-9831.79.1.14	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
13	Afonso C, Bernardo I, Bandarra NM, Martins LL, Cardoso C. The implications of following dietary advice regarding fish consumption frequency and meal size for the benefit (EPA + DHA and Se) versus risk (MeHg) assessment. Int J Food Sci Nutr. 2019;70(5):623-637. doi:10.1080/09637486.2018.1551334	X	X		
14	Afshin A, Micha R, Khatibzadeh S, et al. The impact of dietary habits and metabolic risk factors on cardiovascular and diabetes mortality in countries of the Middle East and North Africa in 2010: a comparative risk assessment analysis. BMJ Open. 2015;5(5):e006385. doi:10.1136/bmjopen-2014-006385	X			
15	Akbaraly T, Wurtz P, Singh-Manoux A, et al. Association of circulating metabolites with healthy diet and risk of cardiovascular disease: analysis of two cohort studies. Sci Rep. 2018;8(1):8620. doi:10.1038/s41598-018-26441-1	X	X		
16	Akerblom HK, Viikari J, Raitakari OT, Uhari M. Cardiovascular Risk in Young Finns Study: general outline and recent developments. Ann Med. 1999. 31(Supp1):45-54. doi:10.1080/07853890.1999.11904399	X			
17	Al Jamal AR, Ibrahim A. Effects of olive oil on lipid profiles and blood glucose in type2 diabetic patients. International Journal of Diabetes and Metabolism. 2011;19(1):19-22.	X			
18	Al Wattar B H, Dodds J, Placzek A, et al. Mediterranean-style diet in pregnant women with metabolic risk factors (ESTEEM): a pragmatic multicentre randomised trial. PLoS Med. 2019;16(7):e1002857. doi:10.1371/journal.pmed.1002857		X	X	
19	Albani V, Celis-Morales C, O'Donovan CB, et al. Within-person reproducibility and sensitivity to dietary change of C15:0 and C17:0 levels in dried blood spots: data from the European Food4Me Study. Mol Nutr Food Res. 2017;61(10). doi:10.1002/mnfr.201700142			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
20	Alexander H, Lockwood LP, Harris MA, Melby CL. Risk factors for cardiovascular disease and diabetes in two groups of Hispanic Americans with differing dietary habits. J Am Coll Nutr. 1999. 18(2):127-36. doi:10.1080/07315724.1999.10718840	X			
21	Alfaddagh A, Elajami TK, Ashfaque H, Saleh M, Bistrian BR, Welty FK. Effect of eicosapentaenoic and docosahexaenoic acids added to statin therapy on coronary artery plaque in patients with coronary artery disease: a randomized clinical trial. J Am Heart Assoc. 2017;6(12): pii: e006981. doi:10.1161/jaha.117.006981		X		Health Status
22	Al-Ghannami SS, Sedlak E, Hussein IS, et al. Lipid-soluble nutrient status of healthy Omani school children before and after intervention with oily fish meal or re-esterified triacylglycerol fish oil. Nutrition. 2016;32(1):73-8. doi:10.1016/j.nut.2015.07.014		X	X	
23	Alipoor B, Haghighian MK, Sadat BE, Asghari M. Effect of sesame seed on lipid profile and redox status in hyperlipidemic patients. Int J Food Sci Nutr. 2012;63(6):674-8. doi:10.3109/09637486.2011.652077				Health Status
24	Aljohi H, Dopler-Nelson M, Cifuentes M, Wilson TA. The consumption of 12 Eggs per week for 1year does not alter fasting serum markers of cardiovascular disease in older adults with early macular degeneration. J Nutr Intermed Metabol. 2019;15:35-41. doi:10.1016/j.jnim.2018.11.004		X		
25	Aller R, de Luis DA, Izaola O, de la Fuente B, Bachiller R. Effect of a high monounsaturated vs high polyunsaturated fat hypocaloric diets in nonalcoholic fatty liver disease. Eur Rev Med Pharmacol Sci. 2014;18(7):1041-7.		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
26	Aller R, Primo D, Izaola O, de Luis DA. Common polymorphism in the cannabinoid receptor gene type 2 (CB2R) rs3123554 are associated with metabolic changes after two different hypocaloric diets with different dietary fatty profiles. Clin Nutr. 2018. 38(6):2632-2638. doi:10.1016/j.clnu.2018.11.013		X		
27	Allison MA, Aragaki A, Eaton C, et al. Effect of dietary modification on incident carotid artery disease in postmenopausal women: results from the women's health initiative dietary modification trial. Stroke. 2014;45(6):1748-56. doi:10.1161/strokeaha.114.005096		X		
28	Allison MA, Aragaki A, Eaton C, et al. Dietary intervention to reduce fat intake does not result in lower incident carotid artery disease: the women's health initiative diet modification trial. Circulation. 2013;128(S22): A10374				Publication Status
29	Alonso A, Zozaya C, Vazquez Z, Alfredo Martinez J, Martinez-Gonzalez MA. The effect of low-fat versus whole-fat dairy product intake on blood pressure and weight in young normotensive adults. J Hum Nutr Diet. 2009. 22(4):336-42. doi:10.1111/j.1365-277X.2009.00967.x		X		
30	Al-Rewashdeh AYA. Blood lipid profileoxidation and pressure of men and women consumed olive oil. Pak J Nutr. 2010;9(1):15-26.		X		
31	Alsaleh A, Frost GS, Griffin BA, et al. PPARgamma2 gene Pro12Ala and PPARalpha gene Leu162Val single nucleotide polymorphisms interact with dietary intake of fat in determination of plasma lipid concentrations. J Nutrigenet Nutrigenomics. 2011;4(6):354-66. doi:10.1159/000336362		X		
32	Alsumari SR, AlNouri DM, El-Sayed MMA, El-Din MFS, Arzoo S. The sociodemographic characteristics and dietary and blood plasma fatty acid profiles of elderly Saudi women with Alzheimer disease. Lipids Health Dis. 2019;18(1):77. doi:10.1186/s12944-019-1029-0	X			Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
33	Alvarez Campano CG, Macleod MJ, Aucott L, Thies F. Marine-derived n-3 fatty acids therapy for stroke. Stroke. 2019;50(11):e314-e315. doi:10.1161/strokeaha.119.026919	X			
34	Alvarez-Alvarez I, Zazpe I, Pérez de Rojas J, et al. Mediterranean dietphysical activity and their combined effect on all-cause mortality: The Seguimiento Universidad de Navarra (SUN) cohort. Prev Med. 2018;106:45-52. doi:10.1016/j.ypmed.2017.09.021			X	
35	Alvarez-Perez J, Sanchez-Villegas A, Diaz-Benitez EM, et al. Influence of a Mediterranean dietary pattern on body fat distribution: results of the PREDIMED-Canarias Intervention Randomized Trial. J Am Coll Nutr. 2016;35(6):568-580. doi:10.1080/07315724.2015.1102102			X	Health Status
36	Alvizouri-Munoz M, Carranza-Madrigal J, Herrera-Abarca JE, Chavez-Carbajal F, Amezcua-Gastelum JL. Effects of avocado as a source of monounsaturated fatty acids on plasma lipid levels. Arch Med Res. 1992. 23(4):163-7.				Country
37	Amba V, Murphy G, Etemadi A, Wang S, Abnet CC, Hashemian M. Nut and peanut butter consumption and mortality in the National Institutes of Health-AARP Diet and Health Study. Nutrients. 2019;11(7): pii: E1508. doi:10.3390/nu11071508		X	X	
38	Amundsen AL, Ose L, Nenseter MS, Ntanios FY. Plant sterol ester-enriched spread lowers plasma total and LDL cholesterol in children with familial hypercholesterolemia. Am J Clin Nutr. 2002;76(2):338-344.		X		
39	Andersen CJ, Lee JY, Blesso CN, Carr TP, Fernandez ML. Egg intake during carbohydrate restriction alters peripheral blood mononuclear cell inflammation and cholesterol homeostasis in metabolic syndrome. Nutrients. 2014;6(7):2650-67. doi:10.3390/nu6072650		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
40	Anderson AD, Anderson MM, Jacobson JL, et al. Metabolic effects of bedtime pistachio consumption for 6 weeks in overweight persons. FASEB journal. 2013;27.				Publication Status
41	Anderson-Vasquez HE, Perez-Martinez P, Ortega Fernandez P, Wanden-Berghe C. Impact of the consumption of a rich diet in butter and it replacement for a rich diet in extra virgin olive oil on anthropometric, metabolic and lipid profile in postmenopausal women. Nutr Hosp. 2015;31(6):2561-70. doi:10.3305/nh.2015.31.6.8732			X	Study Duration
42	Andraski AB, Singh SA, Lee L, et al. A diet high in carbohydrate and low in fat alters the HDL proteome and metabolism of 9 HDL proteins in humans. Circulation. 2019;139(Suppl 1): AMP41. doi:10.1161/circ.139.suppl_1.MP41				Publication Status
43	Annuzzi G, Rivellese AA, Wang H, et al. Lipoprotein subfractions and dietary intake of n-3 fatty acid: the Genetics of Coronary Artery Disease in Alaska Natives study. Am J Clin Nutr. 2012;95(6):1315-22. doi:10.3945/ajcn.111.023887	X			
44	Arora RC, Agarwal N, Arora S, Garg RK, Kumar N, Lakhtakia S. A comparative study of three different test diets in change in plasma total cholesterol in young healthy individuals. Mater Med Pol. 1991. 23(4):296-8.	X			
45	Arora RC, Agarwal N, Arora S, Pandey A. Dietary cholesterol induced changes in serum lipoproteins in healthy females. Mater Med Pol. 1992. 24(1):17-9.				Age of participants at intervention or exposure
46	Asadi Z, Shafiee M, Sadabadi F, et al. Association of dietary patterns and risk of cardiovascular disease events in the MASHAD cohort study. J Hum Nutr Diet. 2019;32(6):789-801. doi:10.1111/jhn.12669		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
47	Asemi Z, Samimi M, Tabassi Z, Shakeri H, Sabihi SS, Esmaillzadeh A. Effects of DASH diet on lipid profiles and biomarkers of oxidative stress in overweight and obese women with polycystic ovary syndrome: a randomized clinical trial. Nutrition. 2014;30(11-12):1287-93. doi:10.1016/j.nut.2014.03.008		X		
48	Asghari G, Yuzbashian E, Mirmiran P, Bahadoran Z, Azizi F. Prediction of metabolic syndrome by a high intake of energy-dense nutrient-poor snacks in Iranian children and adolescents. Pediatr Res. 2016;79(5):697-704. doi:10.1038/pr.2015.270		X		
49	Ashaye A, Gaziano J, Djousse L. Red meat consumption and risk of heart failure in male physicians. Nutr Metab Cardiovasc Dis. 2011;21(12):941-6. doi:10.1016/j.numecd.2010.03.009		X		
50	Aslibekyan S, Campos H, Baylin A. Biomarkers of dairy intake and the risk of heart disease. Nutr Metab Cardiovasc Dis. 2012;22(12):1039-45. doi:10.1016/j.numecd.2011.02.003	X	X		
51	Assaf-Balut C, Garcia de la Torre N, Duran A, et al. A Mediterranean diet with additional extra virgin olive oil and pistachios reduces the incidence of gestational diabetes mellitus (GDM): a randomized controlled trial: The St. Carlos GDM prevention study. PLoS One. 2017;12(10):e0185873. doi:10.1371/journal.pone.0185873		X	X	
52	Assaf-Balut C, Garcia de la Torre N, Duran A, et al. A Mediterranean diet with an enhanced consumption of extra virgin olive oil and pistachios improves pregnancy outcomes in women without gestational diabetes mellitus: a sub-analysis of the St. Carlos Gestational Diabetes Mellitus Prevention Study. Ann Nutr Metab. 2019;74(1):69-79. doi:10.1159/000495793		X	X	
53	Astrup A. Yogurt and dairy product consumption to prevent cardiometabolic diseases: epidemiologic and experimental studies. Am J Clin Nutr. 2014;99(Suppl 5):1235S-1242S. doi:10.3945/ajcn.113.073015	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
54	Atkins JL, Whincup PH, Morris RW, Lennon LT, Papacosta O, Wannamethee SG. Dietary patterns and the risk of CVD and all-cause mortality in older British men. Br J Nutr. 2016;116(7):1246-1255. doi:10.1017/s0007114516003147		X		
55	Austel A, Ranke C, Wagner N, Gorge J, Ellrott T. Weight loss with a modified Mediterranean-type diet using fat modification: a randomized controlled trial. Eur J Clin Nutr. 2015;69(8):878-84. doi:10.1038/ejcn.2015.11		X		
56	Avelino AP, Oliveira GM, Ferreira CC, Luiz RR, Rosa G. Additive effect of linseed oil supplementation on the lipid profiles of older adults. Clin Interv Aging. 2015;10:1679-85. doi:10.2147/cia.S75538		X		
57	Ayer JG, Harmer JA, Xuan W, et al. Dietary supplementation with n-3 polyunsaturated fatty acids in early childhood: effects on blood pressure and arterial structure and function at age 8 y. Am J Clin Nutr. 2009. 90(2):438-46. doi:10.3945/ajcn.2009.27811		X		
58	Aynaci G, Akdemir O. The relationship between lifestyle, health promotion lifestyle profile II and high blood pressure in university students. Open Access Maced J Med Sci. 2018;6(9):1756-1761. doi:10.3889/oamjms.2018.314	X			
59	Azadbakht L, Izadi V, Ehsani S, Esmaillzadeh A. Effects of the Dietary Approaches to Stop Hypertension (DASH) eating plan on the metabolic side effects of corticosteroid medications. J Am Coll Nutr. 2016;35(4):285-90. doi:10.1080/07315724.2014.991459		X		Health Status
60	Azadbakht L, Mirmiran P, Hedayati M, Esmaillzadeh A, Shiva N, Azizi F. Particle size of LDL is affected by the National Cholesterol Education Program (NCEP) step II diet in dyslipidaemic adolescents. Br J Nutr. 2007. 98(1):134-9. doi:10.1017/s0007114507657857				Country

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
61	Azadi-Yazdi M, Karimi-Zarchi M, Salehi-Abargouei A, Fallahzadeh H, Nadjarzadeh A. Effects of Dietary Approach to Stop Hypertension diet on androgens, antioxidant status and body composition in overweight and obese women with polycystic ovary syndrome: a randomised controlled trial. J Hum Nutr Diet. 2017;30(3):275-283. doi:10.1111/jhn.12433		X		
62	Babio N, Becerra-Tomas N, Martinez-Gonzalez MA, et al. Consumption of yogurt, low-fat milk, and other low-fat dairy products is associated with lower risk of metabolic syndrome incidence in an elderly Mediterranean population. J Nutr. 2015;145(10):2308-16. doi:10.3945/jn.115.214593		X		
63	Babio N, Toledo E, Estruch R, et al. Mediterranean diets and metabolic syndrome status in the PREDIMED randomized trial. CMAJ. 2014;186(17):E649-57. doi:10.1503/cmaj.140764		X		
64	Baer DJ, Henderson T, Gebauer SK. High oleic soybean oil improves cardiometabolic health in adults. FASEB journal. 2017;31(Suppl 1)				Publication Status
65	Bagge CN, Strandhave C, Skov CM, Svensson M, Schmidt EB, Christensen JH. Marine n-3 polyunsaturated fatty acids affect the blood pressure control in patients with newly diagnosed hypertension - a 1-year follow-up study. Nutr Res. 2017;38:71-78. doi:10.1016/j.nutres.2017.02.009				Health Status
66	Baik I, Abbott RD, Curb JD, Shin C. Intake of fish and n-3 fatty acids and future risk of metabolic syndrome. J Am Diet Assoc. 2010;110(7):1018-26. doi:10.1016/j.jada.2010.04.013			X	
67	Baila-Rueda L, Mateo-Gallego R, Perez-Calahorra S, et al. Effect of different fat-enriched meats on non-cholesterol sterols and oxysterols as markers of cholesterol metabolism: results of a randomized and cross-over clinical trial. Nutr Metab Cardiovasc Dis. 2015;25(9):853-9. doi:10.1016/j.numecd.2015.06.008		X		Study Duration

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
68	Balk E, Chung M, Lichtenstein A, et al. Effects of omega-3 fatty acids on cardiovascular risk factors and intermediate markers of cardiovascular disease. Evid Rep Technol Assess (Summ). 2004. (93):1- 6.	X			Publication Status
69	Ballesteros MN, Cabrera RM, Del Socorro Saucedo M, Aggarwal D, Shachter NS, Fernandez ML. High intake of saturated fat and early occurence of specific biomarkers may explain the prevalence of chronic disease in northern Mexico. J Nutr. 2005. 135(1):70-73.				Publication Status
70	Bamberger C, Rossmeier A, Lechner K, et al. A walnut-enriched diet reduces lipids in healthy caucasian subjects independent of recommended macronutrient replacement and time point of consumption: a prospective randomized controlled trial. Nutrients. 2017;9(10): pii: E1097. doi:10.3390/nu9101097		X		
71	Barbour JA, Howe PRC, Buckley JD, Bryan J, Coates AM. Cerebrovascular and cognitive benefits of high-oleic peanut consumption in healthy overweight middle-aged adults. Nutr Neurosci. 2017;20(10):555-562. doi:10.1080/1028415x.2016.1204744		X	X	
72	Baril-Gravel L, Labonte ME, Couture P, et al. Docosahexaenoic acid-enriched canola oil increases adiponectin concentrations: a randomized crossover controlled intervention trial. Nutr Metab Cardiovasc Dis. 2015;25(1):52-9. doi:10.1016/j.numecd.2014.08.003			X	
73	Barrubes L, Babio N, Mena-Sanchez G, et al. Dairy product consumption and risk of colorectal cancer in an older Mediterranean population at high cardiovascular risk. Int J Cancer. 2018;143(6):1356-1366. doi:10.1002/ijc.31540			X	
74	Bas M, Altan T, Dincer D, Aran E, Kaya HG, Yuksek O. Determination of dietary habits as a risk factor of cardiovascular heart disease in Turkish adolescents. Eur J Nutr. 2005. 44(3):174-82. doi:10.1007/s00394-004-0509-8	X		X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
75	Bass JA, Moore TA, Stewart KJ. Coronary heart disease risk factors in children and adolescents. Preventive Cardiology. 1999. 2(1):8-12+22.	X			
76	Baumgartner S, Kelly ER, van der Made S, et al. The influence of consuming an egg or an egg-yolk buttermilk drink for 12 wk on serum lipids, inflammationand liver function markers in human volunteers. Nutrition. 2013;29(10):1237-44. doi:10.1016/j.nut.2013.03.020		X		
77	Bazzano LA, Reynolds K, Hu T, et al. Effect of a low-carbohydrate diet on weight and cardiovascular risk factors: a randomized controlled trial. Circulation. 2012;125(10): AP306				Publication Status
78	Bekkouche L, Ait Yahia D. P1-01: Linseed consumption associated with mediterranean diet reduces hyperglycemia and blood pressure among west algerian patients with metabolic syndrome. Ann Cardiol Angeiol. 2015;64S23. doi:10.1016/S0003-3928(16)30048-8				Publication Status
79	Bekkouche L, Bouchenak M, Malaisse WJ, Yahia DA. The Mediterranean diet adoption improves metabolicoxidativeand inflammatory abnormalities in algerian metabolic syndrome patients. Hormone and Metabolic Research. 2014;46(4):274-282. doi:10.1055/s-0033-1363657		X		
80	Benaim C, Freitas-Vilela AA, Pinto TJP, et al. Early pregnancy body mass index modifies the association of pre-pregnancy dietary patterns with serum polyunsaturated fatty acid concentrations throughout pregnancy in Brazilian women. Matern Child Nutr. 2018;14(1): doi:10.1111/mcn.12480			X	
81	Benatar JR, Jones E, White H, Stewart RA. A randomized trial evaluating the effects of change in dairy food consumption on cardio-metabolic risk factors. Eur J Prev Cardiol. 2014;21(11):1376-86. doi:10.1177/2047487313493567		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
82	Bendsen NT, Chabanova E, Thomsen HS, et al. Effect of trans fatty acid intake on abdominal and liver fat deposition and blood lipids: a randomized trial in overweight postmenopausal women. Nutr Diabetes. 2011;1e4. doi:10.1038/nutd.2010.4		X		
83	Bento AP, Cominetti C, Simoes Filho A, Naves MM. Baru almond improves lipid profile in mildly hypercholesterolemic subjects: a randomized, controlled crossover study. Nutr Metab Cardiovasc Dis. 2014;24(12):1330-6. doi:10.1016/j.numecd.2014.07.002		X		Health Status
84	Berard E, Bongard V, Haas B, et al. Score of adherence to 2016 European cardiovascular prevention guidelines is an independent determinant of cardiovascular and all-cause mortality in a French general population. Eur Heart J. 2017;381064. doi:10.1093/eurheartj/ehx502.P5139				Publication Status
85	Berge K, Musa-Veloso K, Harwood M, Hoem N, Burri L. Krill oil supplementation lowers serum triglycerides without increasing low-density lipoprotein cholesterol in adults with borderline high or high triglyceride levels. Nutr Res. 2014;34(2):126-33. doi:10.1016/j.nutres.2013.12.003		X		
86	Berglund L, Oliver EH, Fontanez N, et al. HDL-subpopulation patterns in response to reductions in dietary total and saturated fat intakes in healthy subjects. Am J Clin Nutr. 1999. 70(6):992-1000. doi:10.1093/ajcn/70.6.992				Age of participants at intervention or exposure
87	Bermejo LM, Rodriguez-Duran D, Lopez-Plaza B, et al. Effects of a functional light cheese naturally enriched with CLA and omega-3 improving blood lipid profile in overweight and obese people treatment. Clinical nutrition supplement. 2012;7(1):219. doi:10.1016/S1744-1161(12)70543-4				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
88	Bernic D, Brassard D, Droit A, et al. Comparing the impact of saturated fatty acids from different dairy sources on the proteome of high density lipoproteins. FASEB journal. 2017;31(Suppl 1): lb272-lb272				Publication Status
89	Bernic D, Brassard D, Tessier-Grenier M, et al. Comparing the impact of saturated fatty acids from different dairy sources on LDL particle size phenotype. FASEB journal. 2017;31(Suppl 1): 966-5				Publication Status
90	Berryman CE, Fleming JA, Kris-Etherton PM. Inclusion of almonds in a cholesterol-lowering diet improves plasma HDL subspecies and cholesterol efflux to serum in normal-weight individuals with elevated LDL cholesterol. J Nutr. 2017;147(8):1517-1523. doi:10.3945/jn.116.245126				Health Status
91	Berryman CE, West SG, Fleming JA, Bordi PL, Kris-Etherton PM. Effects of daily almond consumption on cardiometabolic risk and abdominal adiposity in healthy adults with elevated LDL-cholesterol: a randomized controlled trial. J Am Heart Assoc. 2015;4(1):e000993. doi:10.1161/jaha.114.000993		X		Health Status
92	Beydoun MA, Fanelli-Kuczmarski MT, Beydoun HA, et al. Dairy product consumption and its association with metabolic disturbance in a prospective study of urban adults. Br J Nutr. 2018;119(6):706-719. doi:10.1017/s0007114518000028		X		
93	Bhardwaj R, Dod H, Sandhu MS, et al. Acute effects of diets rich in almonds and walnuts on endothelial function. Indian Heart J. 2018;70(4):497-501. doi:10.1016/j.ihj.2018.01.030				Study Duration
94	Bhatt SP, Misra A, Nigam P. Nutrition and physical activity in Asian Indians with non-alcoholic fatty liver: a case control study. Diabetes Metab Syndr. 2019;13(2):1271-1274. doi:10.1016/j.dsx.2019.01.054	X			Country
95	Bian S, Gao Y, Zhang M, et al. Dietary nutrient intake and metabolic syndrome risk in Chinese adults: a case-control study. Nutr J. 2013;12(1):106. doi:10.1186/1475-2891-12-106	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
96	Bigornia SJ, Scott TM, Harris WS, Tucker KL. Prospective associations of erythrocyte composition and dietary intake of n-3 and n-6 PUFA with measures of cognitive function. Nutrients. 2018;10(9):1253. doi:10.3390/nu10091253			X	
97	Bihuniak JD, Ramos A, Huedo-Medina T, Hutchins-Wiese H, Kerstetter JE, Kenny AM. Adherence to a Mediterranean-Style Diet and Its Influence on Cardiovascular Risk Factors in Postmenopausal Women. J Acad Nutr Diet. 2016;116(11):1767-1775. doi:10.1016/j.jand.2016.06.377		X		
98	Bjerregaard P, Pedersen HS, Mulvad G. The associations of a marine diet with plasma lipids blood glucose blood pressure and obesity among the Inuit in Greenland. Eur J Clin Nutr. 2000. 54(9):732-7. doi: 10.1038/sj.ejcn.1601088		X		Age of participants at intervention or exposure
99	Bjerregaard P. The association of n-3 fatty acids with serum High Density Cholesterol (HDL) is modulated by sex but not by Inuit ancestry. Atherosclerosis. 2013;226(1):281-5. doi:10.1016/j.atherosclerosis.2012.10.071	X	X		
100	Bjerve KS, Thoresen L, Bonaa K, Vik T, Johnsen H, Brubakk AM. Clinical studies with alpha-linolenic acid and long-chain n-3 fatty acids. Nutrition. 1992. 8(2):130-2.			X	Health Status
101	Bjornshave A, Holst JJ, Hermansen K. A pre-meal of whey proteins induces differential effects on glucose and lipid metabolism in subjects with the metabolic syndrome: a randomised cross-over trial. Eur J Nutr. 2019;58(2):755-764. doi:10.1007/s00394-018-1684-3		X	X	
102	Blesso CN, Andersen CJ, Barona J, Volk B, Volek JS, Fernandez ML. Effects of carbohydrate restriction and dietary cholesterol provided by eggs on clinical risk factors in metabolic syndrome. J Clin Lipidol. 2013;7(5):463-71. doi:10.1016/j.jacl.2013.03.008				Duplicate

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
103	Blom WAM, Koppenol WP, Hiemstra H, Stojakovic T, Scharnagl H, Trautwein EA. A low-fat spread with added plant sterols and fish omega-3 fatty acids lowers serum triglyceride and LDL-cholesterol concentrations in individuals with modest hypercholesterolaemia and hypertriglyceridaemia. Eur J Nutr. 2019;58(4):1615-1624. doi:10.1007/s00394-018-1706-1		X		Health Status
104	Bobes J, Arango C, Garcia-Garcia M, Rejas J. Healthy lifestyle habits and 10-year cardiovascular risk in schizophrenia spectrum disorders: an analysis of the impact of smoking tobacco in the CLAMORS schizophrenia cohort. Schizophr Res. 2010;119(1-3):101-9. doi:10.1016/j.schres.2010.02.1030	X			Health Status
105	Bodhini D, Gaal S, Shatwan I, et al. Interaction between TCF7L2 polymorphism and dietary fat intake on high density lipoprotein cholesterol. PLoS One. 2017;12(11):e0188382. doi:10.1371/journal.pone.0188382	X			Country
106	Bogl LH, Maranghi M, Rissanen A, Kaprio J, Taskinen MR, Pietilainen KH. Dietary omega-3 polyunsaturated fatty acid intake is related to a protective high-density lipoprotein subspecies profile independent of genetic effects: a monozygotic twin pair study. Atherosclerosis. 2011;219(2):880-6. doi:10.1016/j.atherosclerosis.2011.09.010	X			
107	Bohl M, Bjornshave A, Larsen MK, Gregersen S, Hermansen K. Effects of medium-chain saturated dairy fat on the body composition of abdominal obese subjects (DairyHealth): a 12-weekrandomiseddouble-blindedintervention study. Diabetologia. 2015;58(S1):S335- S336. doi:10.1007/s00125-015-3687-4				Publication Status
108	Bonaccio M, Di Castelnuovo A, Pounis G, et al. High adherence to the Mediterranean diet is associated with cardiovascular protection in higher but not in lower socioeconomic groups: prospective findings from the Moli-sani study. Int J Epidemiol. 2017;46(5):1478-1487. doi:10.1093/ije/dyx145		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
109	Bonaccio M, Ruggiero E, Di Castelnuovo A, et al. Fish intake is associated with lower cardiovascular risk in a Mediterranean population: prospective results from the Moli-sani study. Nutr Metab Cardiovasc Dis. 2017;27(10):865-873. doi:10.1016/j.numecd.2017.08.004		X		
110	Bonafini S, Tagetti A, Gaudino R, et al. Individual fatty acids in erythrocyte membranes are associated with several features of the metabolic syndrome in obese children. Eur J Nutr. 2019;58(2):731-742. doi:10.1007/s00394-018-1677-2	X			
111	Bondia-Pons I, Poho P, Bozzetto L, et al. Isoenergetic diets differing in their n-3 fatty acid and polyphenol content reflect different plasma and HDL-fraction lipidomic profiles in subjects at high cardiovascular risk. Mol Nutr Food Res. 2014;58(9):1873-82. doi:10.1002/mnfr.201400155				Duplicate data
112	Bonet Serra B, Quintanar Rioja A, Viana Arribas M, Iglesias-Gutierrez E, Varela-Moreiras G. The effects of yogurt with isomer enriched conjugated linoleic acid on insulin resistance in obese adolescents. Rev Esp Pediatr. 2008. 64(1):94- 100.				Language
113	Bonthuis M, Hughes MC, Ibiebele TI, Green AC, van der Pols JC. Dairy consumption and patterns of mortality of Australian adults. Eur J Clin Nutr. 2010;64(6):569-77. doi:10.1038/ejcn.2010.45		X		
114	Bosaeus M, Hussain A, Karlsson T, et al. A randomized longitudinal dietary intervention study during pregnancy: effects on fish intakephospholipidsand body composition. Nutr J. 2015;141. doi:10.1186/1475-2891-14-1		X	X	
115	Bouchard-Mercier A, Godin G, Lamarche B, Perusse L, Vohl MC. Effects of peroxisome proliferator-activated receptorsdietary fat intakes and gene-diet interactions on peak particle diameters of low-density lipoproteins. J Nutrigenet Nutrigenomics. 2011;4(1):36-48. doi:10.1159/000324531	X		X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
116	Bouillon K, Singh-Manoux A, Jokela M, et al. Decline in low-density lipoprotein cholesterol concentration: lipid-lowering drugsdietor physical activity? Evidence from the Whitehall II study. Heart. 2011;97(11):923-30. doi:10.1136/hrt.2010.216309		X	X	
117	Boulton TJ, Magarey AM, Cockington RA. Tracking of serum lipids and dietary energy, fat and calcium intake from 1 to 15 years. Acta Paediatr. 1995. 84(9):1050-5. doi:10.1111/j.1651-2227.1995.tb13823.x		X		
118	Bouziotas C, Koutedakis Y, Nevill A, et al. Greek adolescents, fitness, fatness, fat intake, activity, and coronary heart disease risk. Arch Dis Child. 2004. 89(1):41-4.	X			
119	Bouziotas C, Koutedakis Y. A three year study of coronary heart disease risk factors in Greek adolescents. Pediatric Exercise Science. 2003. 15(1):9-18. doi:10.1123/pes.15.1.9	X	X		
120	Bowen J, Brindal E, James-Martin G, Noakes M. Randomized trial of a high protein, partial meal replacement program with or without alternate day fasting: Similar effects on weight loss, retention status, nutritional, metabolic, and behavioral outcomes. Nutrients. 2018;10(9): pii: E1145. doi:10.3390/nu10091145		X		
121	Bowen KJ, Kris-Etherton PM, Jones PJ, Reddivari L. Effects of diets that vary in fatty acid composition on fecal short-chain fatty acid levels and their relationship with circulating lipids and lipoproteins. Circulation. 2019;139(Suppl 1): AP293. doi:10.1161/circ.139.suppl_1.P293				Publication Status
122	Bowen KJ, Kris-Etherton PM, West SG, et al. Canola and high-oleic acid canola oils improve lipid/lipoprotein parameters compared to an oil blend characteristic of a western dietary pattern in individuals at risk for metabolic syndrome: a randomized crossover clinical trial. Circulation. 2018;137(Suppl 1): AP382				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
123	Bozza R, Campos WD, Barbosa Filho VC, Stabelini Neto A, Silva MP, Maziero RS. High blood pressure in adolescents of Curitiba: Prevalence and associated factors. Arq Bras Cardiol. 2016;106(5):411-8. doi:10.5935/abc.20160044	X			
124	Bozzetto L, Annuzzi G, Pacini G, et al. Polyphenol-rich diets improve glucose metabolism in people at high cardiometabolic risk: a controlled randomised intervention trial. Diabetologia. 2015;58(7):1551-60. doi:10.1007/s00125-015-3592-x			X	
125	Brahe LK, Angquist L, Larsen LH, et al. Influence of SNPs in nutrient-sensitive candidate genes and gene-diet interactions on blood lipids: the DiOGenes study. Br J Nutr. 2013;110(5):790-6. doi:10.1017/s0007114512006058		X		
126	Brassard D, Arsenault B, Boyer M, et al. Effects of saturated fatty acids from butter and cheese on high-density lipoprotein (HDL)-mediated cholesterol efflux capacity. FASEB journal. 2017;Conference: Experimental Biology 2017, EB. United States. 31(Suppl 1):146				Publication Status
127	Brassard D, Arsenault BJ, Boyer M, et al. Saturated fats from butter but not from cheese increase HDL-mediated cholesterol efflux capacity from J774 macrophages in men and women with abdominal obesity. J Nutr. 2018;148(4):573-580. doi:10.1093/jn/nxy014				Duplicate data
128	Bray GA, Redman LM, de Jonge L, Rood J, Sutton EF, Smith SR. Plasma fatty acyl-carnitines during 8weeks of overfeeding: relation to diet energy expenditure and body composition: the PROOF study. Metabolism. 2018;831-10. doi:10.1016/j.metabol.2018.01.019		X	X	
129	Brox J, Bjornstad E, Olaussen K, Osterud B, Almdahl S, Lochen ML. Blood lipids, fatty acids, diet and lifestyle parameters in adolescents from a region in northern Norway with a high mortality from coronary heart disease. Eur J Clin Nutr. 2002;56(7):694-700. doi:10.1038/sj.ejcn.1601381		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
130	Bruce B, Spiller GA, Klevay LM, Gallagher SK. A diet high in whole and unrefined foods favorably alters lipids, antioxidant defenses, and colon function. J Am Coll Nutr. 2000. 19(1):61-7. doi:10.1080/07315724.2000.10718915		X		
131	Bruno R, Petrella E, Bertarini V, Pedrielli G, Neri I, Facchinetti F. Adherence to a lifestyle programme in overweight/obese pregnant women and effect on gestational diabetes mellitus: a randomized controlled trial. Matern Child Nutr. 2017;13(3): e12333. doi:10.1111/mcn.12333		X		
132	Bruun S, van Rossem L, Lauritzen L, et al. Content of n-3 LC-PUFA in breast milk four months postpartum is associated with infancy blood pressure in boys and infancy blood lipid profile in girls. Nutrients. 2019;11(2): 235. doi:10.3390/nu11020235		X		
133	Bub A, Malpuech-Brugere C, Orfila C, et al. A Dietary Intervention of Bioactive Enriched Foods Aimed at Adults at Risk of Metabolic Syndrome: Protocol and Results from PATHWAY-27 Pilot Study. Nutrients. 2019;11(8): 1814. doi:10.3390/nu11081814		X		
134	Buckland G, Agudo A, Travier N, et al. Adherence to the Mediterranean diet reduces mortality in the Spanish cohort of the European Prospective Investigation into Cancer and Nutrition (EPIC-Spain). Br J Nutr. 2011;106(10):1581-91. doi:10.1017/S0007114511002078		X	X	
135	Bui Q. Dietary fat modification and the risk of future cardiovascular events and mortality. Am Fam Physician. 2013;87(9):609-10.	X			
136	Bumrungpert A, Chongsuwat R, Phosat C, Butacnum A. Rice bran oil containing gamma-oryzanol improves lipid profiles and antioxidant status in hyperlipidemic subjects: A randomized double-blind controlled trial. J Altern Complement Med. 2019;25(3):353-358. doi:10.1089/acm.2018.0212				Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
137	Butler TJ, Davies I, Mushtaq S. Full fat cheese intake and cardiovascular health: a randomised control trial. Proceedings of the nutrition society. 2017;76(OCE4): E223. doi:10.1017/S0029665117003858				Publication Status
138	Buyken AE, Flood V, Rochtchina E, Nestel P, Brand-Miller J, Mitchell P. Modifications in dietary fat quality are associated with changes in serum lipids of older adults independently of lipid medication. J Nutr. 2010;140(1):88-94. doi:10.3945/jn.109.110486			X	
139	Byrne DW, Rolando LA, Aliyu MH, et al. Modifiable healthy lifestyle behaviors: 10-Year health outcomes from a health promotion program. Am J Prev Med. 2016;51(6):1027-1037. doi:10.1016/j.amepre.2016.09.012		X		
140	Caligiuri SP, Rodriguez-Leyva D, Aukema HM, et al. Dietary flaxseed reduces central aortic blood pressure without cardiac involvement but through changes in plasma oxylipins. Hypertension. 2016;68(4):1031-1038. doi:10.1161/hypertensionaha.116.07834				Health Status
141	Calyniuk B, Grochowska-Niedworok E, Muc-Wierzgon M, Nowakowska-Zajdel E, Osowski M. The effectiveness of the low energy diet in overweight and obese adults. Rocz Panstw Zakl Hig. 2016;67(2):137-46.		X		
142	Camargo A, Rangel-Zuniga OA, Alcala-Diaz J, et al. Dietary fat may modulate adipose tissue homeostasis through the processes of autophagy and apoptosis. Eur J Nutr. 2017;56(4):1621-1628. doi:10.1007/s00394-016-1208-y			X	
143	Campos Mondragón MG, Oliart Ros RM, Martínez Martinez A, Méndez Machado GF, Angulo Guerrero JO. Metabolic syndrome reversion by polyunsaturated fatty acids ingestion. Med Clin. 2013;141(12):513- 518. doi:10.1016/j.medcli.2012.10.030				Language

