USDA-HHS Birth to 24 Months (B-24) Topic Identification Project

Topic Briefs for Potential Systematic Reviews

Period of Sole Nutrient Feeding, 0–6 months

The B-24 expert Work Group 1 identified important nutrition topics relevant to dietary guidance for infants from birth to six months of age (the period of sole nutrient source feeding) to facilitate exploration of the evidence base. Below is a brief description of each topic identified, including the rationale, potential systematic review questions, data needs, research priorities, and key references.

1. Duration of exclusive breastfeeding

Rationale: Current US and global recommendations are largely based on the 2002 World Health Organization's systematic review, "The optimal duration of exclusive breastfeeding," by Michael S. Kramer and Ritsuko Kakuma (2012). However, studies published since the WHO review suggest that this recommendation should be re-evaluated in light of concerns regarding nutritional status, food allergies, iron deficiency, and celiac disease related to delayed introduction of complementary foods.

PICO:

Population: Infants, ages 0–6 months.
Intervention/Exposure: Breastfeeding.
Comparator: Duration of exclusive breastfeeding.
Outcomes: 1) Nutritional status, 2) growth and physical development, 3) cognitive, behavioral and neuromotor development, 4) food allergies and asthma, and 5) long-term health outcomes (e.g., cardiovascular disease, hypertension, Type I and II diabetes, obesity, and inflammatory bowel disease).

Systematic Review Questions:

- What is the optimal duration of exclusive breastfeeding for promoting appropriate nutritional status?
- What is the optimal duration of exclusive breastfeeding for promoting appropriate growth and development?
- What is the optimal duration of exclusive breastfeeding for promoting appropriate cognitive, behavioral and neuromotor development?
- What is the optimal duration of exclusive breastfeeding for preventing food allergies and asthma?
- What is the optimal duration of exclusive breastfeeding for promoting long-term health outcomes (e.g., cardiovascular disease, hypertension, Type I and II diabetes, obesity, and inflammatory bowel disease)?

Data and Research Priorities:

- Data on nutrient and bioactive components of human milk particularly, as these reflect changes in dietary patterns in the US and globally.
- Definition and prevalence of "exclusive breastfeeding." Some research makes very clear what definition was used and others do not. In addition, "exclusive" did not always mean that the infant only received human milk from his or her mother.
- Prevalence of different modes of infant feeding, i.e., who is feeding "at the breast" versus via bottle (pumped fresh expressed human milk, stored mother's human milk, banked human milk, or any combination thereof).
- Relative differences between growth standards for assessing the impact of feeding practices on infants.

1. Duration of exclusive breastfeeding
• Impact of timing of blood sampling on nutrient concentrations relative to feeding, e.g., the timing of the blood draw may matter or the last feeding may be what is reflected in the levels found. • Impact of stage of development on nutrient assessment methodologies. • Factors that impact the definition, prevalence, and effect of food "allergies" versus "sensitivities." • Best methods for defining or confirming "allergy." • Prevalence of confirmed (i.e., by appropriate testing) versus self-reported allergy and comparisons based on method of feeding.
Reference: • Kramer MS, Kakuma R. Optimal duration of exclusive breastfeeding. *Cochrane Database Syst Rev.* 2002;(1):CD003517. Review. Update in: *Cochrane Database Syst Rev.* 2012;8:CD003517. PubMed PMID: 11869667.

2. Relationship between breast milk composition and infant health outcomes

Rationale: Human milk is a complex, biologically active fluid that changes through the course of a feeding and over the course of lactation. Therefore, it is important to understand the specific factors in human milk that either positively or negatively affect infant health outcomes.

PICO:

Population: Lactating women.

Intervention/Exposure: Factors in breast milk that affect infant health and development.

Comparator: Specific factors such as nutrients, micronutrients, PUFAs, nucleotides, oligosaccharides, environmental contaminants (heavy metals, PCBs, etc.), etc.

Outcomes: 1) Infant growth and physical development, 2) infant cognitive, behavioral, and neuromotor development, 3) infant's intake self-regulation based on composition/energy density, and 4) infant immune function (morbidity/mortality).

