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

Topic Briefs for Potential Systematic Reviews

Period of Complementary Feeding, 6–12 months

The B-24 expert Work Group 2 identified important nutrition topics relevant to dietary guidance for infants six to 12 months of age (the period of complementary 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. The impact of differences in protein intake in infants in the first 12 months of life

Rationale: Available data indicate that formula-fed infants have a higher intake of protein compared to infants fed mature human milk (i.e., past the period of colostrum consumption; Hester, 2012). In addition to the consideration of total protein, the source of protein (human milk, cow's milk, soy, hydrolyzed proteins), particularly as it pertains to the amino acid profiles and relative levels of free amino acids of available protein sources, is critical in evaluating the needs of infants through the first 12 months of life. Differences in total protein, free amino acids, and other factors such as peptides associated with hydrolyzed protein formulas, as well as the standard used to evaluate protein quality (the so-called Protein Efficiency Ratio or PER) have been comprehensively reviewed (Journal of Nutrition, 1998). However, the impact of increased free amino acid intake on satiety and growth is still poorly understood. Higher protein intake has been shown to result in increased weight gain in formula-fed, compared to human-milk-fed infants (Koletzko, 2009). The relative impact of differences in protein intake in formula-fed infants, compared to human-milk-fed infants continues to be an open question, particularly with regard to the potential differences in physical growth, including risk of overweight and obesity, neurological development, and renal solute load.

PICO:

Population: Infants, aged 0–12 months.

Intervention/Exposure: 1) High protein intake from infant formula, with variations in protein source (whey, casein, cow, soy, hydrolyzed, etc.), 2) Protein intake from extensively hydrolyzed formulas.

Comparator: 1) Lower protein intake from human milk, 2) Protein intake from cow's milk or soy-based formula.

Outcomes: 1) Growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) overweight/obesity, 4) renal function (unlikely at the levels of protein used in infant formulas), and 5) levels of IGF-one or insulin.

Systematic Review Questions:

- What is the association between relatively high intake of protein in infant formula vs. lower protein intake of human milk on 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) overweight/obesity, 4) renal function, and 5) serum Insulin-like Growth Factor (IGF)-1 and insulin levels?
- What is the association between protein intake on 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) overweight/obesity, 4) renal function and solute load, and 5) serum IGF-1 and insulin levels?

Data and Research Priorities:

- What is the impact of hydrolyzed formulas on cognitive, behavorial, or neuromotor development?
- What is the impact of hydrolyzed formulas on long-term health outcomes, including overweight and obesity?
- How do levels of IGF-one or insulin in human-milk-fed infants compare to those in infant formulas, including those that are extensively

1. The impact of differences in protein intake in infants in the first 12 months of life
hydrolyzed?

References:

- Assessment of nutrient requirements for infant formulas. J Nutr. 1998 Nov;128(11 Suppl):i-iv, 2059S-2293S. Review. Erratum in: *J Nutr* 1999 May;129(5):1090. PubMed PMID: 9826964.
- Hester SN, Hustead DS, Mackey AD, Singhal A, Marriage BJ. Is the macronutrient intake of formula-fed infants greater than breast-fed infants in early infancy? *J Nutr Metab.* 2012;2012:891201. doi: 10.1155/2012/891201. Epub 2012 Sep 27. PubMed PMID: 23056929; PubMed Central PMCID: PMC3463945.
- Koletzko B, von Kries R, Closa R, Escribano J, Scaglioni S, Giovannini M, Beyer J, Demmelmair H, Gruszfeld D, Dobrzanska A, Sengier A, Langhendries JP, Rolland Cachera MF, Grote V; European Childhood Obesity Trial Study Group. Lower protein in infant formula is associated with lower weight up to age 2 y: a randomized clinical trial. *Am J Clin Nutr.* 2009 Jun;89(6):1836-45. doi:10.3945/ajcn.2008.27091. Epub 2009 Apr 22. PubMed PMID: 19386747.

2. The role of beverages (including fruit juices and sugar-sweetened beverages) in complementary feeding between 6 and 12 months

Rationale: The current WIC food packages do not contain any fruit juices for infants. The American Academy of Pediatrics (AAP) recommends no juice prior to six months of age, introduction into the diet only when the infant is drinking from a cup and limited to 4–6oz per day. Fruit juice is not the equivalent to fresh fruit and should not take its place in the diet (Pediatrics, 2001). Type of juice may also be important, e.g., apple juice is low in folate (Skinner, 2004). Sugary drinks such as soda should be avoided, as they are nutrient-poor and decrease the appetite for other, more nutrient-dense foods. Despite these admonitions, the limited available data indicate that infants and toddlers in the US are consuming these beverages at rates that could be a potential concern (Fox, 2004). In addition, the AAP (Pediatric Nutrition Handbook) notes there is very little indication for water, except to mix with infant formula; thus any additional water requirements for infants in this age group is a subject for research.

