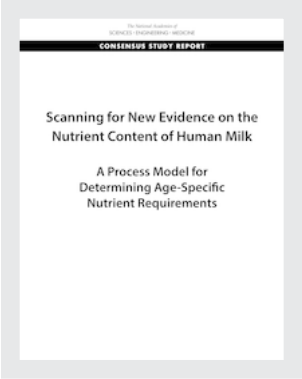

Scanning for New Evidence on the Nutrient Content of Human Milk: A Process Model for Determining Age-Specific Nutrient Requirements (2020)

DETAILS

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Kathleen Rasmussen, Ann L. Yaktine, and Alice Vorosmarti, *Editors*

Committee on Scanning for New Evidence
on the Nutrient Content of Human Milk

Food and Nutrition Board

Health and Medicine Division

A Consensus Study Report of

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This Consensus Study Report was reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise. The purpose of this independent review is to provide candid and critical comments that will assist the National Academies of Sciences, Engineering, and Medicine in making each published report as sound as possible and to ensure that it meets the institutional standards for quality, objectivity, evidence, and responsiveness to the charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process.

We thank the following individuals for their review of this report:

LINDSAY H. ALLEN, U.S. Department of Agriculture; University of California, Davis
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XIAOBIN WANG, Johns Hopkins University School of Medicine and Children’s Center

Although the reviewers listed above provided many constructive comments and suggestions, they were not asked to endorse the content of the proceedings nor did they see the final draft before its release. The review of this proceedings was overseen by **JOHN W. ERDMAN,** University of Illinois at Urbana-Champaign, and **SUZANNE P. MURPHY,** University of Hawai‘i at Mānoa. They were responsible for making certain that an independent examination of this proceedings was carried out in accordance with standards of the National Academies and that all review comments were carefully considered. Responsibility for the final content rests entirely with the authoring committee and the National Academies.

Contents

Summary

Human milk is considered the biologic norm for feeding the human infant during the first 6 months of life, and it is a preferred food from 6 to 12 months. It is a complex food and exerts its biologic effects well beyond its known nutritional value; however, human milk composition and the complexity of its composition is not wholly known or understood. Thus, defining the composition of milk, as well as both the individual and combined effects of milk components and the volume consumed on infant growth and development, is central to optimizing infant health. Furthermore, defining human milk composition, volume, and the myriad factors that influence milk components is needed for developing future Dietary Reference Intake (DRI) values for nutrient intake during the first 12 months of life.

In response to these issues, the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (HHS) asked the National Academies of Sciences, Engineering, and Medicine to conduct an evidence scan of new and emerging evidence describing the nutrient content of human milk as well as the volume of milk consumed, both of which are needed to understand nutrient consumption by healthy breastfed infants. An evidence-scan approach was used to scan the peer-reviewed published literature to determine the status of evidence on the nutrient composition and volume of human milk, and to identify new evidence on nutrients in human milk that could inform the need for a systematic review as a component of the DRI process. The study committee approached its task by designing a literature search strategy, screening, and data abstraction protocol. The committee assessed identified studies to distinguish articles on nutrients that could be used to update the USDA National Nutrient Database for Standard Reference and the Canadian Nutrient File, the reference food composition databases in the United States and Canada, respectively. These databases serve as a reference standard for developing nutrient intake recommendations for infants up to 12 months of age. The committee's steps in development of a literature search strategy are shown in Figure S-1.

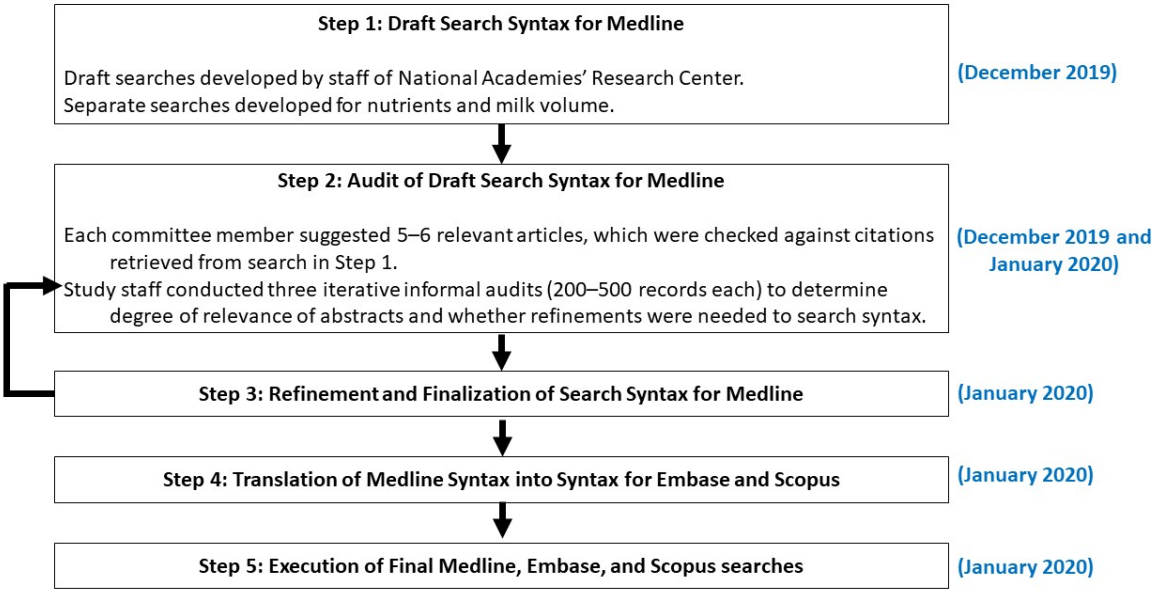

FIGURE S-1 Development of the literature search strategy.

The literature search retrieved 42,762 articles on human milk composition and volume. After removing duplicates, and title and abstract screening, 1,190 articles remained for full-text screening by the committee. The final number of reports remaining for inclusion after full-text screening and subsequent data abstraction was 126. Figure S-2 shows a flow diagram of the screening process and the number of abstracts and articles excluded at each step.

The committee tabulated its results, organized by studies, on nutrient composition, milk volume, and studies that combined composition and volume. Each study was described by population, nutrients included in the study, analytical methodology, and outcome. The selected studies represent the committee's assessment of data that would provide the most reliable estimates of human milk composition and volume. In its assessment, the committee noted the inconsistency in describing study subjects as a healthy population and the variability in the quality of methods used in the milk composition analyses.

Of note, there was a lack of data reported for fluoride, biotin, molybdenum, niacin, pantothenic acid, riboflavin, thiamin, and vitamins B12, C, D, and K. Thus, for the purposes of informing the development of future DRI values for infants from birth through 12 months, the committee found that although it is possible that adequate numbers of participants have been studied so that new DRI values could be developed from the currently available data for some nutrients, for other nutrients additional research will be needed. Other shortfalls noted by the committee included consistency in milk sampling protocols as well as a definition of an appropriate milk sampling strategy. Lastly, the committee recognized the importance of continuing research into less well-understood milk components (e.g., oligosaccharides, bioactive substances, food antigens, hormones, microbes, and growth factors) that contribute to infant growth, development, and overall health.

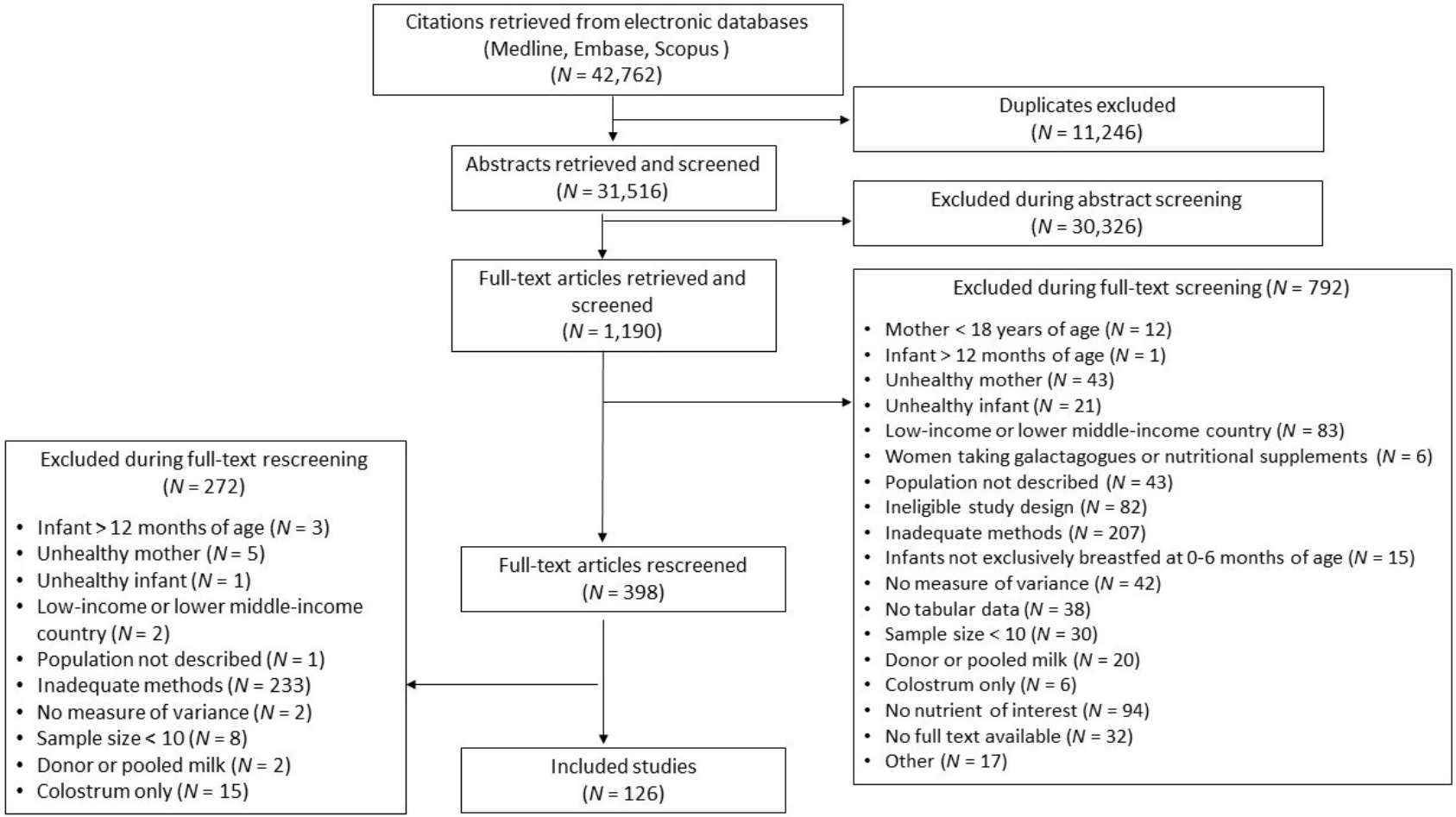

FIGURE S-2 Evidence-scan flow diagram.

1

Introduction

BACKGROUND FOR THE STUDY

From many perspectives, human milk is the biologic norm for feeding the human infant during the first 6 months of life, and it is a preferred food from 6 to 12 months. Human milk is a complex food, and its biologic effects extend well beyond its known nutritional value; however, human milk composition and the complexity of its composition is not wholly known or understood. Thus, describing the composition of human milk, as well as both the individual and combined effects of milk components on infant growth and development, is central to optimizing infant health and development (Neville et al., 2012).

Human milk has a multitude of nutritive and nonnutritive functions and components. These include supporting healthy growth, protecting against infection, supporting immune and intestinal health and cognitive development, and establishing the unique gastrointestinal microbiome (Neville et al., 2012). New analytical tools are now available that provide more quantitative and sensitive analytical methods than were available in recent decades, and these tools are transforming scientific understanding of the diversity and uniqueness of the composition of human milk. For example, human milk has relatively high concentrations of molecules that foster brain development including choline, sialic acid and long-chain polyunsaturated fatty acids (LC-PUFA) (Koletzko et al., 2008; Ojo-Okunola et al., 2020; Salem and Van Dael, 2020). Prenatal exposure to choline and its long-term effects on hippocampal development, learning, memory, and emotional behavior have been studied widely in animal models; however, similarly relevant data for humans are lacking (Blusztajn and Mellott, 2013; Mun et al., 2019). More recently, an important role for LC-PUFA in brain maturation has been recognized. These lipids, particularly docosahexaenoic acid (DHA) and arachidonic acid (AA), are present in human milk at far higher concentrations than in bovine milk. Additionally, they can be increased in human milk by maternal diets containing large amounts of fish oil (Martin et al., 2016; Middleton et al., 2018).

Numerous substances, such as oligosaccharides (e.g., small-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides) have been identified in human milk as potential dietary compounds (Donovan and Comstock, 2016; Plaza-Diaz et al., 2018; Smilowitz et al., 2013). Taken together, new and emerging evidence about the composition of human milk will contribute to better understanding nutrient requirements during infancy and the value of human milk to human health. Furthermore, defining human milk composition, volume, and the myriad factors that influence milk components is needed for developing future Dietary Reference Intake (DRI) values for nutrient intake during the first 12 months of life and beyond.

The request from the U.S. Department of Agriculture (USDA) and the U.S. Department of Health and Human Services (HHS) to scan the new and emerging evidence describing the nutrient content of human milk arose in anticipation of future DRI reviews that would require updated information about nutritional requirements for infants from birth to 5.9 months of age, and from 6 to 12 months of age that would contribute to the totality of data needed to develop

DRI recommendations. The primary data source for infant nutritional requirements is the nutrient content of human milk. However, while knowledge of the range of nutritional compounds in human milk has expanded, only those nutrients with existing DRI values were to be considered in the evidence scan.

COMMITTEE'S TASK AND APPROACH

USDA's Agricultural Research Service (USDA-ARS), HHS, and the U.S. Food and Drug Administration's (FDA's) Center for Food Safety and Applied Nutrition (FDA-CFSAN) requested the National Academies of Sciences, Engineering, and Medicine (the National Academies) to carry out an evidence scan on new and emerging evidence describing the nutrient content of human milk as well as the volume of milk consumed by healthy breastfed infants (see Box 1-1).

In response to the USDA-ARS and FDA-CFSAN request, the Health and Medicine Division of the National Academies established a committee with expertise in epidemiology, public health, physiology of lactation, nutrient composition of human milk, infant growth and development, nutrient requirements during pregnancy and in infancy, DRIs, and systematic evidence reviews. The committee held an open meeting with subject-matter experts (see Appendix B) and worked in closed session and by conference calls to deliberate on its task. To guide its work, the committee constructed a model for the task (see Figure 1-1).

BOX 1-1
Statement of Task

An ad hoc committee under the auspices of the National Academies of Sciences, Engineering, and Medicine will be convened to conduct a literature search and evidence scan of the peer-reviewed published literature on the nutrient content and volume of human milk as an indicator of infant nutritional requirements. The committee will develop prespecified criteria to characterize nutrient levels in human milk and to identify characteristics of the nutritional quality of human milk in relation to infant requirements to support normal growth and development. A 1-day meeting will be convened with selected experts in a discussion of relevant issues. The final product will be a brief summary of the methodology used to conduct the evidence scan, and a table of the reviewed studies and the committee's assessment of the quality of the evidence, but it will not include recommendations. The final product will be designed to serve as a template for use in informing development of future Dietary Reference Intake values for infants from birth through 12 months of age, with consideration toward using this model for other age groups, including the elderly. The committee's final product will be reviewed in accordance with institutional requirements.

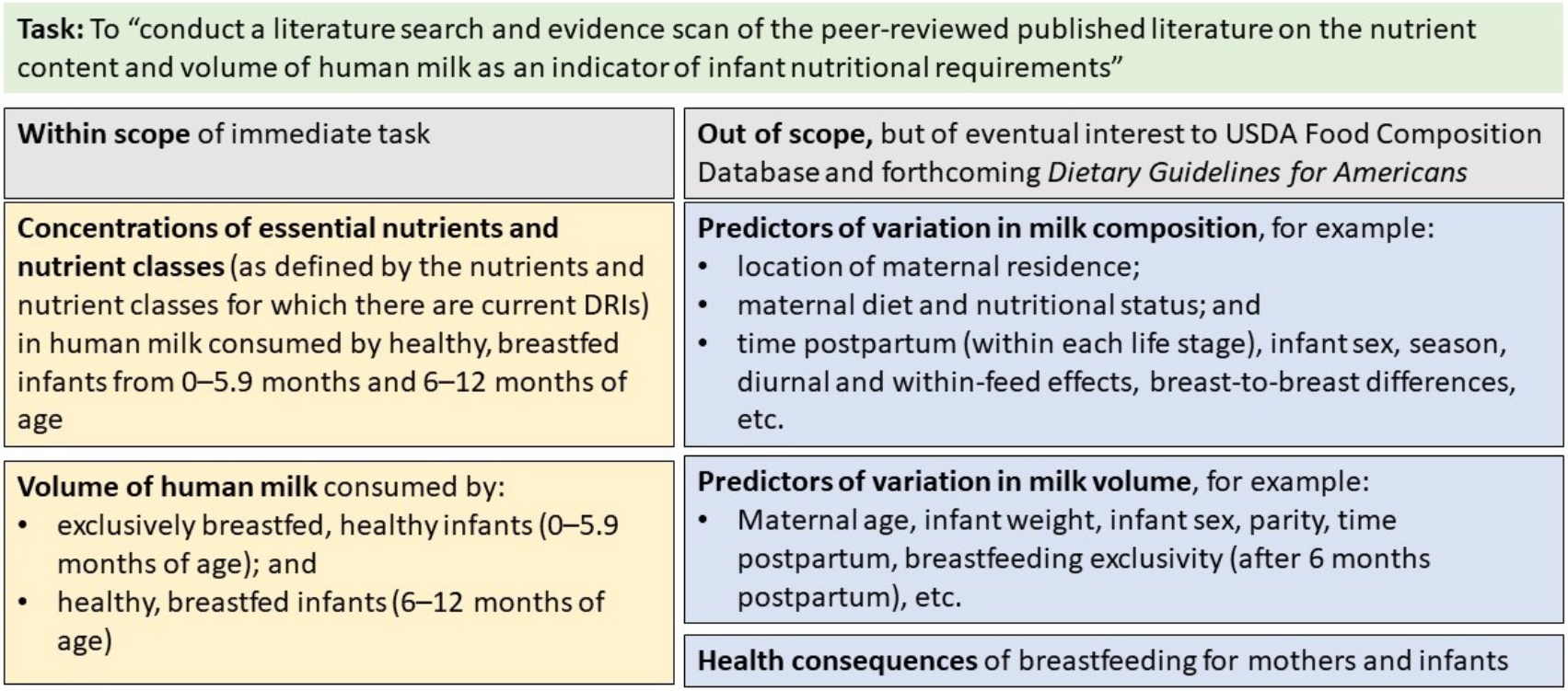

FIGURE 1-1 Scanning for evidence on the nutrient content of human milk: An analytic framework to guide the task.
NOTE: DRI = Dietary Reference Intake; USDA = U.S. Department of Agriculture.