Systematic Review Questions:

- What factors in human milk affect infant growth, body composition, and physical development?
- What factors in human milk affect infant cognitive, behavioral, and neuromotor development?
- What factors in human milk affect infant's intake self-regulation?
- What factors in human milk affect infant's immune function (morbidity/mortality)?

Data and Research Priorities:

- Best methods (biomarkers, intake estimation, etc.) for assessing the impact of maternal diet on nutrient/bioactive components in human milk.
- Data to estimate dietary intake patterns of lactating women in the US and globally, including dietary supplement/herbal/botanical use.
- Confirmation of the role of confounders affecting analysis/composition of human milk including: Time of day of milk collection; time since (mother's) last meal; method of milk collection (one versus both breasts, full versus partial collection, pump versus hand expression); stage of lactation; extent of breastfeeding (exclusive versus predominant), and milk storage.
- Impact of storage method on human milk composition and hedonics.
- Differences in composition of banked human milk from single (mother) or multiple sources.
- Impact of infant on milk composition, e.g., infant sex, parity and number of infants/children nursing.

3. Delivery mechanism for human milk

Rationale: Delivery mechanism (breast versus bottle) for human milk (including oral/motor skills needed for breastfeeding versus bottle feeding) and infant growth. Many infants fed human milk in the US consume expressed human milk by bottle. Numerous studies have demonstrated protective effects of human milk when compared with formula feeding, but these have not distinguished the potential effects of mode of milk delivery on outcomes. For example, not only may differences in the composition of the milk (breast versus formula) influence outcomes such as growth, but the potential for caregiver to influence volume of consumption (bottle versus breast) may also have an effect. Moreover, bottle feeding, regardless of type of milk, may have an effect on an infant's ability to self-regulate milk intake. A recent small study by Bartok (2011) suggested that delivery method for human milk may not affect growth for the first four months of life, but may increase weight velocity from 4–6 months. Using data from the Infant Feeding Practices Study II (IFPS II), Li and colleagues (2012) demonstrated that weight gain during infancy was greater in infants who received a greater proportion of human milk from a bottle than from the breast. Further analysis from IFPS II showed that bottle feeding early in life, regardless of milk type, was associated with increased intake in late infancy than those fed directly at the breast.

PICO:

Population: Infants, ages 0–12 months.
Intervention/Exposure: Human milk consumed via the breast.
Comparator: Human milk consumed via bottle.
Outcomes: Infant 1) growth and physical development, 2) cognitive, behavioral, and neuromotor development, 3) oral health, and 4) long-term health outcomes (e.g., cardiovascular disease, hypertension, Type I and II diabetes, obesity, and inflammatory bowel disease).

Systematic Review Questions:

- Insufficient data exist to support any systematic reviews at this time.

Data and Research Priorities:

- What is the effect of human milk consumed via the breast versus bottle on infant growth and development?
- What is the effect of human milk consumed via the breast versus bottle on infant cognitive, behavioral, and neuromotor development?
- What is the effect of human milk consumed via the breast versus bottle on infant oral health?
- What is the effect of human milk consumed via the breast versus bottle on long-term outcomes (e.g., cardiovascular disease, hypertension, Type I and II diabetes, obesity, and inflammatory bowel disease)?

References:

- Bartok CJ. Babies fed breastmilk by breast versus by bottle: a pilot study evaluating early growth patterns. *Breastfeed Med.* 2011 Jun;6(3):117-24. doi:10.1089/bfm.2010.0055. Epub 2010 Dec 6. PubMed PMID: 21133764.
- Li R, Magadia J, Fein SB, Grummer-Strawn LM. Risk of bottle-feeding for rapid weight gain during the first year of life. *Arch Pediatr Adolesc Med.* 2012 May;166(5):431-6. doi: 10.1001/archpediatrics.2011.1665. PubMed PMID: 22566543.