PICO:

Population: Infants, aged 0–12 months.

Intervention/Exposure: Consuming higher amounts of beverages [>4–6 fl. oz per day; including 100% fruit juices, sugar-sweetened beverages (including fruit juice)].

Comparator: Consuming less/no beverages.

Outcomes: 1) Growth and physical development, 2) oral health, 3) overweight/obesity, and 4) impact on achieving recommended dietary intakes or diet quality.

Systematic Review Questions:

- What is the relationship between beverage consumption (including fruit juices and sugar-sweetened beverages) between six and 12 months of age and 1) growth and physical development, 2) oral health, 3) overweight/obesity, and 4) impact on achieving recommended dietary intake or diet quality?

Data and Research Priorities:

- What is the range of water intake seen in infants in the US?
- What is the prevalence of intakes of different beverages in infants aged six to 12 months in the US?
- How much water is needed between six and 12 months of age?
- What is the impact of water intake on outcomes such as:
  - Growth and physical development
  - Oral health
  - Hyponatremia
  - Overweight/obesity
  - Achieving recommended dietary intake or diet quality?

References:

- Committee on Nutrition. American Academy of Pediatrics: The use and misuse of fruit juice in pediatrics. *Pediatrics.* 2001 May;107(5):1210-3. PubMed PMID:11331711.
- Fox MK, Pac S, Devaney B, Jankowski L. Feeding infants and toddlers study: What foods are infants and toddlers eating? *J Am Diet Assoc.* 2004 Jan;104(1 Suppl1):s22-30. PubMed PMID: 14702014.
- Skinner JD, Ziegler P, Ponza M. Transitions in infants' and toddlers' beverage patterns. *J Am Diet Assoc.* 2004 Jan;104(1 Suppl 1):s45-50. PubMed PMID: 14702017.

3. Can fluid cow's milk be introduced before 12 months of age?

Rationale: Current guidance recommends against introducing fluid cow's milk prior to 12 months of age (Daniels, 2008) and the current WIC Food Package does not allow the introduction of whole milk before 12 months of age. Despite these policies, the use of cow's milk as a source of nutrition for infants under 12 months continues to be prevalent (Siega-Riz, 2011). Factors such as economics and cultural attitude contribute to this use. Moreover, historical concerns about the safety of cow's milk, vis-à-vis the potential to increase gastrointestinal bleeding, have been obviated by recent studies indicating that occult blood losses consequent to cow's milk consumption are minor in infants older than 6 months of age (WHO, 2005). Nevertheless, questions remain about the relative safety and efficacy of cow's milk, particularly in the period beyond exclusive breastfeeding and weaning (i.e., between six and 12 months and in cases where infants have stopped breastfeeding prior to 12 months of age).

PICO:

Population: Infants, aged 0–12 months.
Intervention/Exposure: Consumption of fluid cow's milk before 12 months of age.
Comparator: No exposure to fluid cow's milk before 12 months of age (i.e., continued human milk or infant formula).
Outcomes: 1) Risk of iron deficiency or anemia; 2) growth and physical development.

Systematic Review Questions:

- What is the relationship between consumption of fluid cow's milk between six and 12 months of age and risk of iron deficiency or anemia?
- What is the relationship between consumption of fluid cow's milk between six and 12 months of age and growth and physical development?

Research and Data Priorities:

- What is the prevalence of liquid cow's milk (whole milk, low-fat, or skim) consumption (as sole source of liquid or in combination with human milk) in infants aged six to 12 months in the US?
- Do differences exist based on demographics and race/ethnicity?
- What is the relationship between consumption of liquid cow's milk and
    - Immune function/allergenicity
    - Gastrointestinal problems
    - Risk of other conditions including diabetes, obesity?
- Are there other components of concern in liquid cow's milk for infants six to 12 months of age?
- What is the ideal time for introduction of liquid cow's milk?

References:

- Daniels SR, Greer FR; Committee on Nutrition. Lipid screening and cardiovascular health in childhood. *Pediatrics.* 2008 Jul;122(1):198-208. doi:10.1542/peds.2008-1349. Review. PubMed PMID: 18596007.
- Siega-Riz AM, Kinlaw A, Deming DM, Reidy KC. New findings from the Feeding Infants and Toddlers Study 2008. *Nestle Nutr Workshop Ser Pediatr Program.* 2011;68:83-100; discussion 100-5. doi: 10.1159/000325667. Epub 2011 Oct 3. PubMed PMID: 22044893.
- World Health Organization. Guiding principles for feeding non-breastfed children 6-24 months of age. Switzerland: *World Health Organization,* 2005.