ORGANIZATION OF THE REPORT

This report is organized into four chapters. In this chapter, the background for the study, the Statement of Task, and the study strategy are described. In Chapter 2, the committee describes its search strategy, including the prespecified criteria for assessing relevant evidence, and presents a flow diagram to illustrate the evidence-screening and review process. Chapter 3 presents a table of the evidence-scanning results and the committee's assessment of relevant evidence. Chapter 4 provides the committee's discussion of the findings and perspective on future directions.

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2

Methodological Approach to Evidence Scanning

In response to its charge, the Committee on Scanning for New Evidence on the Nutrient Content of Human Milk held meetings and discussions to develop a systematic approach to searching and summarizing relevant publications on the nutrient content of human milk and the consumption volume of human milk, as indicators of infant nutritional requirements, which will serve as a basis for developing intake recommendation through the Dietary Reference Intake (DRI) process. The committee describes below its approach to the task and the strategy used to carry out the evidence scan.

JUSTIFICATION

The U.S. Department of Agriculture (USDA) National Nutrient Database for Standard Reference (USDA SR Database) (USDA, 2019) and the Canadian Nutrient File (Health Canada, 2015) are the reference food composition databases in the United States and Canada, respectively. These databases serve as a reference standard for developing nutrient intake recommendations for infants up to 12 months of age. The nutrient profiles for human milk found in the USDA SR Database are now almost 40 years old and based on limited data, and the data in the Canadian Nutrient File were derived from the USDA SR Database. Given that new or updated DRI reviews require a systematic review, the usefulness of the USDA SR Database as a data source is limited.

Human milk nutrient profiles are still available, but they are not intended for estimating current exposures. Thus, adequate published data on the macro- and micronutrient content of human milk is needed to update the food composition databases to support systematic reviews for future DRI updates. The goal of this evidence scan was not to conduct a formal systematic review; rather, it was to conduct a thorough scan of the peer-reviewed published literature to (1) determine the status of evidence on the nutrient composition and volume of human milk, and (2) identify new evidence on existing DRI nutrients in human milk that could inform future DRI reviews.

APPROACH

The committee approached its task by designing a literature search strategy with the objective of identifying articles on nutrients to provide information for updating the USDA SR Database and to inform future DRI reviews. The committee focused its approach on evidence describing the nutrient composition based on nutrients specified in the DRIs and on the volume of human milk consumed by the infant (milk volume). The DRI framework structure for a systematic review is grounded in the relationship between nutrient intake (exposure) and health outcomes (Russell et al., 2009). However, for this evidence scan, the committee evaluated nutrient composition and milk volume as predictors of nutrient intake for infants broadly; it did not examine specific associations between nutrient intake and infant/child health outcomes (see methodological descriptions below for detailed information). Therefore, for both human milk

nutrient composition and volume, the committee considered criteria to evaluate whether the evidence would be sufficient to inform a decision to undertake a rereview of a nutrient in the DRI process (Brannon et al., 2017). However, this report does not serve as the basis for a specific nutrient review.

Literature Search Criteria

The committee drew from Brannon et al. (2017) as a paradigm to design this evidence scan. To assure the evidence scan was comprehensive, the committee identified subject-matter experts to provide information relative to the development of an analytic framework. The committee convened a 1-day meeting with subject-matter experts in a discussion of issues relevant to the task (see Appendix B for the meeting agenda). The experts were asked to develop their presentations in response to the following objectives for the evidence scan:

- Identify current evidence on the nutrient content and volume of human milk;
- Develop a literature search strategy for the evidence scan; and
- Identify a methodological strategy for assessing the results of the literature search.

Key Questions

After considering information presented by the subject-matter experts, the committee developed the following key research questions to inform a set of inclusion and exclusion criteria, which were subsequently used to assess potentially relevant studies for eligibility.

1. What is the nutrient[1] composition of human milk produced by healthy[2] lactating mothers of healthy,[3] singleton, full-term infants up to 12 months postpartum?
    a. What is the nutrient composition of milk produced by women who are breastfeeding healthy, singleton, full-term infants, up to 5.9 months postpartum?
    b. What is the nutrient composition of milk produced by women who are breastfeeding healthy, singleton, full-term infants, aged 6 to 12 months?
2. What is the volume of human milk consumed by healthy, singleton, full-term, breastfed infants from birth to 12 months of age who are receiving human milk from a healthy mother?
    a. What is the volume of human milk consumed by healthy, singleton, full-term infants from birth to 5.9 months who are exclusively breastfeeding?
    b. What is the volume of human milk consumed by healthy, singleton, full-term infants ages 6 to 12 months who are breastfeeding?

---

[1] Refers to existing DRI nutrients and does not include bioactive substances in foods.
[2] The committee decided to accept the authors' description of the subjects as being "healthy" when this was provided. These considerations meant that some of the reviewed reports could contain data on participants who may not meet the criteria as defined by a DRI committee (such as those who smoke or have obesity).
[3] The committee also accepted the authors' description of the infant as being healthy when this was provided. However, the criteria for adequate growth in infants changed during the 40-year scope of this evidence scan and were poorly described or not at all by the study investigators so it was difficult for the committee to discern if some of the infants studied would be considered to be growing adequately according to current growth standards.

Eligibility Criteria

The committee developed and refined its prespecified criteria for assessing the relevance of identified evidence (see Tables 2-1 and 2-2). The committee used the National Academies' Research Center as a resource for carrying out the literature search. In its approach, the committee identified a number of relevant articles, which the Research Center staff searched in Medline, Embase, and Scopus (see Appendix C for details on the literature searches). The staff created a list of all the assigned MeSH and Emtree terms, and the committee then reviewed the list of controlled terms and identified additional MeSH terms. The resulting eligibility criteria followed directly from the key questions and are organized using the population, interventions (exposures), comparators, outcomes, and study designs (PI(E)COD) framework in order to focus the key questions into a searchable query. The committee notes that:

1. The interventions (I) element of the framework is not relevant, but the exposures (E) element is. As such, nutrient composition (Key Question 1) and milk volume (Key Question 2) are classified as "exposures."
2. The comparators (C) and outcomes (O) elements of the framework are not relevant for this evidence scan.

TABLE 2-1 Prespecified Criteria for Assessing the Relevance of Identified Evidence: Key Question 1: Nutrient Composition of Human Milk

Component	Criteria
Populations	Human Include • Adult women (≥ 18 years of age) with generally healthy, full-term, singleton infants living in a high-income or upper middle-income country[a] • Generally healthy, full-term infants living in a high-income[b] or upper middle-income country[c] during the study Exclude • Infants older than 12 months of age at the time of study enrollment • Infants with low birth weight or premature birth • Women taking nutritional supplements[d] or galactagogues[e]

Exposures	Milk (e.g., lactation, breastfeeding) containing any of the following:
	• Nutrients, identified as DRI nutrients
	  ○ Micronutrients
	  ▪ Vitamins
	  • A, C, D, E, K, thiamin, riboflavin, niacin, B6, folic acid, B12, pantothenic acid, biotin
	  ▪ Choline
	  ▪ Minerals
	  • Copper, fluorides, iodine, iron, magnesium, manganese, molybdenum, chromium, calcium, phosphorus, sodium, selenium, zinc, potassium, chlorides
	  ○ Protein

	○ Lactose[f] ○ Lipids ▪ Total lipids ▪ Fatty acids • Linoleic, alpha linolenic, eicosapentaenoic, and docosahexaenoic acids Exclude • Colostrum[g] • Nutritional supplements • Oligosaccharides • Bioactive substances[h]
Comparators	Not relevant for this evidence scan
Outcomes	Not relevant for this evidence scan
Study Designs	Include • Publications from 1980 forward[i] • Randomized controlled trials • Observational prospective cohort studies • Case-control studies • Cross-sectional studies Exclude • Case studies, mechanistic studies • Studies without primary data, including systematic reviews, narrative reviews, editorials, conference abstracts, theses, and commentaries • Studies presenting data obtained using methods not considered adequate ○ Nutrients, population size, milk collection procedures, and analytical methods not considered adequate (see Appendix B) • Studies from which nutrient(s) of interest were not able to be assessed independently

[a] Countries are classified according to definitions from the World Bank.

[b] See https://data.worldbank.org/income-level/high-income (accessed September 28, 2020).

[c] See https://data.worldbank.org/income-level/upper-middle-income (accessed September 28, 2020).

[d] The committee acknowledges that contemporary American women have likely received prenatal supplements during gestation and may still have been taking them at the time of milk sampling. Very few reports included information on women's prior or current use of prenatal or other supplements. As a result, it is possible that the milk composition values reported reflect this exposure and, thus, the results must be interpreted in light of this possibility.

[e] Galactagogues are pharmaceutical agents, herbal supplements, or foods for which there is limited or no evidence to support breast milk production. Examples include dopamine antagonists such as domperidone or metoclopramide; shatavari, fenugreek, and malunggay; and parsley, ginger, and garlic.

[f] The committee used lactose rather than carbohydrate as a macronutrient proxy based on the definition in IOM (2002/2005, p. 281).

[g] The committee chose to exclude data regarding milk produced in the first week postpartum to avoid data that may represent the colostral phase of milk production.

[h] Examples of bioactive food substances include polyphenols, carotenoids, tocopherols, tocotrienols, organosulfur compounds, and soluble and insoluble fiber.

[i] The initial literature search was conducted beginning with 1970; however, it was later refined to studies from 1980 onward in order to capture more consistent and up-to-date methodologies in nutrient analyses (see Appendix C).

TABLE 2-2 Prespecified Criteria for Assessing the Relevance of Identified Evidence: Key Question 2: Volume of Human Milk

Component	Criteria
Populations	Human Include • Adult women (≥ 18 years of age) with generally healthy, full-term, singleton infants living in a high-income[a] or upper middle-income[b] country during the study Exclude • Infants older than 6 months at the time of study enrollment • Infants 0–5.9 months not exclusively breastfed • Women taking nutritional supplements or galactogogues[c]
Exposures	Volume of milk (e.g., lactation, breastfeeding) consumed by infant Exclude • Colostrum[d]
Comparators	Not relevant for this evidence scan
Outcomes	Not relevant for this evidence scan
Study Designs	Include • Publications from 1980[e] or more recent • Randomized controlled trials • Observational prospective cohort studies and case-control studies • Cross-sectional studies Exclude • Case studies, mechanistic studies • Studies with no primary data including systematic reviews, narrative reviews, editorials, conference abstracts, theses, and commentaries • Studies presenting data obtained using methods not considered adequate ○ Population size, milk collection procedures, and analytical methods not considered adequate (see Appendix B)

[a] See https://data.worldbank.org/income-level/high-income (accessed September 28, 2020).
[b] See https://data.worldbank.org/income-level/upper-middle-income (accessed September 28, 2020).
[c] Galactagogues are pharmaceutical agents, herbal supplements, or foods for which there is limited or no evidence to support breast milk production. Examples include dopamine antagonists such as domperidone or metoclopramide; shatavari, fenugreek, and malunggay; and parsley, ginger, and garlic.
[d] The committee chose to exclude data regarding milk produced in the first week postpartum to avoid data that may represent the colostral phase of milk production.
[e] The initial literature search was conducted beginning with 1970; however, it was later refined to studies from 1980 onward in order to capture more consistent and up-to-date methodologies in nutrient analyses (see Appendix C).

Search Strategy

Using the prespecified criteria, the committee developed a search strategy that included a search syntax (i.e., specific keywords and controlled vocabulary terms) to be used in searching online databases of the peer-reviewed published literature. The search process is shown in Figure 2-1.

Syntax and Language Terms

The National Academies' research staff compiled a literature search strategy based on the committee's prespecified criteria for nutrient composition and milk volume (see Tables 2-1 and 2-2, respectively). Natural language terms were identified by the committee to be used in the search syntax (see Figure 2-1, Step 1). Two separate searches were conducted, one for nutrient composition and the other for milk volume. Only English language reports were searched. The search was carried out in Medline (using Ovid) and included published articles from January 1980 through December 2019. Details of the literature searches are shown in Appendix C.

Internal Assessment

To assess whether the search strategy was either too broad or too narrow, the committee developed an internal check (Step 2). Committee members suggested five to six key articles that they expected to find in the search results. Research Center staff reran the searches and checked whether the search had identified the submitted articles. Additionally, study staff conducted three abridged checks of 200–500 records to determine whether refinements would be needed to the search syntax. Audit results were consistent with expected outcomes; therefore, no further refinements were made to the literature search, and the search syntax for Medline was finalized (Step 3).

Next, the committee translated the search syntax for use in Embase (using Ovid) and Scopus on peer-reviewed literature published from January 1980 through January 2020 (Steps 4 and 5). Concurrently, the searches were rerun in Medline to capture any articles that had been published since the preliminary search in December 2019. Because human milk composition and volume are often studied in tandem, records from the milk composition and volume search sets were identified that addressed both. To eliminate the need to screen these articles twice, they were removed from the search result sets and put into a third search result set. All result sets were uploaded to a systematic review management program (Covidence[4]) for screening.

[4] See https://www.covidence.org (accessed September 28, 2020).

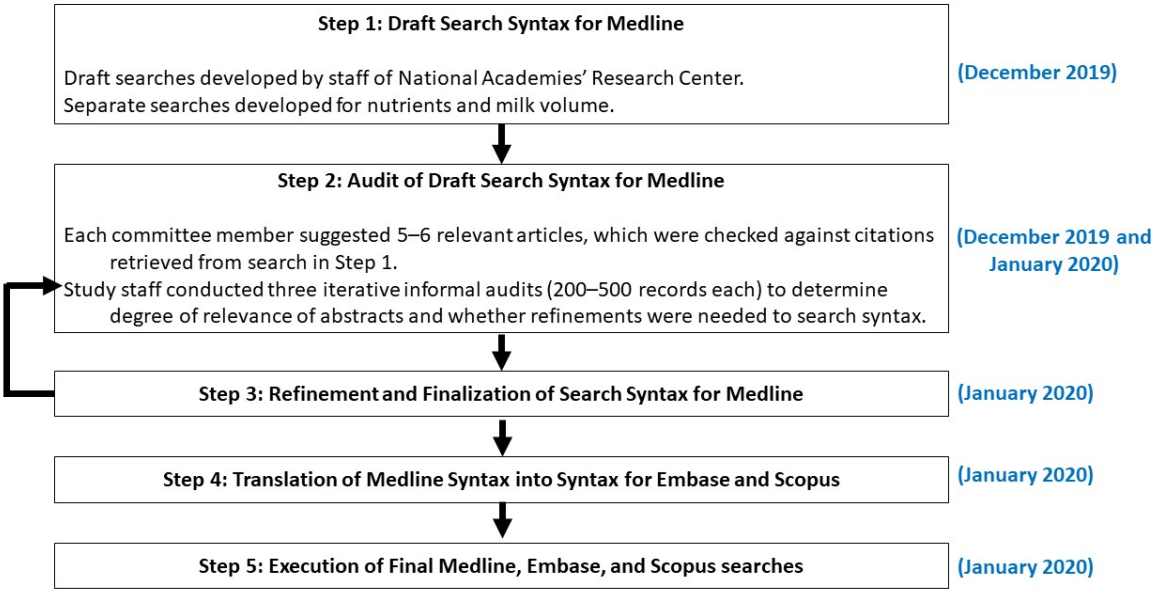

FIGURE 2-1 Development of the literature search strategy.

SCREENING AND DATA ABSTRACTION

Screening

Following the internal assessment, in the first step of the screening process, the Health and Medicine Division (HMD) staff screened the title and abstract of each article retrieved from the literature search using the prespecified criteria presented in Tables 2-1 and 2-2. In the second step, two committee members screened the full text of each article to determine eligibility for data abstraction based on the same prespecified criteria. During the screening process, the committee reevaluated and revised the criteria (see Appendix D) and refined the search strategy. Throughout the screening by committee members, all records were double-screened independently and conflicts were resolved through discussion between the two committee screeners.

Data Abstraction

The data abstraction was carried out using a Web-based (Google) spreadsheet (see Appendix E). At this stage, after the screening process was completed, the committee focused on the methods used to sample and analyze each nutrient in human milk in each study. Studies on milk volume were examined for the methods used to measure milk volume and for infants 0–5.9 months exclusively breastfeeding. Each article was examined by two committee members: one as a primary data extractor and one as a secondary validator who verified extracted data; conflicts were resolved by discussion between the data abstractor and the validator, which confirmed that the study was truly eligible for inclusion. If there was agreement that a study was

eligible, data on the study characteristics, population characteristics, milk sampling methodology, and analysis methodology were abstracted and entered into the spreadsheet.