4. Micronutrient supplements for breast-fed infants (iron, zinc, vitamin D, fluoride)

Rationale: Micronutrient supplements are routinely prescribed for breast-fed infants. Are they necessary, and if so, when, and what is the effective dose, duration, and timing? What are the determinants of the need for supplementation and what is the criterion for efficacy?

PICO:

Population: Breast-fed infants, ages 0–6 months.
Intervention/Exposure: Micronutrient supplements (iron, zinc, vitamin D, fluoride).
Comparator: Different levels of micronutrient intakes (iron, zinc, vitamin D, fluoride)?
Outcomes: 1) Growth and physical development, 2) cognitive, behavioral, and neuromotor development, and 3) iron status/anemia.

Systematic Review Questions:

- What is the impact of specific micronutrient supplements (iron, zinc, vitamin D, and fluoride) for breast-fed infants on:
  - Physical growth?
  - Cognitive, behavioral, and neuromotor development?
  - Relevant health outcomes (e.g., iron and anemia)?

Data and Research Priorities:

- Prevalence of maternal supplement use in the US and globally, and impact on human milk composition.
- Impact of maternal iron supplementation on infant status, including potential interactions with other micronutrients (e.g., zinc, vitamin A, and folate).
- Prevalence of dietary supplement use in infants aged 0–6 months, including relative use in breast-fed versus formula-fed infants.
- Prevalence of micronutrient malnutrition (over- or under-nutrition) in 0–6 month-old infants in the US.
- Specific priority nutrients include:
  - Relative impact of iron form, dose, duration, and compliance on infant iron status.
  - Prevalence of zinc supplement use in mothers and potential impact on maternal status.
  - Better biomarkers for assessing zinc status in this age group.
  - Prevalence of vitamin D use and impact on maternal and infant health.
  - Better data on primary vitamin D exposure scenarios (diet, sunlight) and impact on maternal and infant health, including impact of dose and timing.
  - Data on intake of "dietary" fluoride (water, toothpaste) and potential health implications.

5. Maternal diet and allergy risk

Rationale: Maternal diet during breastfeeding has been implicated in potential increased risk of infant allergy, celiac disease, milk "sensitivities" (i.e., not true allergies), and infant colic. Infant exposure to potential allergens through human milk has been the focus of a number of recent studies (Gdalevich, 2001; Ludvigsson, 2005; Yang, 2009). Sufficient concern has been raised to warrant a closer evaluation of these potential relationships.

PICO:

Population: Pregnant and lactating women.

Intervention/Exposure: Diet [including allergens (milk, egg, wheat, peanut, tree nuts, and fish), probiotics/prebiotics, and polyunsaturated fatty acids (such as alpha-linoleic acid)].

Comparator: Diet, containing or excluding common allergenic foods.

Outcomes: Infant food allergies and asthma, including celiac disease, milk "sensitivities" and infant colic.

Systematic Review Questions:

- What is the relationship between maternal diet during pregnancy on risk of infant allergy and asthma, celiac disease, milk "sensitivities," and infant colic?
- What is the relationship between maternal diet during lactation on risk of infant allergy and asthma, celiac disease, milk "sensitivities," and infant colic?

Data and Research Priorities:

- What is the relative risk of maternal diet in non-atopic versus high-risk atopic families?
- Prevalence of food allergy versus food "sensitivity."
- Best methods for distinguishing between allergic response and sensitivity; the former is a clinical diagnosis based on double-blind, placebo-controlled food challenge versus food sensitivity assessed by skin prick testing or serum-specific Immunoglobulin E (IgE) levels.
- Relative impact of maternal diet on infant asthma or atopic dermatitis (atopic eczema).

References:

- Gdalevich M, Mimouni D, David M, Mimouni M. Breast-feeding and the onset of atopic dermatitis in childhood: a systematic review and meta-analysis of prospective studies. *J Am Acad Dermatol.* 2001 Oct;45(4):520-7. Review. PubMed PMID: 11568741.
- Ludvigsson JF, Mostrom M, Ludvigsson J, Duchen K. Exclusive breastfeeding and risk of atopic dermatitis in some 8300 infants. *Pediatr Allergy Immunol.* 2005 May;16(3):201-8. PubMed PMID: 15853948.
- Yang YW, Tsai CL, Lu CY. Exclusive breastfeeding and incident atopic dermatitis in childhood: a systematic review and meta-analysis of prospective cohort studies. *Br J Dermatol*. 2009 Aug;161(2):373-83. doi:10.1111/j.1365-2133.2009.09049.x. Epub 2009 Feb 23. Review. PubMed PMID:19239469.