4. Micronutrients of concern: Iron, zinc, vitamin D, long-chain polyunsaturated fatty acids (LCPUFA), fluoride, and B12

Rationale: The human milk concentrations of these nutrients are limited in latter stages of lactation; the quality of the other food sources assume greater significance. Currently available infant formulas serve as good sources of all of the nutrients of concern, with the exception of fluoride, which is provided primarily via the fluoride content of the water source used to prepare the formula. For infants who have been formula-fed from birth and are continued on infant formula, along with complementary food through 12 month of age; deficiencies of these nutrients are rare. On the other hand, because human milk is a poor source of vitamin D and cannot meet the needs for iron and zinc by approximately six months, the infant's needs for these nutrients are a concern (Chantry, 2007; Baker, 2010; Savino, 2011; Krebs, 2012). Intake of complementary foods rich in iron and zinc is very important for breast-fed or even infants fed a mixture of formula and human milk after six months. A number of authoritative organizations have addressed the issue of vitamin D supplementation for infants, including Perrine (2010) and the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN; Braegger, 2013). For infants maintained on a mixed vegetarian and human milk diet, intakes of iron, zinc, B12 and vitamin D remain a concern (Mangels, 2012). The question of the need for supplemental LCPUFAs for term infants and infants older than six months remains controversial (Simmer, 2011). Finally, as the fluoride content of human milk is relatively low and is not responsive to maternal intake, breast-fed infants are dependent on other sources of fluoride after six months (CDC, 2001). Based on all these considerations, these nutrients will require further attention in the context of dietary guidance for this age group.

PICO:

Population: Infants and toddlers, aged 0–24 months; sub-populations of interest include: Infants introduced to comp. foods between 4 and 6 months; toddlers, 12–24 months, for whom iron, zinc, and vitamin D may still be nutrients of concern, depending on quality of diets, intake during first year of life (e.g., breast-fed or formula-fed), use of supplements, and sun exposure.

Intervention/Exposure: Low intake or status of micronutrients of concern: Iron, zinc, vitamin D, LCPUFA's, fluoride, B12.

Comparator: Adequate intake or status of micronutrients of concern: Iron, zinc, vitamin D, LCPUFA's, fluoride, B12.

Outcomes: Infant and toddler 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) anemia, 4) immune system development, infection, or inflammation.

Systematic Review Questions:

- What is relationship between iron intake or status and infant and toddler 1) cognitive, behavioral, or neuromotor development, 2) anemia, 3) growth and physical development, and 4) immune function?
- What is relationship between zinc intake or status and infant and toddler 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, and 3) immune function?
- What is relationship between vitamin D intake or status and infant and toddler 1) growth and physical development, 2) immune function, and 3) bone development?
- What is relationship between LCPUFA intake or status and infant and toddler 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) immune function, and 4) visual acuity?
- What is the relationship between fluoride intake or status and infant and toddler growth and physical development (bones, teeth)?
- What is the relationship between vitamin B12 intake or status and infant and toddler 1) cognitive, behavioral, or neuromotor development and 2) risk of anemia?
- What strategies can be used to improve dietary quality and micronutrient intake in infants 6–12 months of age and would different nutrients (e.g.,

4. Micronutrients of concern: Iron, zinc, vitamin D, long-chain polyunsaturated fatty acids (LCPUFA), fluoride, and B12

iron, fluoride) require different strategies?

Data and Research Priorities:

- Data are needed on prevalence of single/multiple micronutrient deficiencies in the US and how these prevalences may differ by:
  - Demographics
  - Method of feeding (human milk plus complementary foods, human milk plus other liquids plus complementary foods, formula plus complementary feeding)
- Research is needed to determine how micronutrient needs can be met with foods from 6–12 months of age or whether supplements are needed
- Sensitive, specific and non-invasive biomarkers of micronutrient status, function and effect are needed for this age group
- Functional biomarkers are needed that reflect high priority health outcomes and potential mechanisms of effect, including biomarkers of growth (beyond anthropometry), immunocompetence, neurological function
- More data from RCT are needed for this age group
- Data on relative contribution of complementary foods introduced between 4 and 6 months, on the nutrient status of exclusively breast-fed infants (to 6 months).

References:

- Baker RD, Greer FR; Committee on Nutrition American Academy of Pediatrics. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0-3 years of age). *Pediatrics.* 2010 Nov;126(5):1040-50. doi:10.1542/peds.2010-2576. Epub 2010 Oct 5. PubMed PMID: 20923825.
- Braegger C, Campoy C, Colomb V, Decsi T, Domellof M, Fewtrell M, Hojsak I, Mihatsch W, Molgaard C, Shamir R, Turck D, van Goudoever J; ESPGHAN Committee on Nutrition. Vitamin D in the Healthy Paediatric Population: A Position Paper by the ESPGHAN Committee on Nutrition. *J Pediatr Gastroenterol Nutr*. 2013 Mar 6. [Epub ahead of print] PubMed PMID: 23471181.
- Chantry CJ, Howard CR, Auinger P. Full breastfeeding duration and risk for iron deficiency in U.S. infants. *Breastfeed Med.* 2007 Jun;2(2):63-73. PubMed PMID: 17661577.
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- Recommendations for using fluoride to prevent and control dental caries in the United States. Centers for Disease Control and Prevention. *MMWR Recomm Rep.* 2001 Aug 17;50(RR-14):1-42. PubMed PMID: 11521913.
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- Simmer K, Patole SK, Rao SC. Long-chain polyunsaturated fatty acid supplementation in infants born at term. *Cochrane Database Syst Rev.* 2011 Dec 7;(12):CD000376. doi: 10.1002/14651858.CD000376.pub3. Review. PubMed PMID:22161363.