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3

Results

LITERATURE SEARCH RESULTS

The objective of this evidence scan was to assess the status of evidence on the nutrient content of human milk and on the volume of milk, both of which are needed to understand nutrient consumption by healthy breastfed infants. The results of the scan are intended to be used to update the U.S. Department of Agriculture's National Nutrient Database for Standard Reference (USDA SR Database) and support future comprehensive systematic reviews to update specific Dietary Reference Intake (DRI) nutrients relevant to the nutrient requirements of infants from birth through 12 months of age in the United States and Canada. This approach took the following five key steps:

1. Develop an analytic framework on the basis of appropriate markers of adequate intake of both nutrients and milk volume.
2. Consult subject-matter experts on nutrients needed to support normal growth and development of infants.
3. Use an analytic framework to develop and carry out a literature scan with relevant key words.
4. Review abstracts and publications for relevance relative to prespecified criteria.
5. Reach a consensus on the relevance of the evidence to updating the USDA SR Database and supporting the DRI process.

The results from the evidence scan are presented in Figure 3-1. The December 2019 searches produced 15,152 records on nutrient composition and 14,807 records on milk volume. The January 2020 searches produced 8,113 articles on nutrient composition and 4,690 articles on milk volume. Combined, the two search sets retrieved 42,762 articles on nutrient composition and milk volume. After removing 8,978 duplicate records from the December search and 2,268 duplicate records from the January search, there remained 31,516 unique citations. During title and abstract screening, 30,236 records were excluded, leaving 1,190 for full-text screening. The committee excluded 792 records during the first round of full-text screening and 272 during the second round (see Chapter 4 for a discussion of exclusion reasons). The final number of reports remaining for inclusion was 126.

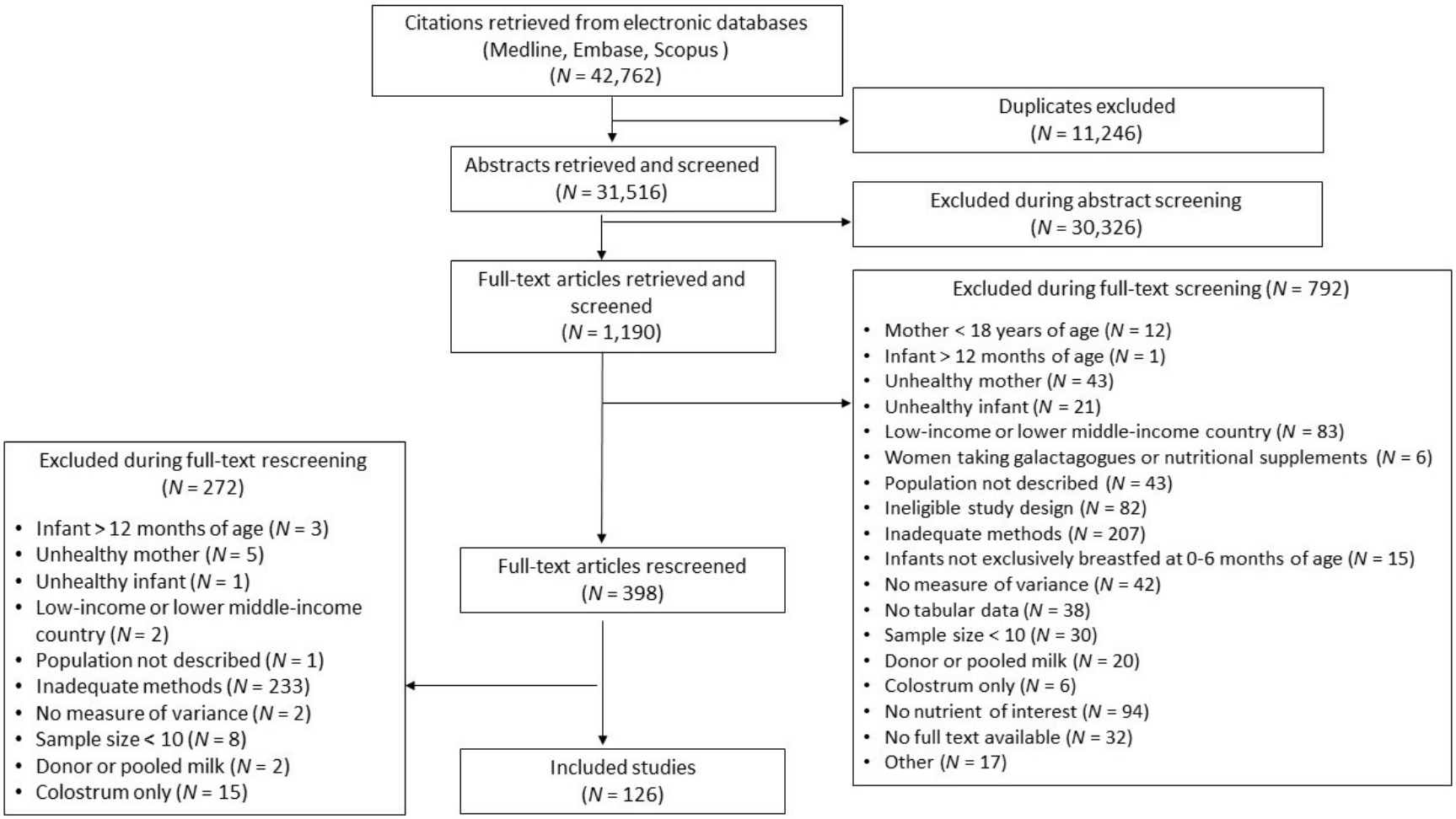

FIGURE 3-1 Evidence-scan flow diagram.

In the process of review and abstraction of the identified studies the committee found no eligible studies on fluoride, vitamin B12, or niacin, and no eligible studies on total carbohydrate (although there were studies on lactose). Additionally, only one to two studies were found for biotin, molybdenum, pantothenic acid, riboflavin, thiamin, and vitamins C, D, and K. This is a result of both the small number of participants studied in any category of infant age as well as the need to use newer methods to analyze milk composition for DRI nutrients. Figure 3-2 compares the number of studies identified by nutrient, and Figure 3-3 shows the number of dyads for each nutrient in the combined results.

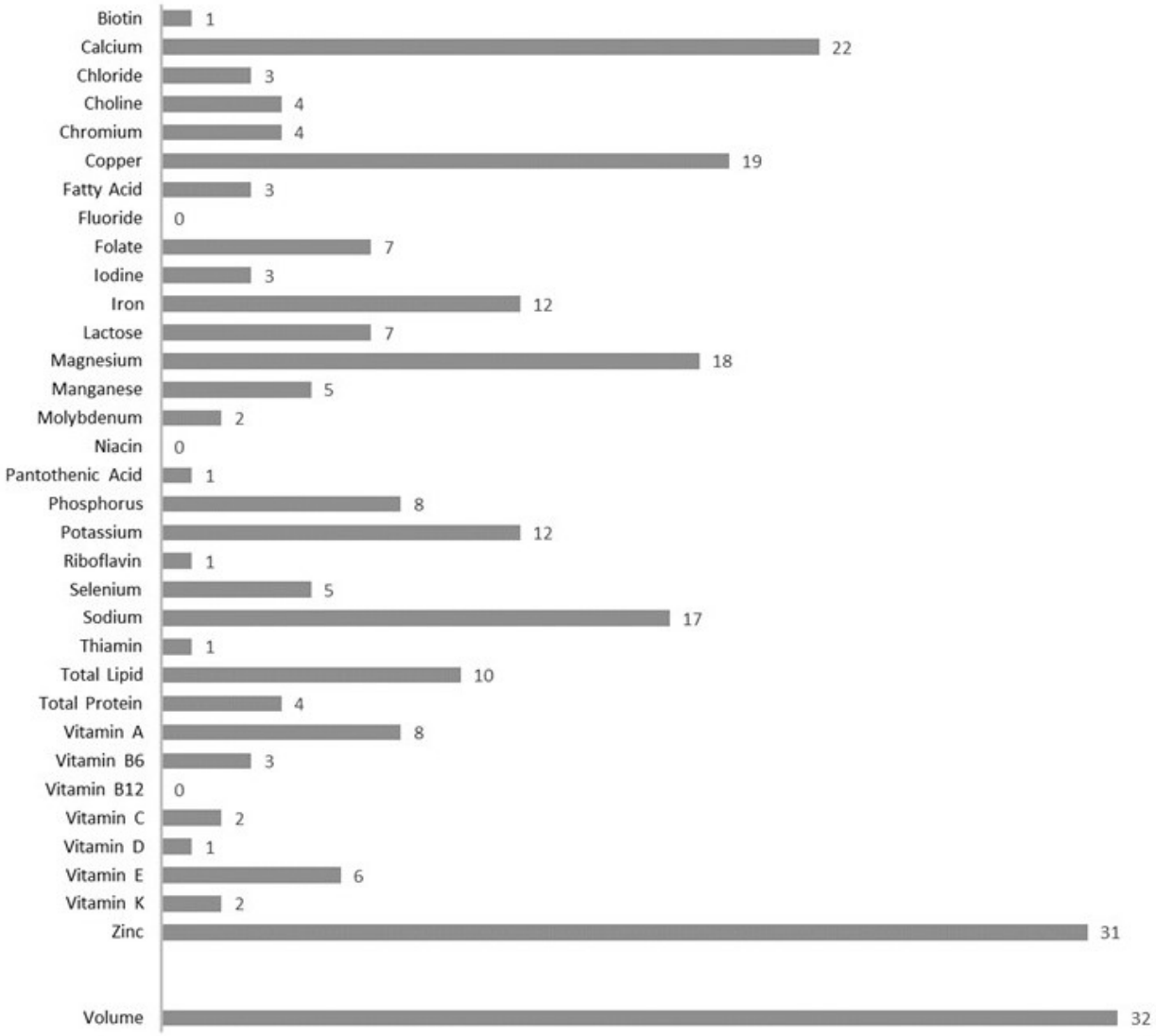

FIGURE 3-2 Total number of studies per nutrient or volume reported.

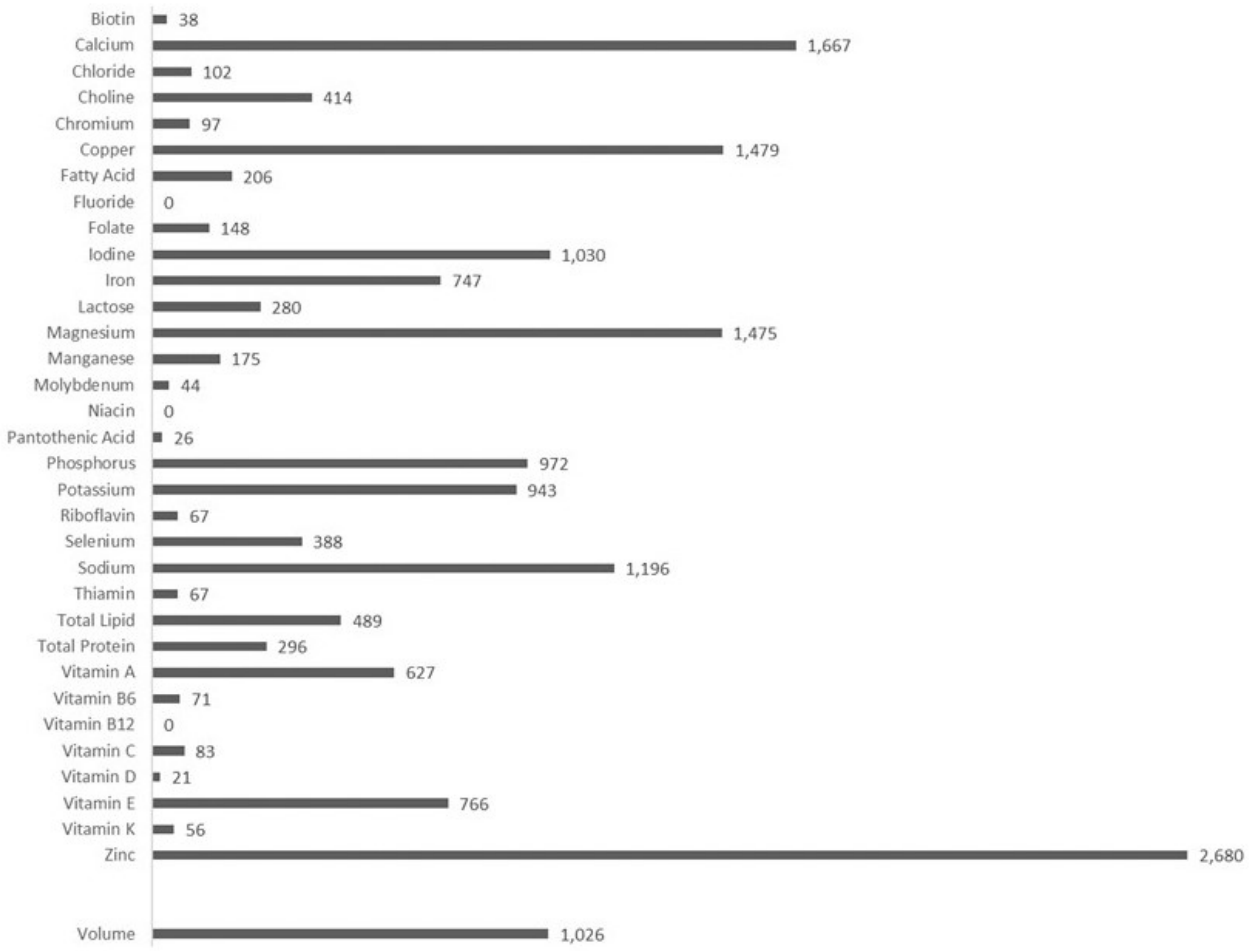

FIGURE 3-3 Total number of dyads per nutrient or volume reported.

Included Studies

Using a Web-based spreadsheet (Google) (see Appendix E), the committee evaluated each of the 398 potentially relevant articles in its entirety. From the initial list, 94 articles relevant to the nutrient content in human milk, 24 relevant to milk volume, and 8 articles relevant to both nutrient content and milk volume combined were determined to be relevant to the committee's criteria. A description of the selected articles is provided in Tables 3-1, 3-2, and 3-3. The committee notes that only three articles in the latter two tables met the committee's general inclusion criteria and also contained data on the milk volumes produced by mothers of infants 6 to 12 months old. These mothers were not exclusively breastfeeding and, thus, these data did not meet the specific inclusion criteria, which required this behavior (see Notes to Tables 3-2 and 3-3). In response to the committee's task, these tables represent the sum of the committee's evidence-scan results.

TABLE 3-1 Assessment of Included Studies of Nutrient Composition in Human Milk on the Basis of Prespecified Criteria (Data Include Infants Who May or May Not Have Been Exclusively Breastfed)

Study Authors, Year	Study Type	Study Population[a]	Nutrient(s)	Nutrient Analysis Methodology	Outcome (mean ± SD)[b]	Additional Comments
Denic et al., 2019	Prospective cohort	43 Serbian dyads, 0–1 mo pp	Vitamin A	HPLC	*Women age ≥ 35 years* 0.48 ± 0.08 μg/mL (1 mo pp) *Women age < 35 years* 0.46 ± 0.11 μg/mL (1 mo pp)	This article reported additional nutrients (total lipids) that did not meet the inclusion criteria
Minato et al., 2019	Prospective cohort	Japanese dyads, 82 at 1 mo pp, 48 at 3 mo pp	Calcium	Multitype emission spectrometer	29.8 (26.7, 33.3) mg/dL (1 mo pp) 28.7 (25.9, 31.9) mg/dL (3 mo pp)	This article reported additional nutrients (total lipids, total proteins, total carbohydrates) that did not meet the inclusion criteria Values are expressed as: median (25%, 75%)
			Phosphorus	Multitype emission spectrometer	16.6 (14.6, 18.3) mg/dL (1 mo pp) 13.4 (11.6, 14.4) mg/dL (3 mo pp)	
Wong et al., 2019	Cross-sectional	49 Chinese dyads, 2–12 mo pp	Fatty acids	Solvent extraction – GC	*2–6 mo pp (%wt/wt of all fatty acids)* 17.89 ± 4.09 (linoleic acid) 2.20 ± 1.02 (α-linolenic acid) 0.36 ± 0.31 (EPA) 0.86 ± 0.66 (DHA) *7–12 mo pp (%wt/wt of all fatty acids)* 16.83 ± 3.63 (linoleic acid) 2.01 ± 0.66 (α-linolenic acid) 0.26 ± 0.28 (EPA) 0.91 ± 0.88 (DHA)	
			Total lipid	Solvent extraction – GC	39.13 ± 14.69 g/L (2–6 mo pp) 36.76 ± 9.76 g/L (7–12 mo pp)	