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
144	Campos-Staffico AM, Costa APR, Carvalho LSF, et al. Omega-3 intake is associated with attenuated inflammatory response and cardiac remodeling after myocardial infarction. Nutr J. 2019;18(1):29. doi:10.1186/s12937-019-0455-1			X	
145	Cao Y, Wittert G, Taylor AW, Adams R, Appleton S, Shi Z. Nutrient patterns and chronic inflammation in a cohort of community dwelling middle-aged men. Clin Nutr. 2017;36(4):1040-1047. doi:10.1016/j.clnu.2016.06.018		X	X	
146	Cardoso Chaves O, Franceschini Sdo C, Machado Rocha Ribeiro S, Ferreira Rocha Sant Ana L, Garcon de Faria C, Priore SE. Anthropometric and biochemical parameters in adolescents and their relationship with eating habits and household food availability. Nutr Hosp. 2013;28(4):1352-6. doi:10.3305/nh.2013.28.4.6467	X	X		
147	Carson JA, Michalsky L, Latson B, et al. The cardiovascular health of urban African Americans: diet-related results from the Genes, Nutrition, Exercise, Wellness, and Spiritual Growth (GoodNEWS) trial. J Acad Nutr Diet. 2012;112(11):1852-8. doi:10.1016/j.jand.2012.06.357		X	X	
148	Carvalho-Wells AL, Jackson KG, Lockyer S, Lovegrove JA, Minihane AM. APOE genotype influences triglyceride and C-reactive protein responses to altered dietary fat intake in UK adults. Am J Clin Nutr. 2012;96(6):1447-53. doi:10.3945/ajcn.112.043240			X	
149	Casas R, Sacanella E, Urpi-Sarda M, et al. The effects of the mediterranean diet on biomarkers of vascular wall inflammation and plaque vulnerability in subjects with high risk for cardiovascular disease. A randomized trial. PLoS One. 2014;9(6):e100084. doi:10.1371/journal.pone.0100084		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
150	Casas R, Sacanella E, Urpi-Sarda M, et al. Long-term immunomodulatory effects of a Mediterranean diet in adults at high risk of cardiovascular disease in the PREvencion con DIeta MEDiterranea (PREDIMED) Randomized Controlled Trial. J Nutr. 2016;146(9):1684-93. doi:10.3945/jn.115.229476		X		Health Status
151	Casas-Agustench P, Serra M, Perez-Heras A, Cofan M, Pinto X, Trautwein EA, Ros E. Effects of plant sterol esters in skimmed milk and vegetable-fat-enriched milk on serum lipids and non-cholesterol sterols in hypercholesterolaemic subjects: a randomised placebo-controlled cross over study. Br J Nutr. 2012;107(12):1766-75. doi:10.1017/s0007114511005162		X		
152	Casazza K, Dulin-Keita A, Gower BA, Fernandez JR. Differential influence of diet and physical activity on components of metabolic syndrome in a multiethnic sample of children. J Am Diet Assoc. 2009. 109(2):236-44. doi:10.1016/j.jada.2008.10.054	X			
153	Celada P, Delgado-Pando G, Olmedilla-Alonso B, Jimenez-Colmenero F, Ruperto M, Sanchez-Muniz FJ. Impact of improved fat-meat products consumption on anthropometric markers and nutrient intakes of male volunteers at increased cardiovascular risk. Nutr Hosp. 2015;32(2):710-21. doi:10.3305/nh.2015.32.2.9231			X	
154	Celada P, Olmedilla-Alonso B, Delgado-Pando G, et al. Coagulation, thrombogenesis, and insulin resistance markers in increased-cardiovascular-risk subjects consuming improved-fat meat products. J Am Coll Nutr. 2019;38(4):334-341. doi:10.1080/07315724.2018.1513345				Health Status
155	Celada P, Sanchez-Muniz FJ, Delgado-Pando G, et al. Effects of improved fat meat products consumption on emergent cardiovascular disease markers of male volunteers at cardiovascular risk. J Physiol Biochem. 2016;72(4):669-678. doi:10.1007/s13105-016-0505-5		X		Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
156	Cervenka MC, Patton K, Eloyan A, Henry B, Kossoff EH. The impact of the modified Atkins diet on lipid profiles in adults with epilepsy. Nutr Neurosci. 2016;19(3):131-7. doi:10.1179/1476830514y.0000000162	X	X		
157	Cha D, Park Y. Association between dietary cholesterol and their food sources and risk for hypercholesterolemia: The 2012-2016 Korea National Health and Nutrition Examination Survey. Nutrients. 2019;11(4): pii: E846. doi:10.3390/nu11040846	X			
158	Cha E, Paul S, Braxter BJ, Umpierrez G, Faulkner MS. Dietary behaviors and glucose metabolism in young adults at risk for type 2 diabetes. Diabetes Educ. 2018;44(2):158-167. doi:10.1177/0145721718756057	X			
159	Chahal N, McCrindle B, Manlhiot C, Wong H. A 4-week randomized clinical trial of flaxseed supplementation in children with hypercholesterolemia. Canadian journal of cardiology. 2011. 27(5 Suppl):S339. doi:10.1016/j.cjca.2011.08.006				Publication Status
160	Champagne CM, Broyles ST, Moran LD, et al. Dietary intakes associated with successful weight loss and maintenance during the Weight Loss Maintenance trial. J Am Diet Assoc. 2011;111(12):1826-35. doi:10.1016/j.jada.2011.09.014		X		
161	Chang L, Vethakkan S, Nesaretnam K, Teng K. Effects of exchanging dietary saturated fatty acids or carbohydrate for monounsaturated fatty acids on inflammatory responses in abdominally obese Malaysians: a randomized controlled trial. Obesity reviews. 2014. 15:94. doi:10.1111/obr.12149				Publication Status
162	Chang WI, Azrina A, Sabariah MN, Irmi Zarina I, Loh SP. Effects of consuming yellowstripe scad versus salmon on lipid profile, fasting glucose, body weight status and blood pressure among healthy overweight Malaysian adults. Malays J Nutr. 2017;23(3):434-452.		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
163	Chee C, Mansell P, Stephens F, et al. Differential effects of carbohydrate vs fat overfeeding on liver fat content and lipid metabolism in healthy overweight males. Diabetologia. 2015. 58(Suppl. 1):S336. doi:10.1007/s00125-015-3687-4				Publication Status
164	Cheenam B, Leena P, Vikas K. Effects of sunflower seeds on cholesterol and low-density lipoprotein levels in patients with dyslipidemia. Asian J Pharm Clin Res. 2019;12(3):556-559. doi:10.22159/ajpcr.2019.v12i3.31032				Health Status, Country
165	Chen BK, Seligman B, Farquhar JW, Goldhaber-Fiebert JD. Multi-Country analysis of palm oil consumption and cardiovascular disease mortality for countries at different stages of economic development: 1980-1997. Global Health. 2011;745. doi:10.1186/1744-8603-7-45	X			
166	Chen M, Li Y, Sun Q, et al. Dairy fat and risk of cardiovascular disease in 3 cohorts of US adults. Am J Clin Nutr. 2016;104(5):1209-1217. doi:10.3945/ajcn.116.134460	X			
167	Chen ST, Maruthur NM, Appel LJ. The effect of dietary patterns on estimated coronary heart disease risk: results from the Dietary Approaches to Stop Hypertension (DASH) trial. Circ Cardiovasc Qual Outcomes. 2010;3(5):484-9. doi:10.1161/circoutcomes.109.930685		X		
168	Chen Y, Estampador AC, Keller M, et al. The combined effects of FADS gene variation and dietary fats in obesity-related traits in a population from the far north of Sweden: the GLACIER Study. Int J Obes (Lond). 2019;43(4):808-820. doi:10.1038/s41366-018-0112-3	X		X	
169	Chen Y, Feng R, Yang X, et al. Yogurt improves insulin resistance and liver fat in obese women with nonalcoholic fatty liver disease and metabolic syndrome: A randomized controlled trial. Am J Clin Nutr. 2019;109(6):1611-1619. doi:10.1093/ajcn/nqy358		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
170	Chiang YL, Haddad E, Rajaram S, Shavlik D, Sabate J. The effect of dietary walnuts compared to fatty fish on eicosanoids, cytokines, soluble endothelial adhesion molecules and lymphocyte subsets: a randomized, controlled crossover trial. Prostaglandins Leukot Essent Fatty Acids. 2012;87(4-5):111-7. doi:10.1016/j.plefa.2012.07.007		X	X	
171	Chiu S, Bergeron N, Williams PT, Bray GA, Sutherland B, Krauss RM. Comparison of the DASH (Dietary Approaches to Stop Hypertension) diet and a higher-fat DASH diet on blood pressure and lipids and lipoproteins: a randomized controlled trial. Am J Clin Nutr. 2016;103(2):341-7. doi:10.3945/ajcn.115.123281		X		
172	Chiu S, Krauss RM. The effects of high saturated fat intake on LDL and HDL subclasses in individuals with atherogenic dyslipidemia. Circulation. 2012;125(Suppl 10): AP348.				Publication Status
173	Chiu S, Williams PT, Krauss RM. Effects of a very high saturated fat diet on LDL particles in adults with atherogenic dyslipidemia: A randomized controlled trial. PLoS One. 2017;12(2):e0170664. doi:10.1371/journal.pone.0170664			X	Study Duration
174	Chiuve SE, Sandhu RK, Moorthy MV, Glynn RJ, Albert CM. Dietary fat intake is differentially associated with risk of paroxysmal compared with sustained atrial fibrillation in women. J Nutr. 2015;145(9):2092-101. doi:10.3945/jn.115.212860			X	Population at Outcome
175	Chiva-Blanch G, Laake K, Myhre P, et al. High adherence to the Nordic diet is associated with lower levels of total and platelet-derived circulating microvesicles in a Norwegian population. Nutrients. 2019;11(5): pii: E1114. doi:10.3390/nu11051114	X	X		
176	Chmurzynska A, Muzsik A, Krzyzanowska-Jankowska P, Walkowiak J, Bajerska J. The effect of habitual fat intake, IL6 polymorphism, and different diet strategies on inflammation in postmenopausal women with central obesity. Nutrients. 2019;11(7): pii: E1557. doi:10.3390/nu11071557			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
177	Cho Y, Cudhea F, Park JH, Mozaffarian D, Singh G, Shin MJ. Burdens of cardiometabolic diseases attributable to dietary and metabolic risks in Korean adults 2012–2013. Yonsei Med J. 2017;58(3):540-551. doi:10.3349/ymj.2017.58.3.540	X			
178	Christofaro DG, Fernandes RA, Oliveira AR, Freitas Junior IF, Barros MV, Ritti-Dias RM. The association between cardiovascular risk factors and high blood pressure in adolescents: a school-based study. Am J Hum Biol. 2014;26(4):518-22. doi:10.1002/ajhb.22555		X		
179	Clark ML, Butler LM, Koh WP, Wang R, Yuan JM. Dietary fiber intake modifies the association between secondhand smoke exposure and coronary heart disease mortality among Chinese non-smokers in Singapore. Nutrition. 2013;29(11-12):1304-9. doi:10.1016/j.nut.2013.04.003		X		
180	Clifton P. Metabolic syndrome-role of dietary fat type and quantity. Nutrients. 2019;11(7): pii: E1438. doi:10.3390/nu11071438	X			
181	Coates AM, Sioutis S, Buckley JD, Howe PRC. Regular consumption of n-3 fatty acid-enriched pork modifies cardiovascular risk factors. Br J Nutr. 2009. 101(4):592-597. doi:10.1017/S0007114508025063				Age of participants at intervention or exposure
182	Colussi G, Catena C, Dialti V, Pezzutto F, Mos L, Sechi LA. Fish meal supplementation and ambulatory blood pressure in patients with hypertension: relevance of baseline membrane fatty acid composition. Am J Hypertens. 2014;27(3):471-81. doi:10.1093/ajh/hpt231		X		Health Status
183	Conte FA, Franz LB, Berlezi EM, Oliveira OB. Nutritional education and olive oil improve dislipidemia of climate women. Journal of Nursing UFPE / Revista de Enfermagem UFPE. 2017;11(8):3100-3107. doi:10.5205/reuol.11064-98681-4-ED.1108201715				Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
184	Conway MC, Mulhern MS, McSorley EM, et al. Dietary determinants of polyunsaturated fatty acid (PUFA) status in a high fish-eating cohort during pregnancy. Nutrients. 2018;10(7): pii: E927. doi:10.3390/nu10070927			X	
185	Conway V, Couture P, Richard C, Gauthier SF, Pouliot Y, Lamarche B. Impact of buttermilk consumption on plasma lipids and surrogate markers of cholesterol homeostasis in men and women. Nutr Metab Cardiovasc Dis. 2013;23(12):1255-62. doi:10.1016/j.numecd.2013.03.003		X		
186	Corella D, Sorli JV, Estruch R, et al. MicroRNA-410 regulated lipoprotein lipase variant rs13702 is associated with stroke incidence and modulated by diet in the randomized controlled PREDIMED trial. Am J Clin Nutr. 2014;100(2):719-31. doi:10.3945/ajcn.113.076992		X		
187	Corina A, Rangel-Zuniga OA, Jimenez-Lucena R, et al. Low intake of vitamin E accelerates cellular aging in patients with established cardiovascular disease: The CORDIOPREV Study. J Gerontol A Biol Sci Med Sci. 2019;74(6):770-777. doi:10.1093/gerona/gly195			X	Health Status
188	Crichton GE, Alkerwi A. Dairy food intake is positively associated with cardiovascular health: findings from Observation of Cardiovascular Risk Factors in Luxembourg study. Nutr Res. 2014;34(12):1036-44. doi:10.1016/j.nutres.2014.04.002	X		X	
189	Crowe-White KM, Cardel MI, Burkhalter HH, Huo T, Fernandez JR. Higher n-6:n-3 fatty acid intake is associated with decreased cardiometabolic risk factors in a racially diverse sample of children. Curr Dev Nutr. 2018;2(5):nzy014. doi:10.1093/cdn/nzy014	X			
190	Cruz ML, Wong WW, Mimouni F, et al. Effects of infant nutrition on cholesterol synthesis rates. Pediatr Res. 1994. 35(2):135-40. doi:10.1203/00006450-199402000-00001		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
191	Cueto-Galan R, Baron FJ, Valdivielso P, et al. Changes in fatty liver index after consuming a Mediterranean diet: 6-year follow-up of the PREDIMED-Malaga trial. Med Clin (Barc). 2017;148(10):435-443. doi:10.1016/j.medcli.2016.11.032			X	
192	Cundiff DK, Lanou AJ, Nigg CR. Relation of omega-3 Fatty Acid intake to other dietary factors known to reduce coronary heart disease risk. Am J Cardiol. 2007. 99(9):1230-3. doi:10.1016/j.amjcard.2006.12.032			X	
193	Curb JD, Wergowske G, Dobbs JC, Abbott RD, Huang B. Serum lipid effects of a high-monounsaturated fat diet based on macadamia nuts. Arch Intern Med. 2000. 160(8):1154-8. doi:10.1001/archinte.160.8.1154				Age of participants at intervention or exposure
194	da Luz P, Nishiyama M, Chagas ACP. Drugs and lifestyle for the treatment and prevention of coronary artery disease - comparative analysis of the scientific basis. Braz J Med Biol Res. 2011;44(10):973-991. doi:10.1590/S0100-879X2011007500111	X			
195	Da Silva MS, Julien P, Couture P, Lemieux S, Vohl MC, Rudkowska I. Associations between dairy intake and metabolic risk parameters in a healthy French-Canadian population. Appl Physiol Nutr Metab. 2014;39(12):1323-31. doi:10.1139/apnm-2014-0154	X	X		
196	Daci A, Ozen G, Uyar I, et al. Omega-3 polyunsaturated fatty acids reduce vascular tone and inflammation in human saphenous vein. Prostaglandins Other Lipid Mediat. 2017;133:29-34. doi:10.1016/j.prostaglandins.2017.08.007				Health Status, Non-human
197	Dai J, Jiang Z, Zhang B. Exercise and nutrition therapy for simple obesity in children. Chinese journal of clinical rehabilitation. 2006. 10(32):20- 22.				Language
198	Dalbeni A, Treggiari D, Tagetti A, et al. Positive effects of tomato paste on vascular function after a fat meal in male healthy subjects. Nutrients. 2018;10(9): pii: E1310. doi:10.3390/nu10091310		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
199	Dalmeijer GW, Struijk EA, van der Schouw YT, et al. Dairy intake and coronary heart disease or stroke--a population-based cohort study. Int J Cardiol. 2013;167(3):925-9. doi:10.1016/j.ijcard.2012.03.094		X		
200	Damasceno NR, Perez-Heras A, Serra M, et al. Crossover study of diets enriched with virgin olive oilwalnuts or almonds. Effects on lipids and other cardiovascular risk markers. Nutr Metab Cardiovasc Dis. 2011;21(Suppl 1):S14-20. doi:10.1016/j.numecd.2010.12.006				Health Status
201	Damasceno NR, Sala-Vila A, Cofan M, et al. Mediterranean diet supplemented with nuts reduces waist circumference and shifts lipoprotein subfractions to a less atherogenic pattern in subjects at high cardiovascular risk. Atherosclerosis. 2013;230(2):347-53. doi:10.1016/j.atherosclerosis.2013.08.014		X		
202	Damsgaard CT, Lauritzen L, Hauger H, et al. Effects of oily fish intake on cardiovascular risk markerscognitive functionand behavior in school-aged children: study protocol for a randomized controlled trial. Trials. 2016;17(1):510. doi:10.1186/s13063-016-1647-z	X	X	X	
203	Damsgaard CT, Ritz C, Dalskov SM, et al. Associations between school meal-induced dietary changes and metabolic syndrome markers in 8-11-year-old Danish children. Eur J Nutr. 2016;55(5):1973-84. doi:10.1007/s00394-015-1013-z		X		
204	Daniels SR. Diet and primordial prevention of cardiovascular disease in children and adolescents. Circulation. 2007. 116(9):973- 974. doi:10.1161/circulationaha.107.723817	X			
205	Daryani A, Becker W, Vessby B, Andersson A. Dietary fat intakefat sources and fatty acid composition in serum among immigrant women from Iran and Turkey compared with women of Swedish ethnicity. Scandinavian Journal of Nutrition. 2005. 49(3):106-115.		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
206	Davinelli S, Corbi G, Zarrelli A, et al. Short-term supplementation with flavanol-rich cocoa improves lipid profileantioxidant status and positively influences the AA/EPA ratio in healthy subjects. J Nutr Biochem. 2018;6133-39. doi:10.1016/j.jnutbio.2018.07.011		X		
207	Davis CR, Bryan J, Hodgson JM, Woodman R, Murphy KJ. A Mediterranean diet reduces F2-isoprostanes and triglycerides among older Australian men and women after 6 months. J Nutr. 2017;147(7):1348-1355. doi:10.3945/jn.117.248419		X		
208	Davis CR, Hodgson JM, Woodman R, Bryan J, Wilson C, Murphy KJ. A Mediterranean diet lowers blood pressure and improves endothelial function: results from the MedLey randomized intervention trial. Am J Clin Nutr. 2017;105(6):1305-1313. doi:10.3945/ajcn.116.146803		X		
209	Davis KE, Prasad C, Imrhan V. Consumption of a diet rich in cottonseed oil (CSO) lowers total and LDL cholesterol in normo-cholesterolemic subjects. Nutrients. 2012;4(7):602-10. doi:10.3390/nu4070602	X			
210	Davison KM, Kaplan BJ. Food intake and blood cholesterol levels of community-based adults with mood disorders. BMC Psychiatry. 2012;1210. doi:10.1186/1471-244x-12-10	X			Health Status
211	Davy BM, Harrell K, Stewart J, King DS. Body weight status, dietary habits and physical activity levels of middle school-aged children in rural Mississippi. South Med J. 2004. 97(6):571-7. doi:10.1097/00007611-200406000-00012			X	
212	Dawczynski C, Massey KA, Ness C, et al. Randomized placebo-controlled intervention with n-3 LC-PUFA-supplemented yoghurt: effects on circulating eicosanoids and cardiovascular risk factors. Clin Nutr. 2013;32(5):686-96. doi:10.1016/j.clnu.2012.12.010		X		Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
213	de Batlle J, Sauleda J, Balcells E, et al. Association between Omega3 and Omega6 fatty acid intakes and serum inflammatory markers in COPD. J Nutr Biochem. 2012;23(7):817-21. doi:10.1016/j.jnutbio.2011.04.005	X		X	
214	de la Torre NG, Assaf-Balut C, Jimenez Varas I, et al. Effectiveness of following Mediterranean diet recommendations in the real world in the incidence of gestational diabetes mellitus (gdm) and adverse maternal-foetal outcomes: a prospective, universal, interventional study with a single group. The St Carlos Study. Nutrients. 2019;11(6): pii: E1210. doi:10.3390/nu11061210		X	X	
215	de Luis D, Izaola O, Primo D, Aller R. Role of rs670 variant of APOA1 gene on metabolic response after a high fat vs. a low fat hypocaloric diets in obese human subjects. J Diabetes Complications. 2019;33(3):249-254. doi:10.1016/j.jdiacomp.2018.10.015		X		
216	de Luis DA, Aller R, Izaola O, Bachiller R, Pacheco D. Cardiovascular risk factors and adipocytokines levels after two hypocaloric diets with different fat distribution in obese subjects and rs6923761 gene variant of glucagon-like peptide 1 receptor. J Endocrinol Invest. 2014;37(9):853-9. doi:10.1007/s40618-014-0116-3		X		
217	de Luis DA, Aller R, Izaola O, Gonzalez Sagrado M, Conde R. Role of G308 promoter variant of tumor necrosis factor alpha gene on weight loss and metabolic parameters after a high monounsaturated versus a high polyunsaturated fat hypocaloric diets. Med Clin (Barc). 2013;141(5):189-93. doi:10.1016/j.medcli.2012.12.021		X		
218	De Luis DA, Aller R, Izaola O, Pacheco D. Role of rs9939609 FTO gene variant in weight loss, insulin resistance and metabolic parameters after a high monounsaturated vs a high polyunsaturated fat hypocaloric diets. Nutr Hosp. 2015;32(1):175-81. doi:10.3305/nh.2015.32.1.9169		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
219	de Luis DA, Izaola O, Primo D, Aller R. Dietary-fat effect of the rs10830963 polymorphism in MTNR1B on insulin resistance in response to 3 months weight-loss diets. Endocrinol Diabetes Nutr. 2019;doi:10.1016/j.endinu.2019.02.007		X		
220	de Luis DA, Izaola O, Primo D, Aller R. Impact of 2 different hypocaloric diets on serum omentin levels in obese subjects. Ann Nutr Metab. 2018;73(2):138-144. doi:10.1159/000489130		X		
221	de Luis DA, Izaola O, Primo D, Aller R. Single nucleotide polymorphisms at the ADIPOQ gene locus rs1501299 interact with different type of dietary fatty acids in two hypocaloric diets. Eur Rev Med Pharmacol Sci. 2019;23(7):2960-2970. doi:10.26355/eurrev_201904_17577	X	X		
222	de Luis DA, Romero E, Izaola O, Primo D, Aller R. Cardiovascular risk factors and insulin resistance after two hypocaloric diets with different fat distribution in obese subjects: effect of the rs10767664 gene variant in brain-derived neurotrophic factor. J Nutrigenet Nutrigenomics. 2017;10(5-6):163-171. doi:10.1159/000485248		X		
223	De Natale C, Minerva V, Patti L, et al. Effects of baked products enriched with n-3 fatty acids, folates, beta-glucans, and tocopherol in patients with mild mixed hyperlipidemia. J Am Coll Nutr. 2012;31(5):311-9. doi:10.1080/07315724.2012.10720427		X		
224	de Oliveira Otto MC, Nettleton JA, Lemaitre RN, et al. Biomarkers of dairy fatty acids and risk of cardiovascular disease in the Multi-ethnic Study of Atherosclerosis. J Am Heart Assoc. 2013;2(4):e000092. doi:10.1161/jaha.113.000092		X		
225	de Roos N, Schouten E, Katan M. Consumption of a solid fat rich in lauric acid results in a more favorable serum lipid profile in healthy men and women than consumption of a solid fat rich in trans-fatty acids. J Nutr. 2001. 131(2):242-5. doi:10.1093/jn/131.2.242		X		Age of participants at intervention or exposure

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
226	Dearborn JL, Qiao Y, Guallar E, et al. Polyunsaturated fats, carbohydrates and carotid disease: The Atherosclerosis Risk in Communities (ARIC) Carotid MRI study. Atherosclerosis. 2016;251361-366. doi:10.1016/j.atherosclerosis.2016.05.024			X	Health Status
227	DeHaven MJ, Ramos-Roman MA, Gimpel N, et al. The GoodNEWS (Genes, Nutrition, Exercise, Wellness, and Spiritual Growth) Trial: a community-based participatory research (CBPR) trial with African-American church congregations for reducing cardiovascular disease risk factors--recruitmentmeasurementand randomization. Contemp Clin Trials. 2011;32(5):630-40. doi:10.1016/j.cct.2011.05.017	X	X		
228	Dehghan M, Mente A, Rangarajan S, et al. Association of dairy intake with cardiovascular disease and mortality in 21 countries from five continents (PURE): a prospective cohort study. Lancet. 2018;392(10161):2288-2297. doi:10.1016/s0140-6736(18)31812-9				Country
229	Dehghan M, Mente A, Zhang X, et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet. 2017;390(10107):2050-2062. doi:10.1016/s0140-6736(17)32252-3				Country
230	Del Bo C, Simonetti P, Gardana C, Riso P, Lucchini G, Ciappellano S. Horse meat consumption affects iron status, lipid profile and fatty acid composition of red blood cells in healthy volunteers. Int J Food Sci Nutr. 2013;64(2):147-54. doi:10.3109/09637486.2012.728198		X		
231	Del Brutto OH, Costa AF, Cano JA, et al. Low prevalence of atrial fibrillation in amerindians: a population-based study in frequent fish consumers livinin rural coastal ecuador (The Atahualpa project). Aging Clin Exp Res. 2018;30(5):539-542. doi:10.1007/s40520-017-0810-z		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
232	Del Brutto OH, Mera RM, Ha JE, et al. Oily fish consumption is inversely correlated with cerebral microbleeds in community-dwelling older adults: results from the Atahualpa Project. Aging Clin Exp Res. 2016. 28(4):737-743. doi:10.1007/s40520-015-0473-6		X	X	
233	dela Paz C, Jimeno C, Sy R, Punzalan FE, dela Pena P. The effect of virgin coconut oil on lipid profile and fasting blood sugar: A phase I clinical trial. Phillippine Journal of Internal Medicine. 2010;48(2):1-6.		X		Country
234	Delgado-Lista J, Perez-Martinez P, Garcia-Rios A, et al. CORonary Diet Intervention with Olive oil and cardiovascular PREVention study (the CORDIOPREV study): Rationalemethodsand baseline characteristics: A clinical trial comparing the efficacy of a Mediterranean diet rich in olive oil versus a low-fat diet on cardiovascular disease in coronary patients. Am Heart J. 2016;177:42-50. doi:10.1016/j.ahj.2016.04.011	X		X	
235	Delgado-Pando G, Celada P, Sanchez-Muniz FJ, Jimenez-Colmenero F, Olmedilla-Alonso B. Effects of improved fat content of frankfurters and pates on lipid and lipoprotein profile of volunteers at increased cardiovascular risk: a placebo-controlled study. Eur J Nutr. 2014;53(1):83-93. doi:10.1007/s00394-013-0502-1				Health Status
236	Demmers TA, Jones PJ, Wang Y, Krug S, Creutzinger V, Heubi JE. Effects of early cholesterol intake on cholesterol biosynthesis and plasma lipids among infants until 18 months of age. Pediatrics. 2005. 115(6):1594-601. doi:10.1542/peds.2004-0997		X		
237	Derkach A, Sampson J, Joseph J, Playdon MC, Stolzenberg-Solomon RZ. Effects of dietary sodium on metabolites: the Dietary Approaches to Stop Hypertension (DASH)-Sodium Feeding Study. Am J Clin Nutr. 2017;106(4):1131-1141. doi:10.3945/ajcn.116.150136		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
238	Detopoulou P, Fragopoulou E, Alepoudea E, Nomikos T, Kalogeropoulos N, Antonopoulou S. Associations between erythrocyte fatty acids and Mediterranean diet in Greek volunteers. Hellenic Journal of Atherosclerosis. 2018;9(1):17-31.	X			
239	Devadawson C, Jayasinghe C, Ramiah S, Kanagasingam A. Assessment of lipid profile and atherogenic indices for cardiovascular disease risk based on different fish consumption habits. Asian J Pharm Clin Res. 2016;9(4):156-160.	X	X		
240	Devarajan S, Singh R, Chatterjee B, Zhang B, Ali A. A blend of sesame oil and rice bran oil lowers blood pressure and improves the lipid profile in mild-to-moderate hypertensive patients. J Clin Lipidol. 2016;10(2):339-49. doi:10.1016/j.jacl.2015.12.011				Health Status, Country
241	Dewailly E, Blanchet C, Gingras S, Lemieux S, Holub BJ. Cardiovascular disease risk factors and n-3 fatty acid status in the adult population of James Bay Cree. Am J Clin Nutr. 2002;76(1):85-92. doi:10.1093/ajcn/76.1.85		X		
242	Dhillon J, Li Z, Ortiz RM. Almond Snacking for 8 wk Increases Alpha-Diversity of the Gastrointestinal Microbiome and Decreases Bacteroides fragilis Abundance Compared with an Isocaloric Snack in College Freshmen. Curr Dev Nutr. 2019;3(8):nzz079. doi:10.1093/cdn/nzz079			X	
243	Di Stefano R, Felice F, Belardinelli E, et al. Extra virgin olive oil and apples enriched-dark chocolate consumption and endothelial function: a randomized crossover trial in patients with cardiovascular risk factors. Eur Heart J. 2017;381119- 1120. doi:10.1093/eurheartj/ehx502.P5319				Publication Status
244	Diaf M, Khaled MB, Sellam F. Correlation between dietary fat intake and atherogenic indices in normaloverweight and obese adults with or without type 2 diabetes. Rom J Diabetes Nutr and Metab Dis. 2015;22(4):347-360. doi:10.1515/rjdnmd-2015-0041		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
245	Dias CB, Amigo N, Wood LG, Mallol R, Correig X, Garg ML. Improvement of the omega 3 index of healthy subjects does not alter the effects of dietary saturated fats or n-6PUFA on LDL profiles. Metabolism. 2017;6811-19. doi:10.1016/j.metabol.2016.11.014				Study Duration
246	Diaz-Lopez A, Bullo M, Martinez-Gonzalez MA, et al. Dairy product consumption and risk of type 2 diabetes in an elderly Spanish Mediterranean population at high cardiovascular risk. Eur J Nutr. 2016;55(1):349-60. doi:10.1007/s00394-015-0855-8			X	
247	Diaz-Lopez A, Bullo M, Martinez-Gonzalez MA, et al. Effects of Mediterranean diets on kidney function: a report from the PREDIMED trial. Am J Kidney Dis. 2012;60(3):380-9. doi:10.1053/j.ajkd.2012.02.334			X	
248	Diekmann C, Huber H, Preuss M, et al. Moderate postmeal walking has no beneficial effects over resting on postprandial lipemia, glycemia, insulinemia, and selected oxidative and inflammatory parameters in older adults with a cardiovascular disease risk phenotype: A randomized crossover trial. J Nutr. 2019;149(11):1930-1941. doi:10.1093/jn/nxz148		X	X	
249	Diez-Espino J, Basterra-Gortari FJ, Salas-Salvado J, et al. Egg consumption and cardiovascular disease according to diabetic status: The PREDIMED study. Clin Nutr. 2017;36(4):1015-1021. doi:10.1016/j.clnu.2016.06.009		X		
250	DiMarco DM, Norris GH, Millar CL, Blesso CN, Fernandez ML. Intake of up to 3 eggs per day is associated with changes in HDL function and increased plasma antioxidants in healthy, young adults. J Nutr. 2017;147(3):323-329. doi:10.3945/jn.116.241877		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
251	Dimitriou M, Rallidis LS, Theodoraki EV, Kalafati IP, Kolovou G, Dedoussis GV. Exclusive olive oil consumption has a protective effect on coronary artery disease; overview of the THISEAS study. Public Health Nutr. 2016;19(6):1081-7. doi:10.1017/s1368980015002244	X			
252	Din JN, Aftab SM, Jubb AW, et al. Effect of moderate walnut consumption on lipid profilearterial stiffness and platelet activation in humans. Eur J Clin Nutr. 2011;65(2):234-9. doi:10.1038/ejcn.2010.233		X	X	
253	DiNicolantonio JJ, O'Keefe JH. Omega-6 vegetable oils as a driver of coronary heart disease: the oxidized linoleic acid hypothesis. Open Heart. 2018;5(2):e000898. doi:10.1136/openhrt-2018-000898	X			
254	Dittrich M, Jahreis G, Bothor K, et al. Benefits of foods supplemented with vegetable oils rich in alpha-linolenic, stearidonic or docosahexaenoic acid in hypertriglyceridemic subjects: a double-blind, randomized, controlled trail. Eur J Nutr. 2015;54(6):881-93. doi:10.1007/s00394-014-0764-2		X		Health Status
255	Dixon LB, Shannon BM, Tershakovec AM, Bennett MJ, Coates PM, Cortner JA. Effects of family history of heart disease, apolipoprotein E phenotype, and lipoprotein(a) on the response of children's plasma lipids to change in dietary lipids. Am J Clin Nutr. 1997. 66(5):1207-17. doi:10.1093/ajcn/66.5.1207		X		Health Status
256	Djousse L, Petrone AB, Gaziano JM. Consumption of fried foods and risk of heart failure in the physicians' health study. J Am Heart Assoc. 2015;4(4): pii: e001740. doi:10.1161/jaha.114.001740		X		
257	Dodevska MS, Sobajic SS, Djordjevic PB, Dimitrijevic-Sreckovic VS, Spasojevic-Kalimanovska VV, Djordjevic BI. Effects of total fibre or resistant starch-rich diets within lifestyle intervention in obese prediabetic adults. Eur J Nutr. 2016;55(1):127-37. doi:10.1007/s00394-015-0831-3		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
258	Dolley G, Boisclair ME, Lamarche B, et al. Interactions between dietary fat intake and FASN genetic variation influence LDL peak particle diameter. J Nutrigenet Nutrigenomics. 2011;4(3):137-45. doi:10.1159/000327778	X	X		
259	Domenech M, Roman P, Lapetra J, et al. Mediterranean diet reduces 24-hour ambulatory blood pressureblood glucose, and lipids: one-year randomized, clinical trial. Hypertension. 2014;64(1):69-76. doi:10.1161/hypertensionaha.113.03353		X		
260	Dominguez-Reyes T, Astudillo-Lopez CC, Salgado-Goytia L, et al. Interaction of dietary fat intake with APOA2, APOA5 and LEPR polymorphisms and its relationship with obesity and dyslipidemia in young subjects. Lipids Health Dis. 2015;14:106. doi:10.1186/s12944-015-0112-4	X			
261	Doo M, Won S, Kim Y. Association between the APOB rs1469513 polymorphism and obesity is modified by dietary fat intake in Koreans. Nutrition. 2015;31(5):653-8. doi:10.1016/j.nut.2014.10.007	X	X		
262	Doostvandi T, Bahadoran Z, Mozaffari-Khosravi H, Tahmasebinejad Z, Mirmiran P, Azizi F. The association of dietary patterns and the incidence of insulin resistance after a 3-year follow-up: Tehran Lipid and Glucose Study. Asia Pac J Clin Nutr. 2017;26(3):531-538. doi:10.6133/apjcn.032016.12		X	X	
263	Dore D, de Hoog J, Giles G, Ding C, Cicuttini F, Jones G. A longitudinal study of the association between dietary factorsserum lipidsand bone marrow lesions of the knee. Arthritis Res Ther. 2012;14(1):R13. doi:10.1186/ar3689			X	
264	Dorgan JF, Hunsberger SA, McMahon RP, et al. Diet and sex hormones in girls: findings from a randomized controlled clinical trial. J Natl Cancer Inst. 2003. 95(2):132-141. doi:10.1093/jnci/95.2.132			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
265	Dorgan JF. Adolescent diet and metabolic syndrome components in young women: results of the dietary intervention study in children (DISC) follow-up study. Am J Epidemiol. 2011;173:S278. doi:10.1093/aje/kwr181				Publication Status
266	Dow CA, Stauffer BL, Greiner JJ, DeSouza CA. Influence of habitual high dietary fat intake on endothelium-dependent vasodilation. Appl Physiol Nutr Metab. 2015;40(7):711-5. doi:10.1139/apnm-2015-0006	X	X		
267	Draper CF, Vassallo I, Di Cara A, et al. A 48-Hour vegan diet challenge in healthy women and men induces a branch-chain amino acid related, health associated, metabolic signature. Mol Nutr Food Res. 2018;62(3). doi:10.1002/mnfr.201700703		X		
268	Drehmer M, Pereira MA, Schmidt MI, et al. Total and full-fat, but not low-fat, dairy product intakes are inversely associated with metabolic syndrome in adults. J Nutr. 2016;146(1):81-9. doi:10.3945/jn.115.220699	X	X		
269	Dreon DM, Fernstrom HA, Williams PT, Krauss RM. Reduced LDL particle size in children consuming a very-low-fat diet is related to parental LDL-subclass patterns. Am J Clin Nutr. 2000. 71(6):1611-6. doi:10.1093/ajcn/71.6.1611	X			
270	Drouin-Chartier JP, Tremblay AJ, Lepine MC, Lemelin V, Lamarche B, Couture P. Substitution of dietary saturated fatty acids with omega-6 polyunsaturated fatty acids decreases ldl apob-100 production rate in men with dyslipidemia associated with insulin-resistance. Circulation. 2016;134(Suppl 1):A14941.				Publication Status
271	Due A, Larsen TM, Mu H, Hermansen K, Stender S, Astrup A. Comparison of 3 ad libitum diets for weight-loss maintenance, risk of cardiovascular disease and diabetes: a 6-mo randomized, controlled trial. Am J Clin Nutr. 2008. 88(5):1232-41. doi:10.3945/ajcn.2007.25695				Age of participants at intervention or exposure