5. Appropriate complementary food choices for human-milk-, formula-, or mixed-fed infants from a macro- and micro-nutrient standpoint

Rationale: The prevalence of obesity in the US and globally is rising at an alarming rate. The factors that contribute to this are myriad, but clearly early dietary exposures and habits make up critical aspects of this scenario and impacts numerous other aspects of short- and long-term health. Timing (Pearce, 2013a) and quality/type (Pearce, 2013b) have been scrutinized for their contributions to the obesity epidemic. The ideal distribution of daily energy intake from human milk, formula (or combination) versus from complementary foods is uncertain. The appropriate amounts and choices of complementary foods are dependent on the percentage of the infant's required caloric intake and DRIs they are to provide. To meet micronutrient needs, the breast-fed infant is dependent on the choices of complementary foods (or supplements), whereas if a formula-fed infant continues to receive a substantial intake of formula, micronutrient inadequacy is unlikely.

PICO:

Population: Infants, aged 0–12 months.

Intervention/Exposure: Optimal distribution of daily energy and macronutrient intake from human milk, infant formula, or a combination of the two, and complementary foods; appropriate amounts and choices of complementary foods.

Comparator: Optimal vs. sub-optimal or excessive intakes based on intake recommendations in the DRIs.

Outcomes: Infant 1) dietary intake (i.e., meeting nutrient requirements established by the DRIs); and infant/toddler health outcomes, such as 2) growth and physical development, 3) cognitive, behavioral, or neuromotor development, 4) food allergies and asthma, and 5) overweight/obesity.

Systematic Review Questions:

- What is the optimal distribution of daily energy and macronutrient intake from complementary foods, human milk, or infant formula (or a combination of the two) that promotes favorable health outcomes, such as 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) prevention of food allergies and asthma, and 4) prevention of overweight/obesity?
- What types and amounts of complementary foods are necessary for infants fed human milk, formula, or mixed feedings to promote favorable health outcomes, such as 1) growth and physical development, 2) cognitive, behavioral, or neuromotor development, 3) prevention of food allergies and asthma, and 4) prevention of overweight/obesity?

Data and Research Priorities:

- Improved content data are needed for common commercially available foods marketed for infants/toddlers.
- Prevalence data on specific dietary intake patterns is needed for infants 6–12 months of age.
- Data on distribution of daily energy and nutrient intake from complementary foods, human milk, or infant formula (or a combination of the two) that ensures meeting the nutrient requirements established by the DRIs.

References:

- Pearce J, Taylor MA, Langley-Evans SC. Timing of the introduction of complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond).* 2013 Oct;37(10):1295-306. doi: 10.1038/ijo.2013.99. Epub 2013 May 27. PubMed PMID: 23736360.
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6. Early dietary influences on food and flavor likes and dislikes, especially for nutrient-dense foods (fruits, vegetables, meat, diary, etc.). What are the evidence-based strategies to enhance acceptance of nutrient-dense foods like fruits and vegetables?

Rationale: Prior to the transition to a mixed diet, a striking contrast exists between the sensory experience of the breast-fed and formula-fed infant (Mennella, 1997; Mennella, 2001). Breast-fed infants have a much more diversified exposure to the volatile elements of the maternal diet via mother's milk, while the formula-fed infant's dietary exposure is more "monotonous." The myriad factors that might contribute to the development of taste preferences in human-milk versus formula-fed infants and their implications for health have been recently reviewed (Trabulsi, 2012). Once weaned to complementary foods, both breast-fed and formula-fed infants learn through repeated exposure to a particular food as well as through exposure to a variety of food (in both flavor and texture) which, in turn, promotes the willingness to eat these complementary foods as well as novel foods. Thus, concerns about "how to" (e.g., order of introduction of foods, types of foods) represent one of the primary matters discussed by mothers/caregivers with their child's pediatrician. Ultimately, the goal is to gradually accustom children to a varied diet that meets nutritional needs for growth and development with appropriate nutrient dense foods, and leads to a preference for nutrient-dense foods.

PICO:

Population: Infants and toddlers, aged 0–24 months; pregnant and lactating women.

Intervention/Exposure: Factors/strategies associated with the development of healthy eating habits; early diet (i.e., maternal diet during pregnancy and lactation, flavor profile of formula, and impact of timing and types of complementary foods introduced during the first year of life); factors/strategies associated with consumption/acceptance of fruits and vegetables.