Butts et al., 2018	Cross-sectional	78 New Zealand mothers of Asian, Māori, Pacific Island, or European ethnicity, 6–8 wk pp	Calcium	ICP-MS	27.5 ± 1.3 mg/100 g (Asian) 29.1 ± 1.0 mg/100 g (Māori and Pacific Island) 30.9 ± 0.7 mg/100 g (New Zealand European)	Sample included women classified as overweight and obese (BMI range 20–39) Values are expressed as: mean ± standard error This article reported additional nutrients (selenium, zinc, fatty acids, total lipid, total protein, carbohydrate) that did not meet the inclusion criteria
			Magnesium	ICP-MS	3.08 ± 0.08 mg/100 g (Asian) 3.01 ± 0.11 mg/100 g (Māori and Pacific Island) 10.19 ± 6.20 mg/100 g (New Zealand European)	
Taravati Javad et al., 2018	Cross-sectional	100 Iranian dyads, 1–12 mo pp	Zinc Copper Magnesium Iron Calcium Sodium	ICP-MS ICP-MS ICP-MS ICP-MS ICP-MS ICP-MS	1.38 ± 1.1 µg/mL 0.35 ± 0.1 µg/mL 34.58 ± 9.5 µg/mL 0.75 ± 1.4 µg/mL 255 ± 68.8 µg/mL 155.72 ± 111.5 µg/mL	
Wang et al., 2018	Prospective cohort	106 Chinese dyads, 0–12 wk pp	Iodine	ICP-MS	221.7 ± 103.5 µg/L (4 wk pp) 175.2 ± 76.2 µg/L (8 wk pp) 148.1 ± 66.2 µg/L (12 wk pp)	
Wiedeman et al., 2018	Cross-sectional	301 Canadian dyads, 8 wk pp	Choline	LC-MS/MS	1106 (1071, 1140) µmol/L (water-soluble choline) (water-soluble choline = sum of free choline, phosphocholine, and glycerophosphocholine)	Values are expressed as: mean (95% CI)
Dold et al., 2017	Cross-sectional	386 Chinese dyads, 109 Croatian dyads; 2–26 wk pp	Iodine	MC-ICP-MS	132 (91, 182) µg/d (China) 97 (72, 146) µg/d (Croatia)	Values are expressed as: median (IQR)

Doneray et al., 2017	Prospective cohort	37 Turkish dyads, measured at 8–12 d pp and 25–30 d pp	Zinc	AAS	*8–12 d pp* 641.1 ± 500.1 µg/dL (foremilk) 455.2 ± 215.1 µg/dL (hindmilk) *25–30 d pp* 575.1 ± 275.1 µg/dL (foremilk) 336.1 ± 235.1 µg/dL (hindmilk)	Milk samples were obtained before (foremilk) and after (hindmilk) a feeding period from the same women
Goran et al., 2017	Prospective cohort	25 dyads, 1–6 mo pp	Lactose	LC-MS/MS	7.8 ± 0.8 g/dL (1 mo pp) 7.5 ± 0.7 g/dL (6 mo pp)	
Huynh et al., 2017b	Cross-sectional	538 Australian dyads, 3 mo pp	Iodine	ICP-MS	127 (84–184) µg/L	Values are expressed as: median (IQR)
Kim et al., 2017	Cross-sectional	165 South Korean mothers from 8 metropolitan cities, 1–11 mo pp	Sodium Potassium Calcium Phosphorus Magnesium	ICP-OES ICP-OES ICP-OES ICP-OES ICP-OES	11.71 ± 6.02 mg/dL 38.58 ± 8.91 mg/dL 27.24 ± 5.62 mg/dL 13.44 ± 3.21 mg/dL 3.01 ± 0.63 mg/dL	Approximately half of the women were taking dietary supplements; data presented in this table are for nonsupplement users This article reported additional nutrients (lactose, total protein, total fat, retinol, vitamin E, iron, zinc, copper, manganese) that did not meet the inclusion criteria
Perrin et al., 2017	Prospective cohort	19 dyads, 11–12 mo pp	Lactose	HPLC	5.7 ± 0.7 g/dL (11 mo pp) 6.0 ± 0.8 g/dL (12 mo pp)	This article reported additional nutrients (total lipid, total protein, iron, zinc) and milk volume that did not meet the inclusion criteria
			Calcium	ICP-OES	200 ± 29 µg/mL (11 mo pp) 200 ± 25 µg/mL (12 mo pp)	
			Sodium	ICP-OES	70 ± 19 µg/mL (11 mo pp) 70 ± 24 µg/mL (12 mo pp)	
			Potassium	ICP-OES	370 ± 51 µg/mL (11 mo pp) 380 ± 69 µg/mL (12 mo pp)	

Sunaric et al., 2017	Cross-sectional	67 Serbian dyads, 0–10 mo pp	Riboflavin	HPLC	0.228 ± 0.035 µg/mL (8–14 d pp) 0.453 ± 0.05 µg/mL (15–300 d pp)	This article reported additional nutrients (total fat, total protein, vitamin E, calcium, magnesium, sodium, potassium, chloride) that did not meet the inclusion criteria
			Thiamin	HPLC	0.094 ± 0.012 µg/mL (8–14 d pp) 0.248 ± 0.05 µg/mL (15–300 d pp)	
			Vitamin C	HPLC	22.6 ± 3.7 µg/mL (8–14 d pp) 35.4 ± 5.2 µg/mL (15–300 d pp)	
Xue et al., 2017	Cross-sectional	509 Chinese dyads, 0–240 d pp	Vitamin E	Ultra HPLC	239 (145–396) µg/mL (12–30 d pp) 206 (126–345) µg/mL (31–60 d pp) 212 (112–300) µg/mL (61–120 d pp) 211 (135–326) µg/mL (121–240 d pp)	
Martysiak-Zurowska et al., 2016	Cross-sectional	16 Polish dyads, 15–90 d pp	Vitamin C	HPLC	43.4 ± 17.1 mg/L (15 d pp) 56.3 ± 12.9 mg/L (30 d pp) 55.2 ± 15.7 mg/L (90 d pp)	
Panagos et al., 2016	Case-control	21 dyads, 4–10 wk pp	Vitamin A	HPLC	4.6 ± 1.7 µg/dL	Study also reported data for obese women This article reported additional nutrients (total fat, total protein, lactose, vitamin B12) that did not meet the inclusion criteria
			Vitamin E	HPLC	378 ± 171.7 µg/dL	
			Vitamin D	Extraction by radio-immunoassay procedure	1.3 ± 0.6 ng/mL	
			Folate	*L. casei* microbial assay	46.4 ± 42.2 ng/mL	
			Fatty acids	Modified Folch method	16.6 ± 3.4 mol% (linoleic acid) 1.7 ± 0.6 mol% (α-linolenic acid)	

					0.8 ± 0.04 mol% (EPA) 0.3 ± 0.1 mol% (DHA)	
Dumrongwongsiri et al., 2015	Cross-sectional	34 Thai dyads, 4–6 mo pp	Zinc	ICP-MS	1.57 (0.5, 3.2) mg/L	Values are expressed as: median (min, max)
Mahdavi et al., 2015	RCT	27 Iranian dyads, 90–120 d pp	Zinc	Flame AAS	2.34 ± 0.79 mg/L (preintervention) 1.74 ± 0.79 mg/L (postintervention)	Study also reports values for women who received synbiotic supplements
			Copper	Flame AAS	0.39 ± 0.23 mg/L (preintervention) 0.23 ± 0.27 mg/L (postintervention)	Values are expressed as: mean ± SEM
			Iron	Flame AAS	0.36 ± 0.28 mg/L (preintervention) 0.18 ± 0.20 mg/L (postintervention)	
			Magnesium	Flame AAS	16.92 ± 0.75 mg/L (preintervention) 16.22 ± 0.71 mg/L (postintervention)	
			Calcium	Flame AAS	195 ± 17.4 mg/L (preintervention) 174.9 ± 16.6 mg/L (postintervention)	

Matos et al., 2014	Prospective cohort	31 Portuguese dyads, 1–16 wk pp	Chromium	ICP-MS	49.74 ± 20.98 µg/kg (4 wk pp) 37.93 ± 13.66 µg/kg (8 wk pp) 35.11 ± 15.55 µg/kg (12 wk pp) 34.94 ± 9.55 µg/kg (16 wk pp)	
			Molybdenum	ICP-MS	3.06 ± 3.73 µg/kg (4 wk pp) 2.69 ± 2.52 µg/kg (8 wk pp) 3.87 ± 3.00 µg/kg (12 wk pp) 3.30 ± 2.64 µg/kg (16 wk pp)	
Ozarda et al., 2014	Prospective cohort	53 Turkish dyads, 1–180 d pp	Choline	HPLC-EC	*Total choline* 1532 (1250–1695) µmol/L (22–180 d pp)	Values are expressed as: median (IQR)
Stimming et al., 2014	Cross-sectional	118 dyads, 8 wk pp	Vitamin E	HPLC	569.3 ± 322.3 µg/100 mL (α-tocopherol) 640.0 ± 354.3 µg/100 mL (total vitamin E)	This article reported additional nutrients (fatty acids) that did not meet the inclusion criteria
Zhao et al., 2014	Cross-sectional	444 Chinese dyads	Sodium	ICP-MS	25.9 ± 26.2 mg/100 g (12–30 d pp) 14.3 ± 6.8 mg/100 g (31–60 d pp) 13.3 ± 6.9 mg/100 g (61–120 d pp) 12.1 ± 9.3 mg/100 g (121–240 d pp)	This article reported additional nutrients (copper, iodine, iron, zinc, selenium) that did not meet the inclusion criteria
			Calcium	ICP-MS	293.6 ± 46.7 mg/kg (12–30 d pp) 309.6 ± 43.1 mg/kg (31–60 d pp) 287.4 ± 40.0 mg/kg (61–120 d pp) 267.4 ± 43.8 mg/kg (121–240 d pp)	

			Phosphorus	ICP-MS	148.0 ± 25.0 mg/kg (12–30 d pp) 136.4 ± 19.3 mg/kg (31–60 d pp) 118.0 ± 11.4 mg/kg (61–120 d pp) 113.4 ± 19.3 mg/kg (121–240 d pp)	
			Potassium	ICP-MS	601.3 ± 79.6 mg/kg (12–30 d pp) 537.6 ± 63.5 mg/kg (31–60 d pp) 489.1 ± 61.4 mg/kg (61–120 d pp) 459.1 ± 48.3 mg/kg (121–240 d pp)	
			Magnesium	ICP-MS	33.1 ± 5.6 mg/kg (12–30 d pp) 32.8 ± 5.1 mg/kg (31–60 d pp) 35.8 ± 3.9 mg/kg (61–120 d pp) 35.9 ± 6.6 mg/kg (121–240 d pp)	
Jozwik et al., 2013	Prospective cohort	13 Polish and American dyads, 1–10 d pp	Lactose	HPLC	171.2 ± 6.1 mmol (d 8 pp) 169.2 ± 6.6 mmol (d 9 pp) 170.1 ± 4.8 mmol (d 10 pp)	Data are reported as: mean ± SEM
Martysiak-Zurowska et al., 2013	Cross-sectional	48 lactating Polish dyads	Vitamin E	NP-HPLC with UV detection	4.59 ± 0.93 TE mg/L (d 14 pp) 3.00 ± 0.85 TE mg/L (d 30 pp) 2.13 ± 0.67 TE mg/L (d 90 pp)	Some women were taking vitamin supplements at time of sampling; milk vitamin E concentrations did not differ significantly between supplement users and nonusers (3.46 ± 1.36 versus 3.35 ± 1.25 TE mg/L) No statement about the health of the mother or infant
			Total lipid	Solvent extraction – HPLC	3.23 ± 0.44% (d 14 pp) 3.68 ± 0.52% (d 30 pp) 3.87 ± 0.40% (d 90 pp)	

Severi et al., 2013	Cross-sectional	123 Uruguayan dyads, 4 mo pp	Zinc	Flame AAS	1.20 (1.10–1.46) mg/L (4 mo pp)	Values are expressed as: median (CI 95%)
Szlagatys-Sidorkiewicz et al., 2013	Cross-sectional	136 Polish dyads, 17–30 d pp	Total lipid	Solvent extraction – HRGC	3.0 ± 1.54 (per 100 g of milk)	Also reported data for women who smoked
			Fatty acids	Solvent extraction – HRGC	*Weight % per 100 g fatty acids* 10.00 ± 1.91 (linoleic acid) 1.17 ± 0.47 (α-linolenic acid) 0.07 ± 0.10 (EPA) 0.33 ± 0.10 (DHA)	
Urzica et al., 2013	RCT	Romanian dyads, 2–4 mo pp; 15 controls; 17 and 19 in two treatment groups	Magnesium	AAS	*Baseline* 1.05 ± 0.10 mmol/L (control) 1.16 ± 0.11 mmol/L (group 1) 0.97 ± 0.16 mmol/L (group 2) *Postintervention* 1.11 ± 0.015 mmol/L (control)	
Yagi et al., 2013	Cross-sectional	20 Japanese dyads, 60–188 d pp	Vitamin B6	HPLC	101 ± 0.32 μmol/L	
Qian et al., 2012	Cross-sectional	750 Chinese dyads, 42 d pp	Zinc	AAS	36.29 ± 7.72 μmol/L	
Szlagatys-Sidorkiewicz et al., 2012	Prospective cohort	49 Polish dyads, 3–32 d pp	Vitamin A	HPLC	84.70 (51.45–134.68) μg/L (d 30–32 pp)	Mother–infant dyads reported taking vitamin supplements; study authors reported no significant difference in mean breast milk concentrations between supplemented and nonsupplemented women Values are expressed as: median (IQR)
			Vitamin E	HPLC	1.10 (0.74–3.94) mg/L (d 30–32 pp)	

Fischer et al., 2010	Case-control	48 dyads, 45 d pp	Choline	Liquid chromatography -electrospray ionization isotope dilution mass spectrometry	83 ± 8 nmol/mL free choline	Values are expressed as: mean ± SE
Mahdavi et al., 2010	Cross-sectional	182 Iranian dyads, 90–120 d pp	Zinc	AAS	1.93 ± 0.5 mg/L (urban) 1.77 ± 0.5 mg/L (rural) 1.85 ± 0.5 mg/L (total)	
			Iron	AAS	0.81 ± 0.2 mg/L (urban 0.9 ± 0.3 mg/L (rural) 0.85 ± 0.2 mg/L (total)	
			Copper	AAS	0.58 ± 0.4 mg/L (urban 0.49 ± 0.2 mg/L (rural) 0.53 ± 0.3 mg/L (total)	
Qian et al., 2010	Cross-sectional	60 Chinese dyads, 8–10 d pp	Calcium	AAS	30 (27, 31) mg/dL (group 1) 29 (28, 30) mg/dL (group 2) 28 (27, 29) mg/dL (group 3) 27 (25, 28) mg/dL (group 4)	Groups 1–3 were urban populations; group 4 was a suburban population This article reported additional nutrients (total lipid, total protein, lactose, iron, copper, zinc) that did not meet the inclusion criteria Values are expressed as: median (IQR)
			Manganese	AAS	1.9 (1.6, 2.1) mg/dL (group 1) 1.9 (1.7, 2.1) mg/dL (group 2) 1.8 (1.6, 2.1) mg/dL (group 3) 0.7 (0.5, 1.3) mg/dL (group 4)	
			Phosphorus	AAS	17 (16, 18) mg/dL (group 1) 16 (14, 17) mg/dL (group 2) 16 (15, 17) mg/dL (group 3) 13 (12, 14) mg/dL (group 4)	
			Potassium	AAS	62 (53, 69) mg/dL (group 1) 61 (56, 68) mg/dL (group 2) 63 (59, 68) mg/dL (group 3)	

					47 (43, 48) mg/dL (group 4)	
			Sodium	AAS	30 (21, 36) mg/dL (group 1) 26 (18, 37) mg/dL (group 2) 24 (19, 30) mg/dL (group 3) 12 (9, 16) mg/dL (group 4)	
Han et al., 2009	Prospective cohort	20 Korean dyads, 0–6 mo pp	Folate	Microbiological assay	365 ± 207 nmol/L (2 mo pp) 201 ± 86 nmol/L (6 mo pp)	
Hannan et al., 2009	Prospective cohort	31 dyads (WIC participants), measured at 30–45 d pp and 75–90 d pp	Zinc	AAS	2.1 ± 1.4 mg/L (30–45 d pp) 2.0 ± 1.7 mg/L (75–90 d pp)	This article reported additional nutrients (selenium, iodine) that did not meet the inclusion criteria
			Iron	AAS	0.5 ± 1.0 mg/L (30–45 d pp) 0.4 ± 0.3 mg/L (75–90 d pp)	
Houghton et al., 2009	Randomized placebo controlled intervention	23 Canadian dyads, 1–16 wk pp	Folate	*L. rhamnoses*	193 ± 62 nmol/L (wk 4 pp) 207 ± 76 nmol/L (wk 8 pp) 183 ± 57 nmol/L (wk 16 pp)	
Matos et al., 2009	Prospective cohort	31 Portuguese dyads, 1–16 wk pp	Copper	ICP-MS	379.6 ± 93.7 µg/kg (4 wk pp) 292.4 ± 77.0 µg/kg (8 wk pp) 259.5 ± 94.6 µg/kg (12 wk pp) 240.7 ± 98.0 µg/kg (16 wk pp)	The study authors note that results are expressed as µg/kg milk, which is roughly equivalent to µg/L milk
			Zinc	ICP-MS	2160.6 ± 589.4 µg/kg (4 wk pp) 1491.4 ± 619.5 µg/kg (8 wk pp) 1084.2 ± 537.2 µg/kg (12 wk pp) 1014.1 ± 461.5 µg/kg (16 wk pp)	
			Manganese	ICP-MS	3.65 ± 1.99 µg/kg (4 wk pp) 2.29 ± 1.13 µg/kg (8 wk pp) 2.86 ± 1.67 µg/kg (12 wk pp) 2.44 ± 1.49 µg/kg (16 wk pp)	
			Selenium	ICP-MS	25.47 ± 7.10 µg/kg (4 wk pp)	