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
272	Dugan CE, Aguilar D, Barona J, Luz Fernandez M. Low-fat dairy (LFD) favorably affects lipoprotein metabolism and C reactive protein (CRP) in subjects with metabolic syndrome. FASEB journal. 2012;26(Suppl 1).				Publication Status
273	Dugan CE, Barona J, Fernandez ML. Low-fat dairy differentially improves metabolic syndrome parameters in male and female adults. FASEB journal. 2013;27. doi:10.1089/met.2013.0109				Publication Status
274	Dumont J, Goumidi L, Grenier-Boley B, et al. Dietary linoleic acid interacts with FADS1 genetic variability to modulate HDL-cholesterol and obesity-related traits. Clin Nutr. 2018;37(5):1683-1689. doi:10.1016/j.clnu.2017.07.012	X			
275	Dyson PA, Beatty S, Matthews DR. An assessment of low-carbohydrate or low-fat diets for weight loss at 2 year's follow-up. Diabet Med. 2010;27(3):363- 364. doi:10.1111/j.1464-5491.2010.02926.x		X		
276	Ebell MH. Omega-3 fatty acids do not prevent cancer or cardiovascular disease events. Am Fam Physician. 2019;100(6):374-375.	X			
277	Ebrahimof S, Hosseini-Esfahani F, Mirmiran P, Fallah-Kezabi M, Azizi F. Food Patterns and Framingham Risk Score in Iranian Adults: Tehran Lipid and Glucose Study: 2005-2011. Metab Syndr Relat Disord. 2018;16(1):64-71. doi:10.1089/met.2017.0125		X	X	
278	Ehsani B, Moslehi N, Mirmiran P, Ramezani Tehrani F, Tahmasebinejad Z, Azizi F. A visceral adiposity index-related dietary pattern and the cardiometabolic profiles in women with polycystic ovary syndrome. Clin Nutr. 2016;35(5):1181-7. doi:10.1016/j.clnu.2015.10.007	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
279	Eloranta AM, Lindi V, Schwab U, et al. Dietary factors associated with metabolic risk score in Finnish children aged 6-8 years: the PANIC study. Eur J Nutr. 2014;53(6):1431-9. doi:10.1007/s00394-013-0646-z	X	X		
280	Engel S, Elhauge M, Tholstrup T. Effect of whole milk compared with skimmed milk on fasting blood lipids in healthy adults: a 3-week randomized crossover study. Eur J Clin Nutr. 2018;72(2):249-254. doi:10.1038/s41430-017-0042-5		X		Study Duration
281	Engel S, Tholstrup T, Bruun JM, Astrup A, Richelsen B, Raben A. Effect of high milk and sugar-sweetened and non-caloric soft drink intake on insulin sensitivity after 6 months in overweight and obese adults: a randomized controlled trial. Eur J Clin Nutr. 2018;72(3):358-366. doi:10.1038/s41430-017-0006-9		X		
282	Engeset D, Braaten T, Teucher B, et al. Fish consumption and mortality in the European Prospective Investigation into Cancer and Nutrition cohort. Eur J Epidemiol. 2015;30(1):57-70. doi:10.1007/s10654-014-9966-4		X		
283	Entezari MH, Salehi R, Kazemi M, Janghorbani M, Kafeshani M. Comparison of the effect of the Dietary Approaches to Stop Hypertension diet with usual dietary advice on expression of peroxisome proliferators-activated receptor gamma gene in women: A randomized controlled clinical trial. ARYA Atheroscler. 2018;14(1):24-31. doi:10.22122/arya.v14i1.1565			X	
284	Ericson U, Brunkwall L, Alves Dias J, et al. Food patterns in relation to weight change and incidence of type 2 diabetes, coronary events and stroke in the Malmö Diet and Cancer cohort. European Journal of Nutrition. 2019;58(5):1801-1814. doi:10.1007/s00394-018-1727-9		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
285	Eshriqui I, Franco-Sena AB, Farias DR, et al. Prepregnancy dietary patterns are associated with blood lipid level changes during pregnancy: a prospective cohort study in Rio de JaneiroBrazil. J Acad Nutr Diet. 2017;117(7):1066-1079.e1. doi:10.1016/j.jand.2016.12.007		X		
286	Essouiri J, Abourazzak FE, Lazrak F, et al. Efficacy of argane oil on metabolic syndrome in a Moroccan knee osteoarthritis population. Curr Rheumatol Rev. 2018;14(1):84-88. doi:10.2174/1573397112666161205103009		X		Country
287	Estruch R, Casas R, Sacanella E, et al. Mediterranean diet and inflammatory biomarkers. Annals of nutrition and metabolism. 2015. 67(Suppl 1):41- 42. doi:10.1159/000440895				Publication Status
288	Estruch R, Martinez-Gonzalez MA, Corella D, et al. Effect of a high-fat Mediterranean diet on bodyweight and waist circumference: a prespecified secondary outcomes analysis of the PREDIMED randomised controlled trial. Lancet Diabetes Endocrinol. 2019;7(5):e6-e17. doi:10.1016/s2213-8587(19)30074-9			X	
289	Estruch R, Martínez-González MA. Mediterranean diets reduced cardiovascular events more than a low-fat diet in high-risk persons. Annals of Internal Medicine. 2013;158(12):JC3. doi:10.7326/0003-4819-158-12-201306180-02003	X			Publication Status
290	Estruch R, Ros E, Salas-Salvado J, et al. Primary prevention of cardiovascular disease with a Mediterranean diet supplemented with extra-virgin olive oil or nuts. N Engl J Med. 2018;378(25):e34. doi:10.1056/NEJMoa1800389		X		
291	Estruch R, Ros E, Salas-Salvadó, et al. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med. 2013;368(14):1279-1290. doi:10.1056/NEJMoa1200303		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
292	Faghihnia N, Mangravite LM, Chiu S, Bergeron N, Krauss RM. Effects of dietary saturated fat on LDL subclasses and apolipoprotein CIII in men. Eur J Clin Nutr. 2012;66(11):1229-33. doi:10.1038/ejcn.2012.118				Study Duration
293	Fahrer H, Hoeflin F, Lauterburg BH, Peheim E, Levy A, Vischer TL. Diet and fatty acids: can fish substitute for fish oil?. Clin Exp Rheumatol. 1991. 9(4):403-6.		X		Age of participants at intervention or exposure
294	Fallaize R, Livingstone KM, Celis-Morales C, et al. Association between diet-quality scores, adiposity, total cholesterol and markers of nutritional status in European adults: findings from the Food4Me study. Nutrients. 2018;10(1): pii: E49. doi:10.3390/nu10010049	X	X		
295	Farras M, Arranz S, Carrion S, et al. A functional virgin olive oil enriched with olive oil and thyme phenolic compounds improves the expression of cholesterol efflux-related genes: a randomized, crossover, controlled trial. Nutrients. 2019;11(8): pii: E1732. doi:10.3390/nu11081732		X	X	
296	Farras M, Castaner O, Martin-Pelaez S, et al. Complementary phenol-enriched olive oil improves HDL characteristics in hypercholesterolemic subjects. A randomized, double-blind, crossover, controlled trial. The VOHF study. Mol Nutr Food Res. 2015;59(9):1758-70. doi:10.1002/mnfr.201500030				Health Status
297	Farvid MS, Malekshah AF, Pourshams A, et al. Dairy food intake and all-cause, cardiovascular disease, and cancer mortality: The Golestan Cohort Study. Am J Epidemiol. 2017;185(8):697-711. doi:10.1093/aje/kww139		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
298	Fathi Y, Ghodrati N, Zibaeenezhad MJ, Faghih S. Kefir drink causes a significant yet similar improvement in serum lipid profile, compared with low-fat milk, in a dairy-rich diet in overweight or obese premenopausal women: A randomized controlled trial. J Clin Lipidol. 2017;11(1):136-146. doi:10.1016/j.jacl.2016.10.016		X		
299	Fava F, Gitau R, Griffin BA, Gibson GR, Tuohy KM, Lovegrove JA. The type and quantity of dietary fat and carbohydrate alter faecal microbiome and short-chain fatty acid excretion in a metabolic syndrome 'at-risk' population. Int J Obes (Lond). 2013;37(2):216-23. doi:10.1038/ijo.2012.33				Duplicate data
300	Fazeli Moghadam E, Tadevosyan A, Fallahi E, Goodarzi R. Nutritional factors and metabolic variables in relation to the risk of coronary heart disease: a case control study in Armenian adults. Diabetes Metab Syndr. 2017;11(1):7-11. doi:10.1016/j.dsx.2016.06.013	X			
301	Feeney EL, Barron R, Dible V, et al. Dairy matrix effects: response to consumption of dairy fat differs when eaten within the cheese matrix-a randomized controlled trial. Am J Clin Nutr. 2018;108(4):667-674. doi:10.1093/ajcn/nqy146		X		
302	Fernández De La Puebla RA, Carmona J, Fuentes F, et al. Response degree of cholesterol LDL to feeding in males with hypercholesterolemia according to baseline value. Medicina clinica. 2002;118(19):737- 740.				Language
303	Fernandez ML, Ballesteros MN, Cabrera RM, Saucedo S, Clark RM. Intake of two eggs per day increases plasma lutein and zeaxanthin without affecting the LDL/HDL ratio in Mexican children aged 8-12 y. FASEB journal. 2011;25.				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
304	Fernandez-Castillejo S, Rubio L, Hernaez A, et al. Determinants of HDL cholesterol efflux capacity after virgin olive oil ingestion: interrelationships with fluidity of HDL monolayer. Mol Nutr Food Res. 2017;61(12). doi:10.1002/mnfr.201700445		X		
305	Fernandez-Castillejo S, Valls RM, Castaner O, et al. Polyphenol rich olive oils improve lipoprotein particle atherogenic ratios and subclasses profile: a randomized, crossover, controlled trial. Mol Nutr Food Res. 2016;60(7):1544-54. doi:10.1002/mnfr.201501068		X		Health Status
306	Feuerstein JS, Bautista LT, Bjerke WS. A dietary approach for treating dyslipidemia and hyperglycemia. Current Nutrition and Food Science. 2011;7(4):271-274.	X	X		
307	Fito M, Estruch R, Salas-Salvado J, et al. Effect of the Mediterranean diet on heart failure biomarkers: a randomized sample from the PREDIMED trial. Eur J Heart Fail. 2014;16(5):543-50. doi:10.1002/ejhf.61		X	X	
308	Fitschen PJ, Rolfhus KR, Winfrey MR, Allen BK, Manzy M, Maher MA. Cardiovascular effects of consumption of black versus English walnuts. J Med Food. 2011;14(9):890-8. doi:10.1089/jmf.2010.0169		X		
309	Fleming J, Kris-Etherton P, Petersen K, Baer D. The dose-response effect of a mediterranean style diet with lean beef on lipids and lipoproteins. Circulation. 2019;139. doi:10.1161/circ.139.suppl_1.045				Publication Status
310	Flynn MM, Reinert SE. Comparing an olive oil-enriched diet to a standard lower-fat diet for weight loss in breast cancer survivors: a pilot study. J Womens Health (Larchmt). 2010;19(6):1155-61. doi:10.1089/jwh.2009.1759		X		
311	Fonolla-Joya J, Reyes-Garcia R, Garcia-Martin A, Lopez-Huertas E, Munoz-Torres M. Daily Intake of Milk Enriched with n-3 Fatty AcidsOleic Acidand Calcium Improves Metabolic and Bone Biomarkers in Postmenopausal Women. J Am Coll Nutr. 2016;35(6):529-536. doi:10.1080/07315724.2014.1003114		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
312	Foraker RE, Pennell M, Sprangers P, Vitolins MZ, DeGraffinreid C, Paskett ED. Effect of a low-fat or low-carbohydrate weight-loss diet on markers of cardiovascular risk among premenopausal women: a randomized trial. J Womens Health (Larchmt). 2014;23(8):675-80. doi:10.1089/jwh.2013.4638		X		
313	Ford PA, Jaceldo-Siegl K, Lee JW, Tonstad S. Trans fatty acid intake is related to emotional affect in the Adventist Health Study-2. Nutr Res. 2016;36(6):509-17. doi:10.1016/j.nutres.2016.01.005			X	
314	Foster GD, Wyatt HR, Hill JO, et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. Ann Intern Med. 2010;153(3):147-57. doi:10.7326/0003-4819-153-3-201008030-00005		X		
315	Frahnow T, Osterhoff MA, Hornemann S, et al. Heritability and responses to high fat diet of plasma lipidomics in a twin study. Sci Rep. 2017;7(1):3750. doi:10.1038/s41598-017-03965-6		X		
316	Francesco Sofi F, Cesari F, Gori AM, et al. The atherosclerotic risk profile is differently affected from fish fed with similar EPA+DHA content but different N-6/N-3 ratio: a single-blinded randomized crossover trial. Eur J Prev Cardiol. 2013. 20(1 SUPPL. 1):S116. doi:10.1177/2047487314530052				Publication Status
317	Freitas-Simoes TM, Cofan M, Serra-Mir M, et al. Walnut supplementation for 2 years in older individuals reduces ldl-cholesterol without adverse effects on adiposity. a sub-study of the walnuts and healthy aging (WAHA) study. Annals of nutrition & metabolism. 2017;71(Suppl 2):988- 989. doi:10.1159/000480486				Publication Status
318	Fretts AM, Mozaffarian D, Siscovick DS, et al. Associations of plasma phospholipid and dietary alpha linolenic acid with incident atrial fibrillation in older adults: the Cardiovascular Health Study. J Am Heart Assoc. 2013;2(1):e003814. doi:10.1161/jaha.112.003814			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
319	Friday KE, Failor RA, Childs MT, Bierman EL. Effects of n-3 and n-6 fatty acid-enriched diets on plasma lipoproteins and apolipoproteins in heterozygous familial hypercholesterolemia. Arterioscler Thromb. 1991. 11(1):47-54. doi:10.1161/01.atv.11.1.47				Age of participants at intervention or exposure
320	Frolich S, Lehmann N, Weyers S, et al. Association of dietary patterns with five-year degree and progression of coronary artery calcification in the Heinz Nixdorf Recall study. Nutr Metab Cardiovasc Dis. 2017;27(11):999-1007. doi:10.1016/j.numecd.2017.09.002		X		
321	Fuchs GJ, Farris RP, DeWier M, Hutchinson S, Strada R, Suskind RM. Effect of dietary fat on cardiovascular risk factors in infancy. Pediatrics. 1994. 93(5):756-63.		X		
322	Fukuoka Y, Nuruki N, Amiya S, Tofuku K, Aosaki S, Tsubouchi H. Effects of a fish-based diet and administration of pure eicosapentaenoic acid on brachial-ankle pulse wave velocity in patients with cardiovascular risk factors. J Cardiol. 2014;63(3):211-7. doi:10.1016/j.jjcc.2013.08.005		X		Health Status
323	Fulgoni VL 3rd, Dreher M, Davenport AJ. Avocado consumption is associated with better diet quality and nutrient intake, and lower metabolic syndrome risk in US adults: results from the National Health and Nutrition Examination Survey (NHANES) 2001-2008. Nutr J. 2013;121. doi:10.1186/1475-2891-12-1	X			
324	Fuller NR, Caterson ID, Sainsbury A, et al. The effect of a high-egg diet on cardiovascular risk factors in people with type 2 diabetes: the Diabetes and Egg (DIABEGG) study-a 3-mo randomized controlled trial. Am J Clin Nutr. 2015;101(4):705-13. doi:10.3945/ajcn.114.096925		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
325	Fumeron F, Lamri A, Abi Khalil C, et al. Dairy consumption and the incidence of hyperglycemia and the metabolic syndrome: results from a French prospective studydata from the epidemiological study on the insulin resistance syndrome (DESIR). Diabetes Care. 2011;34(4):813-817. doi:10.2337/dc10-1772		X		
326	Fumeron F, Lamri A, Emery N, et al. Dairy products and the metabolic syndrome in a prospective study, DESIR. J Am Coll Nutr. 2011;30(5 Suppl 1):454s-63s. doi:10.1080/07315724.2011.10719990		X		
327	Furtado JD, Beqari J, Campos H. Comparison of the utility of total plasma fatty acids versus those in cholesteryl ester, phospholipidand triglyceride as biomarkers of fatty acid intake. Nutrients. 2019;11(9): pii: E2081. doi:10.3390/nu11092081		X	X	
328	Furtado JD, Campos H, Sumner AE, Appel LJ, Carey VJ, Sacks FM. Dietary interventions that lower lipoproteins containing apolipoprotein C-III are more effective in whites than in blacks: results of the OmniHeart trial. Am J Clin Nutr. 2010;92(4):714-22. doi:10.3945/ajcn.2009.28532		X		
329	Garcia A, Gutierrez JM, Fernandez S, Aparicio J, Menendez-Patterson A. Dietary intervention in a hypercholesterolemic school-aged population from Northern Spain. Rev Esp Fisiol. 1996. 52(1):49-58.	X	X		
330	Garcia-Alonso FJ, Jorge-Vidal V, Ros G, Periago MJ. Effect of consumption of tomato juice enriched with n-3 polyunsaturated fatty acids on the lipid profile, antioxidant biomarker status, and cardiovascular disease risk in healthy women. Eur J Nutr. 2012;51(4):415-24. doi:10.1007/s00394-011-0225-0		X		
331	Garcia-Calzon S, Martinez-Gonzalez MA, Razquin C, et al. Mediterranean diet and telomere length in high cardiovascular risk subjects from the PREDIMED-NAVARRA study. Clin Nutr. 2016;35(6):1399-1405. doi:10.1016/j.clnu.2016.03.013		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
332	Garcia-Esquinas E, Ortola R, Banegas JR, Lopez-Garcia E, Rodriguez-Artalejo F. Dietary n-3 polyunsaturated fatty acidsfish intake and healthy ageing. Int J Epidemiol. 2019;48(6):1914-1924. doi:10.1093/ije/dyz196			X	
333	Garcia-Gavilan JF, Bullo M, Canudas S, et al. Extra virgin olive oil consumption reduces the risk of osteoporotic fractures in the PREDIMED trial. Clin Nutr. 2018;37(1):329-335. doi:10.1016/j.clnu.2016.12.030			X	
334	Garcia-Rios A, Alcala-Diaz JF, Gomez-Delgado F, et al. Beneficial effect of CETP gene polymorphism in combination with a Mediterranean diet influencing lipid metabolism in metabolic syndrome patients: CORDIOPREV study. Clin Nutr. 2018;37(1):229-234. doi:10.1016/j.clnu.2016.12.011		X		Health Status
335	Garcia-Rios A, Gomez-Delgado FJ, Delgado-Lista FJ, et al. Beneficial effect of CETP gene polymorphism rs3764261 in combination with a Mediterranean diet on lipid metabolism in metabolic syndrome. Atherosclerosis. 2014. 235(2):e115. doi:10.1016/j.atherosclerosis.2014.05.314				Publication Status
336	Gaskins AJ, Rovner AJ, Mumford SL, et al. Adherence to a Mediterranean diet and plasma concentrations of lipid peroxidation in premenopausal women. Am J Clin Nutr. 2010;92(6):1461-7. doi:10.3945/ajcn.110.000026		X	X	
337	Gebauer SK, Destaillats F, Dionisi F, Krauss RM, Baer DJ. Vaccenic acid and trans fatty acid isomers from partially hydrogenated oil both adversely affect LDL cholesterol: a double-blind, randomized controlled trial. Am J Clin Nutr. 2015;102(6):1339-46. doi:10.3945/ajcn.115.116129		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
338	Georgiopoulos G, Karatzi K, Euthimiou E, et al. Association of macronutrient consumption with arterial aging in adults without clinically overt cardiovascular disease: a 5-year prospective cohort study. Eur J Nutr. 2019;58(6):2305-2314. doi:10.1007/s00394-018-1781-3			X	
339	Gepner Y, Shelef I, Schwarzfuchs D, et al. Effect of distinct lifestyle interventions on mobilization of fat storage pools: CENTRAL Magnetic Resonance Imaging Randomized Controlled Trial. Circulation. 2018;137(11):1143-1157. doi:10.1161/circulationaha.117.030501		X	X	
340	Ghotboddin Mohammadi S, Mirmiran P, Bahadoran Z, Mehrabi Y, Azizi F. The association of dairy intake with metabolic syndrome and its components in adolescents: Tehran Lipid and Glucose Study. Int J Endocrinol Metab. 2015;13(3):e25201. doi:10.5812/ijem.25201v2	X	X		
341	Gillingham LG, Gustafson JA, Han SY, Jassal DS, Jones PJ. High-oleic rapeseed (canola) and flaxseed oils modulate serum lipids and inflammatory biomarkers in hypercholesterolaemic subjects. Br J Nutr. 2011;105(3):417-27. doi:10.1017/s0007114510003697				Health Status
342	Gillingham MB, Elizondo G, Behrend A, et al. Higher dietary protein intake preserves lean body mass, lowers liver lipid deposition, and maintains metabolic control in participants with long-chain fatty acid oxidation disorders. J Inherit Metab Dis. 2019;42(5):857-869. doi:10.1002/jimd.12155		X	X	
343	Giovannini M, Bellu R, Ortisi MT, Incerti P, Riva E. Cholesterol and lipoprotein levels in Milanese children: relation to nutritional and familial factors. J Am Coll Nutr. 1992. 11 Suppl28s-31s. doi:10.1080/07315724.1992.10737980	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
344	Gladine C, Combe N, Vaysse C, et al. Optimized rapeseed oil enriched with healthy micronutrients: a relevant nutritional approach to prevent cardiovascular diseases. Results of the Optim'Oils randomized intervention trial. J Nutr Biochem. 2013;24(3):544-9. doi:10.1016/j.jnutbio.2012.02.003		X		
345	Glassman M, Spark A, Berezin S, Schwarz S, Medow M, Newman LJ. Treatment of type IIa hyperlipidemia in childhood by a simplified American Heart Association diet and fiber supplementation. Am J Dis Child. 1990. 144(9):973-6. doi:10.1001/archpedi.1990.02150330033016		X		
346	Gold K, Wong N, Tong A, et al. Serum apolipoprotein and lipid profile effects of an oat-bran-supplementedlow-fat diet in children with elevated serum cholesterol. Ann N Y Acad Sci. 1991. 623:429-31. doi:10.1111/j.1749-6632.1991.tb43758.x		X		
347	Gomez de la Camara A, De Andres Esteban E, Urrutia Cuchi G, et al. Variability of nutrients intakelipid profile and cardiovascular mortality among geographical areas in Spain: The DRECE study. Geospat Health. 2017;12(2):524. doi:10.4081/gh.2017.524		X		
348	Gomez-Delgado F, Alcala-Diaz JF, Garcia-Rios A, et al. Polymorphism at the TNF-alpha gene interacts with Mediterranean diet to influence triglyceride metabolism and inflammation status in metabolic syndrome patients: From the CORDIOPREV clinical trial. Mol Nutr Food Res. 2014;58(7):1519-27. doi:10.1002/mnfr.201300723		X		Health Status
349	Gomez-Marin B, Gomez-Delgado F, Lopez-Moreno J, et al. Long-term consumption of a Mediterranean diet improves postprandial lipemia in patients with type 2 diabetes: the Cordioprev randomized trial. Am J Clin Nutr. 2018;108(5):963-970. doi:10.1093/ajcn/nqy144				Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
350	Gonciulea AR, Sellmeyer D. The effect of dietary protein source on serum lipids. Endocrine reviews. 2015;36(Suppl 2).				Publication Status
351	Gonzalez-Requejo A, Sanchez-Bayle M, Baeza J, et al. Relations between nutrient intake and serum lipid and apolipoprotein levels. J Pediatr. 1995. 127(1):53-7. doi:10.1016/s0022-3476(95)70256-3	X			
352	Gopinath B, Flood VM, Burlutksy G, Mitchell P. Consumption of nuts and risk of total and cause-specific mortality over 15 years. Nutr Metabol Cardiovasc Dis. 2015;25(12):1125-1131. doi:10.1016/j.numecd.2015.09.006		X		
353	Gorczyca D, Pasciak M, Szponar B, Gamian A, Jankowski A. An impact of the diet on serum fatty acid and lipid profiles in Polish vegetarian children and children with allergy. Eur J Clin Nutr. 2011;65(2):191-5. doi:10.1038/ejcn.2010.231	X	X		
354	Gossell-Williams M, Hyde C, Hunter T, et al. Improvement in HDL cholesterol in postmenopausal women supplemented with pumpkin seed oil: pilot study. Climacteric. 2011;14(5):558-64. doi:10.3109/13697137.2011.563882		X		
355	Goulooze SC, Cohen AF, Rissmann R. Lomitapide. Br J Clin Pharmacol. 2015;80(2):179-81. doi:10.1111/bcp.12612	X	X		
356	Grabovac I, Hochfellner L, Rieger M, et al. Impact of Austria's 2009 trans fatty acids regulation on all-causecardiovascular and coronary heart disease mortality. Eur J Public Health. 2018;28(Suppl 2):4-9. doi:10.1093/eurpub/cky147		X		
357	Graff SK, Mario FM, Magalhaes JA, Moraes RS, Spritzer PM. Saturated fat intake is related to heart rate variability in women with polycystic ovary syndrome. Ann Nutr Metab. 2017;71(3-4):224-233. doi:10.1159/000484325	X		X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
358	Grasgruber P, Sebera M, Hrazdira E, Hrebickova S, Cacek J. Food consumption and the actual statistics of cardiovascular diseases: an epidemiological comparison of 42 European countries. Food Nutr Res. 2016;60:31694. doi:10.3402/fnr.v60.31694	X	X		
359	Greene CM, Zern TL, Wood RJ, et al. Maintenance of the LDL cholesterol: HDL cholesterol ratio in an elderly population given a dietary cholesterol challenge. J Nutr. 2005. 135(12):2793-8. doi:10.1093/jn/135.12.2793				Age of participants at intervention or exposure
360	Greupner T, Kutzner L, Nolte F, et al. Effects of a 12-week high-alpha-linolenic acid intervention on EPA and DHA concentrations in red blood cells and plasma oxylipin pattern in subjects with a low EPA and DHA status. Food Funct. 2018;9(3):1587-1600. doi:10.1039/c7fo01809f	X		X	
361	Griffin BA, Walker CG, Jebb SA, et al. APOE4 genotype exerts greater benefit in lowering plasma cholesterol and apolipoprotein b than wild type (E3/E3), after replacement of dietary saturated fats with low glycaemic index carbohydrates. Nutrients. 2018;10(10): pii: E1524. doi:10.3390/nu10101524		X		
362	Griffin LE, Djuric Z, Angiletta CJ, et al. A Mediterranean diet does not alter plasma trimethylamine N-oxide concentrations in healthy adults at risk for colon cancer. Food Funct. 2019;10(4):2138-2147. doi:10.1039/c9fo00333a			X	
363	Griffith KA, Royak-Schaler R, Nesbitt K, et al. A culturally specific dietary plan to manage weight gain among African American breast cancer survivors: a feasibility study. Nutr Health. 2012;21(2):97-105. doi:10.1177/0260106012459938		X		
364	Grimaldi M, Ciano O, Manzo M, et al. Intensive dietary intervention promoting the Mediterranean diet in people with high cardiometabolic risk: a non-randomized study. Acta Diabetol. 2018;55(3):219-226. doi:10.1007/s00592-017-1078-7		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
365	Grosso G, Stepaniak U, Micek A, et al. A Mediterranean-type diet is associated with better metabolic profile in urban Polish adults: results from the HAPIEE study. Metabolism. 2015;64(6):738-46. doi:10.1016/j.metabol.2015.02.007	X			
366	Grygiel-Górniak B, Kaczmarek E, Mosor M, Przysławski J, Nowak J. The gene-diet associations in postmenopausal women with newly diagnosed dyslipidemia. J Nutr Health Aging. 2017;21(9):1031-1037. doi:10.1007/s12603-017-0877-4	X	X		
367	Grytten E, Laupsa Borge J, Dankel S, et al. Effects of omega-3 and omega-6 fatty acids on lipids and apolipoproteins, glycemic response and endothelial function: a randomized double-blind crossover trial. Obesity facts. 2019;12260. doi:10.1159/000489691				Publication Status
368	Guallar-Castillon P, Rodriguez-Artalejo F, Lopez-Garcia E, et al. Consumption of fried foods and risk of coronary heart disease: Spanish cohort of the European Prospective Investigation into Cancer and Nutrition study. BMJ. 2012;344e363. doi:10.1136/bmj.e363		X		
369	Guallar-Castillon P, Rodriguez-Artalejo F, Tormo MJ, et al. Major dietary patterns and risk of coronary heart disease in middle-aged persons from a Mediterranean country: the EPIC-Spain cohort study. Nutr Metab Cardiovasc Dis. 2012;22(3):192-9. doi:10.1016/j.numecd.2010.06.004		X		
370	Guasch-Ferre M, Bullo M, Martinez-Gonzalez MA, et al. Frequency of nut consumption and risk of total mortality in the predimed study. Annals of nutrition and metabolism. 2013. 62(Suppl 2):17- 18. doi:10.1159/000351281				Publication Status
371	Guasch-Ferre M, Bullo M, Martinez-Gonzalez MA, et al. Frequency of nut consumption and mortality risk in the PREDIMED nutrition intervention trial. BMC Med. 2013;11:164. doi:10.1186/1741-7015-11-164		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
372	Guasch-Ferre M, Zong G, Willett WC, et al. Associations of monounsaturated fatty acids from plant and animal sources with total and cause-specific mortality in two US prospective cohort studies. Circ Res. 2019;124(8):1266-1275. doi:10.1161/circresaha.118.313996	X			
373	Guay V, Lamarche B, Charest A, Tremblay AJ, Couture P. Effect of short-term low- and high-fat diets on low-density lipoprotein particle size in normolipidemic subjects. Metabolism. 2012;61(1):76-83. doi:10.1016/j.metabol.2011.06.002				Study Duration
374	Guevara-Cruz M, Flores-Lopez AG, Aguilar-Lopez M, et al. Improvement of lipoprotein profile and metabolic endotoxemia by a lifestyle intervention that modifies the gut microbiota in subjects with metabolic syndrome. J Am Heart Assoc. 2019;8(17):e012401. doi:10.1161/jaha.119.012401		X		
375	Guillaume M, Lapidus L, Lambert A. Differences in associations of familial and nutritional factors with serum lipids between boys and girls: The Luxombourg Child Study. Am J Clin Nutr. 2000. 72(2):384-388.	X			
376	Gulati S, Misra A, Pandey RM, Bhatt SP, Saluja S. Effects of pistachio nuts on body composition, metabolic, inflammatory and oxidative stress parameters in Asian Indians with metabolic syndrome: a 24-wk, randomized control trial. Nutrition. 2014;30(2):192-7. doi:10.1016/j.nut.2013.08.005		X		Country
377	Gulesserian T, Widhalm K. Effect of a rapeseed oil substituting diet on serum lipids and lipoproteins in children and adolescents with familial hypercholesterolemia. J Am Coll Nutr. 2002;21(2):103-8. doi:10.1080/07315724.2002.10719201		X		Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
378	Gulseth HL, Gjelstad IM, Tierney AC, et al. Dietary fat modifications and blood pressure in subjects with the metabolic syndrome in the LIPGENE dietary intervention study. Br J Nutr. 2010;104(2):160-3. doi:10.1017/s0007114510000565				Duplicate data
379	Güneş Ö, Soylu M, İnanç N, et al. Relationship between red blood cell membrane fatty acid composition and dietary fatty acids level in obese adolescents with/without metabolic syndrome. Progress in Nutrition. 2018;20(4):648-658. doi:10.23751/pn.v20i4.6039	X	X		
380	Guo Z, Miura K, Turin TC, Hozawa A, et al. Relationship of the polyunsaturated to saturated fatty acid ratio to cardiovascular risk factors and metabolic syndrome in Japanese: the INTERLIPID study. J Atheroscler Thromb. 2010;17(8):777-84. doi:10.5551/jat.4135	X			
381	Gustavsson J, Mehlig K, Leander K, et al. FTO gene variationmacronutrient intake and coronary heart disease risk: a gene-diet interaction analysis. Eur J Nutr. 2016;55(1):247-55. doi:10.1007/s00394-015-0842-0	X			
382	Guzel O, Yilmaz U, Uysal U, Arslan N. The effect of olive oil-based ketogenic diet on serum lipid levels in epileptic children. Neurol Sci. 2016;37(3):465-70. doi:10.1007/s10072-015-2436-2	X			Health Status
383	Guzman MA. Diet and chronic diseases: INCAP studies of atherosclerosis and coronary heart disease. Food Nutr Bull. 2010;31(1):141-51. doi:10.1177/156482651003100114	X			
384	Gwynne M, Mounsey A. Mediterranean diet: higher fat but lower risk. J Fam Pract. 2013;62(12):745-748.	X			
385	Ha K, Joung H, Song Y. Inadequate fat or carbohydrate intake was associated with an increased incidence of type 2 diabetes mellitus in Korean adults: a 12-year community-based prospective cohort study. Diabetes Res Clin Pract. 2019;148254-261. doi:10.1016/j.diabres.2019.01.024			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
386	Hajiluian G, Abbasalizad Farhangi M, Jahangiry L. Mediterranean dietary pattern and VEGF +405 G/C gene polymorphisms in patients with metabolic syndrome: an aspect of gene-nutrient interaction. PLoS One. 2017;12(2):e0171637. doi:10.1371/journal.pone.0171637	X			
387	Halliday TM, Polsky S, Schoen JA, et al. Comparison of surgical versus diet-induced weight loss on appetite regulation and metabolic health outcomes. Physiol Rep. 2019;7(7):e14048. doi:10.14814/phy2.14048		X		
388	Hammoud A, Gastaldi M, Maillot M, et al. APOB-516 T allele homozygous subjects are unresponsive to dietary changes in a three-month primary intervention study targeted to reduce fat intake. Genes Nutr. 2010;5(1):29-37. doi:10.1007/s12263-009-0155-0		X		
389	Hamulka J, Glabska D, Guzek D, Bialkowska A, Sulich A. Intake of saturated fatty acids affects atherogenic blood properties in young, caucasian, overweight women even without influencing blood cholesterol. Int J Environ Res Public Health. 2018;15(11): pii: E2530. doi:10.3390/ijerph15112530	X			
390	Hansen CK, Klingenberg L, Larsen LB, Lorenzen JK, Sorensen KV, Astrup A. The effect of UHT-processed dairy milk on cardio-metabolic risk factors. Eur J Clin Nutr. 2017;71(12):1463-1466. doi:10.1038/ejcn.2017.22		X		
391	Hansen-Krone IJ, Enga KF, Njolstad I, Hansen JB, Braekkan SK. Heart healthy diet and risk of myocardial infarction and venous thromboembolism. The Tromso Study. Thromb Haemost. 2012;108(3):554-60. doi:10.1160/th11-11-0818		X		
392	Hansen-Krone IJ, Enga KF, Sudduth-Klinger JM, et al. High fish plus fish oil intake is associated with slightly reduced risk of venous thromboembolism: the Tromso Study. J Nutr. 2014;144(6):861-7. doi:10.3945/jn.113.189548		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
393	Hansson P, Holven KB, Oyri LKL, et al. Sex differences in postprandal responses to different dairy products on lipoprotein subclasses: a randomized controlled cross-over trial. Br J Nutr. 2019;122(7):780-789. doi:10.1017/s0007114519001429	X		X	
394	Haraldsdottir A, Torfadottir JE, Valdimarsdottir UA, et al. Fish and fish-liver oil consumption in adolescence and midlife and risk of CHD in older women. Public Health Nutr. 2016;19(2):318-25. doi:10.1017/s1368980015001020		X		
395	Haring B, Selvin E, Liang M, et al. Dietary protein sources and risk for incident chronic kidney disease: results from the Atherosclerosis Risk in Communities (ARIC) Study. J Ren Nutr. 2017;27(4):233-242. doi:10.1053/j.jrn.2016.11.004		X	X	
396	Harnden KE, Frayn KN, Hodson L. Dietary Approaches to Stop Hypertension (DASH) diet: applicability and acceptability to a UK population. J Hum Nutr Diet. 2010;23(1):3-10. doi:10.1111/j.1365-277X.2009.01007.x		X	X	
397	Harreiter J, Simmons D, Desoye G, et al. Nutritional lifestyle intervention in obese pregnant women, including lower carbohydrate intake, is associated with increased maternal free fatty acids, 3-beta-Hydroxybutyrate, and fasting glucose concentrations: a secondary factorial analysis of the European Multicenter, Randomized Controlled DALI Lifestyle Intervention Trial. Diabetes Care. 2019;42(8):1380-1389. doi:10.2337/dc19-0418		X	X	
398	Harris CP, von Berg A, Berdel D, et al. Association of dietary fatty acids with blood lipids is modified by physical activity in adolescents: results from the GINIplus and LISA birth cohort studies. Nutrients. 2018;10(10). doi:10.3390/nu10101372	X			
399	Harris M, Fryda L, Hutchins A. The impact of virgin coconut and safflower oils on lipids and cytokines in postmenopausal women. FASEB journal. 2015;29(Suppl 1).				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
400	Hart K, Barr S, Reeves S, Sharp K, Jeanes Y. Suboptimal dietary intake is associated with cardiometabolic risk factors in women with polycystic ovary syndrome. Nutrition & Dietetics. 2016;73(2):177-183. doi:10.1111/1747-0080.12188		X		
401	Hartiala J, Gilliam E, Vikman S, Campos H, Allayee H. Association of PLA2G4A with myocardial infarction is modulated by dietary PUFAs. Am J Clin Nutr. 2012;95(4):959-65. doi:10.3945/ajcn.111.032094	X			
402	Haruna M, Shiraishi M, Matsuzaki M, Yatsuki Y, Yeo S. Effect of tailored dietary guidance for pregnant women on nutritional status: A double-cohort study. Matern Child Nutr. 2017;13(4): doi:10.1111/mcn.12391			X	
403	Harvey CJDC, Schofield GM, Zinn C, Thornley SJ, Crofts C, Merien FLR. Low-carbohydrate diets differing in carbohydrate restriction improve cardiometabolic and anthropometric markers in healthy adults: a randomised clinical trial. PeerJ. 2019;2019. 5;7:e6273. doi:10.7717/peerj.6273		X		
404	Hashemi R, Mehdizadeh Khalifani A, Rahimlou M, Manafi M. Comparison of the effect of Dietary Approaches to Stop Hypertension diet and American Diabetes Association nutrition guidelines on lipid profiles in patients with type 2 diabetes: a comparative clinical trial. Nutr Diet. 2019;77(2):204-211. doi:10.1111/1747-0080.12543				Health Status
405	Haufe S, Utz W, Engeli S, et al. Left ventricular mass and function with reduced-fat or reduced-carbohydrate hypocaloric diets in overweight and obese subjects. Hypertension. 2012. 59(1):70- 75. doi:10.1161/hypertensionaha.111.178616		X		
406	Hayman LL. The Dietary Intervention Study in Children (DISC): progress and prospects for primary prevention. Prog Cardiovasc Nurs. 2003. 18(1):4- 5.	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
407	Heine-Broring RC, Brouwer IA, Proenca RV, et al. Intake of fish and marine n-3 fatty acids in relation to coronary calcification: the Rotterdam Study. Am J Clin Nutr. 2010;91(5):1317-23. doi:10.3945/ajcn.2009.28416			X	
408	Helal O, Berrougui H, Loued S, Khalil A. Extra-virgin olive oil consumption improves the capacity of HDL to mediate cholesterol efflux and increases ABCA1 and ABCG1 expression in human macrophages. Br J Nutr. 2013;109(10):1844-55. doi:10.1017/s0007114512003856	X	X		
409	Hellstrand S, Ericson U, Schulz CA, et al. Genetic susceptibility to dyslipidemia and incidence of cardiovascular disease depending on a diet quality index in the Malmö diet and cancer cohort. Genes Nutr. 2016;11(1). doi:10.1186/s12263-016-0536-0		X		
410	Henning SM, Yang J, Woo SL, et al. Hass avocado inclusion in a weight-loss diet supported weight loss and altered gut microbiota: a 12-week randomized, parallel-controlled trial. Curr Dev Nutri. 2019;3(8):nzz068 . doi:10.1093/cdn/nzz068		X		
411	Heraclides A, Mishra GD, Hardy RJ, et al. Dairy intake, blood pressure and incident hypertension in a general British population: the 1946 birth cohort. Eur J Nutr. 2012;51(5):583-591. doi:10.1007/s00394-011-0242-z		X		
412	Hermansen K, Gregersen S, Larsen MK, Bjoernshave A, Larsen MB. Beneficial effects of medium-chain saturated dairy fat on the body composition of abdominal obese subjects (dairyhealth): a 12-week, randomized, double-blinded, intervention study. Diabetes. 2015. 64A208- A209. doi:10.2337/db15742931				Publication Status
413	Hernaez A, Castaner O, Elosua R, et al. Mediterranean diet improves high-density lipoprotein function in high-cardiovascular-risk individuals: a randomized controlled trial. Circulation. 2017;135(7):633-643. doi:10.1161/circulationaha.116.023712		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
414	Hernaez A, Castaner O, Goday A, et al. The Mediterranean diet decreases LDL atherogenicity in high cardiovascular risk individuals: a randomized controlled trial. Mol Nutr Food Res. 2017;61(9). doi:10.1002/mnfr.201601015		X		
415	Hernaez A, Fernandez-Castillejo S, Farras M, et al. Olive oil polyphenols enhance high-density lipoprotein function in humans: a randomized controlled trial. Arterioscler Thromb Vasc Biol. 2014;34(9):2115-9. doi:10.1161/atvbaha.114.303374		X		
416	Hernaez A, Remaley AT, Farras M, et al. Olive oil polyphenols decrease LDL concentrations and LDL atherogenicity in men in a randomized controlled trial. J Nutr. 2015;145(8):1692-7. doi:10.3945/jn.115.211557		X		
417	Hernaez A, Sanllorente A, Castaner O, et al. Increased consumption of virgin olive oil, nuts, legumes, whole grains, and fish promotes HDL Functions in humans. Mol Nutr Food Res. 2019;63(6):e1800847. doi:10.1002/mnfr.201800847			X	
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419	Hernandez-Alonso P, Salas-Salvado J, Baldrich-Mora M, Mallol R, Correig X, Bullo M. Effect of pistachio consumption on plasma lipoprotein subclasses in pre-diabetic subjects. Nutr Metab Cardiovasc Dis. 2015;25(4):396-402. doi:10.1016/j.numecd.2015.01.013		X	X	
420	Hernandez-Alonso P, Salas-Salvado J, Baldrich-Mora M, Mallol R, Correig X, Bullo M. Regular consumption of pistachio modulates plasma lipoprotein subclasses in pre-diabetic subjects. Obesity facts. 2015. 8(Suppl 1):872- 73. doi:10.1159/000382140				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
421	Hernandez-Alonso P, Salas-Salvado J, Ruiz-Canela M, et al. High dietary protein intake is associated with an increased body weight and total death risk. Clin Nutr. 2016;35(2):496-506. doi:10.1016/j.clnu.2015.03.016		X		
422	Herron KL, Lofgren IE, Sharman M, Volek JS, Fernandez ML. High intake of cholesterol results in less atherogenic low-density lipoprotein particles in men and women independent of response classification. Metabolism. 2004. 53(6):823-30. doi:10.1016/j.metabol.2003.12.030		X		
423	Herron KL, Vega-Lopez S, Conde K, et al. Pre-menopausal women, classified as hypo- or hyperresponders, do not alter their LDL/HDL ratio following a high dietary cholesterol challenge. J Am Coll Nutr. 2002;21(3):250-8. doi:10.1080/07315724.2002.10719218				Age of participants at intervention or exposure
424	Herron KL, Vega-Lopez S, Conde K, Ramjiganesh T, Shachter NS, Fernandez ML. Men classified as hypo- or hyperresponders to dietary cholesterol feeding exhibit differences in lipoprotein metabolism. J Nutr. 2003. 133(4):1036-42. doi:10.1093/jn/133.4.1036		X		Age of participants at intervention or exposure
425	Hill AM, Zahradka P, Coates AM, Howe PRC, Taylor CG, Buckley JD. A 12-week randomised controlled trial to evaluate effects of dietary pulse consumption on cardiovascular disease risk factors. FASEB journal. 2017;31(Suppl 1)				Publication Status
426	Hirahatake KM, Jiang L, Wong ND, et al. Diet quality and cardiovascular disease risk in postmenopausal women with type 2 diabetes mellitus: The Women's Health Initiative. J Am Heart Assoc. 2019;8(19):e013249. doi:10.1161/jaha.119.013249		X		Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
427	Hiraoka-Yamamoto J, Ikeda K, Negishi H, et al. Serum lipid effects of a monounsaturated (palmitoleic) fatty acid-rich diet based on macadamia nuts in healthy, young japanese women. Clin Exp Pharmacol Physiol. 2013;31(Suppl 2):S37-8. doi:10.1111/j.1440-1681.2004.04121.x				Study Duration
428	Hirowatari Y, Manita D, Kamachi K, Tanaka A. Effect of dietary modification by calorie restriction on cholesterol levels in lipoprotein(a) and other lipoprotein classes. Annals of Clinical Biochemistry. 2017;54(5):567-576. doi:10.1177/0004563216672247		X		
429	Hisamatsu T, Miura K, Ohkubo T, et al. High long-chain n-3 fatty acid intake attenuates the effect of high resting heart rate on cardiovascular mortality risk: a 24-year follow-up of Japanese general population. J Cardiol. 2014;64(3):218-24. doi:10.1016/j.jjcc.2014.01.005				Duplicate data
430	Hjerpsted J, Leedo E, Tholstrup T. Cheese intake in large amounts lowers LDL-cholesterol concentrations compared with butter intake of equal fat content. Am J Clin Nutr. 2011;94(6):1479-84. doi:10.3945/ajcn.111.022426		X		
431	Hjerpsted JB, Dragsted LO, Tholstrup T. Cheese intake lowers plasma cholesterol concentrations without increasing bile acid excretion. Journal of Nutrition and Intermediary Metabolism. 2016;312-17. doi:10.1016/j.jnim.2015.11.002		X		
432	Hlebowicz J, Persson M, Gullberg B, et al. Food patternsinflammation markers and incidence of cardiovascular disease: the Malmo Diet and Cancer study. J Intern Med. 2011;270(4):365-76. doi:10.1111/j.1365-2796.2011.02382.x		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
433	Hlebowicz J, Persson M, Gullberg B, et al. Food patternsinflammation markers and incidence of cardiovascular disease: The Malmö Diet and Cancer study. Journal of Internal Medicine. 2011;270(4):365-376. doi:10.1111/j.1365-2796.2011.02382.x	X	X		
434	Hoenselaar R. Saturated fat and cardiovascular disease: the discrepancy between the scientific literature and dietary advice. Nutrition. 2012;28(2):118-23. doi:10.1016/j.nut.2011.08.017	X			
435	Hoevenaar-Blom MP, Nooyens AC, Kromhout D, et al. Mediterranean style diet and 12-year incidence of cardiovascular diseases: the EPIC-NL cohort study. PLoS One. 2012;7(9):e45458. doi:10.1371/journal.pone.0045458		X		
436	Holloway CJ, Cochlin LE, Emmanuel Y, et al. A high-fat diet impairs cardiac high-energy phosphate metabolism and cognitive function in healthy human subjects. Am J Clin Nutr. 2011;93(4):748-55. doi:10.3945/ajcn.110.002758		X		
437	Holme I, Retterstol K, Norum KR, Hjermann I. Lifelong benefits on myocardial infarction mortality: 40-year follow-up of the randomized Oslo diet and antismoking study. J Intern Med. 2016;280(2):221-7. doi:10.1111/joim.12485		X		
438	Hooshmand F, Asghari G, Yuzbashian E, Mahdavi M, Mirmiran P, Azizi F. Modified Healthy Eating Index and incidence of metabolic syndrome in children and adolescents: Tehran Lipid and Glucose Study. J Pediatr. 2018;197134-139.e2. doi:10.1016/j.jpeds.2018.01.080		X		
439	Hoppu U, Isolauri E, Koskinen P, Laitinen K. Diet and blood lipids in 1-4 year-old children. Nutr Metab Cardiovasc Dis. 2013;23(10):980-6. doi:10.1016/j.numecd.2012.10.007	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
440	Horowitz JF, Ortega JF, Hinko A, Li M, Nelson RK, Mora-Rodriguez R. Changes in markers for cardio-metabolic disease risk after only 1-2 weeks of a high saturated fat diet in overweight adults. PLoS One. 2018;13(6):e0198372. doi:10.1371/journal.pone.0198372	X			
441	Hoscan Y, Yigit F, Muderrisoglu H. Adherence to Mediterranean diet and its relation with cardiovascular diseases in Turkish population. Int J Clin Exp Med. 2015;8(2):2860-6.		X		
442	Hosseini-Esfahani F, Esfandiar Z, Mirmiran P, Daneshpour MS, Ghanbarian A, Azizi F. The interaction of cholesteryl ester transfer protein gene variations and diet on changes in serum lipid profiles. Eur J Clin Nutr. 2019;73(9):1291-1298. doi:10.1038/s41430-019-0397-x	X		X	
443	Hosseini-Esfahani F, Mirmiran P, Koochakpoor G, Daneshpour MS, Guity K, Azizi F. Some dietary factors can modulate the effect of the zinc transporters 8 polymorphism on the risk of metabolic syndrome. Sci Rep. 2017;7(1):1649. doi:10.1038/s41598-017-01762-9			X	
444	Hosseinpour-Niazi S, Mirmiran P, Hosseini-Esfahani F, Azizi F. Is the metabolic syndrome inversely associates with butternon-hydrogenated- and hydrogenated-vegetable oils consumption: Tehran Lipid and Glucose study. Diabetes Res Clin Pract. 2016;11220-29. doi:10.1016/j.diabres.2015.11.008			X	
445	Hostmark AT, Lunde MSH, Hjellset VT. Short communication: Daily intake of 125 g of cheese for 2 weeks did not alter amount or distribution of serum lipids or desaturase indexes in healthy adults in an exploratory pilot study. J Dairy Sci. 2018;101(11):9625-9629. doi:10.3168/jds.2018-14635		X		
446	Hshieh TT, Petrone AB, Gaziano JM, Djousse L. Nut consumption and risk of mortality in the Physicians' Health Study. Am J Clin Nutr. 2015;101(2):407-12. doi:10.3945/ajcn.114.099846		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
447	Htun NC, Suga H, Imai S, Shimizu W, Takimoto H. Food intake patterns and cardiovascular risk factors in Japanese adults: analyses from the 2012 National Health and nutrition surveyJapan. Nutr J. 2017;16(1):61. doi:10.1186/s12937-017-0284-z	X			
448	Hu EA, Steffen LM, Coresh J, Appel LJ, Rebholz CM. Adherence to the Healthy Eating Index-2015 and Other Dietary Patterns May Reduce Risk of Cardiovascular DiseaseCardiovascular Mortalityand All-Cause Mortality. J Nutr. 2019;150(2):312-321. doi:10.1093/jn/nxz218		X		
449	Hu P, Li Y, Campos H. Fried food intake and risk of nonfatal acute myocardial infarction in the Costa Rica Heart Study. PLoS One. 2018;13(2):e0192960. doi:10.1371/journal.pone.0192960	X			
450	Hu T, Stuchlik P, Yao L, et al. Adherence to low carbohydrate and low fat diets in relation to weight loss and cardiovascular risk factor reduction. Circulation. 2015;131:AMP26				Publication Status
451	Hu XF, Singh K, Kenny TA, Chan HM. Prevalence of heart attack and stroke and associated risk factors among Inuit in Canada: A comparison with the general Canadian population. Int J Hyg Environ Health. 2019;222(2):319-326. doi:10.1016/j.ijheh.2018.12.003	X			
452	Huang X, Gong R, Lin J, Li R, Xiao L, Duan W, Fang D. Effects of lipoprotein lipase gene variationsa high-carbohydrate low-fat diet, and gender on serum lipid profiles in healthy Chinese Han youth. Biosci Trends. 2011;5(5):198-204.	X	X		
453	Huffman KM, Hawk VH, Henes ST, et al. Exercise effects on lipids in persons with varying dietary patterns-does diet matter if they exercise? Responses in Studies of a Targeted Risk Reduction Intervention through Defined Exercise I. Am Heart J. 2012;164(1):117-24. doi:10.1016/j.ahj.2012.04.014		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
454	Huhn S, Masouleh SK, Villringer A, Witte AV. Components of a Mediterranean diet and their impact on cognitive functions in aging. Front Aging Neurosci. 2015;7:132. doi:10.3389/fnagi.2015.00132	X			
455	Hutchins AM, Brown BD, Cunnane SC, Domitrovich SG, Adams ER, Bobowiec CE. Daily flaxseed consumption improves glycemic control in obese men and women with pre-diabetes: a randomized study. Nutr Res. 2013;33(5):367-75. doi:10.1016/j.nutres.2013.02.012		X	X	
456	Iannotti LL, Lutter CK, Waters WF, et al. Eggs early in complementary feeding increase choline pathway biomarkers and DHA: a randomized controlled trial in Ecuador. Am J Clin Nutr. 2017;106(6):1482-1489. doi:10.3945/ajcn.117.160515		X	X	
457	Iggman D, Birgisdottir B, Ramel A, Hill J, Thorsdottir I. Differences in cow's milk composition between Iceland and the other Nordic countries and possible connections to public health. Scandinavian Journal of Nutrition. 2003. 47(4):194-198.			X	
458	Iggman D, Gustafsson IB, Berglund L, Vessby B, Marckmann P, Riserus U. Replacing dairy fat with rapeseed oil causes rapid improvement of hyperlipidaemia: a randomized controlled study. J Intern Med. 2011;270(4):356-64. doi:10.1111/j.1365-2796.2011.02383.x				Health Status
459	Ikem E, Halldorsson TI, Birgisdottir BE, Rasmussen MA, Olsen SF, Maslova E. Dietary patterns and the risk of pregnancy-associated hypertension in the Danish National Birth Cohort: a prospective longitudinal study. BJOG. 2019;126(5):663-673. doi:10.1111/1471-0528.15593		X		
460	Imaizumi T, Ando M, Nakatochi M, et al. Effect of dietary energy and polymorphisms in BRAP and GHRL on obesity and metabolic traits. Obes Res Clin Pract. 2018;12(Suppl 2):39-48. doi:10.1016/j.orcp.2016.05.004		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
461	Imamura F, Lemaitre RN, King IB, et al. Long-chain monounsaturated Fatty acids and incidence of congestive heart failure in 2 prospective cohorts. Circulation. 2013;127(14):1512-21, 1521e1-18. doi:10.1161/circulationaha.112.001197		X		
462	Imran M, Anjum FM, Butt MS, Chatha ZA. Incorporation of nutritionally important fatty acids into eggs and evaluation of "Bio-Omega-3" eggs in humans with moderate hypercholesterolemia. Pakistan Journal of Nutrition. 2014;12(10):907-911.				Country, Study Duration
463	Inamori T, Goda T, Kasezawa N, Yamakawa-Kobayashi K. The combined effects of genetic variation in the SIRT1 gene and dietary intake of n-3 and n-6 polyunsaturated fatty acids on serum LDL-C and HDL-C levels: a population based study. Lipids Health Dis. 2013;124. doi:10.1186/1476-511x-12-4	X			
464	Intorre F, Venneria E, Finotti E, et al. Fatty acid content of serum lipid fractions and blood lipids in normolipidaemic volunteers fed two types of cheese having different fat compositions: a pilot study. Int J Food Sci Nutr. 2013;64(2):185-93. doi:10.3109/09637486.2012.710893				Duplicate data
465	Iraj B, Heidari-Beni M, Bakhtiary-Broujeni M, et al. The effect of walnut consumption on lipid profiles of the first-degree relatives of type two diabetes mellitus patients (T2DM) with prediabetes. Pakistan Journal of Medical Sciences. 2013;29(Suppl 1.):280-284. doi:10.12669/pjms.291(Suppl).3517	X			
466	Jaacks LM, Sher S, Staercke C, et al. Pilot randomized controlled trial of a Mediterranean diet or diet supplemented with fish oil, walnuts, and grape juice in overweight or obese US adults. BMC Nutr. 2018;4:26. doi:10.1186/s40795-018-0234-y		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
467	Jaaskelainen P, Magnussen CG, Pahkala K, et al. Childhood nutrition in predicting metabolic syndrome in adults: the cardiovascular risk in Young Finns Study. Diabetes Care. 2012;35(9):1937-43. doi:10.2337/dc12-0019		X	X	
468	Jacques H, Laurin D, Moorjani S, et al. Influence of diets containing cow's milk or soy protein beverage on plasma lipids in children with familial hypercholesterolemia. J Am Coll Nutr. 1992. 11(Suppl):69s-73s. doi:10.1080/07315724.1992.10737988		X		Health Status
469	Jakicic JM, King WC, Marcus MD, et al. Short-term weight loss with diet and physical activity in young adults: The IDEA study. Obesity. 2015;23(12):2385-97. doi:10.1002/oby.21241		X		
470	Jakobsen MU, Gorst-Rasmussen A, Eriksen HH, et al. Trans fatty acids in adipose tissue and risk of myocardial infarction: a case-cohort study. PLoS One. 2018;13(8):e0202363. doi:10.1371/journal.pone.0202363	X	X		
471	Jamar G, Pisani LP, Medeiros A, et al. Effect of fat intake on the inflammatory process and cardiometabolic risk in obesity after interdisciplinary therapy. Horm Metab Res. 2016;48(2):106-11. doi:10.1055/s-0035-1548871		X		
472	Jang J, Shin MJ, Kim OY, Park K. Longitudinal association between egg consumption and the risk of cardiovascular disease: interaction with type 2 diabetes mellitus. Nutr Diabetes. 2018;8(1):20. doi:10.1038/s41387-018-0033-1		X		
473	Jankovic N, Geelen A, Streppel MT, et al. WHO guidelines for a healthy diet and mortality from cardiovascular disease in European and American elderly: the CHANCES project. Am J Clin Nutr. 2015;102(4):745-56. doi:10.3945/ajcn.114.095117		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
474	Jans A, Van Hees AMJ, Gjelstad IMF, et al. Impact of dietary fat quantity and quality on skeletal muscle fatty acid metabolism in subjects with the metabolic syndrome. Metabolism. 2012;61(11):1554-1565. doi:10.1016/j.metabol.2012.04.003		X		
475	Jenkins DJ, Jones PJ, Lamarche B, et al. Effect of a dietary portfolio of cholesterol-lowering foods given at 2 levels of intensity of dietary advice on serum lipids in hyperlipidemia: a randomized controlled trial. Jama. 2011;306(8):831-9. doi:10.1001/jama.2011.1202		X		
476	Jiang Z, Sim JS. Consumption of n-3 polyunsaturated fatty acid-enriched eggs and changes in plasma lipids of human subjects. Nutrition. 1993. 9(6):513-8.				Age of participants at intervention or exposure
477	Jiao J, Liu G, Shin HJ, et al. Dietary fats and mortality among patients with type 2 diabetes: analysis in two population based cohort studies. BMJ. 2019;366:l4009. doi:10.1136/bmj.l4009				Health Status
478	Jin Y, Kanaya AM, Kandula NR, Rodriguez LA, Talegawkar SA. Vegetarian diets are associated with selected cardiometabolic risk factors among middle-older aged South Asians in the United States. J Nutr. 2018;148(12):1954-1960. doi:10.1093/jn/nxy217	X			
479	Joensen AM, Overvad K, Dethlefsen C, et al. Marine n-3 polyunsaturated fatty acids in adipose tissue and the risk of acute coronary syndrome. Circulation. 2011;124(11):1232-8. doi:10.1161/circulationaha.110.987057		X		
480	Johansson I, Esberg A, Nilsson LM, Jansson JH, Wennberg P, Winkvist A. Dairy Product Intake and Cardiometabolic Diseases in Northern Sweden: A 33-Year Prospective Cohort Study. Nutrients. 2019;11(2): pii: E284. doi:10.3390/nu11020284		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
481	Johns DJ, Lindroos AK, Jebb SA, Sjostrom L, Carlsson LM, Ambrosini GL. Dietary patterns, cardiometabolic risk factors, and the incidence of cardiovascular disease in severe obesity. Obesity (Silver Spring). 2015;23(5):1063-70. doi:10.1002/oby.20920		X		
482	Johnsen SH, Jacobsen BK, Braekkan SK, Hansen JB, Mathiesen EB. Fish consumption, fish oil supplements and risk of atherosclerosis in the Tromso study. Nutr J. 2018;17(1):56. doi:10.1186/s12937-018-0364-8		X		
483	Johnson MB, Burns-Whitmore B, Spalding T, Sancho-Madriz MF. Eating an avocado a day does not change body composition or blood cholesterol in healthy students. FASEB journal. 2013;27(Suppl 1).				Publication Status
484	Jones JL, Fernandez ML, McIntosh MS, et al. A Mediterranean-style low-glycemic-load diet improves variables of metabolic syndrome in women, and addition of a phytochemical-rich medical food enhances benefits on lipoprotein metabolism. J Clin Lipidol. 2011;5(3):188-196. doi:10.1016/j.jacl.2011.03.002		X		
485	Jones PJ, MacKay DS, Senanayake VK, et al. High-oleic canola oil consumption enriches LDL particle cholesteryl oleate content and reduces LDL proteoglycan binding in humans. Atherosclerosis. 2015;238(2):231-8. doi:10.1016/j.atherosclerosis.2014.12.010				Duplicate data
486	Juanola-Falgarona M, Salas-Salvado J, Ibarrola-Jurado N, et al. Effect of the glycemic index of the diet on weight loss, modulation of satiety, inflammation, and other metabolic risk factors: a randomized controlled trial. Am J Clin Nutr. 2014;100(1):27-35. doi:10.3945/ajcn.113.081216		X		
487	Julibert A, Bibiloni MDM, Bouzas C, et al. Total and Subtypes of Dietary Fat Intake and Its Association with Components of the Metabolic Syndrome in a Mediterranean Population at High Cardiovascular Risk. Nutrients. 2019;11(7): pii: E1493. doi:10.3390/nu11071493	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
488	Jung H, Chen CO, Blumberg JB, Kwak HK. The effect of almonds on vitamin E status and cardiovascular risk factors in Korean adults: a randomized clinical trial. Eur J Nutr. 2018;57(6):2069-2079. doi:10.1007/s00394-017-1480-5		X		
489	Juraschek SP, Miller ER 3d, Weaver CM, Appel LJ. Effects of Sodium Reduction and the DASH Diet in Relation to Baseline Blood Pressure. J Am Coll Cardiol. 2017;70(23):2841-2848. doi:10.1016/j.jacc.2017.10.011		X		
490	Kabagambe EK, Ordovas JM, Hopkins PN, Tsai MY, Arnett DK. The relation between erythrocyte trans fat and triglyceride, VLDL- and HDL-cholesterol concentrations depends on polyunsaturated fat. PLoS One. 2012;7(10):e47430. doi:10.1371/journal.pone.0047430		X		
491	Kaippert VC, Dos Santos Lopes MCO, De Carvalho PD, Rosado EL. Effects of unsaturated fatty acids on weight loss, body composition and obesity related biomarkers. Diabetol Metab Syndr. 2015;7(Suppl 1): A139. doi: 10.1186/1758-5996-7-S1-A139				Publication Status
492	Kalantarian S, Rimm EB, Herrington DM, Mozaffarian D. Dietary macronutrientsgenetic variationand progression of coronary atherosclerosis among women. Am Heart J. 2014;167(4):627-635.e1. doi:10.1016/j.ahj.2014.01.001			X	Health Status
493	Karamali M, Samimi M, Bahmani F, Foroozanfard F, Esmaillzadeh A. The effects of DASH diet on lipid profiles and biomarkers of oxidative stress in overweight and obese women with polycystic ovary syndrome: a randomised clinical trial. Human Reproduction. 2014;29i315- i316. doi:10.1093/humrep/29.Supplement_1.1				Publication Status
494	Karatzi K, Aissopou EK, Tsirimiagou C, Fatmeli E, Sfikakis PP, Protogerou AD. Association of consumption of dairy products and meat with retinal vessel calibers in subjects at increased cardiovascular risk. Nutr Metab Cardiovasc Dis. 2016;26(8):752-7. doi:10.1016/j.numecd.2016.03.006	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
495	Karatzi K, Stamatelopoulos K, Lykka M, et al. Sesame oil consumption exerts a beneficial effect on endothelial function in hypertensive men. Eur J Prev Cardiol. 2013;20(2):202-8. doi:10.1177/2047487312437625			X	Health Status
496	Katoku Y, Yamada M, Yonekubo A, Kuwata T, Kobayashi A, Sawa A. Effect of the cholesterol content of a formula on the lipid compositions of plasma lipoproteins and red blood cell membranes in early infancy. Am J Clin Nutr. 1996. 64(6):871-7. doi:10.1093/ajcn/64.6.871		X		
497	Katz DL, Gnanaraj J, Treu JA, Ma Y, Kavak Y, Njike VY. Effects of egg ingestion on endothelial function in adults with coronary artery disease: a randomized, controlled, crossover trial. Am Heart J. 2015;169(1):162-9. doi:10.1016/j.ahj.2014.10.001				Health Status
498	Kelemen L, Anand S. Sexual maturation, BMI, dietary intervention and dietary cholesterol reduced LDL cholesterol in children. Evid Based Cardiovasc Med. 1998. 2(2):58-60.	X			Health Status
499	Kell KP, Cardel MI, Bohan Brown MM, Fernandez JR. Added sugars in the diet are positively associated with diastolic blood pressure and triglycerides in children. Am J Clin Nutr. 2014;100(1):46-52. doi:10.3945/ajcn.113.076505	X			
500	Kemppainen T, Rosendahl A, Nuutinen O, Ebeling T, Pietinen P, Uusitupa M. Validation of a short dietary questionnaire and a qualitative fat index for the assessment of fat intake. Eur J Clin Nutr. 1993. 47(11):765-75.			X	
501	Kent LM, Grant RS, Watts G, Morton DP, Rankin PM, Ward EJ. HDL subfraction changes with a low-fat, plant-based Complete Health Improvement Program (CHIP). Asia Pac J Clin Nutr. 2018;27(5):1002-1009. doi:10.6133/apjcn.052018.05	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
502	Kesse-Guyot E, Fezeu L, Galan P, Hercberg S, Czernichow S, Castetbon K. Adherence to French nutritional guidelines is associated with lower risk of metabolic syndrome. J Nutr. 2011;141(6):1134-1139. doi:10.3945/jn.110.136317			X	
503	Key TJ, Appleby PN, Bradbury KE, et al. Consumption of meat, fish, dairy products, and eggs and risk of ischemic heart disease. Circulation. 2019;139(25):2835-2845. doi:10.1161/circulationaha.118.038813		X		
504	Keys A, Menott A, Karvonen MJ, et al. The diet and 15-year death rate in the seven countries study. Am J Epidemiol. 2017;185(11):1130-1142. doi:10.1093/aje/kwx101	X			
505	Khan SA, Jackson RT. Polyunsaturated fatty acids, inflammationand metabolic syndrome in South Asian Americans in Maryland. Food Sci Nutr. 2018;6(6):1575-1581. doi:10.1002/fsn3.698	X			
506	Khare MM, Carpenter RA, Huber R, et al. Lifestyle intervention and cardiovascular risk reduction in the Illinois WISEWOMAN Program. J Womens Health. 2012. 21(3):294-301. doi:10.1089/jwh.2011.2926		X		
507	Kheirouri S, Mohajeri M, Haghighian HK. Nitric oxide, omega-3 fatty acids and blood pressure in prinzmetal angina. Curr Top Nutraceutical Res. 2015;13(2):89-93.	X			
508	Kiage JN, Merrill PD, Robinson CJ, et al. Intake of trans fat and all-cause mortality in the Reasons for Geographical and Racial Differences in Stroke (REGARDS) cohort. Am J Clin Nutr. 2013;97(5):1121-8. doi:10.3945/ajcn.112.049064		X		
509	Kiefte-de Jong JC, Chowdhury R, Franco OH. Fish intake or omega-3 fatty acids: greater than the sum of all parts?. Eur J Epidemiol. 2012;27(12):891-4. doi:10.1007/s10654-012-9757-8	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
510	Kien CL, Bunn JY, Stevens R, et al. Dietary intake of palmitate and oleate has broad impact on systemic and tissue lipid profiles in humans. Am J Clin Nutr. 2014;99(3):436-45. doi:10.3945/ajcn.113.070557				Study Duration
511	Kim DS, Burt AA, Ranchalis JE, et al. Effects of dietary components on high-density lipoprotein measures in a cohort of 1,566 participants. Nutr Metab. 2014;11(1):44. doi:10.1186/1743-7075-11-44	X	X		
512	Kim JE, Campbell WW. Dietary cholesterol contained in whole eggs is not well absorbed and does not acutely affect plasma total cholesterol concentration in men and women: results from 2 randomized controlled crossover studies. Nutrients. 2018;10(9): pii: E1272. doi:10.3390/nu10091272		X		
513	Kim KY, Park JS. Impact of fish consumption by subjects with prediabetes on the metabolic risk factors: using data in the 2015 (6th) Korea National Health and Nutrition Examination Surveys. Nutr Res Pract. 2018;12(3):233-242. doi:10.4162/nrp.2018.12.3.233	X			
514	Kim M, Chae JS, Kim M, Lee SH, Lee JH. Effects of a 3-year dietary intervention on age-related changes in triglyceride and apolipoprotein A-V levels in patients with impaired fasting glucose or new-onset type 2 diabetes as a function of the APOA5 -1131 T > C polymorphism. Nutr J. 2014;13:40. doi:10.1186/1475-2891-13-40	X	X		
515	Kim M, Kim M, Lee A, et al. Impact of 8-week linoleic acid intake in soy oil on Lp-PLA2 activity in healthy adults. Nutr Metab. 2017;14:32. doi:10.1186/s12986-017-0186-2		X		
516	Kim MS, Hwang SS, Park EJ, Bae JW. Strict vegetarian diet improves the risk factors associated with metabolic diseases by modulating gut microbiota and reducing intestinal inflammation. Environ Microbiol Rep. 2013;5(5):765-75. doi:10.1111/1758-2229.12079		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
517	Kim OY, Chung HK, Shin MJ. Higher levels of serum triglyceride and dietary carbohydrate intake are associated with smaller LDL particle size in healthy Korean women. Nutr Res Pract. 2012;6(2):120-5. doi:10.4162/nrp.2012.6.2.120	X	X		
518	Kim S, Kim J, Lim Y, Kim YJ, Kim JY, Kwon O. A dietary cholesterol challenge study to assess Chlorella supplementation in maintaining healthy lipid levels in adults: a double-blindedrandomizedplacebo-controlled study. Nutr J. 2016;15(1):54. doi:10.1186/s12937-016-0174-9		X		
519	Kim SA, Lee JK, Kang D, Shin S. Oily fish consumption and the risk of dyslipidemia in Korean adults: a prospective cohort study based on the Health Examinees Gem (HEXA-G) study. Nutrients. 2019;11(10): pii: E2506. doi:10.3390/nu11102506		X	X	
520	Kim YS, Xun P, Iribarren C, et al. Intake of fish and long-chain omega-3 polyunsaturated fatty acids and incidence of metabolic syndrome among American young adults: a 25-year follow-up study. Eur J Nutr. 2016;55(4):1707-16. doi:10.1007/s00394-015-0989-8			X	
521	Kingah PL, Luu HN, Volcik KA, Morrison AC, Nettleton JA, Boerwinkle E. Association of NOS3 Glu298Asp SNP with hypertension and possible effect modification of dietary fat intake in the ARIC study. Hypertens Res. 2010;33(2):165-9. doi:10.1038/hr.2009.198	X			
522	Kirkhus B, Lamglait A, Eilertsen KE, et al. Effects of similar intakes of marine n-3 fatty acids from enriched food products and fish oil on cardiovascular risk markers in healthy human subjects. Br J Nutr. 2012;107(9):1339-49. doi:10.1017/s0007114511004508		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
523	Kishawy AT, Amer SA, Abd El-Hack ME, Saadeldin IM, Swelum AA. The impact of dietary linseed oil and pomegranate peel extract on broiler growth, carcass traits, serum lipid profile, and meat fatty acid, phenol, and flavonoid contents. Asian-Australas J Anim Sci. 2019;32(8):1161-1171. doi:10.5713/ajas.18.0522		X		Non-human
524	Kishimoto Y, Taguchi C, Saita E, et al. Additional consumption of one egg per day increases serum lutein plus zeaxanthin concentration and lowers oxidized low-density lipoprotein in moderately hypercholesterolemic males. Food Res Int. 2017;99(Pt 2):944-949. doi:10.1016/j.foodres.2017.03.003	X			Health Status
525	Kishimoto Y, Taguchi C, Suzuki-Sugihara N, et al. The effect of the consumption of egg on serum lipids and antioxidant status in healthy subjects. J Nutr Sci Vitaminol (Tokyo). 2016;62(5):361-365. doi:10.3177/jnsv.62.361	X	X		
526	Knutsen SF, Knutsen R. The Tromso Survey: the Family Intervention study--the effect of intervention on some coronary risk factors and dietary habits, a 6-year follow-up. Prev Med. 1991. 20(2):197-212. doi:10.1016/0091-7435(91)90020-5		X		
527	Kodumuri N, Giamberardino L, Hinderliter A, Sen S. Association of dietary factors with progression of AA in stroke/TIA patients. J Neurol Disord. 2016;4(3): pii: 270. doi:10.4172/2329-6895.1000270				Health Status
528	Kokanovic A, Mandic ML, Banjari I. Does individual dietary intervention have any impact on adolescents with cardiovascular health risks?. Med Glas (Zenica). 2014;11(1):234-7.		X		
529	Kolarzyk E, Skop-Lewandowska A, Jaworska J, Ostachowska-Gasior A, Krzeszowska-Rosiek T. Dietary intake of antioxidants and fats in the context of coronary heart disease prevention among elderly people. Ann Agric Environ Med. 2018;25(1):131-136. doi:10.5604/12321966.1233574			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
530	Koletzko B. Trans fatty acids may impair biosynthesis of long-chain polyunsaturates and growth in man. Acta Paediatr. 1992. 81(4):302-6. doi:10.1111/j.1651-2227.1992.tb12230.x				Health Status
531	Kopecky SL, Klodas E, Alias S, Bauman J, Jew S, Jones PJ. LDL-C response to portfolio foods containing high levels of phytosterols, whole food fiber, and alpha-linoleic acid in statin reluctant patients: impact of CYP7A1-RS3808607 and apoe isoforms. Circulation. 2018;138:A17150				Publication Status
532	Korrapati D, Jeyakumar SM, Putcha UK, et al. Coconut oil consumption improves fat-free mass, plasma HDL-cholesterol and insulin sensitivity in healthy men with normal BMI compared to peanut oil. Clin Nutr. 2018;38(6):2889-2899. doi:10.1016/j.clnu.2018.12.026		X		Country
533	Kovell LC, Yeung E, Miller ER, et al. The effect of healthy diets on subclinical cardiac injury and inflammation: results from the omni-heart trial. Circulation. 2018;138(Suppl 1).				Publication Status
534	Kralova Lesna I, Suchanek P, Brabcova E, Kovar J, Malinska H, Poledne R. Effect of different types of dietary fatty acids on subclinical inflammation in humans. Physiol Res. 2013;62(2):145-52.				Health Status
535	Kratz M, Weigle DS, Breen PA, et al. Exchanging carbohydrate or protein for fat improves lipid-related cardiovascular risk profile in overweight men and women when consumed ad libitum. J Investig Med. 2010;58(5):711-9. doi:10.231/JIM.0b013e3181da4d37		X		
536	Krishna S, Okhovat JP, Kim J, Kim CN. Influence of omega-3 fatty acids on triglyceride levels in patients using isotretinoin. JAMA Dermatol. 2015;151(1):101-2. doi:10.1001/jamadermatol.2014.2402		X		Publication Status
537	Kristensen M, Jensen MG, Aarestrup J, et al. Flaxseed dietary fibers lower cholesterol and increase fecal fat excretion, but magnitude of effect depend on food type. Nutr Metab. 2012;9(1):8-15. doi:10.1186/1743-7075-9-8		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
538	Kromhout D, Menotti A, Alberti-Fidanza A, et al. Comparative ecologic relationships of saturated fat, sucrose, food groups, and a Mediterranean food pattern score to 50-year coronary heart disease mortality rates among 16 cohorts of the Seven Countries Study. Eur J Clin Nutr. 2018;72(8):1103-1110. doi:10.1038/s41430-018-0183-1	X			
539	Ku CY, Gower BA, Nagy TR, Goran MI. Relationships between dietary fat, body fat, and serum lipid profile in prepubertal children. Obes Res. 1998. 6(6):400-7.	X			
540	Kuczmarski MF, Brewer BC, Rawal R, Pohlig RT, Zonderman AB, Evans MK. Aspects of dietary diversity differ in their association with atherosclerotic cardiovascular risk in a racially diverse us adult population. Nutrients. 2019;11(5). pii: E1034. doi:10.3390/nu11051034		X		
541	Kummer K, Jensen PN, Kratz M, et al. Full-fat dairy food intake is associated with a lower risk of incident diabetes among American Indians with low total dairy food intake. J Nutr. 2019;149(7):1238-1244. doi:10.1093/jn/nxz058			X	
542	Kwiterovich PO, Barton BA, McMahon RP, et al. Effects of diet and sexual maturation on low-density lipoprotein cholesterol during puberty: the Dietary Intervention Study in Children (DISC). Circulation. 1997. 96(8):2526-33. doi:10.1161/01.cir.96.8.2526	X			Health Status
543	Kwiterovich PO. Safety and efficacy of treatment of children and adolescents with elevated low density lipoprotein levels with a step two diet or with lovastatin. Nutrition, metabolism, and cardiovascular diseases. Nutr Metab Cardiovasc Dis. 2001. 11(Suppl 5):30- 4.	X			
544	Laake I, Pedersen JI, Selmer R, et al. A prospective study of intake of trans-fatty acids from ruminant fat, partially hydrogenated vegetable oils, and marine oils and mortality from CVD. Br J Nutr. 2012;108(4):743-54. doi:10.1017/s0007114511005897		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
545	Labbe SM, Noll C, Grenier-Larouche T, et al. Improved cardiac function and dietary fatty acid metabolism after modest weight loss in subjects with impaired glucose tolerance. Am J Physiol Endocrinol Metab. 2014;306(12):E1388-96. doi:10.1152/ajpendo.00638.2013		X	X	
546	Labonte ME, Jenkins DJ, Lewis GF, et al. Adding MUFA to a dietary portfolio of cholesterol-lowering foods reduces apoAI fractional catabolic rate in subjects with dyslipidaemia. Br J Nutr. 2013;110(3):426-36. doi:10.1017/s000711451200534x				Health Status
547	Labonte ME, Jenkins DJA, Lewis GF, et al. Impact of adding MUFA to a portfolio diet on in vivo kinetics of apo AI, B100 and B48 in subjects with hypercholesterolemia. FASEB journal. 2011;25(Suppl 1).				Publication Status
548	Labraimi H, Aguenaou H, Charrouf Z, et al. Impact of argane and olive oil consumption on metabolic syndrome indicators among menopausal women in Rabat, Morocco. Obesity Reviews. 2011;1289. doi:10.1111/j.1467-789X.2011.00889.x				Publication Status
549	Ladeia AM, Costa-Matos E, Barata-Passos R, Costa Guimaraes A. A palm oil-rich diet may reduce serum lipids in healthy young individuals. Nutrition. 2008. 24(1):11-5. doi:10.1016/j.nut.2007.08.013	X			
550	Lagström H, Jokinen E, Seppänen R, et al. Fatty acids in serum lipid fractions as indicators of fat intake in 5- year-old children in the STRIP project. Scandinavian Journal of Nutrition. 1998. 42(4):140-144.	X		X	
551	Lahoz C, Castillo E, Mostaza JM, et al. Relationship of the adherence to a Mediterranean diet and its main components with CRP levels in the Spanish population. Nutrients. 2018;10(3). pii: E379. doi:10.3390/nu10030379	X		X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
552	Lai HT, de Oliveira Otto MC, Lemaitre RN, et al. Serial circulating omega 3 polyunsaturated fatty acids and healthy ageing among older adults in the Cardiovascular Health Study: prospective cohort study. BMJ. 2018;363k4445. doi:10.1136/bmj.k4445		X		
553	Laitinen TT, Nuotio J, Juonala M, et al. Success in achieving the targets of the 20-Year infancy-onset dietary intervention: Association with insulin sensitivity and serum lipids. Diabetes Care. 2018;41(10):2236-2244. doi:10.2337/dc18-0869		X		
554	Lamarche B. Dietary sources of saturated fat may influence cardiovascular disease risk. Can Nurse. 2013;109(3):19.	X			
555	Lambert EA, Phillips S, Belski R, et al. Endothelial function in healthy young individuals is associated with dietary consumption of saturated fat. Front Physiol. 2017;8876. doi:10.3389/fphys.2017.00876	X		X	
556	Lambrinoudaki I, Augoulea A, Rizos D, et al. Greek-origin royal jelly improves the lipid profile of postmenopausal women. Gynecol Endocrinol. 2016;32(10):835-839. doi:10.1080/09513590.2016.1188281	X		X	
557	Lana A, Banegas JR, Guallar-Castillon P, Rodriguez-Artalejo F, Lopez-Garcia E. Association of dairy consumption and 24-Hour blood pressure in older adults with hypertension. Am J Med. 2018;131(10):1238-1249. doi:10.1016/j.amjmed.2018.04.039	X			Health Status
558	Lankinen M, Kolehmainen M, Jaaskelainen T, et al. Effects of whole grain, fish and bilberries on serum metabolic profile and lipid transfer protein activities: a randomized trial (Sysdimet). PLoS One. 2014;9(2):e90352. doi:10.1371/journal.pone.0090352		X	X	
559	Lapinleimu H, Jokinen E, Myyrinmaa A, et al. Individualized dietary counselling of families: serum cholesterol concentration and growth of children aged 7-13 months. Acta Paediatr. 1994. 83(4):383-8. doi:10.1111/j.1651-2227.1994.tb18124.x		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
560	Lapinleimu H, Vukari J, Nunikoski H, et al. Impact of gender, apolipoprotein E phenotypes, and diet on serum lipids and lipoproteins in infancy. J Pediatr. 1997. 131(6):825-32. doi:10.1016/s0022-3476(97)70028-3		X		Duplicate data
561	Larsson SC, Virtamo J, Wolk A. Dairy consumption and risk of stroke in Swedish women and men. Stroke. 2012;43(7):1775-80. doi:10.1161/strokeaha.111.641944		X		
562	Larsson SC, Virtamo J, Wolk A. Fish consumption and risk of stroke in Swedish women. Am J Clin Nutr. 2011;93(3):487-93. doi:10.3945/ajcn.110.002287		X		
563	Lassenius MI, Makinen VP, Fogarty CL, et al. Patients with type 1 diabetes show signs of vascular dysfunction in response to multiple high-fat meals. Nutr Metab. 2014;11(1):1-22. doi:10.1186/1743-7075-11-28	X	X		Health Status
564	Lauer RM, Obarzanek E, Hunsberger SA, et al. Efficacy and safety of lowering dietary intake of total fat, saturated fat, and cholesterol in children with elevated LDL cholesterol: the Dietary Intervention Study in Children. Am J Clin Nutr. 2000. 72(Suppl 5):1332s-1342s. doi:10.1093/ajcn/72.5.1332s				Duplicate data
565	Laugesen M, Elliott R. Ischaemic heart diseaseType 1 diabetes, and cow milk A1 beta-casein. N Z Med J. 2003. 116(1168):U295.	X	X		
566	Laupsa Borge J, Veum VL, Eng Ø, et al. Very-high-fat and low-fat isocaloric diets exert similar metabolic benefits but different temporal effects on cardiometabolic risk markers. Obesity facts. 2016;9(Suppl 1):185- 186. doi:10.1159/000446744				Publication Status
567	Lauritzen L, Harslof LB, Hellgren LI, Pedersen MH, Molgaard C, Michaelsen KF. Fish intake, erythrocyte n-3 fatty acid status and metabolic health in Danish adolescent girls and boys. Br J Nutr. 2012;107(5):697-704. doi:10.1017/s0007114511002418	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
568	Laursen ASD, Dahm CC, Johnsen SP, Schmidt EB, Overvad K, Jakobsen MU. Adipose tissue fatty acids present in dairy fat and risk of stroke: the Danish Diet, Cancer and Health cohort. Eur J Nutr. 2019;58(2):529-539. doi:10.1007/s00394-018-1608-2	X	X		
569	Laursen ASD, Dahm CC, Johnsen SP, Tjonneland A, Overvad K, Jakobsen MU. Substitutions of dairy product intake and risk of stroke: a Danish cohort study. Eur J Epidemiol. 2018;33(2):201-212. doi:10.1007/s10654-017-0271-x		X		
570	Laursen ASD, Sluijs I, Boer JMA, Verschuren WMM, van der Schouw YT, Jakobsen MU. Substitutions between dairy products and risk of stroke: results from the European Investigation into Cancer and Nutrition-Netherlands (EPIC-NL) cohort. Br J Nutr. 2019;121(12):1398-1404. doi:10.1017/s0007114519000564		X	X	
571	Lavigne JV, Gidding S, Stevens VJ, et al. A cholesterol-lowering diet does not produce adverse psychological effects in children: three-year results from the dietary intervention study in children. Health Psychol. 1999. 18(6):604-613. doi:10.1037/0278-6133.18.6.604		X	X	
572	Le T, Flatt SW, Natarajan L, et al. Effects of diet composition and insulin resistance status on plasma lipid levels in a weight loss intervention in women. J Am Heart Assoc. 2016;5(1). pii: e002771. doi:10.1161/jaha.115.002771		X		
573	Lee H, Jang HB, Yoo MG, Chung KS, Lee HJ. Protective effects of dietary MUFAs mediating metabolites against hypertension risk in the Korean Genome and Epidemiology Study. Nutrients. 2019;11(8).pii:E1928.doi:10.3390/nu11081928			X	
574	Lee HA, Hwang HJ, Oh SY, et al. The differential effects of changes in individual macronutrient intake on changes in lipid concentrations during childhood: from the Ewha Birth & Growth Cohort. Clin Nutr. 2018;37(3):1027-1033. doi:10.1016/j.clnu.2017.04.017		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
575	Lee J, Kim J. Association between dietary pattern and incidence of cholesterolemia in Korean adults: The Korean Genome and Epidemiology Study. Nutrients. 2018;10(1): pii: E53. doi:10.3390/nu10010053		X		
576	Lee JB, Notay K, Klingel SL, Chabowski A, Mutch DM, Millar PJ. Docosahexaenoic acid reduces resting blood pressure but increases muscle sympathetic outflow compared with eicosapentaenoic acid in healthy men and women. Am J Physiol Heart Circ Physiol. 2019. 316(4):H873- H881. doi:10.1152/ajpheart.00677.2018		X		
577	Lee SP, Dart AM, Walker KZ, O'Dea K, Chin-Dusting JP, Skilton MR. Effect of altering dietary n-6: n-3 PUFA ratio on cardiovascular risk measures in patients treated with statins: a pilot study. Br J Nutr. 2012;108(7):1280-5. doi:10.1017/s0007114511006519				Health Status
578	Lee TC, Ivester P, Hester AG, et al. The impact of polyunsaturated fatty acid-based dietary supplements on disease biomarkers in a metabolic syndrome/diabetes population. Lipids Health Dis. 2014;13:196. doi:10.1186/1476-511x-13-196		X		
579	Lee YJ, Lee A, Yoo HJ, et al. Effect of weight loss on circulating fatty acid profiles in overweight subjects with high visceral fat area: a 12-week randomized controlled trial. Nutr J. 2018;17(1):28. doi:10.1186/s12937-018-0323-4		X		
580	Lee YJ, Seo JA, Yoon T, et al. Effects of low-fat milk consumption on metabolic and atherogenic biomarkers in Korean adults with the metabolic syndrome: a randomised controlled trial. J Hum Nutr Diet. 2016;29(4):477-86. doi:10.1111/jhn.12349		X		
581	Lee YJ, Song S, Song Y. High-carbohydrate diets and food patterns and their associations with metabolic disease in the Korean population. Yonsei Med J. 2018;59(7):834-842. doi:10.3349/ymj.2018.59.7.834	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
582	Lehtimaki T, Moilanen T, Porkka K, et al. Association between serum lipids and apolipoprotein E phenotype is influenced by diet in a population-based sample of free-living children and young adults: the Cardiovascular Risk in Young Finns Study. J Lipid Res. 1995. 36(4):653-61.	X			
583	Leichtle AB, Helmschrodt C, Ceglarek U, et al. Effects of a 2-y dietary weight-loss intervention on cholesterol metabolism in moderately obese men. Am J Clin Nutr. 2011;94(5):1189-1195.		X		
584	Leite MLC, Prinelli F. A compositional data perspective on studying the associations between macronutrient balances and diseases. Eur J Clin Nutr. 2017;71(12):1365-1369. doi:10.1038/ejcn.2017.126	X	X		
585	Lemos BS, Medina-Vera I, Blesso CN, Fernandez ML. Intake of 3 eggs per day when compared to a choline bitartrate supplement, downregulates cholesterol synthesis without changing the LDL/HDL ratio. Nutrients. 2018;10(2). pii: E258. doi:10.3390/nu10020258		X		
586	Lentjes MAH, Keogh RH, Welch AA, et al. Longitudinal associations between marine omega-3 supplement users and coronary heart disease in a UK population-based cohort. BMJ Open. 2017;7(10):e017471. doi:10.1136/bmjopen-2017-017471		X		
587	Letois F, Mura T, Scali J, Gutierrez LA, Féart C, Berr C. Nutrition and mortality in the elderly over 10 years of follow-up: The Three-City study. Br J Nutr. 2016;116(5):882-889. doi:10.1017/S000711451600266X		X	X	
588	Li D, Wan Y, Wang F, et al. Effects of macronutrient distribution on weight change and related cardiometabolic profiles in healthy non-obese Chinese: a randomized, clinical trial. Ann Nutr Metab. 2017;71:689. doi:10.1159/000480486				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
589	Lindstrom T, Kechagias S, Carlsson M, Nystrom FH. Transient increase in HDL-cholesterol during weight gain by hyperalimentation in healthy subjects. Obesity (Silver Spring). 2011;19(4):812-7. doi:10.1038/oby.2010.190		X		
590	Lipscomb ER, Caffrey HM, Hays LM, Finch EA, Saha CK, Ackermann RT. Lifestyle and Behavior. Lower fat intake is associated with lower weight and cholesterol at 4 months in adults with impaired glucose metabolism. Diabetes Spectrum. 2012;25(1):49-55.		X		
591	Liu J, Joshi D, Sempos CT. Non-high-density-lipoprotein cholesterol and cardiovascular risk factors among adolescents with and without impaired fasting glucose. Applied PhysiologyNutrition & Metabolism. 2009. 34(2):136-142. doi:10.1139/H08-149	X	X		
592	Liu JC, Conklin SM, Manuck SB, Yao JK, Muldoon MF. Long-chain omega-3 fatty acids and blood pressure. Am J Hypertens. 2011;24(10):1121-6. doi:10.1038/ajh.2011.120	X			
593	Liu MJ, Li HT, Yu LX, et al. A correlation study of DHA dietary intake and plasma, erythrocyte and breast milk DHA concentrations in lactating women from Coastland, Lakeland, and Inland areas of China. Nutrients. 2016;8(5). pii: E312 doi:10.3390/nu8050312	X		X	
594	Liu PJ, Liu YP, Qin HK, Xing T, Li SS, Bao YY. Effects of polymorphism in FABP2 Ala54Thr on serum lipids and glycemic control in low glycemic index diets are associated with gender among Han Chinese with type 2 diabetes mellitus. Diabetes Metab Syndr Obes. 2019;12:413-421. doi:10.2147/dmso.S196738				Health Status
595	Liu Q, Lichtenstein AH, Matthan NR, et al. Higher lipophilic index indicates higher risk of coronary heart disease in postmenopausal women. Lipids. 2017;52(8):687-702. doi:10.1007/s11745-017-4276-8		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
596	Liu X, Kris-Etherton PM, West SG, et al. Effects of canola and high-oleic-acid canola oils on abdominal fat mass in individuals with central obesity. Obesity (Silver Spring). 2016;24(11):2261-2268. doi:10.1002/oby.21584			X	
597	Liu Y, Poon S, Seeman E, Hare DL, Bui M, Iuliano S. Fat from dairy foods and 'meat' consumed within recommended levels is associated with favourable serum cholesterol levels in institutionalised older adults. J Nutr Sci. 2019;8: e10. doi:10.1017/jns.2019.5	X			
598	Liu Y, Wang J, Zhang R, et al. A good response to oil with medium- and long-chain fatty acids in body fat and blood lipid profiles of male hypertriglyceridemic subjects. Asia Pac J Clin Nutr. 2009. 18(3):351-8.		X		
599	Livingstone KM, Givens DI, Cockcroft JR, Pickering JE, Lovegrove JA. Is fatty acid intake a predictor of arterial stiffness and blood pressure in men? Evidence from the Caerphilly Prospective Study. Nutr Metab Cardiovasc Dis. 2013;23(11):1079-85. doi:10.1016/j.numecd.2012.12.002			X	
600	Loganathan R, Vethakkan SR, Radhakrishnan AK, Razak GA, Kim-Tiu T. Red palm olein supplementation on cytokinese, ndothelial function and lipid profile in centrally overweight individuals: a randomised controlled trial. Eur J Clin Nutr. 2019;73(4):609-616. doi:10.1038/s41430-018-0236-5		X		
601	Loo RL, Zou X, Appel LJ, Nicholson JK, Holmes E. Characterization of metabolic responses to healthy diets and association with blood pressure: application to the Optimal Macronutrient Intake Trial for Heart Health (OmniHeart), a randomized controlled study. Am J Clin Nutr. 2018;107(3):323-334. doi:10.1093/ajcn/nqx072				Duplicate data