Comparator: Factors associated with the development of unhealthy eating habits; different early diet exposures; factors associated with dislike/low intake of fruits and vegetables.

Outcomes: Infant and toddler 1) dietary intake/quality (including nutrients of concern, fruits, meats, and vegetables), 2) dietary behaviors/food preferences, and 3) health outcomes including overweight/obesity (also childhood and adulthood), "healthy eating" and degree of variety of diet during childhood [Note: That is the outcome for some of the long-term studies listed below. Note: Cancer may be another long-term health outcome of interest.].

Systematic Review Questions:

These questions (as well as the Data/Research Priorities) address: 1) The biology underlying the senses that provide acceptance/preference of foods, 2) the relationship of this biology to dietary intake and long-term consequences on health, and 3) evidence-based strategies, based on the biology, to increase the acceptance of nutrient-dense foods.

- Is there a relationship between appropriate/increased intake (quantity, timing, frequency) of nutrient-dense foods (meats, dairy, fruits, vegetables, etc.) by the mother during pregnancy and acceptance/preference of nutrient dense foods in infants?
- Is there a relationship between appropriate/increased intake (quantity, timing, frequency) of nutrient-dense foods (meats, dairy, fruits, vegetables, etc.) by the mother after infants' birth on the acceptance/preference of nutrient-dense foods by their children?
- Are there differences in the acceptance/preference of nutrient-dense foods between breast- and formula-fed infants?
- Does exposure (timing, quantity, frequency) to nutrient-dense foods in weaned infants increase acceptance of nutrient-dense foods?
- Are there differences in pattern or duration of acceptance between infants who were formula- or breast-fed or both during the first few months of life and if so, how does this relate to maternal diet and feeding practices? Are there differences among formula-fed infants, depending on the type of formula fed to infants in early life?

6. Early dietary influences on food and flavor likes and dislikes, especially for nutrient-dense foods (fruits, vegetables, meat, diary, etc.). What are the evidence-based strategies to enhance acceptance of nutrient-dense foods like fruits and vegetables?

- Does increased acceptance/preference for nutrient-dense foods in the first year of life persist? Does it improve dietary intake of nutrient-dense foods at 12–24 months? Does this impact on growth parameters during infancy and childhood?

Data and Research Priorities:

- Improved data on complementary food (type and amount) patterns in the US; particularly with regard to potential differences between breast-fed, formula-fed and mixed-fed infants.
- Improved data/analyses to document impact of maternal dietary patterns during pregnancy and lactation.
- What is the biology (taste, aroma, textures) underlying the preference of foods by infants?
- Using the biology, what are the best strategies to increase the acceptance of nutrient-dense foods and decrease the preference for nutrient-poor, energy-dense foods?
- How does the preference for nutrient-dense foods versus preference for nutrient-poor foods in the first 24 months of life impact on long-term health outcomes?
- What is the relative contribution of protein sources to the development of taste preferences in formula-fed infants?

References:

- Mennella JA, Beauchamp GK. Mothers' milk enhances the acceptance of cereal during weaning. *Pediatr Res.* 1997 Feb;41(2):188-92. PubMed PMID: 9029637.
- Mennella JA, Jagnow CP, Beauchamp GK. Prenatal and postnatal flavor learning by human infants. *Pediatrics.* 2001 Jun;107(6):E88. PubMed PMID: 11389286; PubMed Central PMCID: PMC1351272.
- Trabulsi JC, Mennella JA. Diet, sensitive periods in flavour learning, and growth. *Int Rev Psychiatry.* 2012 Jun;24(3):219-30. doi:10.3109/09540261.2012.675573. Review. PubMed PMID: 22724643.

7. Development of taste preferences for salt and sweet in infants and the impact on dietary intake and long-term health outcomes. How do preferences for foods with added salt and sugars develop?

Rationale: Excessive intakes of foods that contain high amounts of salt (NaCl) and refined sugars (and, consequently, taste salty and sweet) cause or exacerbate a number of illnesses, including hypertension, diabetes, and obesity. The Dietary Guidelines for Americans, as well as other authoritative documents make clear public health concerns that foods with added salt and sugar are foods to be avoided. Despite this, people consume sugar and salt in amounts that most health professionals consider to be unhealthy, starting at a young age. Not only do processed foods, which make up a large part of modern diets, have high quantities of salt and added sugars, but foods that taste sweet or salty and beverages that taste sweet have powerful hedonic appeal, especially for children. The elevated preferences for sugars and salt during childhood reflect the basic biology: Children are programmed to like mother's milk and foods containing energy (signaled by sweet taste) and minerals (signaled by salt taste) during periods of growth (Drenowski, 2012; Stein, 2012). Other biological influences might include maternal status, e.g., hyperemesis gravidarum, which has been suggested as a potential precursor to salt preference (Crystal, 1998). In addition, a body of evidence suggests a role for socio-economic status and race/ethnicity in the development of preferences for salt and sweet (Mennella, 2008). Our ability to develop evidence-based dietary guidance aimed at health promotion and disease prevention is contingent on a better understanding of the factors that contribute to the ontogeny of salt and sweet preferences for during critical periods of development.