					19.95 ± 6.76 µg/kg (8 wk pp) 20.16 ± 5.38 µg/kg (12 wk pp) 19.49 ± 3.58 µg/kg (16 wk pp)	
Zimmerman et al., 2009	Prospective cohort	48 Israeli dyads, 1–6 mo pp	Lactose	HPLC	192.2 ± 10.52 µmol/L (prefast)	This article reported additional nutrients (protein, calcium, phosphorus) that did not meet the inclusion criteria
			Sodium	AAS	0.0138 ± 0.003 mmol/L (prefast)	
Shehadeh et al., 2006	Cross-sectional	41 Israeli dyads, 3 mo pp	Calcium	AAS	25.8 ± 3.9 mg/dL	This article reported additional nutrients (total fat, total protein, carbohydrates) that did not meet the inclusion criteria
			Sodium	AAS	16.2 ± 3.9 mEq/dL	
Hunt et al., 2005	Prospective cohort	45 dyads, 1–4 mo pp	Calcium	ICAP-ES	281 ± 11.5 mg/L (1 mo pp) 268 ± 11.5 mg/L (4 mo pp)	Values are expressed as: mean ± SEM
			Magnesium	ICAP-ES	28.6 ± 2.2 mg/L (1 mo pp) 33.0 ± 2.2 mg/L (4 mo pp)	This article reported additional nutrients (boron) that did not meet the inclusion criteria
			Zinc	ICAP-ES	2.3 ± 0.26 mg/L (1 mo pp) 1.0 ± 0.26 mg/L (4 mo pp)	
Ilcol et al., 2005	Cross-sectional	12 Turkish women, 0–180 d pp	Choline	Enzymatic radiochemical method	19.2 ± 0.9 µmol/L (12–28 d pp) 18.0 ± 0.6 µmol/L (75–90 d pp) 16.2 ± 0.7 µmol/L (165–180 d pp)	
Meneses et al., 2005	Cross-sectional	49 Brazilian dyads, 30–120 d pp	Vitamin A	HPLC	1.4 ± 0.1 µmol/L	Values are expressed as: mean ± SEM
Domellof et al., 2004	Cross-sectional	86 Swedish dyads, 9 mo pp	Iron	AAS	0.29 ± 0.21 mg/L	
			Zinc	AAS	0.46 ± 0.26 mg/L	
			Copper	AAS	0.12 ± 0.22 mg/L	

Schweigert et al., 2004	Prospective cohort	21 German dyads, 4–19 d pp	Vitamin E	HPLC	13.2 ± 5.1 µmol/L (d 19 pp)	
			Vitamin A	HPLC	2.90 ± 1.12 µmol/L (d 19 pp)	
Canfield et al., 2003	Cross-sectional	411 dyads from various countries; 1–12 mo pp	Vitamin A	HPLC	1.086 ± 0.055 µmol/L (Australia) 1.188 ± 0.066 µmol/L (Canada) 1.242 ± 0.085 µmol/L (Chile) 1.043 ± 0.088 µmol/L (China) 1.230 ± 0.063 µmol/L (Japan) 1.321 ± 0.087 µmol/L (Mexico) 1.052 ± 0.050 µmol/L (United Kingdom) 1.227 ± 0.087 µmol/L (United States)	Values are expressed as: mean ± SEM
Carratu et al., 2003	Cross-sectional	195 Italian dyads, 1 mo pp	Total protein	Kjeldahl with correction for NPN by acid precipitation	12.6 ± 2.0 g/L	This paper also reported milk volume, but methods did not meet the inclusion criteria
Gossage et al., 2002	Randomized, placebo controlled trial	21 dyads, 4–32 d pp	Vitamin A	HPLC	2079 ± 207 µmol/L (d 32 pp)	Study reported no significant effect of B-carotene supplementation on milk retinol values; so placebo and supplement group values were combined
Kantola and Vartiainen, 2001	Cross-sectional	256 Finnish dyads, 4 wk pp	Selenium	ETA-AAS	16.4 ± 3.2 µg/L (1987) 18.9 ± 3.0 µg/L (1993–1995)	Two separate groups of women were measured at different times: 1987 and 1993–1995
			Copper	ETA-AAS	0.52 ± 0.11 mg/L (1987) 0.43 ± 0.10 mg/L (1993–1995)	
			Zinc	Flame AAS	3.0 ± 1.0 mg/L (1987) 1.4 ± 0.7 mg/L (1993–1995)	

Silvestre et al., 2001	Prospective cohort	22 Spanish dyads, 0–90 d pp	Copper	Flame AAS	0.43 ± 0.07 mg/L (2nd wk pp) 0.34 ± 0.07 mg/L (d 30 pp) 0.27 ± 0.07 mg/L (d 60 pp) 0.19 ± 0.10 mg/L (d 90 pp)	
			Iron	Flame AAS	0.50 ± 0.19 mg/L (d 2 and 4 pp) 0.39 ± 0.19 mg/L (d 30 pp) 0.43 ± 0.15 mg/L (d 60 pp) 0.40 ± 0.17 mg/L (d 90 pp)	
			Zinc	Flame AAS	3.31 ± 1.06 mg/L (d 2 and 4 pp) 2.41 ± 0.90 mg/L (d 30 pp) 1.40 ± 0.65 mg/L (d 60 pp) 1.05 ± 0.71 mg/L (d 90 pp)	
Wasowicz et al., 2001	Cross-sectional	131 Polish dyads, 1–30 d pp	Zinc	ICP-AES	1.42 ± 0.7 mg/L (10–30 d pp)	This article reported additional nutrients (selenium) that did not meet the inclusion criteria
			Copper	ICP-AES	0.27 ± 0.9 mg/L (10–30 d pp)	
Bocca et al., 2000	Cross-sectional	60 Italian dyads, 1 mo pp	Calcium	UN-ICP-AES	307 ± 11.8 µg/mL	
			Copper	UN-ICP-AES	0.37 ± 0.03 µg/mL	
			Iron	UN-ICP-AES	0.65 ± 0.04 µg/mL	
			Magnesium	UN-ICP-AES	23.0 ± 0.51 µg/mL	
			Manganese	UN-ICP-AES	0.03 ± 0.002 µg/mL	
			Zinc	UN-ICP-AES	2.72 ± 0.07 µg/mL	
Mataloun and Leone, 2000	Prospective case-control	41 Brazilian dyads, 3–30 d pp	Calcium	AAS	9.58 ± 2.01 mmol/L (15 d pp) 10.26 ± 1.83 mmol/L (30 d pp)	
			Phosphorus	Colorimetric method	4.03 ± 1.00 (15 d pp)	
Li et al., 1999	Prospective cohort	38 Austrian dyads, 0–10 mo pp	Selenium	AAS	12.2 ± 2.4 µg/L (15–60 d pp)	
Mackey and Picciano, 1999	Randomized, double-blind, longitudinal	21 dyads, 3–6 mo pp	Folate	*L. casei*	224.4 ± 11.6 nmol/L (3 mo pp) 187.0 ± 11.9 nmol/L (6 mo pp)	This article reported milk volume that did not meet the inclusion criteria

	supplement-ation trial					
Tamari and Kim, 1999	Prospective cohort	51 Korean dyads, 0–90 d pp	Selenium	AAS	13.1 ± 5.8 µg/kg (15–90 d pp)	
Fly et al., 1998	Case-control	14 dyads, 2–8 mo pp	Calcium	ICP-AES	7.77 ± 0.30 mmol/L (d of rest period) 7.95 ± 0.31 mmol/L (d of exercise test)	Values are for baseline mineral concentrations for each treatment day
			Magnesium	ICP-AES	1.52 ± 0.072 mmol/L (d of rest period) 1.54 ± 0.068 mmol/L (d of exercise test)	Values are expressed as: mean ± SE This article reported additional nutrients (phosphorus) that did not meet the inclusion criteria
			Sodium	ICP-AES	5.00 ± 0.48 mmol/L (d of rest period) 4.73 ± 0.22 mmol/L (d of exercise test)	
			Potassium	ICP-AES	11.79 ± 0.62 mmol/L (d of rest period) 11.42 ± 0.40 mmol/L (d of exercise test)	
Lin et al., 1998	Prospective cohort	211 Taiwanese dyads, 0–12 mo pp	Calcium	ICP-AES	264 ± 12 µg/mL (11–30 d pp) 224 ± 9 µg/mL (1–3 mo pp) 225 ± 13 µg/mL (3–6 mo pp) 150 ± 26 µg/mL (6–12 mo pp)	This article reported additional nutrients (iron) that did not meet the inclusion criteria
			Magnesium	ICP-AES	24.7 ± 1.0 µg/mL (11–30 d pp) 26.3 ± 1.3 µg/mL (1–3 mo pp) 24.9 ± 2.0 µg/mL (3–6 mo pp) 18.4 ± 2.0 µg/mL (6–12 mo pp)	Values are expressed as: mean ± SE
			Copper	ICP-AES	0.39 ± 0.02 µg/mL (11–30 d pp) 0.28 ± 0.02 µg/mL (1–3 mo pp)	

					0.20 ± 0.02 µg/mL (3–6 mo pp) 0.09 ± 0.02 µg/mL (6–12 mo pp)	
			Zinc	ICP-AES	2.23 ± 0.19 µg/mL (11–30 d pp) 1.41 ± 0.20 µg/mL (1–3 mo pp) 0.77 ± 0.13 µg/mL (3–6 mo pp) 0.55 ± 0.17 µg/mL (6–12 mo pp)	
Rodriguez-Rodriguez et al., 1998	Cross-sectional	12 Canary Islander dyads, 2–6 mo pp	Selenium	Fluorometric	15.69 ± 4.07 µg/L	
Greer et al., 1997	Randomized, double-blind, placebo-controlled trial	11 dyads, 0–12 wk pp	Vitamin K	HPLC-FLD	1.17 ± 0.70 ng/mL (2 wk pp) 1.14 ± 0.46 ng/mL (6 wk pp) 1.17 ± 0.40 ng/mL (12 wk pp)	
Ortega et al., 1997	Prospective cohort	32 Spanish dyads, 13–40 d pp	Zinc	AAS	51.0 ± 9.2 µmol/L (13–14 d pp) 33.1 ± 8.0 µmol/L (40 d pp)	Values are for women with zinc intakes ≥ 50% of recommended intakes
Wack et al., 1997	Prospective cohort	30 dyads, 0–360+ d pp	Sodium	ICAP-ES	129 ± 61 mg/L (61–120 d pp) 136 ± 76 mg/L (121–180 d pp) 139 ± 142 mg/L (181–240 d pp) 124 ± 65 mg/L (241–300 d pp) 122 ± 123 mg/L (301–360 d pp)	
			Potassium	ICAP-ES	490 ± 85 mg/L (61–120 d pp) 485 ± 66 mg/L (121–180 d pp) 473 ± 63 mg/L (181–240 d pp) 470 ± 72 mg/L (241–300 d pp) 445 ± 53 mg/L (301–360 d pp)	
			Lactose	HPLC	70 ± 4 g/L (61–120 d pp) 70 ± 3 g/L (121–180 d pp) 71 ± 4 g/L (181–240 d pp) 70 ± 4 g/L (241–300 d pp) 71 ± 4 g/L (301–360 d pp)	

			Chloride	Potentiometric method	402 ± 97 mg/L (61–120 d pp) 339 ± 161 mg/L (121–180 d pp) 460 ± 232 mg/L (181–240 d pp) 420 ± 133 mg/L (241–300 d pp) 384 ± 197 mg/L (301–360 d pp)	
Huisman et al., 1996	Prospective cohort	Dutch dyads, 99 measured at 14 and 42 d pp, 25 measured at 89 d pp	Lactose	Capillary gas chromatography	59.0 ± 3.5 g/L (d 14 pp) 60.9 ± 3.0 g/L (d 42 pp) 63.4 ± 3.4 g/L (d 89 pp)	This article reported additional nutrients (fatty acids) that did not meet the inclusion criteria
Coppa et al., 1993		46 Italian dyads, 4–120 d pp	Lactose	HPLC	62.5 ± 5.74 g/L (d 10 pp) 64.1 ± 6.45 g/L (d 30 pp) 66.2 ± 6.88 g/L (d 60 pp) 66.3 ± 7.08 g/L (d 90 pp) 68.9 ± 8.16 g/L (d 120 pp)	This article reported additional nutrients (total carbohydrates) that did not meet the inclusion criteria
Ohtake and Tamura, 1993	Prospective cohort	80 Japanese dyads, 2–201 d pp	Zinc	AAS	1.76 ± 0.90 µg/mL (15–84 d pp) 0.76 ± 0.25 µg/mL (85–201 d pp)	
			Copper	AAS	0.29 ± 0.12 µg/mL (15–84 d pp) 0.19 ± 0.08 µg/mL (85–201 d pp)	
Dagnelie et al., 1992	Case-control	10 Dutch dyads, 2–3 mo pp	Calcium Magnesium Zinc	AAS AAS AAS	29.80 ± 3.87 mg/100 g 3.58 ± 0.50 mg/100 g 0.19 ± 0.10 mg/100 g	This article reported additional nutrients (lactose, total protein, total lipid, vitamin B12) that did not meet the inclusion criteria
Hirano et al., 1992	Prospective cohort	38 Japanese dyads, 0–24 d pp	Biotin	*L. plantarum*	*Free-form biotin* 3.8 ± 1.2 ng/mL (15–24 d pp) *Total biotin* 5.2 ± 2.1 ng/mL (15–24 d pp)	
Canfield et al., 1991	Cross-sectional	45 dyads, 0–6 mo pp	Vitamin K	HPLC	6.98 ± 6.36 nmol/L (1 mo pp) 5.14 ± 4.52 nmol/L (3 mo pp) 5.76 ± 4.48 nmol/L (6 mo pp)	

Nommsen et al., 1991	Prospective cohort	73 dyads, 0–12 mo pp	Total lipid	Modified Folch extraction	36.2 ± 7.0 g/L (3 mo pp) 37.7 ± 9.6 g/L (6 mo pp) 38.1 ± 8.0 g/L (9 mo pp) 37.2 ± 11.3 g/L (12 mo pp)	This article reported additional nutrients (total protein, lactose) and milk volume that did not meet the inclusion criteria
Andon et al., 1989	Cross-sectional	30 healthy, lactating dyads, measured at 60 d pp	Vitamin B6	*Saccharomyces uvarum* method	733 ± 195 nmol/L	Women were not consuming vitamin supplements Foremilk samples
Casey et al., 1989	Prospective cohort	13 dyads, 0–18 mo pp	Zinc	Flame AAS	59.8 ± 14.3 µmol/L (d 14 pp) 54.9 ± 15.0 µmol/L (d 21 pp) 45.8 ± 12.2 µmol/L (d 28 pp) 42.2 ± 10.4 µmol/L (d 38 pp) 33.4 ± 9.8 µmol/L (d 49 pp) 27.4 ± 10.2 µmol/L (d 60 pp) 22.8 ± 8.6 µmol/L (d 90 pp) 19.6 ± 9.3 µmol/L (d 120 pp) 18.5 ± 7.9 µmol/L (d 150 pp) 16.8 ± 9.2 µmol/L (d 180 pp) 14.1 ± 7.0 µmol/L (d 210 pp) 11.4 ± 3.2 µmol/L (d 240 pp) 11.8 ± 6.0 µmol/L (d 270 pp) 8.1 ± 5.0 µmol/L (d 330 pp) 8.3 ± 4.6 µmol/L (d 360 pp)	
			Copper	Graphite furnace AAS	7.6 ± 1.2 µmol/L (d 14 pp) 6.7 ± 1.3 µmol/L (d 21 pp) 6.1 ± 0.7 µmol/L (d 28 pp) 5.8 ± 1.0 µmol/L (d 35 pp) 5.1 ± 0.9 µmol/L (d 49 pp) 4.7 ± 0.7 µmol/L (d 60 pp) 4.2 ± 0.8 µmol/L (d 90 pp) 3.5 ± 1.0 µmol/L (d 120 pp) 3.5 ± 0.8 µmol/L (d 150 pp) 2.8 ± 0.9 µmol/L (d 180 pp)	

					2.6 ± 1.0 µmol/L (d 210 pp) 3.0 ± 0.8 µmol/L (d 240 pp) 2.8 ± 0.9 µmol/L (d 270 pp) 2.4 ± 0.8 µmol/L (d 330 pp) 2.7 ± 1.7 µmol/L (d 360 pp)	
			Manganese	Graphite furnace AAS	70 ± 48 nmol/L (d 14 pp) 64 ± 33 nmol/L (d 21 pp) 68 ± 25 nmol/L (d 28 pp) 60 ± 27 nmol/L (d 35 pp) 46 ± 13 nmol/L (d 49 pp) 36 ± 10 nmol/L (d 90 pp) 35 ± 11 nmol/L (d 120 pp) 41 ± 20 nmol/L (d 150 pp) 39 ± 14 nmol/L (d 180 pp) 40 ± 24 nmol/L (d 210 pp) 45 ± 16 nmol/L (d 240 pp)	
Clark et al., 1989	Cross-sectional	25 milk samples from dyads 2–32 wk pp	Total lipid	Solvent extraction by modified Folch method	4.3 ± 1.6 g/dL	Study did not report the number of dyads This article reported additional nutrients (fatty acids) that did not meet the inclusion criteria
Deelstra et al., 1988	Prospective cohort	10 Belgian dyads, 0–60 d pp	Chromium	AAS	0.14 ± 0.05 ng/mL (30–60 d pp)	
Ferris et al., 1988	Prospective cohort	12 dyads, 2–16 wk pp	Total lipid	Modified Folch extraction	3.98 ± 0.99 g/100 mL (2 wk pp) 4.41 ± 1.07 g/100 mL (6 wk pp) 4.87 ± 1.19 g/100 mL (12 wk pp) 5.50 ± 1.09 g/100 mL (16 wk pp)	This article reported additional nutrients (total protein, lactose) that did not meet the inclusion criteria
Butte et al., 1987	Prospective cohort	45 dyads, 0–4 mo pp	Calcium	AAS	297 ± 37 µg/g (1 mo pp) 301 ± 35 µg/g (2 mo pp) 292 ± 35 µg/g (3 mo pp)	This article reported additional nutrients