6. Introduction of complementary and transitional foods into the diets of infants/toddlers in those at high risk for allergic disease

Rationale: The issue of timing of exposure to food allergens is a core component of questions regarding guidance about infant and young child feeding. The area has been the subject of new studies and reviews (Jarvinen, 2012; Sansotta, 2012; Nwaru, 2013) that reflect a changing approach to this question, e.g., in most patients no delay in introduction is necessary for many of these putative food allergens, and early introduction may prevent food allergy.

PICO:

Population: Infants and toddlers, aged 0–24 months; infants and toddlers at high risk for developing allergies.

Intervention/Exposure: Introduction of complementary foods and highly allergenic foods (milk, egg, wheat, peanut, tree nuts, fish, and shellfish). Late introduction (>6 months for complementary foods, >12 months for highly allergenic foods).

Comparator: Early introduction (4–6 months for complementary foods, 6–12 months for highly allergenic foods).

Outcomes: 1) Food allergies and asthma, 2) immune system development, infection, or inflammation, 3) atopic dermatitis, 4) obesity, 5) Type I and II diabetes, and 6) celiac disease.

Systematic Review Questions:

- What is the relationship between timing of introduction of complementary foods and the development of 1) food allergies and asthma, 2) immune system, infection or inflammation, 3) atopic dermatitis 4) obesity, 5) Type I and II diabetes, and 6) celiac disease among infants and toddlers?
- What is the relationship between consuming highly allergenic complementary foods and the development of 1) food allergies and asthma, 2) immune system, infection, or inflammation, 3) atopic dermatitis, 4) obesity, 5) Type I and II diabetes, and 6) celiac disease among infants and toddlers?

Data and Research Priorities:

- Criteria for definition of high risk (most commonly first-degree relative with an atopic disease).
- Better understanding of the role of confounders in both experimental design and evaluation of outcomes. For example, reverse causation where atopic families delay introduction of complementary foods, therefore appearing as if delaying introduction causes allergy.
- Need well-designed randomized clinical trials.
- Data is needed on prevalence of relevant practices regarding timing of introduction of suspect foods.

References:

- Järvinen KM, Fleischer DM. Can we prevent food allergy by manipulating the timing of food exposure? *Immunol Allergy Clin North Am.* 2012 Feb;32(1):51-65. doi:10.1016/j.iac.2011.11.007. Epub 2011 Dec 16. Review. PubMed PMID: 22244232.
- Nwaru BI, Takkinen HM, Niemelä O, Kaila M, Erkkola M, Ahonen S, Tuomi H, Haapala AM, Kenward MG, Pekkanen J, Lahesmaa R, Kere J, Simell O, Veijola R, Ilonen J, Hyöty H, Knip M, Virtanen SM. Introduction of complementary foods in infancy and atopic sensitization at the age of 5 years: timing and food diversity in a Finnish birth cohort. *Allergy.* 2013 Apr;68(4):507-16. doi:10.1111/all.12118. Epub 2013 Feb 15. PubMed PMID: 23510377.
- Sansotta N, Piacentini GL, Mazzei F, Minniti F, Boner AL, Peroni DG. Timing of introduction of solid food and risk of allergic disease development: Understanding the evidence. *Allergol Immunopathol (Madr).* 2013 Sep-Oct;41(5):337-45. doi: 10.1016/j.aller.2012.08.012. Epub 2012 Dec 31. PubMed PMID: 23287585.