PICO:

Population: Infants 0–12 months (toddlers 12–24 months); pregnant and postpartum women.

Intervention/Exposure: 1) Increased intakes (quantity and frequency) and early introduction (<4 months; timing) of foods with added salt and sugar in infants and toddlers 12-24 months (race, sex, differences?) 2) Pregnant women with hyperemesis gravidarum.

Comparator: 1) Decreased intakes (quantity, frequency) and delayed introduction (> 4 months) of foods with added salt and sugar in infants and toddlers 12-14 months (race, sex, differences?) 2) Pregnant women without hyperemesis gravidarum.

Outcomes: Infant and toddler 1) dietary intake of foods with added salt and sugar 2) dietary behaviors (food preferences), and 3) health outcomes including overweigh and obesity, blood pressure.

Systematic Review Questions:

These questions (as well as the Data and Research Priorities) should address: 1) The biology of preferences for salt and sweet, 2) the relationship between preferences for salt and sweet and dietary intake of foods with added salt and sugar later in childhood and adulthood, as well as long-term consequences on health, and 3) evidence-based strategies to reduce intake of foods with added salt and sugar.

- Do infants and children differ in their preferences for sugar and salt? If there are differences, what are the mechanisms underlying these age-related changes? Are there differences among races? Genetics? Gender? Emotional state of the child (e.g., depression)?
- Is there a relationship between health of the mother prenatally (e.g., hyperemesis gravidarum) and preference for salt and sweet?
- Does the intake of foods with added salt and sugar in infancy influence the preference and analgesic appeal of dietary salt and sweet in infants, young children, and adults?
- Does repeated exposure of foods with added sugar lead to sugar "addiction" later in life (physiologic endorphin response)? How much of the addiction is pre-dispositioned and inborn versus conditioned?
- Is there a relationship in infants between intake of foods with added salt and sugar (timing of introduction, quantity, frequency) and preference for salt and sweet later in childhood and adulthood? Does this impact on growth parameters at 12–24 months and body composition/health later in life?

7. Development of taste preferences for salt and sweet in infants and the impact on dietary intake and long-term health outcomes. How do preferences for foods with added salt and sugars develop?

Data and Research Priorities:

- Additional data about what foods children are eating and what the sources of added sugars and salt are in their diet (Fox, 2004; Siega-Riz, 2011). When are these foods first introduced into infants' diets and why?
- Is there a relationship between an increased or decreased intake (quantity, timing frequency) of foods with added salt and sugar in pregnant women and intake/preference for foods with added salt and sugar in their infants?
- Is there a relationship between an increased or decreased intake (quantity, timing frequency) of foods with added salt and sugar in postpartum women, whether breast- or bottle-feeding) and intake/preference for foods with added salt and sugar in their infants?
- Is there a difference in intake/preference for added salt and sugar between infants who are predominantly breastfed or formula-fed during the first six months after birth?
- How does the amount of salt or sugar vary among formulas and how does it compare to breast milk? Does this mode of differential exposure to salts and sugars affect salt/sugar preference and dietary habits among infants and children?
- What evidence-based strategies are associated with reduced 1) preferences and 2) intake of salt and sugar among children? [Note: One study in adults.]

References:

- Crystal SR, Bernstein IL. Infant salt preference and mother's morning sickness. *Appetite.* 1998 Jun;30(3):297-307. PubMed PMID: 9632460.
- Drewnowski A, Mennella JA, Johnson SL, Bellisle F. Sweetness and food preference. *J Nutr.* 2012 Jun;142(6):1142S-8S. doi: 10.3945/jn.111.149575. Epub 2012 May 9. PubMed PMID: 22573785; PubMed Central PMCID: PMC3738223.
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8. The role, timing, and value of snacking (i.e., food consumed between meals)

Rationale: Snacking continues to be common in this age group (Siega-Riz, 2010), however our understanding about its prevalence, type, effect on growth and development, the development or establishment of eating patterns, and caloric intake need further systematic exploration to help inform dietary guidance for infants/toddlers.

PICO:

Population: Infants and toddlers, aged 6–24 months; caregivers and childcare providers.

Intervention/Exposure: Scheduled timing of snacks (i.e., the caregiver providing snacks at set times); frequent snacks; food/nutrient composition of snacks.

Comparator: Self-regulated snacking (i.e., allowing the infant/toddler to regulate the timing of snacks, and having the caregiver respond to cues); infrequent snacks; food/nutrient composition of snacks.

Outcomes: Infant and toddler 1) growth and physical development, 2) overweight/obesity, and 3) dietary intake.