					285 ± 31 µg/g (4 mo pp)	(phosphorus) that did not meet the inclusion criteria
			Magnesium	AAS	27 ± 4 µg/g (1 mo pp) 30 ± 5 µg/g (2 mo pp) 32 ± 6 µg/g (3 mo pp) 34 ± 6 µg/g (4 mo pp)	This article also reported milk volume that was originally reported in Butte et al. (1984b)
			Zinc	AAS	2.3 ± 0.8 µg/g (1 mo pp) 1.5 ± 0.6 µg/g (2 mo pp) 1.1 ± 0.5 µg/g (3 mo pp) 1.0 ± 0.5 µg/g (4 mo pp)	
			Sodium	AAS	135 ± 33 µg/g (1 mo pp) 106 ± 21 µg/g (2 mo pp) 107 ± 38 µg/g (3 mo pp) 100 ± 28 µg/g (4 mo pp)	
			Potassium	AAS	466 ± 62 µg/g (1 mo pp) 451 ± 60 µg/g (2 mo pp) 437 ± 54 µg/g (3 mo pp) 416 ± 45 µg/g (4 mo pp)	
			Iron	AAS	0.242 ± 0.111 µg/g (1 mo pp) 0.203 ± 0.083 µg/g (2 mo pp) 0.182 ± 0.077 µg/g (3 mo pp) 0.160 ± 0.069 µg/g (4 mo pp)	
			Copper	AAS	0.363 ± 0.058 µg/g (1 mo pp) 0.318 ± 0.071 µg/g (2 mo pp) 0.281 ± 0.065 µg/g (3 mo pp) 0.268 ± 0.067 µg/g (4 mo pp)	
Casey and Neville, 1987	Prospective cohort	13 dyads, 0–38 d pp	Molyb-denum	Graphite furnace AAS	4.5 ± 2.9 ng/mL (d 14 pp)	

Udipi et al., 1987	Prospective cohort	27 dyads, 2–52 wk pp	Folate	*L. casei*	*0.5 mo pp* 37 ± 6 µg/L (0400–0600 hr) 25 ± 4 µg/L (0600–0800 hr) 67 ± 19 µg/L (1000–1200 hr) 52 ± 21 µg/L (1200–1400 hr) 48 ± 9 µg/L (1400–1600 hr) 34 ± 4 µg/L (1800–2000 hr) 45 ± 9 µg/L (2200–2400 hr) *1 mo pp* 32 ± 6 µg/L (0400–0600 hr) 42 ± 6 µg/L (0600–0800 hr) 48 ± 6 µg/L (1000–1200 hr) 58 ± 11 µg/L (1200–1400 hr) 58 ± 7 µg/L (1400–1600 hr) 47 ± 12 µg/L (1800–2000 hr) 54 ± 5 µg/L (2200–2400 hr) *2 mo pp* 22 ± 7 µg/L (0400–0600 hr) 44 ± 8 µg/L (0600–0800 hr) 65 ± 10 µg/L (1000–1200 hr) 88 ± 25 µg/L (1200–1400 hr) 76 ± 12 µg/L (1400–1600 hr) 64 ± 8 µg/L (1800–2000 hr) 84 ± 15 µg/L (2200–2400 hr) *3 mo pp* 52 ± 11 µg/L (0400–0600 hr) 42 ± 10 µg/L (0600–0800 hr) 64 ± 12 µg/L (1000–1200 hr) 97 ± 16 µg/L (1200–1400 hr) 98 ± 32 µg/L (1400–1600 hr) 88 ± 17 µg/L (1800–2000 hr) 59 ± 1 µg/L (2200–2400 hr)	21 of the women were taking daily supplemental folic acid This article reported milk volume that did not meet the inclusion criteria Values are expressed as: mean ± SE

4 mo pp
22 ± 2 µg/L (0400–0600 hr)
47 ± 10 µg/L (0600–0800 hr)
82 ± 14 µg/L (1000–1200 hr)
73 ± 13 µg/L (1200–1400 hr)
101 ± 23 µg/L (1400–1600 hr)
90 ± 16 µg/L (1800–2000 hr)
49 ± 23 µg/L (2200–2400 hr)

5 mo pp
46 ± 16 µg/L (0400–0600 hr)
43 ± 6 µg/L (0600–0800 hr)
78 ± 16 µg/L (1000–1200 hr)
62 ± 11 µg/L (1200–1400 hr)
126 ± 28 µg/L (1400–1600 hr)
90 ± 12 µg/L (1800–2000 hr)
75 ± 16 µg/L (2200–2400 hr)

6 mo pp
51 ± 19 µg/L (0400–0600 hr)
55 ± 11 µg/L (0600–0800 hr)
103 ± 15 µg/L (1000–1200 hr)
107 ± 31 µg/L (1200–1400 hr)
92 ± 17 µg/L (1400–1600 hr)
88 ± 26 µg/L (1800–2000 hr)
39 ± 7 µg/L (2200–2400 hr)

8 mo pp
35 ± 9 µg/L (0400–0600 hr)
36 ± 6 µg/L (0600–0800 hr)
62 ± 13 µg/L (1000–1200 hr)
79 ± 22 µg/L (1200–1400 hr)
79 ± 37 µg/L (1800–2000 hr)
45 ± 9 µg/L (2200–2400 hr)

Morriss et al., 1986	Cross-sectional	52 dyads, 2–180 d pp	Sodium	Flame photometry	7.3 ± 0.5 mEq/L (d 14–21 pp) 4.8 ± 1.0 mEq/L (d 120–180 pp)	This article reported additional nutrients (calcium, magnesium, lactose) that did not meet the inclusion criteria Data are reported as: mean ± SE
			Potassium	Flame photometry	17.1 ± 0.6 mEq/L (d 14–21 pp) 12.8 ± 0.5 mEq/L (d 120–180 pp)	
			Chloride	Colorimetric-amperometric titration	11.8 ± 0.6 mEq/L (d 14–21 pp) 10.5 ± 1.0 mEq/L (d 120–180 pp)	
			Phosphorus	Colorimetric method	5.6 ± 0.3 mEq/L (d 14–21 pp) 3.9 ± 0.2 mEq/L (d 120–180 pp)	
Chappell et al., 1985	Prospective cohort	12 Canadian dyads, 1–5 wk pp	Vitamin A	HPLC	62 ± 3 µg/100 mL (37 d pp)	This article reported additional nutrients (vitamin E) that did not meet the inclusion criteria
Krebs et al., 1985a	Prospective cohort	16 dyads, 1–12 mo pp	Zinc	Flame AAS	*All mo pp* 1.59 ± 1.17 µg/mL (foremilk) 1.60 ± 1.21 µg/mL (midmilk) 1.57 ± 1.30 µg/mL (hindmilk) *1st mo pp* 3.02 ± 1.17 µg/mL (foremilk) 3.05 ± 1.22 µg/mL (midmilk) 2.92 ± 1.20 µg/mL (hindmilk) *2nd mo pp* 1.85 ± 0.97 µg/mL (foremilk) 1.88 ± 0.99 µg/mL (midmilk) 1.81 ± 1.06 µg/mL (hindmilk)	
Krebs et al., 1985b	Case-control	39 dyads, 1–12 mo pp	Zinc	Flame AAS	2.65 ± 0.81 µg/mL (1 mo pp) 0.67 ± 0.40 µg/mL (9 mo pp)	Study also reports values for women who received dietary zinc supplements

Morrison and Driskell, 1985	Cross-sectional	21 dyads, 3–7 mo pp	Vitamin B6	HPLC with fluorometric detection	770 ± 341 pmol/mL	
			Vitamin B6	*S. uvarum*	955 ± 98 pmol/mL	
Butte et al., 1984c	Prospective cohort	13 dyads, 2–12 wk pp	Sodium	AAS	220.0 ± 77 mg/L (2 wk pp) 184.0 ± 54 mg/L (4 wk pp) 173.0 ± 65 mg/L (6 wk pp) 153.0 ± 47 mg/L (8 wk pp) 150.0 ± 49 mg/L (10 wk pp) 130.0 ± 41 mg/L (12 wk pp)	This article reported additional nutrients (total lipid, total protein, phosphorus) and milk volume that did not meet the inclusion criteria
			Calcium	AAS	255.0 ± 53 mg/L (2 wk pp) 254.0 ± 52 mg/L (4 wk pp) 267.0 ± 24 mg/L (6 wk pp) 258.0 ± 22 mg/L (8 wk pp) 270.0 ± 25 mg/L (10 wk pp) 260.0 ± 26 mg/L (12 wk pp)	
			Magnesium	AAS	33.0 ± 8 mg/L (2 wk pp) 31.0 ± 6 mg/L (4 wk pp) 35.0 ± 9 mg/L (6 wk pp) 36.0 ± 9 mg/L (8 wk pp) 38.0 ± 9 mg/L (10 wk pp) 39.0 ± 10 mg/L (12 wk pp)	
			Zinc	AAS	3.4 ± 0.8 mg/L (2 wk pp) 2.9 ± 0.9 mg/L (4 wk pp) 2.1 ± 0.9 mg/L (6 wk pp) 1.9 ± 0.6 mg/L (8 wk pp) 1.8 ± 1.0 mg/L (10 wk pp) 1.4 ± 0.7 mg/L (12 wk pp)	
Casey et al., 1984	Prospective cohort	45 dyads, 0–48 wk pp	Chromium	Graphite furnace AAS	0.28 ± 0.11 ng/mL (1–3 mo pp) 0.26 ± 0.12 mg/mL (4–6 mo pp) 0.46 ± 0.41 ng/mL (7+ mo pp)	

Dewey et al., 1984	Prospective cohort	46 dyads, 7–11 mo pp	Potassium Sodium Copper Calcium Magnesium Iron Zinc	Flame AAS Flame AAS Flame AAS Flame AAS Flame AAS Flame AAS Flame AAS	389 ± 41 µg/mL 84 ± 42 µg/mL 0.17 ± 0.05 µg/mL 236 ± 29 µg/mL 31.9 ± 4.8 µg/mL 0.18 ± 0.10 µg/mL 0.42 ± 0.22 µg/mL	Values given are for women with full lactation (volume > 500 mg/d) This article reported additional nutrients (lactose, total protein, total lipid) and milk volume that did not meet the inclusion criteria
Song et al., 1984	Prospective cohort	26 dyads, 2–12 wk pp	Pantothenic acid	Radio-immunoassay	2.73 ± 0.61 µg/mL foremilk (2 wk pp) 2.40 ± 0.58 µg/mL hindmilk (2 wk pp) 2.54 ± 0.72 µg/mL foremilk (12 wk pp) 2.55 ± 0.73 µg/mL hindmilk (12 wk pp)	
Feeley et al., 1983a	Prospective cohort	102 dyads, 4–45 d pp	Calcium	ICAP-ES	25.0 ± 0.5 mg/100 g (10–14 d pp) 26.2 ± 0.5 mg/100 g (30–45 d pp)	Values are expressed as: mean ± SEM
			Phosphorus	ICAP-ES	14.4 ± 0.3 mg/100 g (10–14 d pp) 13.3 ± 0.3 mg/100 g (30–45 d pp)	
			Magnesium	ICAP-ES	4.9 ± 0.1 mg/100 g (10–14 d pp) 4.9 ± 0.1 mg/100 g (30–45 d pp)	
Feeley et al., 1983b	Prospective cohort	102 dyads, 4–45 d pp	Copper	ICAP-ES	93.9 ± 3.6 µg/100 g (10–14 d pp) 84.7 ± 3.8 µg/100 g (30–45 d pp)	All values are expressed as: mean ± SEM
			Iron	ICAP-ES	85.4 ± 4.5 µg/100 g (10–14 d pp) 76.1 ± 3.8 µg/100 g (30–45 d pp)	

			Zinc	ICAP-ES	0.41 ± 0.01 mg/100 g (10–14 d pp) 0.29 ± 0.01 mg/100 g (30–45 d pp)	
Smith et al., 1983	Prospective cohort	11 dyads, 6–12 wk pp	Folate	*L. casei*	*6 wk pp (ng/mL)* 48.7 ± 17.4 morning/foremilk 69.8 ± 23.8 morning/hindmilk 60.6 ± 28.2 midday/foremilk 77.0 ± 24.0 midday/hindmilk 83.4 ± 37.7 evening/foremilk 100.3 ± 43.7 evening/hindmilk *12 wk pp (ng/mL)* 44.4 ± 27.5 morning/foremilk 70.0 ± 37.1 morning/hindmilk 58.9 ± 34.3 midday/foremilk 98.2 ± 55.6 midday/hindmilk 103.7 ± 52.8 evening/foremilk 131.3 ± 44.2 evening/hindmilk	
Greer et al., 1982	Prospective cohort	18 dyads, 3–26 wk pp	Calcium	AAS	25.9 ± 0.96 mg/dL (3 wk pp) 27.7 ± 0.86 mg/dL (6 wk pp) 24.8 ± 0.97 mg/dL (26 wk pp)	Values are expressed as: mean ± SE This article reported additional nutrients (phosphorus) that did not meet the inclusion criteria
			Magnesium	AAS	14.7 ± 0.6 mg/dL (3 wk pp) 12.7 ± 0.4 mg/dL (6 wk pp) 10.7 ± 0.4 mg/dL (26 wk pp)	
Keenan et al., 1992	Prospective cohort	28 dyads, 3.5–32 wk pp	Sodium	Flame photometry	7.9 ± 3.0 mEq/L (3.5–6 wk pp) 4.7 ± 2.0 mEq/L (8.5–18 wk pp) 5.4 ± 1.3 mEq/L (20–32 wk pp)	
			Potassium	Flame photometry	15.2 ± 1.8 mEq/L (3.5–6 wk pp) 13.8 ± 1.3 mEq/L (8.5–18 wk pp) 13.3 ± 1.1 mEq/L (20–32 wk pp)	

Koo and Gupta, 1982	Prospective cohort	45 Australian dyads, 0–28 d pp	Sodium	Flame photometry	9.8 ± 0.6 mmol/L (8–14 d pp) 6.9 ± 0.2 mmol/L (15–28 d pp)	Values are expressed as: mean ± SEM
Ohtake et al., 1981	Prospective cohort	30 Japanese dyads, 1–3 mo pp	Zinc	AAS	3.80 ± 1.24 μg/mL (27–47 d pp)	
			Copper	AAS	0.38 ± 0.08 μg/mL (27–47 d pp)	
Tamura et al., 1980	Cross-sectional	25 Japanese dyads, 3–25 wk pp	Folate	*L. casei*	141.4 ± 47.9 ng/mL	

NOTES: A number of authors claimed that fatty acids do not change within a feed and used this as their rationale for not using a complete breast expression as their sample. However, the fatty acids are part of the lipid component of milk, which varies remarkably during a feed. If all you want to know is the proportion of fatty acids, something other than a full expression may suffice, but for estimating an infant's needs, it is not acceptable. The amount of a fatty acid actually delivered is the key information needed. This is the product of the total lipid in the whole feed and the proportion of that lipid represented by the particular fatty acid.

AAS = atomic absorption spectrometry; B-carotene = beta-carotene; BMI = body mass index; CI = confidence interval; d = day; DHA = docosahexaenoic acid; dL = deciliter; EPA = eicosapentaenoic acid; ETA-AAS = electro thermal atomization-atomic absorption spectroscopy; g = gram; GC = gas chromatography; HPLC = high-performance liquid chromatography; HPLC-EC = high-performance liquid chromatography-electrochemical detection; HPLC-FLD = high-performance liquid chromatography with fluorescence detection; hr = hour; HRGC = high resolution gas chromatography; ICAP-ES = inductively coupled argon plasma emission spectrometry; ICP-AES = inductively coupled plasma atomic emission spectrometry; ICP-MS = inductively coupled plasma-mass spectrometry; ICP-OES = inductively coupled plasma-optical emission spectrometry; IQR = interquartile range; kg = kilogram; L = liter; LC-MS/MS = liquid chromatography tandem mass spectrometry; MC-ICP-MS = multicollector inductively coupled plasma mass spectrometry; mEq = milliequivalent; mg = milligram; mL = milliliter; mmol = millimole; mo = month; mol = mole; ng = nanogram; NP-HPLC = normal-phase high-performance liquid chromatography; NPN = nonprotein nitrogen; pmol = picomole; pp = postpartum; RCT = randomized, double-blind, placebo-controlled trial; SD = standard deviation; SE = standard error; SEM = standard error of the mean; TE = alpha-tocopherol equivalent; UN-ICP-AES = ultrasonic nebulization-inductively coupled plasma atomic emission spectrometry; UV = ultraviolet; WIC = Special Supplemental Nutrition Program for Women, Infants, and Children; wk = week; wt/wt = weight/weight.

[a] Study was done in the United States, unless noted otherwise.

[b] Values are presented as the mean ± standard deviation unless noted otherwise.