7. Infant formula

Rationale: Notwithstanding the universal recognition of human milk as the "gold standard" for infant feeding, infant formulas continue to play a large role in infant feeding in the US. Commercially available infant formulas have a remarkable success record in safely providing adequate nutrition for normal growth and development. However, the ongoing effort to create a food that mimics the composition of human milk has resulted in periodic additions of new components. These changes demand ongoing vigilance to ensure continued safety and efficacy. Areas of continued interest include the nature and effect of available protein sources, e.g., cow milk (casein/whey) or soy-based, or addition of such ingredients as specific long-chain polyunsaturated fatty acids (LCPUFA) and other bioactive components including prebiotics/probiotics. Further knowledge is needed about the best formulation in order to inform recommendations on what to feed non- or partially breast-fed infants.

PICO:

Population: Infants, aged 0–12 months.

Intervention/Exposure: Infant formula (including formulas with different sources and forms of protein, and formulas containing LCPUFAs or pre-/probiotics).

Comparator: Breast milk or different types of infant formula.

Outcomes: 1) Food allergies and asthma, 2) diabetes mellitus, and 3) diet quality.

Systematic Review Questions:

- Which type of infant formula results in similar risk of food allergies and asthma between formula-fed infants and breast-fed infants?
- Which type of infant formula results in similar risk of diabetes mellitus between formula-fed infants and breast-fed infants?
- Which type of infant formula results in similar diet quality between formula-fed infants and breast-fed infants?

Data and Research Priorities:

- Improved data on composition of currently available commercial formulas.
- Specific data are needed with regard to how "extensively" or "partially" hydrolyzed formulas are defined.
- Better data on physic-chemical properties of components of infant formula are needed to better evaluate the biological impact and to address issues such as potential allergenicity.
- Impact of other components in human milk on protein metabolism to provide better context for evaluating this issue with regard to infant formula matrix.
- Estimates of the exposure of infants to the range of new ingredients that have been added to infant formulas in recent years, e.g., LCPUFA; and comparison to intakes in breast-fed infants.

8. Health outcomes in formula versus breastfed infants

Rationale: Short-, medium-, and long-term health outcomes likely linked with different infant-feeding practices (exclusive breastfeeding, exclusive formula feeding, mixed feeding, etc.). It is crucial to better characterize relationship between infant feeding practices, obesity, and related chronic diseases. Focal points include the influence of infant feeding mode(s) on infant body composition and the immune system (e.g., inflammation). Other key health outcomes might include the impact of infant feeding modes on oral health.

PICO:

Population: Infants, ages 0–12 months.
Intervention/Exposure: Infant feeding practices (exclusive breastfeeding, exclusive formula feeding, mixed feeding, etc.).
Comparator: Different infant feeding practices (exclusive breastfeeding, exclusive formula feeding, mixed feeding, etc.).
Outcomes: 1) Cognitive, behavioral, or neuromotor development, 2) immune system development, infection, or inflammation, and 3) body composition/overweight/obesity (all outcomes considered in short-, medium-, and long-term).

Systematic Review Questions:

- What is the relationship between infant feeding practices (i.e., exclusive breastfeeding, exclusive formula feeding) and cognitive, behavioral, or neuromotor development?
- What is the relationship between infant feeding practices (i.e., exclusive breastfeeding, exclusive formula feeding) and immune system development, infection, or inflammation?
- What is the relationship between infant feeding practices (i.e., exclusive breastfeeding, exclusive formula feeding) and overweight/obesity?

Data and Research Priorities: (in addition to those highlighted above in #8)

- Need to standardize definitions of different infant feeding modes.
- Prevalence and type of mixed feeding during months 0–6 in the US.
- Impact of mixed feeding during months 0–6 (solids, water, and either human milk or infant formula) and health outcomes.
- Need for good prospective cohort studies since randomized controlled trials are unethical in this area.
- Need for household socio-economic status and maternal education, as they are critical distal confounders.
- Need to have a better understanding of the role of maternal lifestyles and quality of caregiving as intermediate confounders.
- Need for better data on type of formula, quality, and amount of complementary foods and drinks, as well as infant's physical activity patterns, as each is likely to be a key proximal determinant or effect modifier.