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
602	Lopes MP, Giudici KV, Marchioni DM, Fisberg RM, Martini LA. Relationships between n-3 polyunsaturated fatty acid intake, serum 25 hydroxyvitamin D, food consumption, and nutritional status among adolescents. Nutr Res. 2015;35(8):681-8. doi:10.1016/j.nutres.2015.05.018	X			
603	Lopez-Moreno J, Garcia-Carpintero S, Gomez-Delgado F, et al. Endotoxemia is modulated by quantity and quality of dietary fat in older adults. Exp Gerontol. 2018;109:119-125. doi:10.1016/j.exger.2017.11.006			X	
604	Lorenzen J, Astrup A. The effect of dairy fat and calcium intake on fat digestibility and blood lipid profile. Obesity reviews. 2011;1290. doi:10.1111/j.1467-789X.2011.00889.x				Publication Status
605	Lorenzen JK, Astrup A. Dairy calcium intake modifies responsiveness of fat metabolism and blood lipids to a high-fat diet. Br J Nutr. 2011;105(12):1823-31. doi:10.1017/s0007114510005581		X		
606	Loring PA, Duffy LK, Murray MS. A risk-benefit analysis of wild fish consumption for various species in Alaska reveals shortcomings in data and monitoring needs. Sci Total Environ. 2010;408(20):4532-4541. doi:10.1016/j.scitotenv.2010.07.013	X	X		
607	Loued S, Berrougui H, Componova P, Ikhlef S, Helal O, Khalil A. Extra-virgin olive oil consumption reduces the age-related decrease in HDL and Paraoxonase 1 anti-inflammatory activities. Br J Nutr. 2013;110(7):1272-1284. doi:10.1017/S0007114513000482	X			
608	Louie JC, Flood VM, Burlutsky G, Rangan AM, Gill TP, Mitchell P. Dairy consumption and the risk of 15-year cardiovascular disease mortality in a cohort of older Australians. Nutrients. 2013;5(2):441-54. doi:10.3390/nu5020441		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
609	Louie JC, Flood VM, Rangan AM, et al. Higher regular fat dairy consumption is associated with lower incidence of metabolic syndrome but not type 2 diabetes. Nutr Metab Cardiovasc Dis. 2013;23(9):816-21. doi:10.1016/j.numecd.2012.08.004			X	
610	Lu Y, Feskens EJ, Dolle ME, et al. Dietary n-3 and n-6 polyunsaturated fatty acid intake interacts with FADS1 genetic variation to affect total and HDL-cholesterol concentrations in the Doetinchem Cohort Study. Am J Clin Nutr. 2010;92(1):258-65. doi:10.3945/ajcn.2009.29130	X			
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612	Lund ASQ, Hasselbalch AL, Gamborg M, et al. N-3 polyunsaturated fatty acids, body fat and inflammation. Obesity Facts. 2013;6(4):369-379. doi:10.1159/000354663	X			
613	Lund EK, Lee-Finglas WE, Southon S, et al. Dietary fat intake and plasma lipid levels in adolescents. Eur J Clin Nutr. 1992. 46(12):857-64.	X			
614	Lutjohann D, Meyer S, von Bergmann K, Stellaard F. Cholesterol absorption and synthesis in vegetarians and omnivores. Mol Nutr Food Res. 2018;62(6):e1700689. doi:10.1002/mnfr.201700689	X		X	
615	Luukkonen PK, Sadevirta S, Umpleby M, et al. Effect of overfeeding diets enriched with unsaturated or saturated fatty acids or sugars on de novo lipogenesislipolysis and liver fat in humans. Diabetologia. 2016;59(1):S10- S11. doi:10.1007/s00125-016-4046-9				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
616	Luukkonen PK, Sadevirta S, Zhou Y, et al. Saturated fat is more metabolically harmful for the human liver than unsaturated fat or simple sugars. Diabetes Care. 2018;41(8):1732-1739. doi:10.2337/dc18-0071				Study Duration
617	Ma W, Wu JH, Wang Q, et al. Prospective association of fatty acids in the de novo lipogenesis pathway with risk of type 2 diabetes: the Cardiovascular Health Study. Am J Clin Nutr. 2015;101(1):153-63. doi:10.3945/ajcn.114.092601			X	
618	Machado AM, de Paula H, Cardoso LD, Costa NM. Effects of brown and golden flaxseed on the lipid profile, glycemia, inflammatory biomarkers, blood pressure and body composition in overweight adolescents. Nutrition. 2015;31(1):90-6. doi:10.1016/j.nut.2014.05.002		X		
619	Machin DR, Park W, Alkatan M, Mouton M, Tanaka H. Effects of non-fat dairy products added to the routine diet on vascular function: a randomized controlled crossover trial. Nutr Metab Cardiovasc Dis. 2015;25(4):364-9. doi:10.1016/j.numecd.2015.01.005		X		
620	Machin DR, Park W, Alkatan M, Mouton M, Tanaka H. Hypotensive effects of solitary addition of conventional nonfat dairy products to the routine diet: a randomized controlled trial. Am J Clin Nutr. 2014;100(1):80-7. doi:10.3945/ajcn.114.085761		X		
621	MacKay DS, Cardillo A, Mollard RC, Jones PJ. Hemp food product consumption for 4 weeks raises red blood cell alpha linolenic acid, but not total n-3 polyunsaturated fatty acid content, compared to a soybean and sesame control product in free living participants who are overweight or obese. FASEB journal. 2017;31(1)				Publication Status
622	Macknin M, Kong T, Weier A, et al. Plant-based, no-added-fat or American Heart Association diets: impact on cardiovascular risk in obese children with hypercholesterolemia and their parents. J Pediatr. 2015;166(4):953-9.e1-3. doi:10.1016/j.jpeds.2014.12.058		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
623	Madjd A, Taylor MA, Mousavi N, et al. Comparison of the effect of daily consumption of probiotic compared with low-fat conventional yogurt on weight loss in healthy obese women following an energy-restricted diet: a randomized controlled trial. Am J Clin Nutr. 2016;103(2):323-9. doi:10.3945/ajcn.115.120170		X		
624	Madsen MTB, Bjerregaard AA, Furtado JD, et al. Comparisons of estimated intakes and plasma concentrations of selected fatty acids in pregnancy. Nutrients. 2019;11(3): pii: E568. doi:10.3390/nu11030568	X		X	
625	Magriplis E, Mitsopoulou AV, Karageorgou D, et al. Frequency and quantity of egg intake is not associated with dyslipidemia: the Hellenic National Nutrition and Health Survey (HNNHS). Nutrients. 2019;11(5): pii: E1105. doi:10.3390/nu11051105	X	X		
626	Mah E, Sapper TN, Chitchumroonchokchai C, et al. alpha-Tocopherol bioavailability is lower in adults with metabolic syndrome regardless of dairy fat co-ingestion: a randomized, double-blind, crossover trial. Am J Clin Nutr. 2015;102(5):1070-80. doi:10.3945/ajcn.115.118570			X	
627	Mah E, Schulz JA, Kaden VN, et al. Cashew consumption reduces total and ldl cholesterol in mildly hypercholesterolemic men and women: a randomized, crossover, controlled feeding trial. FASEB journal. 2017;31(Suppl 1)				Publication Status
628	Mah E, Schulz JA, Kaden VN, et al. Cashew consumption reduces total and LDL cholesterol: a randomized, crossover, controlled-feeding trial. Am J Clin Nutr. 2017;105(5):1070-1078. doi:10.3945/ajcn.116.150037				Health Status
629	Mahe G, Ronziere T, Laviolle B, et al. An unfavorable dietary pattern is associated with symptomatic ischemic stroke and carotid atherosclerosis. J Vasc Surg. 2010;52(1):62-8. doi:10.1016/j.jvs.2010.02.258	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
630	Maki KC, Hasse W, Dicklin MR, et al. Corn oil lowers plasma cholesterol compared with coconut oil in adults with above-desirable levels of cholesterol in a randomized crossover trial. J Nutr. 2018;148(10):1556-1563. doi:10.1093/jn/nxy156				Health Status
631	Maki KC, Lawless AL, Kelley KM, Kaden VN, Geiger CJ, Dicklin MR. Corn oil improves the plasma lipoprotein lipid profile compared with extra-virgin olive oil consumption in men and women with elevated cholesterol: results from a randomized controlled feeding trial. J Clin Lipidol. 2015;9(1):49-57. doi:10.1016/j.jacl.2014.10.006				Health Status
632	Maki KC, Lawless AL, Kelley KM, et al. Corn oil intake favorably impacts lipoprotein cholesterolapolipoprotein and lipoprotein particle levels compared with extra-virgin olive oil. Eur J Clin Nutr. 2017;71(1):33-38. doi:10.1038/ejcn.2016.169			X	Study Duration
633	Maki KC, Palacios OM, Lindner E, Nieman KM, Bell M, Sorce J. Replacement of refined starches and added sugars with egg protein and unsaturated fats increases insulin sensitivity and lowers triglycerides in overweight or obese adults with elevated triglycerides. J Nutr. 2017;147(7):1267-1274. doi:10.3945/jn.117.248641		X		Health Status
634	Maki KC, Rains TM, Schild AL, et al. Effects of low-fat dairy intake on blood pressureendothelial function, and lipoprotein lipids in subjects with prehypertension or stage 1 hypertension. Vasc Health Risk Manag. 2013;9369-79. doi:10.2147/vhrm.S45684		X		
635	Malpuech-Brugere C, Mouriot J, Boue-Vaysse C, et al. Differential impact of milk fatty acid profiles on cardiovascular risk biomarkers in healthy men and women. Eur J Clin Nutr. 2010;64(7):752-9. doi:10.1038/ejcn.2010.73		X		Study Duration