TABLE 3-2 Assessment of Included Studies of the Volume[a] of Human Milk on the Basis of Prespecified Criteria (Results Include Studies of Healthy, Singleton, Full-Term Infants Who Were Exclusively Breastfed from Birth to 5.9 Months)

Study Authors, Year	Study Type	Study Population[b]	Methodology	Outcome (mean ± SD)[c]	Additional Comments
Mohd Shukri et al., 2019	RCT	11 Malaysian dyads, 2–18 wk pp	Deuterium dilution	534.1 ± 169 g/d (2 wk pp)	
Buntuchai et al., 2017	Cross-sectional	36 Thai dyads, 1–3 mo pp	24-hr test weighing	598.7 ± 182.4 mL/d	
Bandara et al., 2015	Cross-sectional	48 Sri Lankan dyads, 0–6 mo pp	Deuterium oxide to the mother	773 ± 219 g/d (2 to < 4 mo pp) 802 ± 156 g/d (4–6 mo pp)	Volume was measured over a 14-day period Dyads were randomly selected from health clinics
Wells et al., 2012	Randomized trial	50 Icelandic dyads, 6 mo pp	Deuterium dilution	901 ± 158 g/d	
Nielsen et al., 2011	Prospective cohort	36 Scottish dyads, 15–25 wk pp	Deuterium dilution	923 ± 122 g/d (15 wk pp) 999 ± 146 g/d (25 wk pp)	
Kent et al., 2006	Cross-sectional	71 Australian dyads, 4–26 wk pp	24-hr test weighing	788 ± 169 g/d	
Sekiyama et al., 2003	Prospective cohort	13 Japanese dyads, 30–90 d pp	Test weighing	712 ± 188 g/d (30 d pp) 809 ± 164 g/d (60 d pp) 798 ± 120 g/d (90 d pp)	
Mitoulas et al., 2002	Cross-sectional	30 Australian dyads, 1–6 mo pp	Test weighing	750 ± 200 mL/d	
Butte et al., 2001	Prospective cohort	24 dyads, 3–24 mo pp	3-day test weighing	763 ± 144 g/d (3 mo pp)	
Chen et al., 1998	Cross-sectional	Dyads (19 primiparous; 16 multiparous), 0–2 wk pp	24-hr test weighing	*Day 14 pp* 766 ± 196 g/d (primiparous) 960 ± 166 g/d (multiparous)	A third subgroup of primiparous women who delivered by cesarean was not included because they did not meet the inclusion criteria

Dewey et al., 1991	Prospective cohort	67 dyads, 3 mo pp	24-hr test weighing	914 ± 194 g/d	
Vio et al., 1991	Case-control	10 Chilean dyads (nonsmokers), 1–3 mo pp	Deuterium dilution	961 ± 120 g/d (1–3 mo pp)	
Woodward and Cumming, 1990	Cross-sectional	35 Australian dyads, 6–12 wk pp	Test weighing	830 ± 152 g/24 hr	
Neville et al., 1988	Prospective cohort	13 dyads, 0–5 mo pp	Test weighing	615 ± 130 g/d (7–14 d pp) 689 ± 148 g/d (15–28 d pp) 707 ± 104 g/d (30–59 d pp) 753 ± 89 g/d (60–150 d pp)	
Lucas et al., 1987	Prospective cohort	12 dyads, 5–11 wk pp	Deuterium dilution	767 ± 20 mL/d (5 wk pp) 868 ± 39 mL/d (11 wk pp)	Values are expressed as: mean ± SE
Dewey and Lonnerdal, 1986	Prospective cohort	18 dyads, 6–21 wk pp	24-hr test weighing	753 ± 121 g/24 hr	
Forsum and Sadurskis, 1986	Prospective cohort	22 Swedish dyads, 2–10 wk pp	24-hr test weighing	666 ± 129 g/24 hr (2 wk pp) 765 ± 126 g/24 hr (4 wk pp) 778 ± 146 g/24 hr (6 wk pp) 778 ± 147 g/24 hr (8 wk pp) 789 ± 132 g/24 hr (10 wk pp)	
Janas and Picciano, 1986	Prospective cohort	10 dyads, 2–8 wk pp	Test weighing	634 ± 43 mL/d (2 wk pp) 691 ± 43 mL/d (4 wk pp) 701 ± 47 mL/d (8 wk pp)	
Matheny and Picciano, 1986	Prospective cohorts (3 combined)	50 dyads, 2–16 wk pp	Test weighing	628 ± 127 mL/d (4 wk pp) 644 ± 138 mL/d (8 wk pp) 676 ± 140 mL/d (12 wk pp)	The authors noted that 1 g of milk consumed was taken to represent 1 mL of milk ingested
Strode et al., 1986	Intervention trial	14 dyads, 6–24 wk pp	Test weighing	736 ± 168 g/24 hr (6–24 wk pp)	
Butte et al., 1985	Prospective cohort	45 dyads, 0–4 mo pp	24-hr test weighing	*Feeding Pattern A* 798.2 ± 159.0 g/24 hr (1 mo pp)	Feeding pattern A = feedings distributed throughout the 24-hr day

				781.5 ± 172.7 g/24 hr (2 mo pp) 751.2 ± 112.2 g/24 hr (3 mo pp) 787.9 ± 149.0 g/24 hr (4 mo pp) *Feeding Pattern B* 795.2 ± 176.4 g/24 hr (3 mo pp) 841.7 ± 101.6 g/24 hr (4 mo pp)	Feeding Pattern B = no feeding from 12 am to 6 am
Butte et al., 1984a	Prospective cohort	45 dyads, 0–4 mo pp	24-hr test weighing	751 ± 130 g/d (1 mo pp) 725 ± 131 g/d (2 mo pp) 723 ± 114 g/d (3 mo pp) 740 ± 128 g/d (4 mo pp)	
De Carvalho et al., 1982	Prospective cohort	46 dyads, 1 mo pp	24-hr test weighing	681 ± 136 mL/d	
Pao et al., 1980	Prospective cohort	11 dyads, 1–6 mo pp	Test weighing	600 ± 159 mL/d (1 mo pp)	

NOTE: d = day; g = gram; hr = hour; mL = milliliter; mo = month; pp = postpartum; RCT = randomized controlled trial; SD = standard deviation; wk = week.

[a] To measure milk volume, infant intake is assessed (not maternal weight change or total production, which can be higher as infants leave milk in the breast). However, weighing the baby before and after a feed underestimates the volume consumed because of insensible water loss (sweat that has evaporated and exhaled water). Because very few reports corrected for this, often without having estimated this amount themselves, the committee did not use correction for insensible water loss as an exclusion criteria.

[b] Study was done in the United States, unless noted otherwise.

[c] Values are presented as the mean ± standard deviation unless noted otherwise.

TABLE 3-3 Assessment of Included Studies of Both Nutrient Composition and Milk Volume[a] on the Basis of Prespecified Criteria (Results Include Volume Studies of Healthy, Singleton, Full-Term Infants Who Were Exclusively Breastfed from Birth to 5.9 Months)

Study Authors, Year	Study Type	Study Population[b]	Nutrient(s)	Nutrient Analysis Methodology	Outcome (mean ±SD)[c]	Additional Comments
McCrory et al., 1999	Randomized intervention	23 dyads, 8–16 wk pp	Volume	Test weighing	801 ± 115 g/d	
			Total lipid	Folch extraction	34.1 ± 6.0 g/L	
			Total protein	Micro Kjeldahl	9.10 ± 1.36 g/L	
Dewey et al., 1994	Case-control	33 dyads, 6–8 wk pp	Total protein	Kjeldahl with correction for NPN by acid precipitation	9.1 ± 1.0 g/L	This article reported additional nutrients (lactose) that did not meet the inclusion criteria
			Total lipid	Folch assay (solvent extraction)	32.7 ± 5.1 g/L	
			Volume	Test weighing	838 ± 176 g/d	
Krebs et al., 1994	Prospective cohort	71 healthy dyads, followed from 2 wk to 9 mo pp	Volume	Test weighing	600 ± 120 g/d (2 wk pp) 690 ± 110 g/d (3 mo pp)	Study only reported daily zinc intake from human milk, not zinc concentration
			Zinc	Flame AAS	Zinc intake from human milk: 2.30 ± 0.68 mg/d (2 wk pp) 1.00 ± 0.43 mg/d (3 mo pp)	
Stuff and Nichols, 1989	Prospective cohort	45 dyads, 16–24 wk pp	Volume	Test weighing	792 ± 111 g/d (16 wk pp) 734 ± 150 g/d (16 wk pp) 729 ± 165 g/d (20 wk pp)	This article reported additional nutrients (lactose) that did not meet the inclusion criteria
			Total lipid	Gravimetric analysis	29.3 ± 7.0 mg/g (16 wk pp) 28.4 ± 7.0 mg/g (16 wk pp) 29.2 ± 6.4 mg/g (20 wk pp)	

					32.1 ± 7.7 mg/g (20 wk pp) 30.8 ± 9.0 mg/g (24 wk pp) 30.1 ± 6.6 mg/g (24 wk pp) 33.8 ± 10.4 mg/g (28 wk pp) 32.7 ± 12.7 mg/g (28 wk pp) 34.3 ± 13.9 mg/g (32 wk pp)
			Protein nitrogen	Kjeldahl	1.29 ± 0.17 mg/g (16 wk pp) 1.30 ± 0.14 mg/g (16 wk pp) 1.25 ± 0.21 mg/g (20 wk pp) 1.33 ± 0.15 mg/g (20 wk pp) 1.20 ± 0.15 mg/g (24 wk pp) 1.27 ± 0.16 mg/g (24 wk pp) 1.21 ± 0.18 mg/g (28 wk pp) 1.26 ± 0.14 mg/g (28 wk pp) 1.27 ± 0.17 mg/g (32 wk pp)
Casey et al., 1985	Prospective cohort	11 dyads, 0–31 d pp	Chromium	Graphite furnace AAS	0.22 ± 0.09 ng/mL (14 d pp)
			Zinc	Flame AAS	4.74 ± 1.02 µg/mL (8 d pp) 3.88 ± 0.91 µg/mL (14 d pp)
			Copper	Graphite furnace AAS	0.49 ± 0.06 µg/mL (14 d pp)
			Manganese	Graphite furnace AAS	3.8 ± 2.4 ng/mL (14 d pp)
			Volume	24-hr test weighing	542 ± 103 mL/d (8 d pp) 615 ± 108 mL/d (14 d pp)

Butte et al., 1984b	Prospective cohort	45 dyads, 0–4 mo pp	Total lipid	Solvent extraction	36.2 ± 7.5 mg/g (1 mo pp) 34.4 ± 6.8 mg/g (2 mo pp) 32.2 ± 7.8 mg/g (3 mo pp) 34.8 ± 10.8 mg/g (4 mo pp)	
			Volume	24-hr test weighing	751.0 ± 130.0 g/d (1 mo pp) 725.0 ± 131.0 g/d (2 mo pp) 723.0 ± 114.0 g/d (3 mo pp) 740.0 ± 128.0 g/d (4 mo pp)	
Dewey et al., 1983	Prospective cohort	20 dyads, 1–6 mo pp	Potassium	Flame AAS	527 ± 70 µg/mL (1 mo pp) 477 ± 79 µg/mL (2 mo pp) 470 ± 81 µg/mL (3 mo pp) 464 ± 89 µg/mL (4 mo pp) 460 ± 85 µg/mL (5 mo pp) 430 ± 63 µg/mL (6 mo pp)	This article reported additional nutrients (lactose, total protein, total lipid) that did not meet the inclusion criteria. Study authors defined exclusive breastfeeding as receiving ≤ 50 kcal/d from other sources
			Sodium	Flame AAS	227 ± 152 µg/mL (1 mo pp) 264 ± 223 µg/mL (2 mo pp) 184 ± 139 µg/mL (3 mo pp) 175 ± 138 µg/mL (4 mo pp) 166 ± 130 µg/mL (5 mo pp) 134 ± 78 µg/mL (6 mo pp)	
			Copper	Flame AAS	0.36 ± 0.08 µg/mL (1 mo pp) 0.28 ± 0.06 µg/mL (2 mo pp) 0.27 ± 0.07 µg/mL (3 mo pp) 0.24 ± 0.05 µg/mL (4 mo pp) 0.20 ± 0.09 µg/mL (5 mo pp) 0.21 ± 0.07 µg/mL (6 mo pp)	
			Calcium	Flame AAS	261 ± 44 µg/mL (1 mo pp) 275 ± 48 µg/mL (2 mo pp) 270 ± 61 µg/mL (3 mo pp) 255 ± 43 µg/mL (4 mo pp) 248 ± 40 µg/mL (5 mo pp)	

					256 ± 42 µg/mL (6 mo pp)
			Magnesium	Flame AAS	27.6 ± 4.7 µg/mL (1 mo pp) 32.4 ± 4.1 µg/mL (2 mo pp) 33.6 ± 4.7 µg/mL (3 mo pp) 35.1 ± 8.0 µg/mL (4 mo pp) 33.8 ± 7.1 µg/mL (5 mo pp) 33.9 ± 4.4 µg/mL (6 mo pp)
			Iron	Flame AAS	0.31 ± 0.11 µg/mL (1 mo pp) 0.22 ± 0.07 µg/mL (2 mo pp) 0.25 ± 0.11 µg/mL (3 mo pp) 0.22 ± 0.09 µg/mL (4 mo pp) 0.20 ± 0.08 µg/mL (5 mo pp) 0.21 ± 0.10 µg/mL (6 mo pp)
			Zinc	Flame AAS	2.71 ± 0.36 µg/mL (1 mo pp) 1.67 ± 0.68 µg/mL (2 mo pp) 1.35 ± 0.54 µg/mL (3 mo pp) 0.89 ± 0.39 µg/mL (4 mo pp) 0.57 ± 0.20 µg/mL (5 mo pp) 0.64 ± 0.28 µg/mL (6 mo pp)
			Volume	24-hr test weighing	673 ± 192 mL/d (1 mo pp) 756 ± 170 mL/d (2 mo pp) 782 ± 172 mL/d (3 mo pp) 810 ± 142 mL/d (4 mo pp) 805 ± 117 mL/d (5 mo pp) 896 ± 122 mL/d (6 mo pp)
Picciano et al., 1981	Prospective cohort	26 dyads, 1–3 mo pp	Iron	AAS	5.87 ± 2.09 µmol/L (1 mo pp) 6.62 ± 2.17 µmol/L (2 mo pp) 7.36 ± 3.03 µmol/L (3 mo pp)
			Zinc	AAS	33.8 ± 19.8 µmol/L (1 mo pp) 31.8 ± 16.8 µmol/L (2 mo pp)

		29.5 ± 13.8 μmol/L (3 mo pp)
Calcium	AAS	7.24 ± 1.52 mmol/L (1 mo pp) 7.31 ± 1.40 mmol/L (2 mo pp) 7.14 ± 1.25 mmol/L (3 mo pp)
Copper	AAS	3.35 ± 1.07 μmol/L (1 mo pp) 3.24 ± 1.21 μmol/L (2 mo pp) 3.26 ± 1.35 μmol/L (3 mo pp)
Phosphorus	Colorimetric assay	5.04 ± 0.84 mmol/L (1 mo pp) 4.78 ± 0.84 mmol/L (2 mo pp) 4.68 ± 0.81 mmol/L (3 mo pp)
Magnesium	AAS	1.15 ± 0.25 mmol/L (1 mo pp) 1.27 ± 0.21 mmol/L (2 mo pp) 1.36 ± 0.21 mmol/L (3 mo pp)
Sodium	AAS	6.57 ± 2.39 mmol/L (1 mo pp) 5.26 ± 2.18 mmol/L (2 mo pp) 5.48 ± 2.04 mmol/L (3 mo pp)
Potassium	AAS	11.92 ± 2.38 mmol/L (1 mo pp) 10.92 ± 2.23 mmol/L (2 mo pp) 10.41 ± 2.05 mmol/L (3 mo pp)
Chlorine	Ion electrode	12.04 ± 2.37 mmol/L (1 mo pp) 11.70 ± 2.09 mmol/L (2 mo pp) 11.96 ± 2.57 mmol/L (3 mo pp)
Volume	Test weighing	606 ± 135 mL/d (1 mo pp)

NOTE: AAS = atomic absorption spectrometry; d = day; g = gram; kcal = kilocalories; L = liter; mg = milligram; mL = milliliter; mmol = millimole; mo = month; mol = mole; ng = nanogram; NPN = nonprotein nitrogen; pp = postpartum; wk = week.

[a] To measure milk volume, infant intake is assessed (not maternal weight change or total production, which can be higher as infants leave milk in the breast). However, weighing the baby before and after a feed underestimates the volume consumed because of insensible water loss (sweat

that has evaporated and exhaled water). Because very few reports corrected for this, often without having estimated this amount themselves, the committee did not use correction for insensible water loss as an exclusion criteria.

[b] Study was done in the United States, unless noted otherwise.

[c] Values are presented as the mean ± standard deviation unless noted otherwise.

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4

Discussion and Future Directions

An objective assessment of the totality and quality of the evidence based on a comprehensive systematic review is required to support an update of a Dietary Reference Intake (DRI) nutrient review. The scanning process described herein is not intended to replace the need for a comprehensive systematic review. Rather, an evidence scan, as operationalized in this report, enables a cost-effective and objective means of assessing whether there is sufficient new evidence to merit a formal reexamination of a nutrient or nutrients to support a DRI review.

This evidence scan was carried out to elicit new information on a range of micro- and macronutrients in human milk and the volume of milk consumed by breastfeeding infants. The scanning process required continuous evaluation and adjustment to obtain the most relevant evidence to inform development of future DRI values. Although the committee was not charged to make recommendations, it offers comments on the approach to the evidence-scan process, and discusses its findings and interpretation of the evidence in this chapter.

APPROACH TO THE EVIDENCE-SCANNING PROCESS

Design of the Search Process

The committee made a deliberate choice to be inclusive in the design of its search. An example of this approach was the committee's choice to go beyond the United States and Canada to accept data from countries that were ranked as high-income or high middle-income by the World Bank. The committee used its own judgment to decide whether to exclude reports from high middle-income countries that would have not been in this classification when the investigation was done, often decades ago. The committee chose to use these two groups of countries as they helped it to distinguish environments that might produce results for milk volume and composition that would be similar to those obtained among contemporary American women.

The committee further acknowledges that contemporary American women have likely received prenatal supplements during gestation and may still have been taking them at the time of milk sampling. Very few reports included information on women's prior or current use of prenatal or other supplements. As a result, it is possible that the milk composition values reported here reflect this exposure and, thus, these results must be interpreted in light of this possibility.