9. Type of human milk consumed

Rationale: Numerous modes exist for feeding human milk, including directly suckled from the breast, freshly expressed via a bottle, stored mother's milk, banked human milk, or any combination thereof. It is therefore important to assess the impact of changes in composition (i.e., nutritional and immunological content; Bertino, 2013) and hedonics (taste or smell; Spitzer, 2013) over time (e.g., during a feeding, over a day or longer, consequent to these different modes of feeding/storage).

PICO:

Population: Lactating women.

Intervention/Exposure: Type of human milk (milk suckled directly from the mother's breasts, fresh expressed human milk, stored mother's human milk, banked human milk, or any combination thereof); human milk storage methods.

Comparator: Different type of human milk (milk suckled directly from the mother's breasts, fresh expressed human milk, stored mother's human milk, banked human milk, or any combination thereof); human milk storage methods.

Outcomes: Differences in human milk composition/taste (i.e., nutritional and immunological content) and changes over time; infant health outcomes, including 1) immune system development, infection, or inflammations, 2) growth and physical development, 3) cognitive, behavioral, and neuromotor development, and 4) weight status (overweight/obesity).

Systematic Review Questions:

- Insufficient data exist to support any systematic reviews at this time.

Data and Research Priorities:

- Do different human milk storage methods result in differences in the composition or taste of different types of human milk (i.e., milk suckled directly from the mother's breasts, fresh expressed human milk, stored mother's human milk, banked human milk, or any combination thereof)?
- Are there differences in the composition or taste of different types of human milk (i.e., milk suckled directly from the mother's breasts, fresh expressed human milk, stored mother's human milk, banked human milk, or any combination thereof)?
- Are there differences in changes over time in the composition or taste of different types of human milk (i.e., milk suckled directly from the mother's breasts, fresh expressed human milk, stored mother's human milk, banked human milk, or any combination thereof)?
- Are there differences in infant health outcomes when different types of human milk are consumed, including 1) immune system development, infection, or inflammation, 2) growth and physical development, 3) cognitive, behavioral, and neuromotor development, and 4) weight status (overweight/obesity)?

References:

- Bertino E, Giribaldi M, Baro C, Giancotti V, Pazzi M, Peila C, Tonetto P, Arslanoglu S, Moro GE, Cavallarin L, Gastaldi D. Effect of prolonged refrigeration on the lipid profile, lipase activity, and oxidative status of human milk. *J Pediatr Gastroenterol Nutr.* 2013 Apr;56(4):390-6. doi:10.1097/MPG.0b013e31827af155. PubMed PMID: 23149807.
- Spitzer J, Klos K, Buettner A. Monitoring aroma changes during human milk storage at +4 °C by sensory and quantification experiments. *Clin Nutr.* 2013 Feb 6. doi:pii: S0261-5614(13)00041-1. 10.1016/j.clnu.2013.01.015. [Epub ahead of print] PubMed PMID: 23433895.

10. Factors influencing infant appetite

Rationale: Infant appetite is likely affected by the method of feeding, the nutrient content of the food [e.g., the amino acid tryptophan may make an infant sleepy and thus less interested in feeding (Arslanoglu, 2011); free glutamate may be associated with early satiety (Ventura, 2012); timing of feeds and the hormone profile of the infant (Savino, 2006)]. Thus, an understanding of appetite regulation and factors that can alter that regulation are of importance for the immediate health of the infant and likely affect long-term health outcomes.

PICO:

Population: Infants, ages 0–12 months.

Intervention/Exposure: Factors influencing appetite regulation [e.g., method of feeding, the nutrient content of the food (tryptophan may make an infant sleepy and thus less interested in feeding; free glutamate may be associated with early satiety and thus less intake), timing of feeds, the hormone profile of the infant, the socio-economic security of the care providers, and the psychological health of the family, especially the mother].

Comparator: Factors influencing appetite regulation [e.g., method of feeding, the nutrient content of the food (tryptophan may make an infant sleepy and thus less interested in feeding; free glutamate may be associated with early satiety and thus less intake), timing of feeds, the hormone profile of the infant, the socio-economic security of the care providers and the psychological health of the family, especially the mother].