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
636	Malve H, Kerkar P, Mishra N, et al. LDL-cholesterol lowering activity of a blend of rice bran oil and safflower oil (8:2) in patients with hyperlipidaemia: a proof of concept, double blind, controlled, randomised parallel group study. J Indian Med Assoc. 2010;108(11):785-8.				Country
637	Manios Y, Moschandreas J, Hatzis C, Kafatos A. Health and nutrition education in primary schools of Crete: changes in chronic disease risk factors following a 6-year intervention programme. Br J Nutr. 2002;88(3):315-24. doi:10.1079/bjn2002672		X		
638	Mann JI, Appleby PN, Key TJ, Thorogood M. Dietary determinants of ischaemic heart disease in health conscious individuals. Heart. 1997. 78(5):450-5. doi:10.1136/hrt.78.5.450				Age of participants at intervention or exposure
639	Manninen S, Lankinen M, Erkkila A, et al. The effect of intakes of fish and Camelina sativa oil on atherogenic and anti-atherogenic functions of LDL and HDL particles: a randomized controlled trial. Atherosclerosis. 2019;281:56-61. doi:10.1016/j.atherosclerosis.2018.12.017			X	
640	Manninen SM, Lankinen MA, de Mello VD, Laaksonen DE, Schwab US, Erkkila AT. Intake of fatty fish alters the size and the concentration of lipid components of HDL particles and camelina sativa oil decreases IDL particle concentration in subjects with impaired glucose metabolism. Mol Nutr Food Res. 2018;62(10):e1701042. doi:10.1002/mnfr.201701042				Product not widely available in US
641	Mansoorian B, Chen Y, Mullen W, Combet E. Impact of dietary fat replacement with rapeseed or sunflower oils on biomarkers of cardiovascular disease in healthy adults with overweight / obesity. Obesity facts. 2019;12205- . doi:10.1159/000489691				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
642	Mansour M, Nassef YE, Shady MA, Aziz AA, Malt HA. Metabolic syndrome and cardiovascular risk factors in obese adolescent. Open Access Maced J Med Sci. 2016;4(1):118-21. doi:10.3889/oamjms.2016.037	X			Country
643	Maranhao PA, Kraemer-Aguiar LG, de Oliveira CL, et al. Brazil nuts intake improves lipid profile, oxidative stress and microvascular function in obese adolescents: a randomized controlled trial. Nutr Metab (Lond). 2011;8(1):32. doi:10.1186/1743-7075-8-32		X		
644	Marchioni DM, de Oliveira MF, Carioca AAF, et al. Plasma fatty acids: Biomarkers of dietary intake?. Nutrition. 2019;59:77-82. doi:10.1016/j.nut.2018.08.008	X		X	
645	Markey O, Vasilopoulou D, Jackson KG, Todd S, Givens DI, Lovegrove JA. Postprandial lipid responses after long-term intake of dairy products varying in fatty acid composition. Ann Nutr Metab. 2017;71346- . doi:10.1159/000480486				Publication Status
646	Markey O, Vasilopoulou D, Kliem KE, et al. Plasma phospholipid fatty acid profile confirms compliance to a novel saturated fat-reduced, monounsaturated fat-enriched dairy product intervention in adults at moderate cardiovascular risk: a randomized controlled trial. Nutr J. 2017;16(1):33. doi:10.1186/s12937-017-0249-2			X	
647	Markhus MW, Rasinger JD, Malde MK, et al. Docosahexaenoic acid status in pregnancy determines the maternal docosahexaenoic acid status 3-, 6- and 12 months postpartum. Results from a longitudinal observational study. PLoS One. 2015;10(9):e0136409. doi:10.1371/journal.pone.0136409		X	X	
648	Markun S. Cardiovascular primary prevention with omega 3 fatty acids: no effect on mortality. Praxis. 2013;102(17):1076- 1077. doi:10.1024/1661-8157/a001392				Language

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
649	Martinez-Gonzalez MA, Sanchez-Tainta A, Corella D, et al. A provegetarian food pattern and reduction in total mortality in the Prevencion con Dieta Mediterranea (PREDIMED) study. Am J Clin Nutr. 2014;100(Suppl 1):320s-8s. doi:10.3945/ajcn.113.071431		X		
650	Martinez-Gonzalez MA, Toledo E, Aros F, et al. Extravirgin olive oil consumption reduces risk of atrial fibrillation: the PREDIMED (Prevencion con Dieta Mediterranea) trial. Circulation. 2014;130(1):18-26. doi:10.1161/circulationaha.113.006921		X	X	
651	Martinez-Gonzalez MA, Zazpe I, Razquin C, et al. Empirically-derived food patterns and the risk of total mortality and cardiovascular events in the PREDIMED study. Clin Nutr. 2015;34(5):859-67. doi:10.1016/j.clnu.2014.09.006		X		
652	Martino F, Martino E, Versacci P, Niglio T, Zanoni C, Puddu PE. Lifestyle and awareness of cholesterol blood levels among 29159 community school children in Italy. Nutr Metab Cardiovasc Dis. 2019;29(8):802-807. doi:10.1016/j.numecd.2019.05.060	X	X		
653	Maruyama C, Nakano R, Shima M, et al. Effects of a Japan diet intake program on metabolic parameters in middle-aged men. J Atheroscler Thromb. 2017;24(4):393-401. doi:10.5551/jat.36780	X		X	
654	Marzuki A, Arshad F, Razak TA, Jaarin K. Influence of dietary fat on plasma lipid profiles of Malaysian adolescents. Am J Clin Nutr. 1991. 53(Suppl 4):1010s-1014s. doi:10.1093/ajcn/53.4.1010S				Country
655	Maslova E, Rifas-Shiman SL, Olsen SF, Gillman MW, Oken E. Prenatal n-3 long-chain fatty acid status and offspring metabolic health in early and mid-childhood: results from Project Viva. Nutr Diabetes. 2018;8(1):29. doi:10.1038/s41387-018-0040-2				Population at Outcome
656	Mason AE, Saslow LR, Moran PJ, et al. Lipid findings from the Diabetes Education to Lower Insulin Sugars and Hunger (DELISH) Study. Nutr Metab (Lond). 2019;16:58. doi:10.1186/s12986-019-0383-2				Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
657	Masquio DC, de Piano A, Campos RM, et al. Saturated fatty acid intake can influence increase in plasminogen activator inhibitor-1 in obese adolescents. Horm Metab Res. 2014;46(4):245-51. doi:10.1055/s-0034-1370908	X			
658	Masquio DC, de Piano-Ganen A, Oyama LM, et al. The role of free fatty acids in the inflammatory and cardiometabolic profile in adolescents with metabolic syndrome engaged in interdisciplinary therapy. J Nutr Biochem. 2016;33:136-44. doi:10.1016/j.jnutbio.2016.03.017		X		
659	Mateo-Gallego R, Perez-Calahorra S, Bea AM, et al. Effects of lean red meat or lean white meat intake on the lipid profile in women: a randomized crossover study. Atheroscler Suppl. 2011;12(1):141.				Publication Status
660	Mateo-Gallego R, Perez-Calahorra S, Cenarro A, et al. Effect of lean red meat from lamb v. lean white meat from chicken on the serum lipid profile: a randomised cross-over study in women. Br J Nutr. 2012;107(10):1403-7. doi:10.1017/s0007114511004545		X		
661	Matsumoto C, Yoruk A, Wang L, Gaziano JM, Sesso HD. Fish and omega-3 fatty acid consumption and risk of hypertension. J Hypertens. 2019;37(6):1223-1229. doi:10.1097/hjh.0000000000002062			X	
662	Mayneris-Perxachs J, Bondia-Pons I, Serra-Majem L, Castellote AI, López-Sabater MC. Long-chain n-3 fatty acids and classical cardiovascular disease risk factors among the Catalan population. Food Chem. 2010;119(1):54-61. doi:10.1016/j.foodchem.2009.05.073	X			
663	Mayr H, Bendall C, Tierney A, Kingsley M, Radcliffe J, Itsiopoulos C, Thomas C. A multi-ethnic australian cohort with coronary heart disease adhere well to a Mediterranean diet intervention and improve plasma adiponectin levels. Ann Nutr Metab. 2017;71:906- 907. doi:10.1159/000480486				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
664	Mayr HL, Tierney AC, Kucianski T, Thomas CJ, Itsiopoulos C. Australian patients with coronary heart disease achieve high adherence to 6-month Mediterranean diet intervention: preliminary results of the AUSMED Heart Trial. Nutrition. 2019;61:21-31. doi:10.1016/j.nut.2018.10.027			X	Health Status
665	Mazidi M, Pennathur S, Afshinnia F. Link of dietary patterns with metabolic syndrome: analysis of the National Health and Nutrition Examination Survey. Nutr Diabetes. 2017;7(3): e255. doi:10.1038/nutd.2017.11	X			
666	Mazza E, Ferro Y, Lamprinoudi T, et al. Relationship between high sodium and low PUFA intake and carotid atherosclerosis in elderly women. Exp Gerontol. 2018;108256-261. doi:10.1016/j.exger.2018.05.004	X			
667	McCaffery JM, Poque-Geile MF, Muldoon MF, Debski TT, Wing RR, Manuck SB. The nature of the association between diet and serum lipids in the community: a twin study. Health Psychol. 2001. 20(5):341-50. doi:10.1037//0278-6133.20.5.341	X			
668	McEneny J, McPherson P, Spence M, et al. Does a diet high or low in fat influence the oxidation potential of VLDL, LDL and HDL subfractions?. Nutr Metab Cardiovasc Dis. 2013;23(7):612-8. doi:10.1016/j.numecd.2011.12.007		X		
669	McKay DL, Chen CY, Yeum KJ, Matthan NR, Lichtenstein AH, Blumberg JB. Chronic and acute effects of walnuts on antioxidant capacity and nutritional status in humans: a randomized, cross-over pilot study. Nutr J. 2010;9:21. doi:10.1186/1475-2891-9-21		X		
670	Medenwald D, Kluttig A, Lacruz ME, Schumann J. Serum dietary fatty acids and coronary heart disease risk - A nested case-control-study within the CARLA cohort. Nutr Metab Cardiovasc Dis. 2019;29(2):152-158. doi:10.1016/j.numecd.2018.10.006	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
671	Meier T, Grafe K, Senn F, et al. Cardiovascular mortality attributable to dietary risk factors in 51 countries in the WHO European Region from 1990 to 2016: a systematic analysis of the Global Burden of Disease Study. Eur J Epidemiol. 2019;34(1):37-55. doi:10.1007/s10654-018-0473-x	X	X		
672	Melanson KJ, Summers A, Nguyen V, et al. Body compositiondietary composition and components of metabolic syndrome in overweight and obese adults after a 12-week trial on dietary treatments focused on portion control, energy density, or glycemic index. Nutr J. 2012;11(57). doi:10.1186/1475-2891-11-57		X		
673	Mellendick K, Shanahan L, Wideman L, Calkins S, Keane S, Lovelady C. Diets rich in fruits and vegetables are associated with lower cardiovascular disease risk in adolescents. Nutrients. 2018;10(2):E136. doi:10.3390/nu10020136	X	X		
674	Meng H, Matthan NR, Wu D, et al. Comparison of diets enriched in stearic, oleic, and palmitic acids on inflammation, immune response, cardiometabolic risk factors, and fecal bile acid concentrations in mildly hypercholesterolemic postmenopausal women-randomized crossover trial. Am J Clin Nutr. 2019;110(2):305-315. doi:10.1093/ajcn/nqz095		X		Health Status
675	Menotti A, Kromhout D, Puddu PE, et al. Baseline fatty acids food groups a diet score and 50-year all-cause mortality rates. An ecological analysis of the Seven Countries Study. Ann Med. 2017;49(8):718-727. doi:10.1080/07853890.2017.1372622			X	
676	Mente A, Dehghan M, Rangarajan S, et al. Association of dietary nutrients with blood lipids and blood pressure in 18 countries: a cross-sectional analysis from the PURE study. Lancet Diabetes Endocrinol. 2017;5(10):774-787. doi:10.1016/s2213-8587(17)30283-8	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
677	Merino J, Sala-Vila A, Kones R, et al. Increasing long-chain n-3PUFA consumption improves small peripheral artery function in patients at intermediate-high cardiovascular risk. J Nutr Biochem. 2014;25(6):642-6. doi:10.1016/j.jnutbio.2014.02.004			X	
678	Mertens E, Markey O, Geleijnse JM, Givens DI, Lovegrove JA. Dietary patterns in relation to cardiovascular disease incidence and risk markers in a middle-aged British male population: data from the Caerphilly Prospective Study. Nutrients. 2017;9(1): pii: E75. doi:10.3390/nu9010075		X		
679	Metkus TS, Dobrosielski D, Stewart K. Effect of a low carbohydrate versus a low fat diet on the metabolic syndrome. J Am Coll Cardiol. 2012;59(13 Suppl 1):e1753. doi: 10.1016/s0735-1097(12)61754-9				Publication Status
680	Micha R, Penalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association between dietary factors and mortality from heart disease, stroke and type 2 diabetes in the United States. JAMA. 2017;317(9):912-924. doi:10.1001/jama.2017.0947	X			
681	Mielgo-Ayuso J, Collado PS, Urdampilleta A, Martinez-Sanz JM, Seco J. Changes induced by diet and nutritional intake in the lipid profile of female professional volleyball players after 11 weeks of training. J Int Soc Sports Nutr. 2013;10(1):55. doi:10.1186/1550-2783-10-55		X		
682	Mietus-Snyder M, Baker AL, Neufeld EJ, et al. Effects of nutritional counseling on lipoprotein levels in a pediatric lipid clinic. Am J Dis Child. 1993. 147(4):378-81. doi:10.1001/archpedi.1993.02160280028012	X	X		
683	Miglani N, Bains K, Singh P. Diet and physical activity in relation to metabolic syndrome among urban Indian men and women. Ecol Food Nutr. 2015;54(1):43-56. doi:10.1080/03670244.2014.947403	X			Country