Systematic Review Questions:

- What is the association between scheduled vs. self-regulated snacking on infant and toddler 1) growth and physical development, 2) overweight/obesity, and 3) dietary intake?
- Are there differences between breast- and formula-fed infants?
- What is the association between frequency of snacks and infant/toddler's 1) growth and physical development, 2) overweight/obesity, and 3) dietary intake?
- What snacks optimize nutrient intakes in infants and toddlers and are there differences between breast- and formula-fed infants?

Data and Research Priorities:

- What are infants/toddlers currently eating for snacks?
- How frequently are infants/toddlers eating snacks or meals?
- What is the definition of snacking? Sometimes it is defined by researchers as the number of foods or calories consumed "between meals," or by respondents as to whether they called it a meal or a snack. In infants, the name does not mean much, since infants eat frequently, so snacks and meals may be interchangeable for this population.
- Are there longitudinal data that provide measured health outcomes needed to supplement existing cross-sectional data?

References:

- Siega-Riz AM, Deming DM, Reidy KC, Fox MK, Condon E, Briefel RR. Food consumption patterns of infants and toddlers: where are we now? *J Am Diet Assoc*. 2010 Dec;110(12 Suppl):S38-51. doi: 10.1016/j.jada.2010.09.001. PubMed PMID:21092767

9. Method of complementary feeding

Rationale: Aside from the potential health impact of the timing of introduction of complementary foods (Jonsdottir, 2012; Pearce, 2013; Woo, 2013), the methods of introducing both liquids/beverages and solids complementary foods may also have important implications for the infant growth and development. The ease of accepting complementary foods is dependent on developmental readiness, and this should be demonstrated before complementary foods are introduced. Because strategies for introducing complementary foods are varied and can occur before children are developmentally ready, parents need guidance on the best methods for introducing complementary foods. Another area in need of guidance is the timing of use of complementary foods within a given feeding episode, i.e., before or after breast- or bottle-feeding. These practices may result in over-feeding, the displacement of nutrients or calories from human milk or infant formula, or other health consequences.

PICO:

Population: Infants and toddlers, aged 6–24 months; caregivers and childcare providers.

Intervention/Exposure: Adding solids to bottles; putting a baby to bed with a bottle (including human milk, infant formula, and other beverages (water, juice, etc.); signs that infant is not developmentally ready for solids foods.

Comparator: Not providing solids in bottles; not putting a bottle in bed with a baby; signs that a baby is developmentally ready for solid foods (i.e., gumming, swallowing head control); appropriate methods of introducing solid foods.

Outcomes: Infant/toddler 1) oral health, 2) overweight/obesity, and 3) dietary intake.

Systematic Review Questions:

- What is the relationship between adding solids to bottles and infant/toddler 1) oral health, 2) overweight/obesity, and 3) dietary intake (e.g., macro- including calorie and micro-nutrient intake)?
- What is the relationship between putting a baby to bed with a bottle and infant/toddler 1) oral health, 2) overweight/obesity, and 3) risk of otitis media?
- What methods of introducing solids results in optimal infant/toddler 1) oral health, 2) overweight/obesity, and 3) dietary (quality and quantity) intake?

Data and Research Priorities:

- Improved data on the prevalence of different methods for introduction and use of complementary foods.
- Does it make a difference whether or not complementary foods are introduced before breastfeeding or bottle feeding at a given meal time?

References:

- Jonsdottir OH, Thorsdottir I, Hibberd PL, Fewtrell MS, Wells JC, Palsson GI, Lucas A, Gunnlaugsson G, Kleinman RE. Timing of the introduction of complementary foods in infancy: a randomized controlled trial. *Pediatrics.* 2012 Dec;130(6):1038-45. doi: 10.1542/peds.2011-3838. Epub 2012 Nov 12. PubMed PMID:23147979.
- Pearce J, Taylor MA, Langley-Evans SC. Timing of the introduction of complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond).* 2013 Oct;37(10):1295-306. doi: 10.1038/ijo.2013.99. Epub 2013 May 27. PubMed PMID: 23736360.
- Woo JG, Guerrero ML, Ruiz-Palacios GM, Peng YM, Herbers PM, Yao W, Ortega H, Davidson BS, McMahon RJ, Morrow AL. Specific infant feeding practices do not consistently explain variation in anthropometry at age 1 year in urban United States, Mexico, and China cohorts. *J Nutr.* 2013 Feb;143(2):166-74. doi:10.3945/jn.112.163857. Epub 2012 Dec 12. PubMed PMID: 23236024; PubMed Central PMCID: PMC3542908.