Outcomes: 1) Appetite regulation, 2) growth and physical development, 2) cognitive, behavioral, or neuromotor development, and 3) dietary behaviors.

Systematic Review Questions:

- How is infant appetite regulated?
- What infant cues of development readiness for complementary foods should be used to determine timing of introduction of complementary foods?
- What factors in the infant diet and environment impact appetite regulation in infants?
- What is the impact of appetite regulation on infant health, including growth and physical development, and cognitive, behavioral, or neuromotor development?

Data and Research Priorities:

- Biomarkers of relevant neurological function.
- Methodologies to distinguish between biological and environmental factors.
- Better appreciation of critical periods in development specific to appetite (hedonics and mechanics of eating).

References:

- Arslanoglu S, Bertino E, Nicocia M, Moro GE. WAPM Working Group on Nutrition: potential chronobiotic role of human milk in sleep regulation. *J Perinat Med.* 2011 Jan;40(1):1-8. Review. PubMed PMID: 22848905.
- Savino F, Grassino EC, Fissore MF, Guidi C, Liguori SA, Silvestro L, Oggero R, Miniero R. Ghrelin, motilin, insulin concentration in healthy infants in the first months of life: relation to fasting time and anthropometry. *Clin Endocrinol (Oxf).* 2006 Aug;65(2):158-62. PubMed PMID: 16886954.
- Ventura AK, Beauchamp GK, Mennella JA. Infant regulation of intake: the effect of free glutamate content in infant formulas. *Am J Clin Nutr.* 2012 Apr;95(4):875-81. doi: 10.3945/ajcn.111.024919. Epub 2012 Feb 22. PubMed PMID:22357724; PubMed Central PMCID: PMC3302362.

11. Infant microbiome

Rationale: Study of the infant microbiome (considered to be the collective genomes and genes, products of bacteria resident within and on the infant) is a new field where information that may directly impact health is rapidly accruing. The infant gastrointestinal tract microbiome is highly variable and can be influenced by mode of delivery, type of feeding, time, and infectious events the infant experiences. The gut microbiome may directly affect infant health by playing a role in the types of infections and the infant's nutritional status. It also may have long-term effects on allergy, obesity, and chronic inflammatory diseases, among others. The key issue is to understand if or how the infant microbiome affects health outcomes in infancy and later in life and how infant feedings can be manipulated to provide desirable outcomes.

PICO:

Population: Infants, aged 0–12 months (breast-fed infants serve as the reference group).

Intervention/Exposure: Gut microbiome; infant feeding practices that impact the gut microbiome; infant dietary intake (e.g., related to human milk, infant formula, etc.).

Comparator: Gut microbiome; infant feeding practices that impact the gut microbiome; reference group will be infants following optimal breastfeeding practices (exclusive breastfeeding for six months; any breastfeeding for at least one year).

Outcomes: Development of 1) food allergies and asthma, 2) immune system, infection, or inflammation, and 3) overweight/obesity during infancy and later in childhood and adulthood.

Systematic Review Questions:

- Insufficient data exist to support any systematic reviews at this time.

Data and Research Priorities:

- Characterization of the nature and ontology of the gut/oral/dermal microbiome including:
  - Characterization of gut microbiome across different populations and racial/ethnic groups
  - The relative impact of genetics versus environment
- Characterization of the bi-directional relationships between diet/specific nutrients and the gut microbiome, i.e.,
  - What is the role of diet and specific nutrients in the ontogeny of the gut microbiome?
  - What is the impact of the gut microbiome on nutrient absorption and metabolism?
- How does the infant gut microbiome impact development of food allergies and asthma?
- What is the contribution of the gut microbiome to the metabolome and what is the potential for this relationship in terms of biomarkers of nutrition exposure, status, and function?
- How does the infant gut microbiome impact development of the immune system, infection, or inflammation?
- How does the infant gut microbiome impact development of overweight or obesity and other chronic non-communicable diseases?
- How can infant feeding practices be manipulated to impact infant gut microbiome in such a way to improve health outcomes?