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
684	Mikkila V, Rasanen L, Raitakari OT, et al. Major dietary patterns and cardiovascular risk factors from childhood to adulthood. The Cardiovascular Risk in Young Finns Study. Br J Nutr. 2007. 98(1):218-25. doi:10.1017/s0007114507691831		X		
685	Milajerdi A, Shakeri F, Keshteli AH, et al. Dietary total antioxidant capacity in relation to stroke among Iranian adults. Nutr Neurosci. 2019;1-6. doi:10.1080/1028415x.2018.1520478	X	X		
686	Miller C, Karimi R, Silbernagel S, et al. Mercury, omega-3 fatty acids and seafood intake are not associated with heart rate variability or QT interval. Arch Environ Occup Health. 2018;73(4):251-257. doi:10.1080/19338244.2017.1315360	X			
687	Miller ER, Cooper LA, Carson KA, et al. A dietary intervention in urban African Americans: results of the "Five Plus Nuts and Beans" randomized trial. Am J Prev Med. 2016;50(1):87- 95. doi:10.1016/j.amepre.2015.06.010		X		
688	Min C, Noh H, Kang YS, et al. Skipping breakfast is associated with diet quality and metabolic syndrome risk factors of adults. Nutr Res Pract. 2011;5(5):455-63. doi:10.4162/nrp.2011.5.5.455	X	X		
689	Minoura A, Wang DH, Sato Y, et al. Association of dietary fat and carbohydrate consumption and predicted ten-year risk for developing coronary heart disease in a general Japanese population. Acta Med Okayama. 2014;68(3):129-35. doi:10.18926/amo/52652	X			
690	Mirmiran P, Asghari G, Farhadnejad H, Eslamian G, Hosseini-Esfahani F, Azizi F. Low carbohydrate diet is associated with reduced risk of metabolic syndrome in Tehranian adults. Int J Food Sci Nutr. 2017;68(3):358-365. doi:10.1080/09637486.2016.1242119		X		
691	Mirmiran P, Yousefi R, Mottaghi A, Azizi F. Advanced glycation end products and risk of hypertension in Iranian adults: Tehran lipid and glucose study. J Res Med Sci. 2018;23:43. doi:10.4103/jrms.JRMS_982_17		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
692	Mitra SR, Tan PY, Amini F. Association of ADRB2 rs1042713 with obesity and obesity-related phenotypes and its interaction with dietary fat in modulating Glycaemic Indices in Malaysian Adults. J Nutr Metab. 2019;2019:8718795. doi:10.1155/2019/8718795	X			
693	Miura K, Stamler J, Brown IJ, et al. Relationship of dietary monounsaturated fatty acids to blood pressure: the International Study of Macro/Micronutrients and Blood Pressure. J Hypertens. 2013;31(6):1144- 1150. doi:10.1097/HJH.0b013e3283604016	X			
694	Mize CE, Uauy R, Kramer R, Benser M, Allen S, Grundy SM. Lipoprotein-cholesterol responses in healthy infants fed defined diets from ages 1 to 12 months: comparison of diets predominant in oleic acid versus linoleic acidwith parallel observations in infants fed a human milk-based diet. J Lipid Res. 1995. 36(6):1178-87.		X		
695	Mohammadifard N, Hosseini M, Sajjadi F, Maghroun M, Boshtam M, Nouri F. Comparison of effects of soft margarine, blended, ghee, and unhydrogenated oil with hydrogenated oil on serum lipids: A randomized clinical trail. ARYA Atheroscler. 2013;9(6):363-71.		X		
696	Mohammadifard N, Nazem M, Naderi GA, et al. Effect of hydrogenated, liquid and ghee oils on serum lipids profile. ARYA Atheroscler. 2010;6(1):16-22.		X		
697	Mohammadifard N, Talaei M, Sadeghi M, et al. Dietary patterns and mortality from cardiovascular disease: Isfahan Cohort Study. Eur J Clin Nutr. 2017;71(2):252- 258. doi:10.1038/ejcn.2016.170		X		Country
698	Molero-Conejo E, Morales LM, Fernandez V, et al. Lean adolescents with increased risk for metabolic syndrome. Arch Latinoam Nutr. 2003. 53(1):39-46.				Country
699	Monge R, Beita O. Prevalence of coronary heart disease risk factors in Costa Rican adolescents. J Adolesc Health. 2000. 27(3):210-7. doi:10.1016/s1054-139x(99)00017-8	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
700	Monge-Rojas R, Campos H, Fernandez Rojas X. Saturated and cis- and trans-unsaturated fatty acids intake in rural and urban Costa Rican adolescents. J Am Coll Nutr. 2005. 24(4):286-93. doi:10.1080/07315724.2005.10719476	X			
701	Montserrat-de la Paz S, Lopez S, Bermudez B, Guerrero JM, Abia R, Muriana FJ. Effects of immediate-release niacin and dietary fatty acids on acute insulin and lipid status in individuals with metabolic syndrome. J Sci Food Agric. 2018;98(6):2194-2200. doi:10.1002/jsfa.8704			X	
702	Moreno JP, Johnston CA, El-Mubasher AA, et al. Peanut consumption in adolescents is associated with improved weight status. Nutr Res. 2013;33(7):552-6. doi:10.1016/j.nutres.2013.05.005	X	X		
703	Moreno-Luna R, Munoz-Hernandez R, Miranda ML, et al. Olive oil polyphenols decrease blood pressure and improve endothelial function in young women with mild hypertension. Am J Hypertens. 2012;25(12):1299-304. doi:10.1038/ajh.2012.128		X		
704	Morgantini C, Trifiro S, Trico D, et al. A short-term increase in dietary cholesterol and fat intake affects high-density lipoprotein composition in healthy subjects. Nutr Metab Cardiovasc Dis. 2018;28(6):575-581. doi:10.1016/j.numecd.2018.03.005		X		
705	Morrison MC, Mulder P, Stavro PM, et al. Replacement of dietary saturated fat by PUFA-rich pumpkin seed oil attenuates non-alcoholic fatty liver disease and atherosclerosis development, with additional health effects of virgin over refined oil. PLoS One. 2015;10(9):e0139196. doi:10.1371/journal.pone.0139196				Non-human
706	Mossaheb N, Papageorgiou K, Schafer MR, Becker J, Schloegelhofer M, Amminger GP. Changes in triglyceride levels in ultra-high risk for psychosis individuals treated with omega-3 fatty acids. Early Interv Psychiatry. 2018;12(1):30-36. doi:10.1111/eip.12275		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
707	Mousavi SM, Milajerdi A, Pouraram H, et al. Adherence to alternative Healthy Eating Index (AHEI-2010) is not associated with risk of stroke in Iranian adults: a case-control study. Int J Vitam Nutr Res. 2019;1-8. doi:10.1024/0300-9831/a000603	X			
708	Mozaffarian D, Appel LJ, Van Horn L. Components of a cardioprotective diet: New insights. Circulation. 2011;123(24):2870-2891. doi:10.1161/circulationaha.110.968735	X			
709	Mueller C, Masri B, Hogg J, Mastrogiacomo M, Chiu YL. Carbohydrate- vs fat-controlled diet effect on weight loss and coronary artery disease risk: a pilot feeding study. Nutr Clin Pract. 2010;25(5):542-7. doi:10.1177/0884533610379854		X		
710	Mueller NT. Effects of macronutrients on serum short chain fatty acids (SCFA): results from the optimal macro-nutrient intake to prevent heart disease (OmniHeart) trial. Circulation. 2019;139. doi:10.1161/circ.139.suppl_1.MP68				Publication Status
711	Muka T, Blekkenhorst LC, Lewis JR, et al. Dietary fat compositiontotal body fat and regional body fat distribution in two Caucasian populations of middle-aged and older adult women. Clin Nutr. 2017;36(5):1411-1419. doi:10.1016/j.clnu.2016.09.018			X	
712	Mytton OT, Forouhi NG, Scarborough P, et al. Association between intake of less-healthy foods defined by the United Kingdom's nutrient profile model and cardiovascular disease: a population-based cohort study. PLoS Med. 2018;15(1):e1002484. doi:10.1371/journal.pmed.1002484		X		
713	Nagashree RS, Manjunath NK, Indu M, et al. Effect of a diet enriched with fresh coconut saturated fats on plasma lipids and erythrocyte fatty acid composition in normal adults. J Am Coll Nutr. 2017;36(5):330-334. doi:10.1080/07315724.2017.1280713				Country

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
714	Nakabou M, Kai T, Maeshima T, Kanamasa K. Relationship between EPA or EPA/AA and arteriosclerosis in elderly patients over 80 years old. Japanese Journal of Geriatrics. 2011;48(6):672-678. doi:10.3143/geriatrics.48.672				Language
715	Nakamura Y, Okuda N, Turin TC, et al. Fatty acids intakes and serum lipid profiles: NIPPON DATA90 and the national nutrition monitoring. J Epidemiol. 2010;20(Suppl 3):S544-8. doi:10.2188/jea.je20090223	X			
716	Nakamura Y, Ueshima H, Okuda N, et al. Relationship of three different types of low-carbohydrate diet to cardiometabolic risk factors in a Japanese population: the INTERMAP/INTERLIPID Study. Eur J Nutr. 2016;55(4):1515-24. doi:10.1007/s00394-015-0969-z		X		
717	Nakamura Y, Okuda N, Okamura T. Low-carbohydrate diets and cardiovascular and total mortality in Japanese: a 29-year follow-up of NIPPON DATA80. Br J Nutr. 2014;112(6):916-924. doi:10.1017/S0007114514001627		X		
718	Namayandeh SM, Kaseb F, Lesan S. Olive and sesame oil effect on lipid profile in hypercholesterolemic patientswhich better?. Int J Prev Med. 2013;4(9):1059-62.				Health Status
719	Navas-Carretero S, Zulet MA, Abete I, Planes J, Avellaneda A, Martinez JA. Influence on health markers of the regular consumption of anew meat product designed with an optimized nutritional profile. Annals of Nutrition and Metabolism. 2013. 63(Suppl 1):1678. doi:10.1159/000354245				Publication Status
720	Negele L, Schneider B, Ristl R, et al. Effect of a low-fat diet enriched either with rapeseed oil or sunflower oil on plasma lipoproteins in children and adolescents with familial hypercholesterolaemia. Results of a pilot study. Eur J Clin Nutr. 2015;69(3):337-43. doi:10.1038/ejcn.2014.234		X		Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
721	Nejatinamini S, Ataie-Jafari A, Ghasemian A, et al. Burden of ischemic heart disease attributable to low omega-3 fatty acids intake in Iran: findings from the Global Burden of Disease Study 2010. J Tehran Heart Cent. 2016;11(1):21-9.	X			
722	Nettleton JA, Brouwer IA, Geleijnse JM, Hornstra G. Saturated fat consumption and risk of coronary heart disease and ischemic stroke: a science update. Ann Nutr Metab. 2017;70(1):26-33. doi:10.1159/000455681	X			
723	Neuhouser ML, Howard B, Lu J, et al. A low-fat dietary pattern and risk of metabolic syndrome in postmenopausal women: the Women's Health Initiative. Metabolism. 2012;61(11):1572-81. doi:10.1016/j.metabol.2012.04.007		X		
724	Neville MM, Geppert J, Min Y, Grimble G, Crawford MA, Ghebremeskel K. Dietary fat intake body composition and blood lipids of university men and women. Nutr Health. 2012;21(3):173-85. doi:10.1177/0260106012467242	X			
725	Ng CPS, Kwok JSL, Zhou J, Cheung PYB, Tzang LCH, Sundaram S. Effect of whole grains and unsaturated fatty acids dietary intervention on health in Hong Kong overweight population. Gut. 2018;67(Suppl 2):A71. doi:10.1136/gutjnl-2018-IDDFabstracts.153				Publication Status
726	Nicklas JM, Sacks FM, Smith SR, et al. Effect of dietary composition of weight loss diets on high-sensitivity c-reactive protein: the Randomized POUNDS LOST trial. Obesity (Silver Spring). 2013;21(4):681-9. doi:10.1002/oby.20072		X		
727	Nicklas TA, O'Neil CE, Fulgoni VL 3rd. Snacking patterns diet quality, and cardiovascular risk factors in adults. BMC Public Health. 2014;14:388. doi:10.1186/1471-2458-14-388	X		X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
728	Nieman DC, Gillitt N, Jin F, et al. Chia seed supplementation and disease risk factors in overweight women: a metabolomics investigation. J Altern Complement Med. 2012;18(7):700-8. doi:10.1089/acm.2011.0443		X		
729	Nieman KM, Maki KC, Palacios OM, Lindner E, Huebner M, Sorce J. Replacement of refined carbohydrates with a combination of egg protein and unsaturated fatty acids: effects on lipoprotein particle concentrations and LDL peak size in adults with elevated triglycerides. FASEB journal. 2017;31(Suppl 1).				Publication Status
730	Niinikoski H, Pahkala K, Viikari J, et al. The STRIP Study: long-Term Impact of a Low Saturated Fat/Low Cholesterol Diet. Current cardiovascular risk reports. 2014;8(11):1- 7. doi:10.1007/s12170-014-0410-9	X			Duplicate data
731	Niinikoski H, Viikari J, Ronnemaa T, et al. Prospective randomized trial of low-saturated-fat, low-cholesterol diet during the first 3 years of life. The STRIP baby project. Circulation. 1996. 94(6):1386-93. doi:10.1161/01.cir.94.6.1386				Duplicate data
732	Nilsen R, Hostmark AT, Haug A, Skeie S. Effect of a high intake of cheese on cholesterol and metabolic syndrome: results of a randomized trial. Food Nutr Res. 2015;59:27651. doi:10.3402/fnr.v59.27651		X		
733	Niswender KD, Fazio S, Gower BA, Silver HJ. Balanced high fat diet reduces cardiovascular risk in obese women although changes in adipose tissue, lipoproteins, and insulin resistance differ by race. Metabolism. 2018;82:125-134. doi:10.1016/j.metabol.2018.01.020	X	X		
734	Nordgren TM, Anderson Berry A, Van Ormer M, et al. Omega-3 fatty acid supplementation, pro-resolving mediators, and clinical outcomes in maternal-infant pairs. Nutrients. 2019;11(1). pii: E98. doi:10.3390/nu11010098		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
735	Normia J, Laitinen K, Isolauri E, Poussa T, Jaakkola J, Ojala T. Impact of intrauterine and post-natal nutritional determinants on blood pressure at 4 years of age. J Hum Nutr Diet. 2013;26(6):544-52. doi:10.1111/jhn.12115	X	X		
736	Noto D, Fayer F, Cefalu AB, et al. Myristic acid is associated to low plasma HDL cholesterol levels in a Mediterranean population and increases HDL catabolism by enhancing HDL particles trapping to cell surface proteoglycans in a liver hepatoma cell model. Atherosclerosis. 2016;246:50-6. doi:10.1016/j.atherosclerosis.2015.12.036		X		
737	Nybacka A, Hellstrom PM, Hirschberg AL. Increased fibre and reduced trans fatty acid intake are primary predictors of metabolic improvement in overweight polycystic ovary syndrome-substudy of randomized trial between diet, exercise and diet plus exercise for weight control. Clin Endocrinol (Oxf). 2017;87(6):680-688. doi:10.1111/cen.13427		X		
738	Nykanen T, Pihlainen K, Santtila M, Vasankari T, Fogelholm M, Kyrolainen H. Diet macronutrient composition, physical activity, and body composition in soldiers during 6 months deployment. Mil Med. 2019;184(3-4):e231-e237. doi:10.1093/milmed/usy232			X	
739	O'Connor J, Steinbeck K, Hill A, et al. Evaluation of a community-based weight management program for overweight and obese adolescents: the Loozit study. Nutrition & Dietetics. 2008. 65(2):121-127.		X		
740	O'Connor LE, Paddon-Jones D, Wright AJ, Campbell WW. A Mediterranean-style eating pattern with lean unprocessed red meat has cardiometabolic benefits for adults who are overweight or obese in a randomized, crossover, controlled feeding trial. American Journal of Clinical Nutrition. 2018;108(1):33-40. doi:10.1093/ajcn/nqy075		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
741	Okburan G, Mercanligil SM. Effects of walnut consumption on blood lipids and lipoproteins in hyperlipidemic individuals. Clinical Nutrition. 2016. 35(Suppl 1):S83. doi:10.1016/S0261-5614(16)30448-4				Publication Status
742	Oliveira-de-Lira L, Santos EMC, de Souza RF, et al. Supplementation-dependent effects of vegetable oils with varying fatty acid compositions on anthropometric and biochemical parameters in obese women. Nutrients. 2018;10(7): pii: E932. doi:10.3390/nu10070932		X		
743	Oliver MF. Free fatty acids and acute coronary syndromes--the history. QJM. 2011;104(7):625-7. doi:10.1093/qjmed/hcr016	X			
744	Omega-3 fatty acid supplements and cardiovascular disease. Drug Ther Bull. 2018;56(4):39. doi:10.1136/dtb.2018.4.0606	X			
745	O'Neil CE, Nicklas TA, Myers L, Johnson CC, Berenson GS. Cardiovascular risk factors and behavior lifestyles of young women: implications from findings of the Bogalusa Heart Study. Am J Med Sci. 1997. 314(6):385-95. doi:10.1097/00000441-199712000-00005	X			
746	Oranta O, Pahkala K, Ruottinen S, et al. Infancy-onset dietary counseling of low-saturated-fat diet improves insulin sensitivity in healthy adolescents 15-20 years of age: the Special Turku Coronary Risk Factor Intervention Project (STRIP) study. Diabetes Care. 2013;36(10):2952-9. doi:10.2337/dc13-0361			X	
747	Orem A, Yucesan FB, Orem C, et al. Hazelnut-enriched diet improves cardiovascular risk biomarkers beyond a lipid-lowering effect in hypercholesterolemic subjects. J Clin Lipidol. 2013;7(2):123-31. doi:10.1016/j.jacl.2012.10.005				Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
748	Ortega JF, Morales-Palomo F, Fernandez-Elias V, et al. Dietary supplementation with omega-3 fatty acids and oleate enhances exercise training effects in patients with metabolic syndrome. Ob. 2016;24(8):1704-11. doi:10.1002/oby.21552		X		
749	Ortega RM, Requejo AM, Navia B, et al. Effect of saturated fatty acid consumption on energy and nutrient intake and blood lipid levels in preschool children. Ann Nutr Metab. 2001. 45(3):121-7. doi:10.1159/000046717	X			
750	Ortega RM, Requejo AM, Navia B, et al. The consumption of milk products in a group of pre-school children: influence on serum lipid profile. Nutrition Research. 2000. 20(6):779-790. doi:10.1016/S0271-5317(00)00175-5		X		
751	Ortiz RM, Garcia S, Kim AD. Is almond consumption more effective than reduced dietary saturated fat at decreasing plasma total cholesterol and LDL-c Levels? A theoretical approach. J Nutr Metab. 2012;2012:265712. doi:10.1155/2012/265712	X			
752	O'Sullivan TA, Ambrosini GL, Mori TA, Beilin LJ, Oddy WH. Omega-3 Index correlates with healthier food consumption in adolescents and with reduced cardiovascular disease risk factors in adolescent boys. Lipids. 2011;46(1):59-67. doi:10.1007/s11745-010-3499-8	X	X		
753	O'Sullivan TA, Bremner AP, Mori TA, et al. Regular fat and reduced fat dairy products show similar associations with markers of adolescent cardiometabolic health. Nutrients. 2016;8(1): pii: E22. doi:10.3390/nu8010022		X		
754	Otsuka R, Tange C, Nishita Y, et al. Fish and meat intake, serum eicosapentaenoic acid and docosahexaenoic acid levels, and mortality in community-dwelling Japanese older persons. Int J Environ Res Public Health. 2019;16(10): pii: E1806. doi:10.3390/ijerph16101806			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
755	Otten J, Mellberg C, Ryberg M, et al. Strong and persistent effect on liver fat with a Paleolithic diet during a two-year intervention. Int J Obes (Lond). 2016;40(5):747-53. doi:10.1038/ijo.2016.4		X	X	
756	Oudin A, Wennberg M. Fish consumption and ischemic stroke in southern Sweden. Nutr J. 2011;10109. doi:10.1186/1475-2891-10-109		X		
757	Oyri LKL, Narverud I, Bogsrud MP, et al. Postprandial changes in gene expression of cholesterol influx and efflux mediators after intake of SFA compared with n-6 PUFA in subjects with and without familial hypercholesterolaemia: secondary outcomes of a randomised controlled trial. J Nutr Sci. 2019;8:e27. doi:10.1017/jns.2019.25	X		X	
758	Pagliai G, Russo E, Niccolai E, et al. Influence of a 3-month low-calorie Mediterranean diet compared to the vegetarian diet on human gut microbiota and SCFA: the CARDIVEG Study. Eur J Nutr. 2019;doi:10.1007/s00394-019-02050-0			X	
759	Pahkala K, Hietalampi H, Laitinen TT, et al. Ideal cardiovascular health in adolescence: effect of lifestyle intervention and association with vascular intima-media thickness and elasticity (the Special Turku Coronary Risk Factor Intervention Project for Children [STRIP] study). Circulation. 2013;127(21):2088-96. doi:10.1161/circulationaha.112.000761		X	X	
760	Palazhy S, Kamath P, Rajesh PC, Vaidyanathan K, Nair SK, Vasudevan DM. Composition of plasma and atheromatous plaque among coronary artery disease subjects consuming coconut oil or sunflower oil as the cooking medium. J Am Coll Nutr. 2012;31(6):392-6. doi:10.1080/07315724.2012.10720464			X	Country
761	Paletas K, Athanasiadou E, Sarigianni M, et al. The protective role of the Mediterranean diet on the prevalence of metabolic syndrome in a population of Greek obese subjects. J Am Coll Nutr. 2010;29(1):41-5. doi:10.1080/07315724.2010.10719815	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
762	Pałkowska E, Bartnikowska E, Owsiak D. The use of low-caloric diet with modified fatty acids pool in the therapy of the metabolic syndrome. Rocz Panstw Zakl Hig. 2012;63(2):163- 169.				Language
763	Pang D, Allman-Farinelli MA, Wong T, Barnes R, Kingham KM. Replacement of linoleic acid with alpha-linolenic acid does not alter blood lipids in normolipidaemic men. Br J Nutr. 1998. 80(2):163-7.				Age of participants at intervention or exposure
764	Pang SJ, Jia SS, Man QQ, et al. Dietary cholesterol in the elderly Chinese population: an analysis of CNHS 2010-2012. Nutrients. 2017;9(9). pii: E934. doi:10.3390/nu9090934	X			
765	Paniagua JA, Perez-Martinez P, Gjelstad IM, et al. A low-fat high-carbohydrate diet supplemented with long-chain n-3 PUFA reduces the risk of the metabolic syndrome. Atherosclerosis. 2011;218(2):443-50. doi:10.1016/j.atherosclerosis.2011.07.003				Duplicate data
766	Paoli A, Cenci L, Grimaldi KA. Effect of ketogenic Mediterranean diet with phytoextracts and low carbohydrates/high-protein meals on weight, cardiovascular risk factorsbody composition and diet compliance in Italian council employees. Nutr J. 2011;10112. doi:10.1186/1475-2891-10-112		X		
767	Papadaki A, Martinez-Gonzalez MA, Alonso-Gomez A, et al. Mediterranean diet and risk of heart failure: results from the PREDIMED randomized controlled trial. Eur J Heart Fail. 2017;19(9):1179-1185. doi:10.1002/ejhf.750		X		
768	Papandreou D, Karabouta Z, Rousso I. Are dietary cholesterol intake and serum cholesterol levels related to nonalcoholic Fatty liver disease in obese children?. Cholesterol. 2012;doi: 10.1155/2012/572820	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
769	Paquet C, Propsting SL, Daniel M. Total n-3 fatty acid and SFA intakes in relation to insulin resistance in a Canadian First Nation at risk for the development of type 2 diabetes. Public Health Nutr. 2014;17(6):1337-41. doi:10.1017/s1368980013000542	X		X	
770	Park BS, Ryu CM, Ahn YS, Park SO. The consumption of low animal food with low n-6/n-3 ratio reduce LDL cholesterol in humans. Res J Med Sci. 2012;6(3):107-112. doi:10.3923/rjmsci.2012.107.112			X	Study Duration
771	Park JE, Miller M, Rhyne J, Wang Z, Hazen SL. Differential effect of short-term popular diets on TMAO and other cardio-metabolic risk markers. Nutr Metab Cardiovasc Dis. 2019;29(5):513-517. doi:10.1016/j.numecd.2019.02.003			X	
772	Park JK, Koehler KM. Probabilistic quantitative assessment of coronary heart disease risk from dietary exposure to industrially-produced trans fatty acids in partially hydrogenated oils. Toxicol Sci. 2019;171(1):213-224. doi:10.1093/toxsci/kfz170	X	X		
773	Park S, Kim DS, Kang S. Carrying minor allele of FADS1 and haplotype of FADS1 and FADS2 increased the risk of metabolic syndrome and moderate but not low fat diets lowered the risk in two Korean cohorts. Eur J Nutr. 2019;58(2):831-842. doi:10.1007/s00394-018-1719-9	X			
774	Park Y, Oh SH, Rhee MY. Association between 24-hour ambulatory blood pressure and erythrocyte n-3 polyunsaturated fatty acids in Korean subjects with hypertension. Nutr Res. 2010;30(12):807-14. doi:10.1016/j.nutres.2010.09.013	X			
775	Parletta N, Zarnowiecki D, Cho J, et al. A Mediterranean-style dietary intervention supplemented with fish oil improves diet quality and mental health in people with depression: a randomized controlled trial (HELFIMED). Nutr Neurosci. 2019;22(7):474-487. doi:10.1080/1028415x.2017.1411320			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
776	Pavithra N, Bannikoppa PS, Uthappa S, Kurpad AV, Mani I. Plasma fatty acid composition and estimated desaturase activities reflect dietary patterns in subjects with metabolic syndrome. Indian J Clin Biochem. 2018;33(3):290-296. doi:10.1007/s12291-017-0674-1		X		Country
777	Pawelczyk T, Trafalska E, Kotlicka-Antczak M, Pawelczyk A. The association between polyunsaturated fatty acid consumption and the transition to psychosis in ultra-high risk individuals. Prostaglandins Leukot Essent Fatty Acids. 2016;108:30-7. doi:10.1016/j.plefa.2016.03.010			X	Health Status
778	Pegington M, Evans DG, Howell A, et al. Lifestyle behaviours and health measures of women at increased risk of breast cancer taking chemoprevention. Eur J Cancer Prev. 2019;28(6):500-506. doi:10.1097/cej.0000000000000493		X	X	
779	Pei R, DiMarco DM, Putt KK, et al. Low-fat yogurt consumption reduces biomarkers of chronic inflammation and inhibits markers of endotoxin exposure in healthy premenopausal women: a randomised controlled trial. Br J Nutr. 2017;118(12):1043-1051. doi:10.1017/s0007114517003038		X	X	
780	Pellizzer AM, Straznicky NE, Lim S, Kamen PW, Krum H. Reduced dietary fat intake increases parasympathetic activity in healthy premenopausal women. Clin Exp Pharmacol Physiol. 1999. 26(8):656-60. doi:10.1046/j.1440-1681.1999.03103.x		X		
781	Penedo LA, Nunes JC, Gama MA, Leite PE, Quirico-Santos TF, Torres AG. Intake of butter naturally enriched with cis9,trans11 conjugated linoleic acid reduces systemic inflammatory mediators in healthy young adults. J Nutr Biochem. 2013;24(12):2144-51. doi:10.1016/j.jnutbio.2013.08.006		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
782	Perelman D, Coghlan N, Lamendola C, Carter S, Abbasi F, McLaughlin T. Substituting poly- and mono-unsaturated fat for dietary carbohydrate reduces hyperinsulinemia in women with polycystic ovary syndrome. Gynecol Endocrinol. 2017;33(4):324-327. doi:10.1080/09513590.2016.1259407			X	Study Duration
783	Perez-Cornago A, Brennan L, Ibero-Baraibar I, et al. Metabolomics identifies changes in fatty acid and amino acid profiles in serum of overweight older adults following a weight loss intervention. J Physiol Biochem. 2014;70(2):593-602. doi:10.1007/s13105-013-0311-2		X	X	
784	Perez-Heras AM, Mayneris-Perxachs J, Cofan M, et al. Long-chain n-3 PUFA supplied by the usual diet decrease plasma stearoyl-CoA desaturase index in non-hypertriglyceridemic older adults at high vascular risk. Clin Nutr. 2018;37(1):157-162. doi:10.1016/j.clnu.2016.11.009			X	
785	Perichart-Perera O, Balas-Nakash M, Rodriguez-Cano A, et al. Correlates of dietary energy sources with cardiovascular disease risk markers in Mexican school-age children. J Am Diet Assoc. 2010;110(2):253-60. doi:10.1016/j.jada.2009.10.031	X	X		
786	Perona JS, Covas MI, Fito M, Cabello-Moruno R, Aros F, Corella D, Ros E, Garcia M, Estruch R, Martinez-Gonzalez MA, Ruiz-Gutierrez V. Reduction in systemic and VLDL triacylglycerol concentration after a 3-month Mediterranean-style diet in high-cardiovascular-risk subjects. J Nutr Biochem. 2010;21(9):892-8. doi:10.1016/j.jnutbio.2009.07.005		X		
787	Perry AC, Tremblay LM, Signorile JF, Kaplan TA, Miller PC. Fitness diet and coronary risk factors in a sample of southeastern U.S. children. Appl Human Sci. 1997. 16(4):133-41.	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
788	Pertiwi K, Kok DE, Wanders AJ, de Goede J, Zock PL, Geleijnse JM. Circulating n-3 fatty acids and linoleic acid as indicators of dietary fatty acid intake in post-myocardial infarction patients. Nutr Metab Cardiovasc Dis. 2019;29(4):343-350. doi:10.1016/j.numecd.2018.12.010	X			Health Status
789	Petrogianni M, Grammatikaki E, Kalogeropoulos N, et al. Additional benefit in CVD risk indices derived from the consumption of fortified milk when combined with a lifestyle intervention. Public Health Nutr. 2014;17(2):440-9. doi:10.1017/s1368980012005265		X		Health Status
790	Phillips CM, Kesse-Guyot E, Ahluwalia N, et al. Dietary fat abdominal obesity and smoking modulate the relationship between plasma complement component 3 concentrations and metabolic syndrome risk. Atherosclerosis. 2012;220(2):513-9. doi:10.1016/j.atherosclerosis.2011.11.007		X	X	
791	Pieters DJ, Zock PL, Fuchs D, Mensink RP. Effect of alpha-linolenic acid on 24-h ambulatory blood pressure in untreated high-normal and stage I hypertensive subjects. Br J Nutr. 2019;121(2):155-163. doi:10.1017/s0007114518003094			X	
792	Pignitter M, Lindenmeier M, Andersen G, et al. Effect of 1- and 2-month high-dose alpha-linolenic acid treatment on (13) C-labeled alpha-linolenic acid incorporation and conversion in healthy subjects. Mol Nutr Food Res. 2018;62(20):e1800271. doi:10.1002/mnfr.201800271			X	
793	Pihlajamaki JA, Schwab U, Kaminska D, et al. Dietary polyunsaturated fatty acids and the Pro12Ala polymorphisms of PPARG regulate serum lipids through divergent pathways: a randomised crossover clinical trial. Diabetologia. 2013. 56(Suppl 1):S154. doi:10.1007/s00125-013-3012-z				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
794	Pilis K, Pilis A, Stec K, et al. Three-year chronic consumption of low-carbohydrate diet impairs exercise performance and has a small unfavorable effect on lipid profile in middle-aged men. Nutrients. 2018;10(12):pii:E1914. doi:10.3390/nu10121914	X	X		
795	Pinto X, Fanlo-Maresma M, Corbella E, et al. A Mediterranean diet rich in extra-virgin olive oil is associated with a reduced prevalence of nonalcoholic fatty liver disease in older individuals at high cardiovascular risk. J Nutr. 2019;149(11):1920-1929. doi:10.1093/jn/nxz147		X	X	
796	Pintus S, Murru E, Carta G, et al. Sheep cheese naturally enriched in alpha-linolenic, conjugated linoleic and vaccenic acids improves the lipid profile and reduces anandamide in the plasma of hypercholesterolaemic subjects. Br J Nutr. 2013;109(8):1453-62. doi:10.1017/s0007114512003224		X		
797	Pisinger C, Jacobsen RK, Jørgensen T. Final results from one of world's largest population-based randomized interventions on lifestyle. The Inter99 study. Circulation. 2013;127(12)				Publication Status
798	Polley KR, Oswell NJ, Pegg RB, Paton CM, Cooper JA. A 5-day high-fat diet rich in cottonseed oil improves cholesterol profiles and triglycerides compared to olive oil in healthy men. Nutr Res. 2018;60:43-53. doi:10.1016/j.nutres.2018.09.001			X	Study Duration
799	Polychronopoulos E, Pounis G, Bountziouka V, et al. Dietary meat fats and burden of cardiovascular disease risk factors, in the elderly: a report from the MEDIS study. Lipids Health Dis. 2010;9:30. doi:10.1186/1476-511x-9-30	X			
800	Porkka KV, Raitakari OT, Leino A, et al. Trends in serum lipid levels during 1980-1992 in children and young adults. The Cardiovascular Risk in Young Finns Study. Am J Epidemiol. 1997. 146(1):64-77. doi:10.1093/oxfordjournals.aje.a009192	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
801	Praagman J, Franco OH, Ikram MA, et al. Dairy products and the risk of stroke and coronary heart disease: the Rotterdam Study. Eur J Nutr. 2015;54(6):981-90. doi:10.1007/s00394-014-0774-0		X		
802	Pranger IG, Corpeleijn E, Muskiet FAJ, Kema IP, Singh-Povel C, Bakker SJL. Circulating fatty acids as biomarkers of dairy fat intake: data from the lifelines biobank and cohort study. Biomarkers. 2019;24(4):360-372. doi:10.1080/1354750x.2019.1583770	X	X		
803	Prentice RL, Aragaki AK, Howard BV, et al. Low-fat dietary pattern among postmenopausal women influences long-term cancer cardiovascular disease and diabetes outcomes. J Nutr. 2019;149(9):1565-1574. doi:10.1093/jn/nxz107		X		
804	Prentice RL, Aragaki AK, Van Horn L, et al. Low-fat dietary pattern and cardiovascular disease: results from the Women's Health Initiative randomized controlled trial. Am J Clin Nutr. 2017;106(1):35-43. doi:10.3945/ajcn.117.153270		X		
805	Properzi C, Sullivan T, Sherriff J, et al. Ad libitum Mediterranean and low fat diets both significantly reduce hepatic steatosis: a randomized controlled trial. Hepatol Int. 2018;12(2):S232. doi:10.1007/s12072-018-9852-3				Publication Status
806	Pu S, Rodriguez-Perez C, Ramprasath VR, Segura-Carretero A, Jones PJ. Dietary high oleic canola oil supplemented with docosahexaenoic acid attenuates plasma proprotein convertase subtilisin kexin type 9 (PCSK9) levels in participants with cardiovascular disease risk: a randomized control trial. Vascul Pharmacol. 2016;87:60-65. doi:10.1016/j.vph.2016.06.007			X	Duplicate data
807	Quintanilha BJ, Pinto Ferreira LR, Ferreira FM, Neto EC, Sampaio GR, Rogero MM. Circulating plasma microRNAs dysregulation and metabolic endotoxemia induced by a high-fat high-saturated diet. Clin Nutr. 2019;39(2):554-562. doi:10.1016/j.clnu.2019.02.042		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
808	Quivers ES, Driscoll DJ, Garvey CD, et al. The effects of diet on serum cholesterol in children. Ann N Y Acad Sci. 1991. 623:133-4. doi:10.1111/j.1749-6632.1991.tb43724.x	X	X		
809	Raatz SK, Johnson LK, Rosenberger TA, Picklo MJ. Twice weekly intake of farmed Atlantic salmon (Salmo salar) positively influences lipoprotein concentration and particle size in overweight men and women. Nutr Res. 2016;36(9):899-906. doi:10.1016/j.nutres.2016.06.011		X		
810	Radtke T, Schmid A, Trepp A, et al. Short-term effects of trans fatty acids from ruminant and industrial sources on surrogate markers of cardiovascular risk in healthy men and women: a randomized, controlled, double-blind trial. Eur J Prev Cardiol. 2017;24(5):534-543. doi:10.1177/2047487316680691		X		
811	Raitakari OT, Porkka KV, Rasanen L, Ronnemaa T, Viikari JS. Clustering and six year cluster-tracking of serum total cholesterol, HDL-cholesterol and diastolic blood pressure in children and young adults. The Cardiovascular Risk in Young Finns Study. J Clin Epidemiol. 1994. 47(10):1085-93. doi:10.1016/0895-4356(94)90094-9	X		X	
812	Raitakari OT, Porkka KV, Rasanen L, Viikari JS. Relations of life-style with lipids, blood pressure and insulin in adolescents and young adults. The Cardiovascular Risk in Young Finns Study. Atherosclerosis. 1994. 111(2):237-46. doi:10.1016/0021-9150(94)90098-1	X			
813	Rajaie S, Azadbakht L, Khazaei M, Esmaillzadeh A. Effects of a moderately-restricted carbohydrate diet on cardiovascular risk factors among women with metabolic syndrome. Journal of Isfahan Medical School. 2012;29(171).				Language

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
814	Rajaie S, Azadbakht L, Khazaei M, Sherbafchi M, Esmaillzadeh A. Moderate replacement of carbohydrates by dietary fats affects features of metabolic syndrome: a randomized crossover clinical trial. Nutrition. 2014;30(1):61-8. doi:10.1016/j.nut.2013.06.011		X		
815	Rajaram S, Yip EL, Reghunathan R, Mohan S, Sabate J. Effect of altering dietary n-6: n-3 polyunsaturated fatty acid ratio with plant and marine-based supplement on biomarkers of bone turnover in healthy adults. Nutrients. 2017;9(10): pii: E1162. doi:10.3390/nu9101162			X	
816	Rajendiran E, She Y, Tessier-Grenier M, et al. Apolipoprotein E variants and sex modify the action of dairy fat intake on plasma HDL-cholesterol and adiponectin concentration. J Nutrigenet Nutrigenomics. 2017;10(3- 4):114. doi:10.1159/000480052				Publication Status
817	Ramel A, Martinez JA, Kiely M, Bandarra NM, Thorsdottir I. Moderate consumption of fatty fish reduces diastolic blood pressure in overweight and obese European young adults during energy restriction. Nutrition. 2010;26(2):168-74. doi:10.1016/j.nut.2009.04.002			X	
818	Ramos-Lopez O, Riezu-Boj JI, Milagro FI, Goni L, Cuervo M, Martinez JA. Differential lipid metabolism outcomes associated with ADRB2 gene polymorphisms in response to two dietary interventions in overweight/obese subjects. Nutr Metab Cardiovasc Dis. 2018;28(2):165-172. doi:10.1016/j.numecd.2017.11.006		X		
819	Ramprasath VR, Jones PJ, Buckley DD, Woollett LA, Heubi JE. Decreased plasma cholesterol concentrations after PUFA-rich diets are not due to reduced cholesterol absorption/synthesis. Lipids. 2012;47(11):1063-71. doi:10.1007/s11745-012-3708-8				Study Duration
820	Ramsden CE, Zamora D, Faurot K, Majchrzak S, Hibbeln J. The Sydney diet heart study: a randomised controlled trial of linoleic acid for secondary prevention of coronary heart disease and death. FASEB journal. 2013;27(Suppl 1).				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
821	Ramsden CE, Zamora D, Leelarthaepin B, et al. Use of dietary linoleic acid for secondary prevention of coronary heart disease and death: Evaluation of recovered data from the Sydney Diet Heart Study and updated meta-analysis. BMJ. 2013. 346(7894):e8707. doi:10.1136/bmj.e8707				Health Status
822	Ramsden CE, Zamora D, Majchrzak-Hong S, et al. Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73). BMJ. 2016;353:i1246. doi:10.1136/bmj.i1246				Health Status
823	Rancourt-Bouchard M, Gigleux I, Guay V, et al. Effects of regular-fat and low-fat dairy consumption on daytime ambulatory blood pressure and other cardiometabolic risk factors: a randomized controlled feeding trial. Am J Clin Nutr. 2019;111(1):42-51. doi:10.1093/ajcn/nqz251		X		
824	Ras R, Demonty I, Zebregs Y, Quadt F, Olsson J, Trautwein E. The combined effect on blood lipids of plant sterols and different low doses of omega-3 fatty acids. Atherosclerosis. 2014. 235(2):e112. doi:10.1016/j.atherosclerosis.2014.05.304				Publication Status
825	Rashid NA, Nawi AM, Khadijah S. Exploratory analysis of traditional risk factors of ischemic heart disease (IHD) among predominantly Malay Malaysian women. BMC Public Health. 2019;19(Suppl 4):545. doi:10.1186/s12889-019-6855-5	X	X		
826	Rask-Nissila L, Jokinen E, Viikari J, et al. Impact of dietary intervention, sex, and apolipoprotein E phenotype on tracking of serum lipids and apolipoproteins in 1- to 5-year-old children: the Special Turku Coronary Risk Factor Intervention Project (STRIP). Arterioscler Thromb Vasc Biol. 2002;22(3):492-8. doi:10.1161/hq0302.104516				Duplicate data