10. Physical activity in the prevention of childhood obesity

Rationale: A need exists for consistent messaging related to structured and unstructured activity, including play for infants and toddlers. The type and amount of activity will impact energy expenditure/needs, the development of healthful activity habits at an early age, physical and social development, and overall well-being. The National Association of Sports and Physical Education (NASPE) has developed specific guidelines for the physical activity of children from birth to age 5 that address the developing child's unique characteristics (NASPE, 2013). These guidelines reflect the current evidence with regard to motor development, movement and exercise, and the physical activity needs of young children during the first years of life. Including activity guidelines from birth to 24 months is consistent with transitioning to DGA goals of health-promotion and disease prevention. Of specific interest is the relationship between "tummy time" (Kadey, 2012), other developmentally appropriate activities, and inactivity ("containerization") on short- and long-term health. Specific physical activities to consider at 6–12 months include locomotor activities (crawling, walking, etc.), non-manipulative activity [tummy time (e.g., pushing up on extended arms and pivoting on stomach) and unrestrained sitting time], and manipulative activity (encouraging infants to manipulate objects). In addition, there are concerns about "containment" of infants" and "back-to-sleep practices" that do not promote the physical activities listed above, and it is recommended that caregivers allow periods for tummy time and unrestrained activity.

PICO:

Population: Infants and toddlers, aged 0–24 months; caregivers and childcare providers.
Intervention/Exposure: Participation in tummy time or developmentally appropriate physical activity.
Comparator: Different amounts of tummy time or developmentally appropriate physical activity.
Outcomes: Infant/toddler 1) growth and physical development, 2) cognitive and behavioral or neuromotor development, and 3) overweight/obesity.

Systematic Review Questions:

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

Data and Research Priorities:

- What is the relationship between tummy time or other unrestrained activity on 1) growth and physical development, 2) cognitive, behavioral or neuromotor development, and 3) overweight/obesity?
- What is the relationship between participation in developmentally appropriate physical activity and 1) growth and physical development, 2) cognitive, behavioral or neuromotor development, and 3) overweight/obesity?
- What is the relationship of physical inactivity due to restrained/contained time (including TV/video exposure) and 1) growth and physical development, and 2) cognitive, behavioral or neuromotor development, and 3) overweight?

References:

- Kadey HJ, Roane HS. Effects of access to a stimulating object on infant behavior during tummy time. *J Appl Behav Anal.* 2012 Summer;45(2):395-9. doi:10.1901/jaba.2012.45-395. PubMed PMID: 22844145; PubMed Central PMCID:PMC3405933.
- The National Association of Sports and Physical Education. Active start: A statement of physical activity guidelines for children from birth to age 5. 2nd edition. 2013. Internet: Active Start.

11. Impact of the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC) food package on infant and child diet

Rationale: Nearly half of infants born in the United States participate in the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). WIC is designed to help families with limited resources meet the nutrition needs of pregnant, breastfeeding, and non-breastfeeding postpartum women, infants, and children to five years of age who are at nutritional risk. WIC provides supplemental food and nutrition education to program participations to improve dietary quality and practices. For infants, the contents of the WIC food package are dependent on whether the infant is formula-fed, breast-fed, or fed both formula and breast milk (FNS, 2012). By October 2009, all WIC clinics introduced a new WIC food package to reflect the Dietary Guidelines for Americans, as well as the infant-feeding practice guidelines of the American Academy of Pediatrics. The new food package was designed in response to concerns raised by the Institute of Medicine and others regarding breastfeeding duration, juice consumption, age at introduction to solid foods and cow's milk, consumption of fruits and vegetables, and frequency of exposure to new foods among WIC participants. The impact of the new food packages on the dietary intake and behavior of infant and toddlers participating in WIC is of importance. Another priority is the comparison of the diets of participating infants and young children to diets of those not participating in WIC.

PICO:

Population: Infants and toddlers, aged 0–24 months.

Intervention/Exposure: Participation in WIC/receipt of WIC food package.

Comparator: Infants and toddlers not participating in WIC (both WIC-eligible and not WIC-eligible)/WIC participants (infant and toddlers) who did not receiving the new WIC food package.

Outcomes: 1) Overweight/obesity, 2) dietary intake (quality), and 3) dietary behaviors (human milk feeding/formula feeding/juice intake; introduction to solids (fruits and vegetables).

Systematic Review Questions: The Work Group suggested that each of the following study questions be repeated, comparing new vs. old WIC food packages

- Is participation in WIC associated with improved breastfeeding initiation, duration and exclusivity?
- With regard to complementary feeding, is participation in WIC associated with:
  - Age at which infants are introduced to solid foods?
  - The types of first food introduced?
  - A specific pattern of complementary feeding during infancy (dietary pattern, types of foods consumed, added sugar and salt content of complementary foods, or age in which whole milk is introduced)?
- How do associations between WIC participation and infant and young child feeding differ for breast-fed compared to formula-fed infants?
- How do associations between WIC participation and infant and young child feeding differ for children of different races and ethnic groups?
- Is participation in WIC associated with childhood obesity or other diet-related adverse health outcomes?
- Is participation in WIC associated with improved food security (compared to non-WIC/WIC-ineligible and non-WIC/WIC-eligible)?

Data and Research Priorities:

The Work Group was aware of ongoing data analyses of the WIC programs (Harrison, 2013).

References:

- Food and Nutrition Service. WIC Food Packages. 2012. Internet: WIC Food Packages.