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
827	Rathnayake KM, Weech M, Jackson KG, Lovegrove JA. Impact of the Apolipoprotein E (epsilon) genotype on cardiometabolic risk markers and responsiveness to acute and chronic dietary fat manipulation. Nutrients. 2019;11(9): pii: E2044. doi:10.3390/nu11092044		X		
828	Raziani F, Ebrahimi P, Engelsen SB, Astrup A, Raben A, Tholstrup T. Consumption of regular-fat vs reduced-fat cheese reveals gender-specific changes in LDL particle size - a randomized controlled trial. Nutrition & Metabolism. 2018;15(61). doi:10.1186/s12986-018-0300-0		X		
829	Razny, Polus, Wnek, et al. The effect of N-3 PUFA supplementation on postprandial triglycerides and insulin in obesity. The BIOCLAIMS study. Obesity facts. 2014. 7(Suppl 1)798- 99. doi:10.1159/000363668				Publication Status
830	Razquin C, Sanchez-Tainta A, Salas-Salvado J, et al. Dietary energy density and body weight changes after 3 years in the PREDIMED study. Int J Food Sci Nutr. 2017;68(7):865-872. doi:10.1080/09637486.2017.1295028			X	
831	Redondo N, García-González N, Diaz-Prieto LE, et al. Effects of ewe's milk yogurt (whole and semi-skimmed) and cow's milk yogurt on inflammation markers and gut microbiota of subjects with borderline-high plasma cholesterol levels: a crossover study. Eur J Nutr. 2019;58(3):1113-1124. doi:10.1007/s00394-018-1626-0		X		
832	Reeves JL, Otahal P, Magnussen CG, et al. DHA mediates the protective effect of fish consumption on new episodes of depression among women. Br J Nutr. 2017;118(9):743-749. doi:10.1017/s0007114517002768			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
833	Reidlinger DP, Darzi J, Hall WL, et al. The effectiveness of an integrated dietary intervention compared with an average UK diet in reducing cardiovascular disease risk factors in older men and women aged 40 to 70 years: the CRESSIDA Study. Proceedings of the nutrition society. 2013;72(OCE4):E249. doi:10.1017/S0029665113002747				Publication Status
834	Reidlinger DP, Darzi J, Hall WL, et al. How effective are current dietary guidelines for cardiovascular disease prevention in healthy middle-aged and older men and women? A randomized controlled trial. Am J Clin Nutr. 2015;101(5):922-930. doi:10.3945/ajcn.114.097352		X		
835	Reiner MF, Stivala S, Limacher A, et al. Omega-3 fatty acids predict recurrent venous thromboembolism or total mortality in elderly patients with acute venous thromboembolism. J Thromb Haemost. 2017;15(1):47-56. doi:10.1111/jth.13553		X		Health Status
836	Reis RS, Dalle Molle R, Machado TD, et al. Impulsivity-based thrifty eating phenotype and the protective role of n-3 PUFAs intake in adolescents. Transl Psychiatry. 2016;15:6e755. doi:10.1038/tp.2016.16		X	X	
837	Renu M, Khushbu A. Diet and lipid profile of menopausal women as risk factors of cardiovascular disease. Indian Journal of Public Health Research and Development. 2014;5(3):104-108. doi:10.5958/0976-5506.2014.00283.6				Country
838	Retterstol K, Svendsen M, Narverud I, Holven KB. Effect of low carbohydrate high fat diet on LDL cholesterol and gene expression in normal-weight, young adults: a randomized controlled study. Atherosclerosis. 2018;279:52-61. doi:10.1016/j.atherosclerosis.2018.10.013		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
839	Riestra P, Lopez-Simon L, Ortega H, et al. Fat intake influences the effect of the hepatic lipase C-514T polymorphism on HDL-cholesterol levels in children. Exp Biol Med (Maywood). 2009. 234(7):744-9. doi:10.3181/0812-rm-373	X			
840	Rietman A, Schwarz J, Blokker BA, et al. Increasing protein intake modulates lipid metabolism in healthy young men and women consuming a high-fat hypercaloric diet. J Nutr. 2014;144(8):1174-80. doi:10.3945/jn.114.191072		X		
841	Rix TA, Joensen AM, Riahi S, et al. A U-shaped association between consumption of marine n-3 fatty acids and development of atrial fibrillation/atrial flutter - A Danish cohort study. Europace. 2014;16(11):1554-1561. doi:10.1093/europace/euu019			X	
842	Roberge JB, Van Hulst A, Barnett TA, et al. Lifestyle habits, dietary factors, and the metabolically unhealthy obese phenotype in youth. J Pediatr. 2019;46-52.e1. doi:10.1016/j.jpeds.2018.08.063			X	
843	Rock CL, Flatt SW, Barkai HS, Pakiz B, Heath DD. Walnut consumption in a weight reduction intervention: effects on body weight, biological measures blood pressure and satiety. Nutr J. 2017;16(1):76. doi:10.1186/s12937-017-0304-z		X		
844	Rodriguez-Perez C, Ramprasath VR, Pu S, et al. Docosahexaenoic acid attenuates cardiovascular risk factors via a decline in proprotein convertase subtilisin/kexin type 9 (PCSK9) plasma levels. Lipids. 2016;51(1):75-83. doi:10.1007/s11745-015-4099-4				Duplicate data
845	Rogers IS, Emmett PM. Fat content of the diet among preschool children in southwest Britain: II. relationship with growth blood lipids and iron status. Pediatrics. 2001. 108(3):E49. doi:10.1542/peds.108.3.e49		X		
846	Rogers TS, Seehusen DA. Omega-3 Fatty Acids and Cardiovascular Disease. Am Fam Physician. 2018;97(9):562-564.	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
847	Rogerson D, Macas D, Milner M, Liu Y, Klonizakis M. Contrasting effects of short-term Mediterranean and vegan diets on microvascular function and cholesterol in younger adults: a comparative pilot study. Nutrients. 2018;10(12): pii: E1897. doi:10.3390/nu10121897		X		
848	Roncero-Ramos I, Rangel-Zuniga OA, Lopez-Moreno J, et al. Mediterranean diet, glucose homeostasis, and inflammasome genetic variants: The CORDIOPREV Study. Mol Nutr Food Res. 2018;62(9):e1700960. doi:10.1002/mnfr.201700960				Health Status
849	Rondanelli M, Klersy C, Perna S, et al. Effects of two-months balanced diet in metabolically healthy obesity: lipid correlations with gender and BMI-related differences. Lipids Health Dis. 2015;14:139. doi:10.1186/s12944-015-0131-1	X		X	
850	Ros E, Hu FB. Consumption of plant seeds and cardiovascular health: Epidemiological and clinical trial evidence. Circulation. 2013;128(5):553-565. doi:10.1161/circulationaha.112.001119	X			
851	Rosado JL, Garcia OP, Ronquillo D, et al. Intake of milk with added micronutrients increases the effectiveness of an energy-restricted diet to reduce body weight: a randomized controlled clinical trial in Mexican women. J Am Diet Assoc. 2011;111(10):1507-16. doi:10.1016/j.jada.2011.07.011		X		
852	Rosenbaum M, Hall KD, Guo J, et al. Glucose and lipid homeostasis and inflammation in humans following an isocaloric ketogenic diet. Obesity (Silver Spring). 2019;27(6):971-981. doi:10.1002/oby.22468	X	X		
853	Rosqvist F, Smedman A, Lindmark-Mansson H, et al. Potential role of milk fat globule membrane in modulating plasma lipoproteins, gene expression, and cholesterol metabolism in humans: a randomized study. Am J Clin Nutr. 2015;102(1):20-30. doi:10.3945/ajcn.115.107045		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
854	Rousseaux J, Duhamel A, Dumont J, et al. The n-3 long-chain PUFAs modulate the impact of the GCKR Pro446Leu polymorphism on triglycerides in adolescents. J Lipid Res. 2015;56(9):1774-80. doi:10.1194/jlr.M057570	X			
855	Roussell MA, Hill AM, Gaugler TL, et al. Beef in an optimal lean diet study: effects on lipids, lipoproteins, and apolipoproteins. Am J Clin Nutr. 2012;95(1):9-16. doi:10.3945/ajcn.111.016261				Health Status
856	Roussell MA, Hill AM, Gaugler TL, et al. Effects of a DASH-like diet containing lean beef on vascular health. J Hum Hypertens. 2014;28(10):600-5. doi:10.1038/jhh.2014.34		X		
857	Roy SJ, Fico BG, Baker BD, et al. Effects of full-fat dairy products on subclinical vascular function in adults with elevated blood pressure: a randomized clinical trial. Eur J Clin Nutr. 2019;74(1):9-16. doi:10.1038/s41430-019-0435-8		X		
858	Roy SJ, Lapierre SS, Baker BD, Delfausse LA, Machin DR, Tanaka H. High dietary intake of whole milk and full-fat dairy products does not exert hypotensive effects in adults with elevated blood pressure. Nutr Res. 2019;6472-81. doi:10.1016/j.nutres.2019.01.003		X		Health Status
859	Ruel G, Shi Z, Zhen S, Zuo H, et al. Association between nutrition and the evolution of multimorbidity: the importance of fruits and vegetables and whole grain products. Clin Nutr. 2014;33(3):513-20. doi:10.1016/j.clnu.2013.07.009		X		Country
860	Ruisinger JF, Gibson CA, Backes JM, et al. Statins and almonds to lower lipoproteins (the STALL Study). J Clin Lipidol. 2015;9(1):58-64. doi:10.1016/j.jacl.2014.10.001		X		Health Status
861	Ruixing Y, Qiming F, Dezhai Y, et al. Comparison of demography, diet, lifestyle, and serum lipid levels between the Guangxi Bai Ku Yao and Han populations. J Lipid Res. 2007. 48(12):2673-2681. doi:10.1194/jlr.M700335-JLR200		X		Country

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862	Ruiz N, Segarra AB, Lara L, Ramirez-Sanchez M, Prieto I. Diet and oxidative status. The dietary pattern and urinary 8-isoprostane in healthy Spanish women. Antioxidants (Basel). 2019;8(8): pii: E271. doi:10.3390/antiox8080271			X	
863	Ruiz-Nunez B, Kuipers RS, Luxwolda MF, et al. Saturated fatty acid (SFA) status and SFA intake exhibit different relations with serum total cholesterol and lipoprotein cholesterol: a mechanistic explanation centered around lifestyle-induced low-grade inflammation. J Nutr Biochem. 2014;25(3):304-12. doi:10.1016/j.jnutbio.2013.11.004	X			Country
864	Ruscica M, Pavanello C, Gandini S, et al. Effect of soy on metabolic syndrome and cardiovascular risk factors: a randomized controlled trial. Eur J Nutr. 2018;57(2):499-511. doi:10.1007/s00394-016-1333-7		X		
865	Ryberg M, Sandberg S, Mellberg C, et al. A Palaeolithic-type diet causes strong tissue-specific effects on ectopic fat deposition in obese postmenopausal women. J Intern Med. 2013;274(1):67-76. doi:10.1111/joim.12048	X	X		
866	Saarinen HJ, Sittiwet C, Simonen P, et al. Determining the mechanisms of dietary turnip rapeseed oil on cholesterol metabolism in men with metabolic syndrome. J Investig Med. 2018;66(1):11-16. doi:10.1136/jim-2017-000495			X	Duplicate data
867	Sabour H, Norouzi-Javidan A, Soltani Z, et al. The correlation between dietary fat intake and blood pressure among people with spinal cord injury. Iran J Neurol. 2016;15(3):121-7.	X			Health Status
868	Saedi S, Noroozi M, Khosrotabar N, Mazandarani S, Ghadrdoost B. How canola and sunflower oils affect lipid profile and anthropometric parameters of participants with dyslipidemia. Med J Islam Repub Iran. 2017;315:5. doi:10.18869/mjiri.31.5				Health Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
869	Sagawa N, Olson NC, Ahuja V, et al. Long chain n-3 polyunsaturated fatty acids are not associated with circulating T-helper type 1 cells: results from the Multi-Ethnic Study of Atherosclerosis (MESA). Prostaglandins Leukot Essent Fatty Acids. 2017;12537-42. doi:10.1016/j.plefa.2017.08.012			X	
870	Saha S, Mundle M, Ghosh S, Koley M. Effects of medical nutrition therapy on plasma lipoproteins of type II dyslipidemic patients: a short-term pilot study. Asian Journal of Pharmaceutical and Clinical Research. 2012;5(Suppl 4):207-211.		X		Country
871	Sala-Vila A, Romero-Mamani ES, Gilabert R, et al. Changes in ultrasound-assessed carotid intima-media thickness and plaque with a Mediterranean diet: a substudy of the PREDIMED trial. Arterioscler Thromb Vasc Biol. 2014;34(2):439-45. doi:10.1161/atvbaha.113.302327		X	X	
872	Sala-Vila A, Ros E. Mounting evidence that increased consumption of α-linolenic acid, the vegetable n-3 fatty acid, may benefit cardiovascular health. Clin Lipidol. 2011;6(4):365-369. doi:10.2217/clp.11.36	X			
873	Salo P, Viikari J, Rask-Nissila L, et al. Effect of low-saturated fat, low-cholesterol dietary intervention on fatty acid compositions in serum lipid fractions in 5-year-old children. The STRIP project. Eur J Clin Nutr. 1999. 53(12):927-32.				Duplicate data
874	Samieri C, Lorrain S, Buaud B, et al. Relationship between diet and plasma long-chain n-3 PUFAs in older people: impact of apolipoprotein E genotype. J Lipid Res. 2013;54(9):2559-67. doi:10.1194/jlr.P036475	X			
875	Samuelson G, Bratteby LE, Mohsen R, Vessby B. Dietary fat intake in healthy adolescents: inverse relationships between the estimated intake of saturated fatty acids and serum cholesterol. Br J Nutr. 2001. 85(3):333-41. doi:10.1079/bjn2000279	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
876	Sanchez-Rodriguez E, Biel-Glesson S, Fernandez-Navarro JR, et al. Effects of virgin olive oils differing in their bioactive compound contents on biomarkers of oxidative stress and inflammation in healthy adults: a randomized double-blind controlled trial. Nutrients. 2019;11(3): pii: E561. doi:10.3390/nu11030561		X	X	
877	Sanchez-Rodriguez E, Lima-Cabello E, Biel-Glesson S, et al. Effects of virgin olive oils differing in their bioactive compound contents on metabolic syndrome and endothelial functional risk biomarkers in healthy adults: a randomized double-blind controlled trial. Nutrients. 2018. 10(5): pii: E626. doi:10.3390/nu10050626		X		
878	Sanders TA, Lewis FJ, Goff LM, Chowienczyk PJ. SFAs do not impair endothelial function and arterial stiffness. Am J Clin Nutr. 2013;98(3):677-83. doi:10.3945/ajcn.113.063644			X	
879	Saneei P, Hashemipour M, Kelishadi R, Rajaei S, Esmaillzadeh A. Effects of recommendations to follow the Dietary Approaches to Stop Hypertension (DASH) diet v. usual dietary advice on childhood metabolic syndrome: a randomised cross-over clinical trial. Br J Nutr. 2013;110(12):2250-9. doi:10.1017/s0007114513001724		X		
880	Santaren ID, Bazinet RP, Liu Z, et al. The distribution of fatty acid biomarkers of dairy intake across serum lipid fractions: the prospective metabolism and islet cell evaluation (PROMISE) Cohort. Lipids. 2019;54(10):617-627. doi:10.1002/lipd.12185	X	X		
881	Sayer RD, Wright AJ, Chen N, Campbell WW. Dietary Approaches to Stop Hypertension diet retains effectiveness to reduce blood pressure when lean pork is substituted for chicken and fish as the predominant source of protein. Am J Clin Nutr. 2015;102(2):302-8. doi:10.3945/ajcn.115.111757		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
882	Sayon-Orea C, Razquin C, Bullo M, et al. Effect of a nutritional and behavioral intervention on energy-reduced Mediterranean diet adherence among patients with metabolic syndrome: interim analysis of the PREDIMED-Plus randomized clinical trial. JAMA. 2019;322(15):1486-1499. doi:10.1001/jama.2019.14630		X		
883	Schaefer EJ, Tani M. Nutrition and coronary heart disease prevention. In Gang, A, eds. *Dyslipidemias: Pathophysiology, Evaluation and Management.* 2015:329-341. doi:10.1007/978-1-60761-424-1_19	X			Publication Status
884	Schlienger JL, Paillard F, Lecerf JM, et al. Effect on blood lipids of two daily servings of Camembert cheese. An intervention trial in mildly hypercholesterolemic subjects. Int J Food Sci Nutr. 2014;65(8):1013-8. doi:10.3109/09637486.2014.945156				Health Status
885	Schreuder YJ, Hutten BA, van Eijsden M, et al. Ethnic differences in maternal total cholesterol and triglyceride levels during pregnancy: the contribution of demographics, behavioural factors and clinical characteristics. Eur J Clin Nutr. 2011;65(5):580-9. doi:10.1038/ejcn.2010.282	X	X		
886	Schroder H, Salas-Salvado J, Martinez-Gonzalez MA, et al. Baseline adherence to the Mediterranean diet and major cardiovascular events: Prevencion con Dieta Mediterranea trial. JAMA Intern Med. 2014;174(10):1690-2. doi:10.1001/jamainternmed.2014.3463		X		
887	Schuler R, Osterhoff MA, Frahnow T, et al. High-saturated-fat diet increases circulating angiotensin-converting enzyme, which is enhanced by the rs4343 polymorphism defining persons at risk of nutrient-dependent increases of blood pressure. J Am Heart Assoc. 2017;6(1):p ii: e004465. doi:10.1161/jaha.116.004465		X	X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
888	Schumacher TL, Burrows TL, Rollo ME, Wood LG, Callister R, Collins CE. Comparison of fatty acid intakes assessed by a cardiovascular-specific food frequency questionnaire with red blood cell membrane fatty acids in hyperlipidaemic Australian adults: a validation study. Eur J Clin Nutr. 2016. 70(12):1433-1438. doi:10.1038/ejcn.2016.144	X		X	
889	Schwab US, Lankinen MA, de Mello VD, et al. Camelina sativa oil, but not fatty fish or lean fish, improves serum lipid profile in subjects with impaired glucose metabolism-a randomized controlled trial. Mol Nutr Food Res. 2018;62(4). doi:10.1002/mnfr.201700503				Product not widely available in the US
890	Schwandt P, Bertsch T, Haas GM. Sustained lifestyle advice and cardiovascular risk factors in 687 biological child-parent pairs: the PEP Family Heart Study. Atherosclerosis. 2011;219(2):937-45. doi:10.1016/j.atherosclerosis.2011.09.032		X		
891	Schwandt P, Haas GM, Bertsch T. Nutrition and cardiovascular risk factors in four age groups of female individuals: The PEP family heart study. International Journal of Preventive Medicine. 2010;1(2):103-109.	X			
892	Schwandt P, Haas GM, Liepold E. Lifestyle and cardiovascular risk factors in 2001 child-parent pairs: the PEP Family Heart Study. Atherosclerosis. 2010;213(2):642-8. doi:10.1016/j.atherosclerosis.2010.09.032	X	X		
893	Sciarrillo CM, Koemel NA, Tomko PM, Bode KB, Emerson SR. Postprandial lipemic responses to various sources of saturated and monounsaturated fat in adults. Nutrients. 2019;11(5): pii: E1089. doi:10.3390/nu11051089	X		X	
894	Seah JY, Ong CN, Koh WP, Yuan JM, van Dam RM. A dietary pattern derived from reduced rank regression and fatty acid biomarkers is associated with lower risk of type 2 diabetes and coronary artery disease in Chinese adults. J Nutr. 2019;149(11):2001-2010. doi:10.1093/jn/nxz164		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
895	Seidel C, Deufel T, Jahreis G. Effects of fat-modified dairy products on blood lipids in humans in comparison with other fats. Ann Nutr Metab. 2005. 49(1):42-8. doi:10.1159/000084176				Study Duration
896	Seki K, Hasuike-Seo M, Kondo S, Sato N, Suzuki E, Hasumi K. Effects of intake of sesame oil (kadoya pure sesame oil) on the level of serum cholesterol in volunteers with slightly higher serum cholesterol - A randomized, double-blind, parallel-group, placebo-controlled study. Japanese Pharmacology and Therapeutics. 2015;43(5):687-696.				Health Status
897	Seki K, Ishikawa T, Hasuike-Seo M, Suzuki E, Kondo S, Hasumi K. Hypocholesterolemic effect of sesame oil (Kadoya Pure Sesame Oil) - A verification test with a randomized, double-blind, parallel-group, placebo-controlled study. Japanese Pharmacology and Therapeutics. 2015;43(10):1473-1480.				Health Status
898	Sellem L, Srour B, Gueraud F, et al. Saturated, mono- and polyunsaturated fatty acid intake and cancer risk: results from the French prospective cohort NutriNet-Sante. Eur J Nutr. 2019;58(4):1515-1527. doi:10.1007/s00394-018-1682-5			X	
899	Setayeshgar S, Ekwaru JP, Maximova K, et al. Dietary intake and prospective changes in cardiometabolic risk factors in children and youth. Appl Physiol Nutr Metab. 2017;42(1):39-45. doi:10.1139/apnm-2016-0215		X		
900	Severins N, Mensink RP, Plat J. Effects of lutein-enriched egg yolk in buttermilk or skimmed milk on serum lipids & lipoproteins of mildly hypercholesterolemic subjects. Nutr Metab Cardiovasc Dis. 2015;25(2):210-7. doi:10.1016/j.numecd.2014.10.003		X		
901	Shah BS, Freeland-Graves JH, Cahill JM, Lu H, Graves GR. Diet quality as measured by the healthy eating index and the association with lipid profile in low-income women in early postpartum. J Am Diet Assoc. 2010;110(2):274-9. doi:10.1016/j.jada.2009.10.038	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
902	Shah M, Adams-Huet B, Franklin B, Phillips M, Mitchell J. The effects of high-protein and high-monounsaturated fat meals on postprandial lipids, lipoprotein particle numbers, cytokines, and leptin responses in overweight/obese subjects. Metab Syndr Relat Disord. 2018;16(3):150-158. doi:10.1089/met.2017.0167	X		X	
903	Shang X, Sanders KM, Scott D, et al. Dietary alpha-linolenic acid and total omega-3 fatty acids are inversely associated with abdominal aortic calcification in older women but not in older men. J Nutr. 2015;145(8):1778-86. doi:10.3945/jn.115.211789			X	
904	Shannon BM, Tershakovec AM, Martel JK, et al. Reduction of elevated LDL-cholesterol levels of 4- to 10-year-old children through home-based dietary education. Pediatrics. 1994. 94(6 Pt 1):923-7.		X		
905	Shatwan IM, Weech M, Jackson KG, Lovegrove JA, Vimaleswaran KS. Apolipoprotein E gene polymorphism modifies fasting total cholesterol concentrations in response to replacement of dietary saturated with monounsaturated fatty acids in adults at moderate cardiovascular disease risk. Lipids Health Dis. 2017;16(1):222. doi:10.1186/s12944-017-0606-3		X		
906	Shay CM, Stamler J, Dyer AR, et al. Nutrient and food intakes of middle-aged adults at low risk of cardiovascular disease: the international study of macro-/micronutrients and blood pressure (INTERMAP). Eur J Nutr. 2012;51(8):917-26. doi:10.1007/s00394-011-0268-2	X			
907	Shea S, Basch CE, Irigoyen M, Zybert P, Contento I, Gutin B. Relationships between diet and blood lipid levels in Hispanic preschool children. Ann N Y Acad Sci. 1991. 623:462-3. doi:10.1111/j.1749-6632.1991.tb43772.x	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
908	Shea S, Basch CE, Irigoyen M, et al. Relationships of dietary fat consumption to serum total and low-density lipoprotein cholesterol in hispanic preschool children. Prev Med. 1991. 20(2):237-49. doi:10.1016/0091-7435(91)90023-w	X			
909	Shi Z, Riley M, Brown A, Page A. Chilli intake is inversely associated with hypertension among adults. Clin Nutr ESPEN. 2018;2367-72. doi:10.1016/j.clnesp.2017.12.007	X	X		
910	Shih CW, Hauser ME, Aronica L, Rigdon J, Gardner CD. Changes in blood lipid concentrations associated with changes in intake of dietary saturated fat in the context of a healthy low-carbohydrate weight-loss diet: a secondary analysis of the Diet Intervention Examining The Factors Interacting with Treatment Success (DIETFITS) trial. Am J Clin Nutr. 2019;109(2):433-441. doi:10.1093/ajcn/nqy305	X		X	
911	Shiue I, Arima H, Hankey GJ, Anderson CS. Dietary intake of key nutrients and subarachnoid hemorrhage: a population-based case-control study in Australasia. Cerebrovasc Dis. 2011;31(5):464-70. doi:10.1159/000324386	X	X		
912	Shojasaadat F, Ayremlou P, Hashemi A, Mehdizadeh A, Zarrin R. A randomized controlled trial comparing effects of a low-energy diet with n-3 polyunsaturated fatty acid supplementation in patients with non-alcoholic fatty liver disease. J Res Med Sci. 2019;2421. doi:10.4103/jrms.JRMS_282_18		X		Health Status
913	Silva S, Bronze MR, Figueira ME, et al. Impact of a 6-wk olive oil supplementation in healthy adults on urinary proteomic biomarkers of coronary artery disease, chronic kidney disease, and diabetes (types 1 and 2): a randomized, parallel, controlled, double-blind study. Am J Clin Nutr. 2015;101(1):44-54. doi:10.3945/ajcn.114.094219		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
914	Silva S, Bronze MR, Figueira ME, et al. Impact of a six-week olive oil supplementation in healthy adults on urinary proteomic biomarkers of coronary artery disease, chronic kidney disease and diabetes. Atherosclerosis. 2015;241(1):e41. doi:10.1016/j.atherosclerosis.2015.04.146				Publication Status
915	Silva VM, Vinagre CGC, Dallan LAO, Chacra APM, Maranhão RC. Plasma lipids, lipoprotein metabolism and HDL lipid transfers are equally altered in metabolic syndrome and in type 2 diabetes. Lipids. 2014;49(7):677-684. doi:10.1007/s11745-014-3899-2		X		
916	Silver HJ, Kang H, Keil CD, et al. Consuming a balanced high fat diet for 16 weeks improves body composition, inflammation and vascular function parameters in obese premenopausal women. Metabolism. 2014;63(4):562-73. doi:10.1016/j.metabol.2014.01.004		X		
917	Silver HJ, Niswender KD, Keil CD, et al. CNR1 genotype influences HDL-cholesterol response to change in dietary fat intake. PLoS One. 2012;7(5):e36166. doi:10.1371/journal.pone.0036166		X		
918	Simell O, Niinikoski H, Viikari J, Rask-Nissila L, Tammi A, Ronnemaa T. Cardiovascular disease risk factors in young children in the STRIP baby project. Special Turku coronary risk factor intervention project for children. Ann Med. 1999. 31 Suppl 155-61.				Duplicate data
919	Simon JA, Morrison JA, Similo SL, McMahon RP, Schreiber GB. Correlates of high-density lipoprotein cholesterol in Black girls and White girls: the NHLBI Growth and Health Study. Am J Public Health. 1995. 85(12):1698-702. doi:10.2105/ajph.85.12.1698	X			
920	Simprini LA, Villines TC, Rich M, Taylor AJ. The relationship between subclinical atherosclerosis, non-high-density lipoprotein cholesterol, exercise, and diet among male participants of the PACC Project. J Clin Lipidol. 2012;6(2):174-9. doi:10.1016/j.jacl.2011.11.005	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
921	Skilton MR, Mikkila V, Wurtz P, et al. Fetal growthomega-3 (n-3) fatty acids, and progression of subclinical atherosclerosis: preventing fetal origins of disease? The Cardiovascular Risk in Young Finns Study. Am J Clin Nutr. 2013;97(1):58-65. doi:10.3945/ajcn.112.044198			X	Health Status
922	Skorkowska-Telichowska K, Kosinska J, Chwojnicka M, et al. Positive effects of egg-derived phospholipids in patients with metabolic syndrome. Adv Med Sci. 2016;61(1):169-74. doi:10.1016/j.advms.2015.12.003		X		
923	Skouroliakou M, Grosomanidis D, Massara P, Kostara C, et al. Serum antioxidant capacity, biochemical profile and body composition of breast cancer survivors in a randomized Mediterranean dietary intervention study. Eur J Nutr. 2018;57(6):2133-2145. doi:10.1007/s00394-017-1489-9		X		Health Status
924	Skuladottir M, Ramel A, Rytter D, et al. Examining confounding by diet in the association between perfluoroalkyl acids and serum cholesterol in pregnancy. Environ Res. 2015;143(Pt A):33-8. doi:10.1016/j.envres.2015.09.001	X	X		
925	Slade AN, Kim H. Dietary responses to a hypertension diagnosis: evidence from the National Health and Nutrition Examination Survey (NHANES) 2007-2010. Behav Med. 2014;40(1):1-13. doi:10.1080/08964289.2013.826171	X			
926	Sluijs I, Praagman J, Boer JMA, Verschuren WMM, van der Schouw YT. Fluidity of the dietary fatty acid profile and risk of coronary heart disease and ischemic stroke: results from the EPIC-Netherlands cohort study. Nutr Metab Cardiovasc Dis. 2017;27(9):799-805. doi:10.1016/j.numecd.2017.06.008	X	X		
927	Smidowicz A, Regula J. Dietary gender differences in terms of the risk of atherogenesis in Poland. Acta Sci Pol Technol Aliment. 2015;14(3):257-267. doi:10.17306/j.Afs.2015.3.37	X	X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
928	Smit LA, Baylin A, Campos H. Conjugated linoleic acid in adipose tissue and risk of myocardial infarction. Am J Clin Nutr. 2010;92(1):34-40. doi:10.3945/ajcn.2010.29524	X			
929	Smith KM, Barraj LM, Kantor M, Sahyoun NR. Relationship between fish intake, n-3 fatty acids, mercury and risk markers of CHD (National Health and Nutrition Examination Survey 1999-2002). Public Health Nutr. 2009. 12(8):1261-9. doi:10.1017/s1368980008003844	X			
930	Snetselaar L, Stumbo P, Chenard C, Ahrens L, Smith K, Zimmerman B. Adolescents eating diets rich in either lean beef or lean poultry and fish reduced fat and saturated fat intake and those eating beef maintained serum ferritin status. J Am Diet Assoc. 2004. 104(3):424-8. doi:10.1016/j.jada.2003.12.016		X	X	
931	Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, Brunner EJ. Consumption of dairy products and associations with incident diabetes, CHD and mortality in the Whitehall II study. Br J Nutr. 2013;109(4):718-26. doi:10.1017/s0007114512001845		X		
932	Soerensen KV, Thorning TK, Astrup A, Kristensen M, Lorenzen JK. Effect of dairy calcium from cheese and milk on fecal fat excretion, blood lipids, and appetite in young men. Am J Clin Nutr. 2014;99(5):984-91. doi:10.3945/ajcn.113.077735		X		Study Duration
933	Sola R, Fito M, Estruch R, Salas-Salvado J, et al. Effect of a traditional Mediterranean diet on apolipoproteins B, A-I, and their ratio: a randomized, controlled trial. Atherosclerosis. 2011;218(1):174-80. doi:10.1016/j.atherosclerosis.2011.04.026		X		
934	Sola R, Valls RM, Godas G, Perez-Busquets G, et al. Cocoa, hazelnuts, sterols and soluble fiber cream reduces lipids and inflammation biomarkers in hypertensive patients: a randomized controlled trial. PLoS One. 2012;7(2):e31103. doi:10.1371/journal.pone.0031103		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
935	Somerset S, Graham L, Markwell K, Colquhoun D. Isoenergetic replacement of dietary saturated with monounsaturated fat via macadamia nuts can affect coronary risk in overweight subjects. Atherosclerosis supplements. 2011;12(1):143- 144. doi: 10.1016/S1567-5688(11)70684-5				Publication Status
936	Somerset SM, Graham L, Markwell K. Isoenergetic replacement of dietary saturated with monounsaturated fat via macadamia nuts enhances endothelial function in overweight subjects. Clin Nutr ESPEN. 2013;8(3):e113-e119. doi:10.1016/j.clnme.2013.02.003		X		
937	Sondike SB, Copperman N, Jacobson MS. Effects of a low-carbohydrate diet on weight loss and cardiovascular risk factor in overweight adolescents. J Pediatr. 2003. 142(3):253-8. doi:10.1067/mpd.2003.4		X		
938	Sonestedt E, Gullberg B, Ericson U, Wirfalt E, Hedblad B, Orho-Melander M. Association between fat intake, physical activity and mortality depending on genetic variation in FTO. Int J Obes (Lond). 2011;35(8):1041-9. doi:10.1038/ijo.2010.263		X		
939	Sonestedt E, Hellstrand S, Drake I, et al. Diet quality and change in blood lipids during 16 years of follow-up and their interaction with genetic risk for dyslipidemia. Nutrients. 2016;8(5): pii: E274. doi:10.3390/nu8050274			X	
940	Song J, Jiang X, Cao Y, Juan J, Wu T, Hu Y. Interaction between an ATP-binding cassette A1 (ABCA1) variant and egg consumption for the risk of ischemic stroke and carotid atherosclerosis: a family-based study in the Chinese population. J Atheroscler Thromb. 2019;26(9):835-845. doi:10.5551/jat.46615		X		
941	Song S, Paik HY, Park M, Song Y. Dyslipidemia patterns are differentially associated with dietary factors. Clin Nutr. 2016;35(4):885-91. doi:10.1016/j.clnu.2015.06.002	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
942	Song X, Huang Y, Neuhouser ML, et al. Dietary long-chain fatty acids and carbohydrate biomarker evaluation in a controlled feeding study in participants from the Women's Health Initiative cohort. Am J Clin Nutr. 2017;105(6):1272-1282. doi:10.3945/ajcn.117.153072			X	
943	Srour B, Fezeu LK, Kesse-Guyot E, et al. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Sante). BMJ. 2019;365:l1451. doi:10.1136/bmj.l1451		X		
944	Stelmach-Mardas M, Walkowiak J, Wieckowska B, Przyslawski J. Polyunsaturated fatty acids and not plant sterols naturally-occurring in food influence lipid profile in obese women. Acta Sci Pol Technol Aliment. 2014;13(1):111-7.	X			Health Status
945	Stevenson JL, Miller MK, Skillman HE, Paton CM, Cooper JA. A PUFA-rich diet improves fat oxidation following saturated fat-rich meal. Eur J Nutr. 2017;56(5):1845-1857. doi:10.1007/s00394-016-1226-9				Study Duration
946	Stocks T, Taylor MA, Angquist L, et al. Change in proportional protein intake in a 10-week energy-restricted low- or high-fat diet, in relation to changes in body size and metabolic factors. Obes Facts. 2013;6(3):217-27. doi:10.1159/000351726		X		
947	Storniolo CE, Casillas R, Bullo M, et al. A Mediterranean diet supplemented with extra virgin olive oil or nuts improves endothelial markers involved in blood pressure control in hypertensive women. Eur J Nutr. 2017;56(1):89-97. doi:10.1007/s00394-015-1060-5		X		Health Status
948	Streppel MT, Sluik D, van Yperen JF, et al. Nutrient-rich foodscardiovascular diseases and all-cause mortality: the Rotterdam study. Eur J Clin Nutr. 2014;68(6):741-7. doi:10.1038/ejcn.2014.35		X		
949	Strom M, Mortensen EL, Henriksen TB, Olsen SF. Fish consumption measured during pregnancy and risk of cardiovascular diseases later in life: an observational prospective study. PLoS One. 2011;6(11):e27330. doi:10.1371/journal.pone.0027330		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
950	Stulnig TM, Leitner L, Marculescu R, Zeyda M, Itariu BK. Does treatment with n-3 polyunsaturated fatty acids influence vitamin D status in severely obese non-diabetic subjects?. Diabetologia. 2012;55:S363- . doi:10.1007/s00125-012-2688-9				Publication Status
951	Stupin A, Rasic L, Matic A, et al. Omega-3 polyunsaturated fatty acids-enriched hen eggs consumption enhances microvascular reactivity in young healthy individuals. Appl Physiol Nutr Metab. 2018;43(10):988-995. doi:10.1139/apnm-2017-0735			X	Study Duration
952	Sundfor TM, Svendsen M, Heggen E, Dushanov S, Klemsdal TO, Tonstad S. BMI modifies the effect of dietary fat on atherogenic lipids: a randomized clinical trial. Am J Clin Nutr. 2019;110(4):832-841. doi:10.1093/ajcn/nqz113				Health Status
953	Sureda A, Bibiloni MD, Martorell M, et al. Mediterranean diets supplemented with virgin olive oil and nuts enhance plasmatic antioxidant capabilities and decrease xanthine oxidase activity in people with metabolic syndrome: The PREDIMED study. Mol Nutr Food Res. 2016;60(12):2654-2664. doi:10.1002/mnfr.201600450		X	X	
954	Suter E, Hawes MR. Relationship of physical activity, body fat, diet, and blood lipid profile in youths 10-15 yr. Med Sci Sports Exerc. 1993. 25(6):748-54.	X	X		
955	Svendsen K, Henriksen HB, Ostengen B, et al. Evaluation of a short Food Frequency Questionnaire to assess cardiovascular disease-related diet and lifestyle factors. Food Nutr Res. 2018;19:62. doi:10.29219/fnr.v62.1370			X	
956	Szymlek-Gay EA, Gray AR, Heath AM, Ferguson EL, Skeaff CM. Red meat consumption and serum lipids and fatty acids in toddlers: secondary outcomes of a randomized controlled trial. J Pediatr Gastroenterol Nutr. 2018;67(3):395-400. doi:10.1097/mpg.0000000000002018		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
957	Taba N, Fischer K, Esko T, Metspalu A, Pirastu N. Investigating causal relationships between dietary items and blood metabolites using 2-sample mendelian randomization. Human Heredity. 2017;83(5):244- 245. doi:10.1159/000499459				Publication Status
958	Tagetti A, Ericson U, Montagnana M, et al. Intakes of omega-3 polyunsaturated fatty acids and blood pressure change over time: possible interaction with genes involved in 20-HETE and EETs metabolism. Prostaglandins Other Lipid Mediat. 2015;120:126-33. doi:10.1016/j.prostaglandins.2015.05.003			X	
959	Taguchi C, Kishimoto Y, Suzuki-Sugihara N, et al. Regular egg consumption at breakfast by Japanese woman university students improves daily nutrient intakes: open-labeled observations. Asia Pac J Clin Nutr. 2018;27(2):359-365. doi:10.6133/apjcn.042017.17	X	X		
960	Tahir FN, Danyal M, Shah SIA, Qureshi JA. Lipid lowering effect of almonds (Prunus dulcis) in healthy adults. Pakistan Journal of Medical and Health Sciences. 2018;12(4):1356-1358.				Country
961	Taing CY, Gibson AA, Colagiuri S, et al. Primary analysis of the Mandarin-speaking sub-study within the Sydney diabetes prevention program. Diabetes Res Clin Pract. 2017;132:118-126. doi:10.1016/j.diabres.2017.07.032		X		
962	Takagi H, Kobayashi Y, Taguchi O, Takei Y, Sumida Y. Influence of dietary intake of fish oil, magnesium, and zinc on metabolic parameters among individuals tested for diabetes. Nutrition. 2015;31(7-8):988-93. doi:10.1016/j.nut.2015.02.019	X			
963	Takata Y, Zhang X, Li H, et al. Fish intake and risks of total and cause-specific mortality in 2 population-based cohort studies of 134,296 men and women. Am J Epidemiol. 2013;178(1):46-57. doi:10.1093/aje/kws584				Country

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
964	Tammi A, Ronnemaa T, Gylling H, et al. Plant stanol ester margarine lowers serum total and low-density lipoprotein cholesterol concentrations of healthy children: the STRIP project. Special Turku Coronary Risk Factors Intervention Project. J Pediatr. 2000. 136(4):503-10. doi:10.1016/s0022-3476(00)90014-3		X		
965	Tammi A, Ronnemaa T, Miettinen TA, et al. Effects of gender, apolipoprotein E phenotype and cholesterol-lowering by plant stanol esters in children: the STRIP study. Special Turku Coronary Risk Factor Intervention Project. Acta Paediatr. 2002;91(11):1155-62. doi:10.1080/080352502320777379		X		
966	Tang H, Zhang Z, Li Z, Lin J, Fang DZ. High-carbohydrate/low-fat diet-induced gender-specific serum lipid profile changes are associated with LEPR polymorphisms in Chinese youth. Ann Nutr Metab. 2017;70(1):1-8. doi:10.1159/000455165		X		
967	Tani S, Matsuo R, Matsumoto N. A longitudinal study of the association of the eicosapentaenoic acid/arachidonic acid ratio derived from fish consumption with the serum lipid levels: a pilot study. Heart Vessels. 2019;34(1):189-196. doi:10.1007/s00380-018-1226-1		X		
968	Taylor C, Perera D, Wilson A, Zahradka P. Arterial stiffness interferes with LDL-cholesterol lowering by canola oil in persons with mild hypercholesterolemia. FASEB journal. 2017;31(1):.				Publication Status
969	Tayyem RF, Al-Shudifat AE, Johannessen A, et al. Dietary patterns and the risk of coronary heart disease among Jordanians: a case-control study. Nutr Metab Cardiovasc Dis. 2018;28(3):262-269. doi:10.1016/j.numecd.2017.10.026		X		
970	Te Morenga LA, Levers MT, Williams SM, Brown RC, Mann J. Comparison of high protein and high fiber weight-loss diets in women with risk factors for the metabolic syndrome: a randomized trial. Nutr J. 2011. 10:40. doi:10.1186/1475-2891-10-40		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
971	te Velde SJ, Snijder MB, van Dijk AE, et al. Dairy intake from adolescence into adulthood is not associated with being overweight and metabolic syndrome in adulthood: the Amsterdam Growth and Health Longitudinal Study. J Hum Nutr Diet. 2011. 24(3):233-244. doi:10.1111/j.1365-277X.2010.01149.x		X		
972	Tektonidis TG, Akesson A, Gigante B, Wolk A, Larsson SC. A Mediterranean diet and risk of myocardial infarctionheart failure and stroke: a population-based cohort study. Atherosclerosis. 2015;243(1):93-8. doi:10.1016/j.atherosclerosis.2015.08.039		X		
973	Telford RD, Cunningham RB, Waring P, et al. Sensitivity of blood lipids to changes in adiposity, exercise, and diet in children. Med Sci Sports Exerc. 2015;47(5):974-82. doi:10.1249/mss.0000000000000493		X		
974	Telle-Hansen VH, Larsen LN, Hostmark AT, et al. Daily intake of cod or salmon for 2 weeks decreases the 18:1n-9/18:0 ratio and serum triacylglycerols in healthy subjects. Lipids. 2012;47(2):151-60. doi:10.1007/s11745-011-3637-y		X		
975	Telle-Hansen VH, Narverud I, Retterstol K, et al. Substitution of TAG oil with diacylglycerol oil in food items improves the predicted 10 years cardiovascular risk score in healthy, overweight subjects. J Nutr Sci. 2012;1. doi:10.1017/jns.2012.18		X		
976	Tennakoon SU, Kumar BN, Meyer HE. Differences in selected lifestyle risk factors for cardiovascular disease between Sri Lankans in Oslo, Norway, and in Kandy, Sri Lanka. Asia Pac J Public Health. 2015. 27(2):Np616-25. doi:10.1177/1010539513485973	X		X	
977	Teymoori F, Asghari G, Salehi P, Sadeghian S, Mirmiran P, Azizi F. Are dietary amino acids prospectively predicts changes in serum lipid profile?. Diabetes Metab Syndr. 2019. 13(3):1837-1843. doi:10.1016/j.dsx.2019.04.013		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
978	Thiengwiboonwong S, Chongsuwat R, Temcharoen P, Pandii W, Pavadhgul P. Efficacy of dietary modification following the National Cholesterol Education Program (NCEP) recommendation on lipid profiles among hyperlipidemia subjects. J Med Assoc Thai. 2013;96(10):1257-67.				Health Status
979	Tholstrup T, Hjerpsted J, Raff M. Palm olein increases plasma cholesterol moderately compared with olive oil in healthy individuals. Am J Clin Nutr. 2011;94(6):1426-32. doi:10.3945/ajcn.111.018846				Study Duration
980	Thomas J, Chan L, Wray A, et al. Does the presence of cardiovascular disease risk factors or established disease influence the dietary intake of affected adults and their children residing in the same household? A secondary analysis of the Australian Health Survey (2011-2013). BMC Cardiovasc Disord. 2017. 17(1):146. doi:10.1186/s12872-017-0578-2	X		X	
981	Thomson CA, Stopeck AT, Bea JW, et al. Changes in body weight and metabolic indexes in overweight breast cancer survivors enrolled in a randomized trial of low-fat vs. reduced carbohydrate diets. Nutr Cancer. 2010. 62(8):1142-52. doi:10.1080/01635581.2010.513803		X		
982	Thorning TK, Raziani F, Bendsen NT, Astrup A, Tholstrup T, Raben A. Diets with high-fat cheese, high-fat meat, or carbohydrate on cardiovascular risk markers in overweight postmenopausal women: a randomized crossover trial. Am J Clin Nutr. 2015;102(3):573-81. doi:10.3945/ajcn.115.109116				Study Duration
983	Tierney AC, McMonagle J, Shaw DI, et al. Effects of dietary fat modification on insulin sensitivity and on other risk factors of the metabolic syndrome-LIPGENE: a European randomized dietary intervention study. Int J Obes. 2011. 35(6):800-809. doi:10.1038/ijo.2010.209		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
984	Toledo E, Hu FB, Estruch R, et al. Effect of the Mediterranean diet on blood pressure in the PREDIMED trial: results from a randomized controlled trial. BMC Med. 2013. 11:207. doi:10.1186/1741-7015-11-207		X		
985	Toledo E, Wang DD, Ruiz-Canela M, et al. Plasma lipidomic profiles and cardiovascular events in a randomized intervention trial with the Mediterranean diet. Am J Clin Nutr. 2017;106(4):973-983. doi:10.3945/ajcn.116.151159		X		
986	Tomdio A, Ritchie M, Miller AC. Omega-3 fatty acids and cardiovascular disease prevention. Am Fam Physician. 2019. 100(4):209-210.	X			
987	Torres-Pena JD, Garcia-Rios A, Delgado-Casado N, et al. Mediterranean diet improves endothelial function in patients with diabetes and prediabetes: a report from the CORDIOPREV study. Atherosclerosis. 2018;269:50-56. doi:10.1016/j.atherosclerosis.2017.12.012		X		Health Status
988	Tørris C, Molin M, Cvancarova Småstuen M. Lean fish consumption is associated with beneficial changes in the metabolic syndrome components: a 13-year follow-up study from the Norwegian Tromsø Study. Nutrients. 2017;9(3). pii: E247 doi:10.3390/nu9030247		X		
989	Torvik K, Narverud I, Ottestad I, et al. Dietary counseling is associated with an improved lipid profile in children with familial hypercholesterolemia. Atherosclerosis. 2016;252:21-27. doi:10.1016/j.atherosclerosis.2016.07.913	X			Health Status
990	Tran N, Barraj L. Contribution of specific dietary factors to CHD in US females. Public Health Nutr. 2010. 13(2):154-62. doi:10.1017/s1368980009990693	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
991	Trico D, Trifiro S, Mengozzi A, et al. Reducing Cholesterol and Fat Intake Improves Glucose Tolerance by Enhancing beta Cell Function in Nondiabetic Subjects. J Clin Endocrinol Metab. 2018. 103(2):622-631. doi:10.1210/jc.2017-02089		X	X	
992	Tröbs M, Renner T, Scherer G, et al. Nutrition, antioxidants, and risk factor profile of nonsmokers, passive smokers and smokers of the Prevention Education Program (PEP) in Nuremberg, Germany. Prev Med. 2002. 34(6):600-607. doi:10.1006/pmed.2002.1024		X		
993	Trude AC, Kharmats A, Jock B, et al. Patterns of food consumption are associated with obesity, self-reported diabetes and cardiovascular disease in five American Indian communities. Ecol Food Nutr. 2015. 54(5):437-54. doi:10.1080/03670244.2014.922070	X	X		
994	Tsaban G, Wolak A, Avni-Hassid H, et al. Dynamics of intrapericardial and extrapericardial fat tissues during long-term, dietary-induced, moderate weight loss. Am J Clin Nutr. 2017;106(4):984-995. doi:10.3945/ajcn.117.157115		X		
995	Tsugane S, Sawada N. The JPHC study: design and some findings on the typical Japanese diet. Jpn J Clin Oncol. 2014. 44(9):777-82. doi:10.1093/jjco/hyu096	X			
996	Tura A, Conte B, Caparrotto C, et al. Insulin sensitivity and secretion in young, healthy subjects are not changed by Zone and Mediterranean diets. Med J Nutrition Metab. 2010. 3(3):233-237. doi:10.1007/s12349-010-0026-7		X		
997	Turcot V, Brunet J, Daneault C, Tardif JC, Des Rosiers C, Lettre G. Validation of fatty acid intakes estimated by a food frequency questionnaire using erythrocyte fatty acid profiling in the Montreal Heart Institute Biobank. J Hum Nutr Diet. 2015;28(6):646-58. doi:10.1111/jhn.12272			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
998	Turner KM, Keogh JB, Meikle PJ, Clifton PM. Changes in lipids and inflammatory markers after consuming diets high in red meat or dairy for four weeks. Nutrients. 2017;9(8): pii: E886. doi:10.3390/nu9080886		X		
999	Turunen AW, Jula A, Suominen AL, et al. Fish consumption, omega-3 fatty acids, and environmental contaminants in relation to low-grade inflammation and early atherosclerosis. Environ Res. 2013;12043-54. doi:10.1016/j.envres.2012.09.007	X	X		
1000	Ugidos IF, Perez-Rodriguez D, Fernandez-Lopez A. A role for lipids as agents to alleviate stroke damage: the neuroprotective effect of 2-hydroxy arachidonic acid. Neural Regen Res. 2017. 12(8):1273-1275. doi:10.4103/1673-5374.213545	X			
1001	Ulven SM, Christensen JJ, Nygard O, et al. Using metabolic profiling and gene expression analyses to explore molecular effects of replacing saturated fat with polyunsaturated fat-a randomized controlled dietary intervention study. Am J Clin Nutr. 2019;109(5):1239-1250. doi:10.1093/ajcn/nqy356				Health Status
1002	Ulven SM, Leder L, Elind E, et al. Exchanging key food items in daily diet improves fat quality and reduces total cholesterol and LDL cholesterol-a randomized controlled trial. Ann Nut Metab. 2015. 67(Suppl 1):370- 371. doi:10.1159/000440895				Publication Status
1003	Ulven SM, Leder L, Elind E, et al. Replacing dietary saturated fat with polyunsaturated fat reduces total cholesterol and LDL cholesterol in healthy subjects with moderate hypercholesterolaemia-a randomized controlled trial. Atherosclerosis. 2015. 241(1): E194-E194. doi: 10.1016/j.atherosclerosis.2015.04.946				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1004	Ulven SM, Leder L, Elind E, et al. Exchanging a few commercial regularly consumed food items with improved fat quality reduces total cholesterol and LDL-cholesterol: A double-blind randomised controlled trial. Br J Nutr. 2016;116(8):1383-1393. doi:10.1017/s0007114516003445				Health Status
1005	Um CY, Judd SE, Flanders WD, Fedirko V, Bostick RM. Associations of calcium and dairy products with all-cause and cause-specific mortality in the REasons for Geographic and Racial Differences in Stroke (REGARDS) Prospective Cohort Study. Nutr Cancer. 2017;69(8):1185-1195. doi:10.1080/01635581.2017.1367946		X		
1006	Um CY, Prizment A, Hong CP, Lazovich D, Bostick RM. Associations of calcium and dairy product intakes with all-cause, all-cancer, colorectal cancer and coronary heart disease mortality among older women in the Iowa Women's Health Study. Br J Nutr. 2019. 121(10):1188-1200. doi:10.1017/S000711451900045X		X		
1007	Um YJ, Oh SW, Lee CM, et al. Dietary fat intake and the risk of metabolic syndrome in Korean Adults. Korean J Fam Med. 2015;36(5):245-52. doi:10.4082/kjfm.2015.36.5.245			X	
1008	Upadya H, Devaraju CJ, Joshi SR. Anti-inflammatory properties of blended edible oil with synergistic antioxidants. Indian J Endocrinol Metab. 2015;19(4):511-9. doi:10.4103/2230-8210.159063				Health Status, Country
1009	Uusitalo L, Nevalainen J, Salminen I, et al. Fatty acids in serum and diet--a canonical correlation analysis among toddlers. Matern Child Nutr. 2013;9(3):381-95. doi:10.1111/j.1740-8709.2011.00374.x			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1010	Uusitupa M, Hermansen K, Savolainen MJ, et al. Effects of an isocaloric healthy Nordic diet on insulin sensitivity, lipid profile and inflammation markers in metabolic syndrome -- a randomized study (SYSDIET). J Intern Med. 2013;274(1):52-66. doi:10.1111/joim.12044		X		
1011	Valente FX, Candido FG, Lopes LL, et al. Effects of coconut oil consumption on energy metabolism, cardiometabolic risk markers, and appetitive responses in women with excess body fat. Eur J Nutr. 2018;57(4):1627-1637. doi:10.1007/s00394-017-1448-5			X	
1012	Valera B, Suhas E, Counil E, Poirier P, Dewailly E. Influence of polyunsaturated fatty acids on blood pressure, resting heart rate and heart rate variability among French Polynesians. J Am Coll Nutr. 2014. 33(4):288-296. doi:10.1080/07315724.2013.874913	X	X		
1013	Valsta LM, Jauhiainen M, Aro A, Katan MB, Mutanen M. Effects of a monounsaturated rapeseed oil and a polyunsaturated sunflower oil diet on lipoprotein levels in humans. Arterioscler Thromb.1992. 12(1):50-7. doi:10.1161/01.atv.12.1.50				Age of participants at intervention or exposure
1014	van der Gaag EJ, Wieffer R, van der Kraats J. Advising consumption of green vegetables, beef, and full-fat dairy products has no adverse effects on the lipid profiles in children. Nutrients. 2017. 9(5). pii: E518. doi:10.3390/nu9050518		X		
1015	van Hees AM, Saris WH, Hul GB, et al. Effects of dietary fat modification on skeletal muscle fatty acid handling in the metabolic syndrome. Int J Obes (Lond). 2010. 34(5):859-70. doi:10.1038/ijo.2010.6				Duplicate data
1016	Van Rooijen M, Plat J, Blom W, Zock P, Mensink R. The saturated fatty acids palmitic acid and stearic acid do not differently affect cholesterol efflux capacity: Results of A human dietary intervention trial. Atherosclerosis. 2019;287e56- . doi:10.1016/j.atherosclerosis.2019.06.159				Publication Status

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1017	Varady KA, Dam VT, Klempel MC, et al. Effects of weight loss via high fat vs. low fat alternate day fasting diets on free fatty acid profiles. Sci Rep. 2015. 5:7561. doi:10.1038/srep07561		X		
1018	Vasilopoulou D, Markey O, Fagan CC, et al. Chronic consumption of conventional and saturated-fat reduced dairy products have differential effects on low-density lipoprotein cholesterol levels in adults at moderate cardiovascular disease risk. Proceedings of the Nutrition Society. 2016;75(OCE3):E169. doi:10.1017/S0029665116001841				Publication Status
1019	Vedtofte MS, Jakobsen MU, Lauritzen L, et al. Association between the intake of alpha-linolenic acid and the risk of CHD. Br J Nutr. 2014;112(5):735-43. doi:10.1017/s000711451400138x	X			
1020	Velazquez-Lopez L, Santiago-Diaz G, Nava-Hernandez J, Munoz-Torres AV, Medina-Bravo P, Torres-Tamayo M. Mediterranean-style diet reduces metabolic syndrome components in obese children and adolescents with obesity. BMC Pediatr. 2014;14:175. doi:10.1186/1471-2431-14-175		X		
1021	Venkatramanan S, Joseph SV, Chouinard PY, Jacques H, Farnworth ER, Jones PJ. Milk enriched with conjugated linoleic acid fails to alter blood lipids or body composition in moderately overweight, borderline hyperlipidemic individuals. J Am Coll Nutr. 2010;29(2):152-9. doi:10.1080/07315724.2010.10719829		X		Health Status
1022	Viikari J, Akerblom HK, Rasanen L, Kalavainen M, Pietarinen O. Cardiovascular risk in young Finns. Experiences from the Finnish Multicentre Study regarding the prevention of coronary heart disease. Acta Paediatr Scand Suppl. 1990. 365:13-9. doi:10.1111/j.1651-2227.1990.tb11579.x	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1023	Vildmyren I, Halstensen A, Oterhals A, Gudbrandsen OA. Cod protein powder lowered serum nonesterified fatty acids and increased total bile acid concentrations in healthy, lean, physically active adults: A randomized double-blind study. Food Nutr Res. 2019;63. doi:10.29219/fnr.v63.3437		X		
1024	Villalpando S, Lara Zamudio Y, Shamah-Levy T, Mundo-Rosas V, Manzano AC, Lamadrid-Figueroa H. Substitution of whole cows' milk with defatted milk for 4 months reduced serum total cholesterol HDL-cholesterol and total apoB in a sample of Mexican school-age children (6-16 years of age). Br J Nutr. 2015. 114(5):788-95. doi:10.1017/s0007114515002330		X		
1025	Villamor E, Marin C, Mora-Plazas M, Casale M, Vargas LN, Baylin A. Cooking with soyabean oil increases whole-blood alpha-linolenic acid in school-aged children: Results from a randomized trial. Public Health Nutr. 2015;18(18):3420-8. doi:10.1017/s1368980015000762			X	
1026	Villaverde P, Lajous M, MacDonald CJ, Fagherazzi G, Bonnet F, Boutron-Ruault MC. High dietary total antioxidant capacity is associated with a reduced risk of hypertension in French women. Nutr J. 2019;18(1):31. doi:10.1186/s12937-019-0456-0		X		
1027	Vincent MJ, Allen B, Palacios OM, Haber LT, Maki KC. Meta-regression analysis of the effects of dietary cholesterol intake on LDL and HDL cholesterol. Am J Clin Nutr. 2019;109(1):7-16. doi:10.1093/ajcn/nqy273	X			
1028	Violi F, Loffredo L, Pignatelli P, et al. Extra virgin olive oil use is associated with improved post-prandial blood glucose and LDL cholesterol in healthy subjects. Nutr Diabetes. 2015;5e172. doi:10.1038/nutd.2015.23			X	

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1029	Vishwanathan R, Gendron CM, Goodrow-Kotyla EF, Wilson TA, Nicolosi RJ. Increased consumption of dietary cholesterolluteinand zeaxanthin as egg yolks does not decrease serum concentrations and lipoprotein distribution of other carotenoidsretinoland tocopherols. Nutr Res. 2010;30(11):747-55. doi:10.1016/j.nutres.2010.10.007		X	X	
1030	Vissers LET, Waller M, van der Schouw YT, et al. A pro-inflammatory diet is associated with increased risk of developing hypertension among middle-aged women. Nutr Metab Cardiovasc Dis. 2017;27(6):564-570. doi:10.1016/j.numecd.2017.03.005		X		
1031	Viturro E, de Oya M, Lasuncion MA, et al. Cholesterol and saturated fat intake determine the effect of polymorphisms at ABCG5/ABCG8 genes on lipid levels in children. Genet Med. 2006. 8(9):594-9. doi:10.109701.gim.0000237760.25195.e7	X	X		
1032	von Ruesten A, Feller S, Bergmann MM, Boeing H. Diet and risk of chronic diseases: Results from the first 8 years of follow-up in the EPIC-Potsdam study. Eur J Clin Nutr. 2013;67(4):412-9. doi:10.1038/ejcn.2013.7		X		
1033	Voortman T, Kiefte-de Jong JC, Ikram MA, et al. Adherence to the 2015 Dutch dietary guidelines and risk of non-communicable diseases and mortality in the Rotterdam Study. Eur J Epidemiol. 2017;32(11):993-1005. doi:10.1007/s10654-017-0295-2		X		
1034	Vors C, Joumard-Cubizolles L, Lecomte M, et al. Milk polar lipids reduce lipid cardiovascular risk factors in overweight postmenopausal women: Towards a gut sphingomyelin-cholesterol interplay. Gut. 2019;69(3):487-501. doi:10.1136/gutjnl-2018-318155		X		Health Status
1035	Vorster HH, Benade AJ, Barnard HC, et al. Egg intake does not change plasma lipoprotein and coagulation profiles. Am J Clin Nutr.1992. 55(2):400-10. doi:10.1093/ajcn/55.2.400				Age of participants at intervention or exposure

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1036	Vyncke K, Huybrechts I, Van Winckel M, et al. Dietary lipid intake only partially influences variance in serum phospholipid fatty acid composition in adolescents: Impact of other dietary factors. Lipids. 2014;49(9):881-93. doi:10.1007/s11745-014-3935-2	X		X	
1037	Wade AT, Davis CR, Dyer KA, Hodgson JM, Woodman RJ, Murphy KJ. A Mediterranean diet supplemented with dairy foods improves markers of cardiovascular risk: Results from the MedDairy randomized controlled trial. Am J Clin Nutr. 2018;108(6):1166-1182. doi:10.1093/ajcn/nqy207		X		
1038	Wan Y, Wang F, Yuan J, et al. Effects of dietary fat on gut microbiota and faecal metabolitesand their relationship with cardiometabolic risk factors: A 6-month randomised controlled-feeding trial. Gut. 2019;68(8):1417-1429. doi:10.1136/gutjnl-2018-317609		X	X	
1039	Wan Y, Yuan J, Li J, et al. Unconjugated and secondary bile acid profiles in response to higher-fat, lower-carbohydrate diet and associated with related gut microbiota: A 6-month randomized controlled-feeding trial. Clin Nutr. 2019;39(2):395-404. doi:10.1016/j.clnu.2019.02.037		X	X	
1040	Wanders AJ, Brouwer IA, Siebelink E, Katan MB. Effect of a high intake of conjugated linoleic acid on lipoprotein levels in healthy human subjects. PLoS One. 2010;5(2):e9000. doi:10.1371/journal.pone.0009000		X		
1041	Wang D, Campos H, Baylin A. Red meat intake is positively associated with non-fatal acute myocardial infarction in the Costa Rica Heart Study. Br J Nutr. 2017;118(4):303-311. doi:10.1017/s000711451700201x	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1042	Wang DD, Toledo E, Hruby A, et al. Plasma ceramides, Mediterranean diet, and incident cardiovascular disease in the PREDIMED trial (prevención con dieta mediterránea). Circulation. 2017;135(21):2028-2040. doi:10.1161/CIRCULATIONAHA.116.024261		X		
1043	Wang DD, Zheng Y, Toledo E, et al. Lipid metabolic networks, Mediterranean diet and cardiovascular disease in the PREDIMED trial. Int J Epidemiol. 2018. 47(6):1830-1845. doi:10.1093/ije/dyy198	X	X		
1044	Wang H, Fox CS, Troy LM, McKeown NM, Jacques PF. Longitudinal association of dairy consumption with the changes in blood pressure and the risk of incident hypertension: The Framingham Heart Study. Br J Nutr. 2015;114(11):1887-99. doi:10.1017/s0007114515003578		X		
1045	Wang L, Manson JE, Forman JP, Gaziano JM, Buring JE, Sesso HD. Dietary fatty acids and the risk of hypertension in middle-aged and older women. Hypertension. 2010;56(4):598-604. doi:10.1161/hypertensionaha.110.154187			X	
1046	Wang L, Tao L, Hao L, et al. A Moderate-fat diet with one avocado per day increases plasma antioxidants and decreases the oxidation of small, dense LDL in adults with overweight and obesity: A randomized controlled trial. J Nutr. 2019;150(2):276-284. doi:10.1093/jn/nxz231			X	
1047	Wang MP, Thomas GN, Ho SY, Lai HK, Mak KH, Lam TH. Fish consumption and mortality in Hong Kong Chinese--the LIMOR study. Ann Epidemiol. 2011;21(3):164-9. doi:10.1016/j.annepidem.2010.10.010		X		
1048	Wannamethee SG, Jefferis BJ, Lennon L, Papacosta O, Whincup PH, Hingorani AD. Serum conjugated linoleic acid and risk of incident heart failure in older men: The British Regional Heart Study. J Am Heart Assoc. 2018;7(1). pii: e006653. doi:10.1161/jaha.117.006653		X		

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1049	Ward RE, Cho K, Nguyen XT, et al. Omega-3 supplement usefish intakeand risk of non-fatal coronary artery disease and ischemic stroke in the Million Veteran Program. Clin Nutr. 2019;39(2):574-579. doi:10.1016/j.clnu.2019.03.005		X		
1050	Weech M, Altowaijri H, Mayneris-Perxachs J, et al. Replacement of dietary saturated fat with unsaturated fats increases numbers of circulating endothelial progenitor cells and decreases numbers of microparticles: findings from the randomized, controlled Dietary Intervention and VAScular function (DIVAS) study. Am J Clin Nutr. 2018;107(6):876-882. doi:10.1093/ajcn/nqy018			X	
1051	Weech M, Vafeiadou K, Hasaj M, et al. Development of a food-exchange model to replace saturated fat with MUFAs and n-6 PUFAs in adults at moderate cardiovascular risk. J Nutr. 2014;144(6):846-55. doi:10.3945/jn.114.190645			X	
1052	Weech M, Vafeiadou K, Mihaylova R, et al. Substitution of dietary saturated fatty acids with either monounsaturated or n-6 polyunsaturated fatty acids improves the plasma lipid profile in those at risk from CVD: results from the DIVAS study. Proceedings of the nutrition society.2013. 72.E182. doi:10.1017/S0029665113002073				Publication Status
1053	Weech M, Vafeiadou K, Todd S, Yaqoob P, Jackson KG, Lovegrove JA. Replacing dietary saturated with unsaturated fat reduces the cardiovascular risk score in men and women at moderate cardiovascular risk: DIVAS study. Proceedings of the nutrition society. 2015;74(OCE1): E123. doi:10.1017/S002966511500138X				Publication Status
1054	Weggemans RM, Zock PL, Ordovas JM, Pedro-Botet J, Katan MB. Apoprotein E genotype and the response of serum cholesterol to dietary fat, cholesterol and cafestol. Atherosclerosis. 2001. 154(3):547-555. doi:10.1016/S0021-9150(00)00720-6				Age of participants at intervention or exposure

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1055	Weihua Mmed L, Yougang W, Jing W. Reduced or modified dietary fat for preventing cardiovascular disease. J Cardiovasc Nurs. 2013;28(3):204-5. doi:10.1097/JCN.0b013e3182816005	X			
1056	West CE, Sullivan DR, Katan MB, Halferkamps IL, van der Torre HW. Boys from populations with high-carbohydrate intake have higher fasting triglyceride levels than boys from populations with high-fat intake. Am J Epidemiol. 1990. 131(2):271-82. doi:10.1093/oxfordjournals.aje.a115497	X			
1057	West SG, Gebauer SK, Kay CD, et al. Diets containing pistachios reduce systolic blood pressure and peripheral vascular responses to stress in adults with dyslipidemia. Hypertension. 2012;60(1):58-63. doi:10.1161/hypertensionaha.111.182147				Health Status
1058	West SG, Krick AL, Klein LC, et al. Effects of diets high in walnuts and flax oil on hemodynamic responses to stress and vascular endothelial function. J Am Coll Nutr. 2010;29(6):595-603. doi:10.1080/07315724.2010.10719898				Health Status
1059	White AA, Klimis-Tavantzis DJ. Dietary risk assessment for cardiovascular disease among central Maine adolescents. J Sch Health. 1992. 62(9):428-32. doi:10.1111/j.1746-1561.1992.tb01262.x	X		X	
1060	Williams PT, Bergeron N, Chiu S, Krauss RM. A randomized, controlled trial on the effects of almonds on lipoprotein response to a higher carbohydrate, lower fat diet in men and women with abdominal adiposity. Lipids Health Dis. 2019;18(1):83. doi:10.1186/s12944-019-1025-4			X	Study Duration
1061	Wilson DK, Lewis NM. Weight-for-height measurement and saturated fatty acid intake are predictors of serum cholesterol level in children. J Am Diet Assoc. 1992. 92(2):192-6.	X			

	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1062	Winkvist A, Klingberg S, Nilsson LM, et al. Longitudinal 10-year changes in dietary intake and associations with cardio-metabolic risk factors in the Northern Sweden Health and Disease Study. Nutr J. 2017;16(1):20. doi:10.1186/s12937-017-0241-x			X	
1063	Wolff E, Vergnes MF, Portugal H, et al. Cholesterol-absorber status modifies the LDL cholesterol-lowering effect of a Mediterranean-type diet in adults with moderate cardiovascular risk factors. J Nutr. 2011;141(10):1791-8. doi:10.3945/jn.111.141333		X		
1064	Wong H, Chahal N, Manlhiot C, Niedra E, McCrindle BW. Flaxseed in pediatric hyperlipidemia: a placebo-controlled, blinded, randomized clinical trial of dietary flaxseed supplementation for children and adolescents with hypercholesterolemia. JAMA Pediatr. 2013;167(8):708-13. doi:10.1001/jamapediatrics.2013.1442		X		Health Status
1065	Wong VCH, Maguire JL, Omand JA, et al. A Positive Association Between Dietary Intake of Higher Cow's Milk-Fat Percentage and Non-High-Density Lipoprotein Cholesterol in Young Children. J Pediatr. 2019;211105-111.e2. doi:10.1016/j.jpeds.2019.03.047		X		
1066	Wong WW, Hachey DL, Insull W, Opekun AR, Klein PD. Effect of dietary cholesterol on cholesterol synthesis in breast-fed and formula-fed infants. J Lipid Res. 1993. 34(8):1403-11.		X		
1067	Wu Y, Sun G, Zhou X, et al. Pregnancy dietary cholesterol intake, major dietary cholesterol sourcesand the risk of gestational diabetes mellitus: A prospective cohort study. Clin Nutr. 2019; 5614(19)30272-9. doi:10.1016/j.clnu.2019.06.016			X	
1068	Wulan SN, Westerterp KR, Plasqui G. Metabolic profile before and after short-term overfeeding with a high-fat diet: A comparison between South Asian and white men. British Journal of Nutrition. 2014;111(10):1853-1861. doi:10.1017/S0007114514000014		X		

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1069	Wurtz AM, Hansen MD, Tjonneland A, et al. Substitution of meat and fish with vegetables or potatoes and risk of myocardial infarction. Br J Nutr. 2016;116(9):1602-1610. doi:10.1017/s0007114516003500		X		
1070	Wurtz AM, Hansen MD, Tjonneland A, et al. Substitutions of red meat poultry and fish and risk of myocardial infarction. Br J Nutr. 2016;115(9):1571-8. doi:10.1017/s0007114516000507		X		
1071	Xu Y, Wahlberg K, Love TM, et al. Associations of blood mercury and fatty acid concentrations with blood mitochondrial DNA copy number in the Seychelles Child Development Nutrition Study. Environ Int. 2019;124278-283. doi:10.1016/j.envint.2019.01.019		X	X	
1072	Xun P, Hou N, Daviglus M, et al. Fish oilselenium and mercury in relation to incidence of hypertension: a 20-year follow-up study. J Intern Med. 2011;270(2):175-86. doi:10.1111/j.1365-2796.2010.02338.x			X	
1073	Yaemsiri S, Sen S, Tinker LF, et al. Serum fatty acids and incidence of ischemic stroke among postmenopausal women. Stroke. 2013;44(10):2710-7. doi:10.1161/strokeaha.111.000834		X		
1074	Yagalla MV, Hoerr SL, Song WO, Enas E, Garg A. Relationship of dietabdominal obesity, and physical activity to plasma lipoprotein levels in Asian Indian physicians residing in the United States. Journal of the American Dietetic Association. 1996. 96(3):257-261.				Age of participants at intervention or exposure
1075	Yamagishi K, Iso H, Shimazu T, et al. Fish intake and risk of mortality due to aortic dissection and aneurysm: A pooled analysis of the Japan cohort consortium. Clin Nutr. 2019;38(4):1678-1683. doi:10.1016/j.clnu.2018.08.007	X	X		

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1076	Yamanaka M, Sakuma M, Matsushita A, et al. The Effects of Long-Term Dietary Therapy on Patients with Hypertriglyceridemia. J Atheroscler Thromb. 2019;26(1):39-49. doi:10.5551/jat.42440		X		Health Status
1077	Yao Y, Liu W, Zhou H, et al. The Relations between Minor Components and Antioxidant Capacity of Five Fruits and Vegetables Seed Oils in China. J Oleo Sci. 2019;68(7):625-635. doi:10.5650/jos.ess19005			X	
1078	Yu D, Sonderman J, Buchowski MS, et al. Healthy Eating and Risks of Total and Cause-Specific Death among Low-Income Populations of African-Americans and Other Adults in the Southeastern United States: A Prospective Cohort Study. PLoS Med. 2015;12(5):e1001830; discussion e1001830. doi:10.1371/journal.pmed.1001830		X		
1079	Yu E, Ruiz-Canela M, Guasch-Ferre M, et al. Increases in Plasma Tryptophan Are Inversely Associated with Incident Cardiovascular Disease in the Prevencion con Dieta Mediterranea (PREDIMED) Study. J Nutr. 2017;147(3):314-322. doi:10.3945/jn.116.241711		X		
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1081	Zarrazquin I, Torres-Unda J, Ruiz F, et al. Longitudinal study: lifestyle and cardiovascular health in health science students. Nutr Hosp. 2014;30(5):1144-51. doi:10.3305/nh.2014.30.5.7833	X			
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	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1083	Zhang HW, Zhao X, Guo YL, et al. Free fatty acids and cardiovascular outcome: a Chinese cohort study on stable coronary artery disease. Nutr Metab (Lond). 2017;14(41). doi:10.1186/s12986-017-0195-1		X		
1084	Zhang J, Wang C, Li L, et al. Dietary inclusion of salmon, herring and pompano as oily fish reduces CVD risk markers in dyslipidaemic middle-aged and elderly Chinese women. Br J Nutr. 2012;108(8):1455-65. doi:10.1017/s0007114511006866				Health Status
1085	Zhang J, Wang C, Li L, et al. Inclusion of Atlantic salmon in the Chinese diet reduces cardiovascular disease risk markers in dyslipidemic adult men. Nutr Res. 2010;30(7):447-54. doi:10.1016/j.nutres.2010.06.010		X		Country
1086	Zhang S, Lin X, Lynn H, et al. Dietary cholesterol interacts with SREBF1 to modulate obesity in Chinese children. Mol Nutr Food Res. 2017;61(9). doi:10.1002/mnfr.201700105	X			
1087	Zhang X, Qi Q, Bray GA, Hu FB, Sacks FM, Qi L. APOA5 genotype modulates 2-y changes in lipid profile in response to weight-loss diet intervention: the Pounds Lost Trial. Am J Clin Nutr. 2012;96(4):917-22. doi:10.3945/ajcn.112.040907		X		
1088	Zhang Z, Gillespie C, Yang Q. Plasma trans-fatty acid concentrations continue to be associated with metabolic syndrome among US adults after reductions in trans-fatty acid intake. Nutr Res. 2017;4351-59. doi:10.1016/j.nutres.2017.05.008	X	X		
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1090	Zhao JV, Schooling CM. Effect of linoleic acid on ischemic heart disease and its risk factors: a Mendelian randomization study. BMC Med. 2019;17(1):61. doi:10.1186/s12916-019-1293-x	X	X		
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1094	Zhu WL, Feng NP, Ma J, Wang Y, Ye GJ. The effect of dietary intervention on lipidemia in school-aged children. Zhonghua liu xing bing xue za zhi. 2003. 24(9):794- 797.				Language
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	Reference	Study Design	Intervention /Exposure or Comparator	Outcome	Other
1097	Zibaeenezhad MJ, Ghavipisheh M, Attar A, Aslani A. Comparison of the effect of omega-3 supplements and fresh fish on lipid profile: a randomizedopen-labeled trial. Nutr Diabetes. 2017;7(12):1. doi:10.1038/s41387-017-0007-8		X		
1098	Zibaeenezhad MJ, Ostovan P, Mosavat SH, Zamirian M, Attar A. Almond oil for patients with hyperlipidemia: A randomized open-label controlled clinical trial. Complement Ther Med. 2019;42:33-36. doi:10.1016/j.ctim.2018.10.013				Health Status
1099	Zinn C, McPhee J, Harris N, Williden M, Prendergast K, Schofield G. A 12-week low-carbohydratehigh-fat diet improves metabolic health outcomes over a control diet in a randomised controlled trial with overweight defence force personnel. Appl Physiol Nutr Metab. 2017;42(11):1158-1164. doi:10.1139/apnm-2017-0260		X		
1100	Zock PL, de Vries JH, Katan MB. Impact of myristic acid versus palmitic acid on serum lipid and lipoprotein levels in healthy women and men. Arterioscler Thromb. 1994. 14(4):567-75.				Age of participants at intervention or exposure
1101	Zock PL, Katan MB. Hydrogenation alternatives: effects of trans fatty acids and stearic acid versus linoleic acid on serum lipids and lipoproteins in humans. J Lipid Res. 1992. 33(3):399-410.				Age of participants at intervention or exposure
1102	Zong G, Sun Q, Yu D, et al. Dairy consumptiontype 2 diabetesand changes in cardiometabolic traits: A prospective cohort study of middle-aged and older chinese in beijing and shanghai. Diabetes Care. 2014;37(1):56-63. doi:10.2337/dc13-0975		X		
1103	Zubair N, Kuzawa CW, Lee NR, McDade TW, Adair LS. Clustering and determinants of cardiometabolic risk factors among Filipino young adults. Asia Pac J Clin Nutr. 2014;23(1):148-58. doi:10.6133/apjcn.2014.23.1.06				Country