Selection of Inclusion and Exclusion Criteria

The committee selected its inclusion and exclusion criteria on the basis of identifying studies (or a subset of data within them) that would provide the most reliable estimate of milk volume (measured as infant milk intake, not milk production) and nutrient composition. The selected criteria reflect the expertise of the committee as well as that of subject-matter experts

who provided information about approaches for milk sampling and analysis to the committee in a public session. This approach was useful because it eliminated studies that, while well established in the literature, were not relevant to the committee's task because of small sample sizes (often fewer than 10 women per group) or methods now considered less rigorous than currently accepted methodologies. The criteria for milk sampling further allowed the committee to discriminate among studies that included data for some nutrients that could be used and data for other nutrients that could not. This process reinforced the importance the committee placed on the proper sampling of milk for the nutrient(s) to be analyzed. (See Chapter 2 and Appendix D for more information about milk collection and analytical methods.) It should be noted, however, that there are currently insufficient data to determine optimal sampling protocols for all nutrients.

The Screening Process

The number of records retrieved in the committee's search, even after the criteria were refined and revised iteratively, was much larger than anticipated. However, the abstract-screening process, as expected, revealed a large number of records that did not meet the committee's inclusion criteria. For example, many studies focused on oligosaccharides in human milk. These were not included because there are, at present, no DRI values for these milk components. Among studies on trace minerals, some were eliminated when the research objective was analysis of toxic levels of minerals or contaminants (e.g., lead) while others were eliminated because care was not exercised in using trace mineral-free collection containers.

Notably, a high proportion of studies were conducted outside of the United States and Canada. At the stage of full-text screening many of these studies were excluded when the committee determined that the populations studied across low- and middle-income countries were not comparable to those in the United States and Canada. Among the remaining studies reviewed, a report was deemed relevant only when it described participants (e.g., mothers of term infants who served as the comparison group for mothers of preterm infants were included in the study population) who met the criteria. In numerous other cases, the population studied, methods used, or the data obtained were reported with insufficient rigor for the findings to be useful to the committee. Altogether, the majority of studies were excluded owing to inadequate methods at both the full-text screen (26 percent) and the final full-text rescreen (86 percent). Thus, at the final, full-text rescreening, only 126 of the 398 fully evaluated articles were determined eligible for final assessment.

FINDINGS

A striking feature of Tables 3-1, 3-2, and 3-3 is the disproportionate number among the types of relevant studies reported. The committee found only 32 eligible reports that included data on milk volume since 1980, compared to 102 eligible reports on milk composition in the same time period. Given the public health messages about the importance of human milk and the increasing proportion of women who breastfeed or feed pumped milk, the committee considered this result disproportionately low. Additionally, given the recommendation to introduce complementary foods to infants' diets at about 6 months of age, and the fact that only a minority of U.S. infants are exclusively breastfed at and after this age, the committee expected to find few reports of the measurement of milk volume in infants older than 6 months. Indeed, only three

such reports met all of the committee's inclusion criteria, except that the mothers should be exclusively breastfeeding their infants (Neville et al., 1988, and Stuff and Nichols, 1989, in Table 3-2; and Krebs et al., 1994, in Table 3-3). Krebs et al. (1994) found that 93 percent of infants were not exclusively breast fed by 7 months of age. Neville et al. (1988), the only report that included longitudinal data, documented the expected decline in milk volume from 6–12 months of age. While it has long been known that milk composition also changes as milk volume declines after the introduction of complementary foods, the committee notes that additional research will be needed to define the volume and composition of milk produced by women for infants 6 months of age and older.

In another observation, the committee found that despite increased interest in essential fatty acids within the research community, only three of the identified studies met the screening criteria. Exclusion of other studies on this subject was based primarily on the fact that relative amounts (rather than absolute concentrations) of the fatty acids were reported without also reporting total lipids. As described above, in some studies, collection methods were not optimized (e.g., not a full breast expression) and/or the method (e.g., creamatocrit) used for measuring total lipid was not deemed adequate by the committee. This finding highlights that some data uses, such as DRIs, require calculation of the total amount of fatty acids that a nursing infant consumes. This means that it is important to determine both the total amount of lipid in the milk sample as well as the absolute amounts of each fatty acid per unit volume of milk.

Assessment of Findings Relative to Methodologies Used

Among reports published since 1980, only a small number met the committee's inclusion criteria. Given the many new methods that have been developed for measuring these components (see Appendix D), researchers are now poised for a reexamination of these essential nutrients. The committee found a similar number of studies on trace minerals (81),[1] macrominerals (80),[2] and electrolytes (80),[3] in human milk. There were 24 studies on macronutrients. Two aspects of the scanning process merit further comment related to the methodologies reported and limitations in the evidence. First, one of the committee's criteria was that the lactating women studied should be "healthy." Some study authors asserted that participants were healthy but did not provide further details about what this meant and how it was determined. Other authors were clear about the selection process for their study population(s), and they provided data about their characteristics (e.g., age, body mass index, absence of specific conditions and/or behaviors, such as smoking). The committee decided to accept the authors' description of the subjects as being "healthy." These considerations meant that some of the reviewed reports could contain data on participants who may not meet the criteria as defined by a DRI committee (such as those who smoke or have obesity).

The problem of defining what is meant by "healthy" also applied to infants. The committee also accepted the authors' description of the infant as being healthy when this was

[1] Trace minerals are classified as minerals required in the diet in daily amounts of 100 milligrams or less. These include copper, zinc, selenium, iodine, chromium, fluoride, manganese, molybdenum, and others.
[2] Macrominerals are classified as minerals required in the diet in daily amounts greater than 100 milligrams. These include calcium, phosphorus, magnesium, sodium, potassium, chloride, and sulfur.
[3] Electrolytes are charged minerals whose functions include maintenance of intra- and extracellular fluid balance, maintenance of metabolic pH, and nerve transduction. Electrolytes include sodium, calcium, potassium, chloride, phosphate, and magnesium.

provided. However, the criteria for adequate growth in infants changed during the 40-year scope of this evidence scan and were poorly described or not at all by the study investigators, thus it was difficult for the committee to discern if some of the infants studied would be considered to be growing adequately according to current growth standards.

Second, there was substantial variation in the quality of the methods used for analysis of milk composition. This variation meant that some of the articles, such as those with more limited descriptions of how the work was done, may be adequate while others may not. Thus, articles with limited details should be used with caution. The committee's criteria related to how milk was sampled and the methods that were used to analyze it. These criteria did not require reporting of the quality-control procedures used in the analyses, for example. This factor will therefore require attention in future applications of the evidence presented in this report.

The committee adhered to the DRI framework when it reported milk volume and composition values separately from birth to 5.9 and from 6 to 12 months. Given that the composition of colostrum differs greatly from that of more mature milk, the committee eliminated reports or parts of reports that included data on colostrum. Consequently, as can be seen from the values in Table 3-1, the concentrations of some nutrients vary widely within the period from birth to 5.9 months and the period from 6 to 12 months, respectively. For other non-DRI applications, users of these data may find it advantageous to subdivide the age ranges further.

FUTURE DIRECTIONS

In this evidence scan, which covered over a 40-year period, a total of 126 studies were identified as relevant to milk composition and volume based on the committee's criteria. From among these, the committee identified only 8 final articles that included data on both the volume of milk consumed by the infant and its nutrient composition combined. As is clear from this evidence scan, both milk volume and milk composition are highly variable among individuals. Information on both, preferably from the same mother–infant dyad, are required to estimate an infant's nutrient requirement accurately.

To inform development of future DRI values for infants from birth through 12 months, for at least some nutrients, it is possible that sufficient numbers of participants have been studied so that new DRIs s could be developed from the data available. For other nutrients additional research will be needed before sufficient data are available to consider a revision of the current DRIs (see Figures 3-2 and 3-3).

In developing its criteria for methodologic rigor, it became clear to the committee that more research would be needed on the question of what constitutes an appropriate milk sampling strategy, as this is poorly understood for many nutrients. In addition, many intriguing components of human milk have been identified in recent years, and the research community is gaining a better understanding of the implications of some milk components (e.g., oligosaccharides) for infant health. However, for others (e.g., pluripotent stem cells), their importance is not yet understood. Thus, attention to these several kinds of components of human milk will be important in the future.

A

Acronyms and Abbreviations

AA	arachidonic acid
AAS	atomic absorption spectrometry
AI	Adequate Intake
B-carotene	beta-carotene
BMI	body mass index
CI	confidence interval
CPBA	competitive protein-binding assay
d	day
DHA	docosahexaenoic acid
dL	deciliter
DRI	Dietary Reference Intake
EPA	eicosapentaenoic acid
ETA-AAS	electro thermal atomization-atomic absorption spectroscopy
FDA	U.S. Food and Drug Administration
FDA-CFSAN	FDA Center for Food Safety and Applied Nutrition
g	gram
GC-MS	gas chromatography–mass spectrometry
HHS	U.S. Department of Health and Human Services
HMD	Health and Medicine Division
HPLC	high-performance liquid chromatography
HPLC-EC	high-performance liquid chromatography-electrochemical detection
HPLC-FLD	high-performance liquid chromatography with fluorescence detection
hr	hour
ICAP-ES	inductively coupled argon plasma emission spectrometry
ICP-AES	inductively coupled plasma-atomic emission spectrometry
ICP-MS	inductively coupled plasma-mass spectrometry
ICP-OES	inductively coupled plasma-optical emission spectrometry
IQR	interquartile range
kg	kilogram

L	liter
LC-MS/MS	liquid chromatography-tandem mass spectrometry
LC-PUFA	long-chain polyunsaturated fatty acids
MC-ICP-MS	multicollector inductively coupled plasma mass spectrometry
mEq	milliequivalent
mg	milligram
mL	milliliter
mmol	millimole
mo	month
mol	mole
MS	mass spectrometry
MS/MS	tandem mass spectrometry
ng	nanogram
NP-HPLC	normal-phase high-performance liquid chromatography
NPN	nonprotein nitrogen
PI(E)COD	population, interventions (exposures), comparators, outcomes, and study designs
pmol	picomole
pp	postpartum
RCT	randomized, double-blind, placebo-controlled trial
RIA	radioimmunoassay
SD	standard deviation
SE	standard error
SEM	standard error of the mean
TE	alpha-tocopherol equivalents
UN-ICP-AES	ultrasonic nebulization-inductively coupled plasma atomic emission spectrometry
UV	ultraviolet
USDA	U.S. Department of Agriculture
USDA-ARS	USDA Agricultural Research Service
USDA SR Database	USDA National Nutrient Database for Standard Reference
WIC	Special Supplemental Nutrition Program for Women, Infants, and Children
wk	week
wt	weight
wt/wt	weight/weight

B

Open Session Agenda

Committee on Scanning for New Evidence on the Nutrient Content of Human Milk

Open Session with Experts
November 7, 2019
Keck Center Conference Room 800, Washington, DC

9:00 a.m.	Welcome and chair's opening statement *Kathleen Rasmussen, Cornell University (committee chair)*
9:15	Trace minerals in human milk: Typical concentrations, factors affecting variability, and insights relevant to estimating infant requirements *Donna Geddes, The University of Western Australia*
9:35	Q&A
9:45	Major minerals and vitamin D in human milk: Typical concentrations, factors affecting variability, and insights relevant to estimating infant requirements *Donna Geddes, The University of Western Australia*
10:05	Q&A
10:15	Break
10:45	Water-soluble vitamins in human milk: Typical concentrations, factors affecting variability, and insights relevant to estimating infant requirements *Lindsay Allen and Daniela Hampel, University of California, Davis*
11:05	Q&A
11:15	Total protein and essential amino acids in human milk: Typical concentrations, factors affecting variability, and insights relevant to estimating infant requirements *Stephanie Atkinson, McMaster University*
11:35	Q&A
11:45	Break for lunch
12:00 p.m.	Working lunch: Overview of the Human Milk Composition Initiative (HMCI) *Kellie O. Casavale, Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration*

1:00	Volume of human milk: Factors affecting variability, and insights relevant to estimating infant requirements *Margaret Neville, Emeritus, University of Colorado Denver*
1:20	Q&A
1:40	Total lipids and essential/conditionally essential fatty acids in human milk: Typical concentrations, factors affecting variability, and insights relevant to estimating infant requirements *Mark McGuire, University of Idaho*
2:00	Q&A
2:10	General discussion with participants *Kathleen Rasmussen, Cornell University (committee chair)*
3:00 pm	Adjourn open session

C

Literature Search Results

Two sets of literature searches were performed for nutrient composition and milk volume. The first set was performed in Medline (Ovid) in December 2019. The second search set was conducted in Embase (Ovid), PubMed, and Scopus in January 2020. At this time, the Medline searches were also rerun to capture any reports published since the December search. Each set contained separate searches for nutrient composition and milk volume. The initial literature search was conducted beginning with 1970; however, it was later refined to studies from 1980 onward in order to capture more consistent and up-to-date methodologies in nutrient analyses. The search results are presented in the following tables.

Search Topic: Nutrient Composition of Human Milk
Database: Medline (Ovid)
Search Date: December 12, 2019

Search No.	Syntax	Results
1	Milk, Human/	18,742
2	Breast Feeding/	36,452
3	Breast Milk Expression/	278
4	(human milk or breast milk or breastmilk).ti,ab,kw,kf.	19,975
5	or/1-4	54,373
6	Nutrients/	1,171
7	Micronutrients/	5,548
8	Vitamins/	30,511
9	Minerals/	22,945
10	“Infant Nutritional Physiological Phenomena”/	14,784
11	Lactose/	11,298
12	Milk Proteins/	11,536

13	Fatty Acids/	83,454
14	Linoleic Acid/	6,188
15	alpha-Linolenic Acid/	2,874
16	Eicosapentaenoic Acid/	5,965
17	Docosahexaenoic Acids/	8,425
18	Vitamin A/	23,704
19	Vitamin D/	33,449
20	Vitamin E/	26,307
21	Vitamin K/	11,529
22	Thiamine/	9,923
23	Riboflavin/	8,339
24	Niacin/	10,703
25	Vitamin B 6/	2,717
26	Folic Acid/	26,641
27	Vitamin B 12/	20,604
28	Pantothenic Acid/	2,902
29	Biotin/	13,788
30	Choline/	18,155
31	Copper/	67,164
32	Fluorides/	25,727
33	Iodine/	24,936
34	Iron/	92,331

35	Magnesium/	66,614
36	Manganese/	24,087
37	Molybdenum/	7,730
38	Chromium/	14,165
39	Calcium/	264,939
40	Phosphorus/	41,882
41	Selenium/	20,253
42	Zinc/	58,592
43	Sodium/	104,877
44	Potassium/	100,571
45	Chlorides/	44,005
46	Oligosaccharides/	24,010
47	(nutrient* or micronutrient* or macronutrient* or vitamin* or mineral* or lactose* or protein* or fat* or lipid* or linoleic acid* or alpha linolenic acid* or eicosapentaenoic acid* or docosahexaenoic acid* or vitamin a or vitamin c or vitamin d or vitamin e or vitamin k or thiamin* or riboflavin* or niacin* or vitamin b6 or vitamin b 6 or folate* or folacin* or folic* or folic acid* or vitamin b12 or vitamin b 12 or pantothenic acid* or biotin* or choline* or copper* or fluoride* or iodine* or iron* or magnesium* or manganese* or molybdenum* or chromium* or calcium* or phosphorus* or selenium* or zinc* or sodium* or potassium* or chloride* or cobalamin* or oligosaccharide*).ti,ab,kw,kf.	4,669,392
48	composition*.ti,ab,kw,kf.	337,426
49	or/6-48	5,143,025
50	Case Reports/	1,963,775
51	Editorial/	456,019

52	Comment/	764,287
53	or/50-52	3,015,432
54	5 and 49	19,432
55	54 not (Animals/ not (Animals/ and Humans/))	18,885
56	55 not 53	17,926
57	56	17,926
58	limit 57 to (english language and yr="1970-Current")	15,163

Search Topic: Nutrient Composition of Human Milk
Database: Medline (Ovid)
Search Date: January 8, 2020

Search No.	Syntax	Results
1	Milk, Human/	18,795
2	Breast Feeding/	36,578
3	Breast Milk Expression/	280
4	(human milk or breast milk or breastmilk).ti,ab,kw,kf.	20,054
5	or/1-4	54,555
6	Nutrients/	1,274
7	Micronutrients/	5,579
8	Vitamins/	30,569
9	Minerals/	23,004
10	"Infant Nutritional Physiological Phenomena"/	14,811
11	Lactose/	11,324
12	Milk Proteins/	11,560

13	Fatty Acids/	83,660
14	Linoleic Acid/	6,197
15	alpha-Linolenic Acid/	2,884
16	Eicosapentaenoic Acid/	5,992
17	Docosahexaenoic Acids/	8,455
18	Vitamin A/	23,733
19	Vitamin D/	33,612
20	Vitamin E/	26,341
21	Vitamin K/	11,569
22	Thiamine/	9,935
23	Riboflavin/	8,373
24	Niacin/	10,708
25	Vitamin B 6/	2,721
26	Folic Acid/	26,706
27	Vitamin B 12/	20,637
28	Pantothenic Acid/	2,904
29	Biotin/	13,821
30	Choline/	18,179
31	Copper/	67,332
32	Fluorides/	25,794
33	Iodine/	24,966

34	Iron/	92,572
35	Magnesium/	66,673
36	Manganese/	24,136
37	Molybdenum/	7,749
38	Chromium/	14,202
39	Calcium/	265,305
40	Phosphorus/	41,998
41	Selenium/	20,311
42	Zinc/	58,706
43	Sodium/	104,967
44	Potassium/	100,632
45	Chlorides/	44,034
46	Oligosaccharides/	24,049
47	(nutrient* or micronutrient* or macronutrient* or vitamin* or mineral* or lactose* or protein* or fat* or lipid* or linoleic acid* or alpha linolenic acid* or eicosapentaenoic acid* or docosahexaenoic acid* or vitamin a or vitamin c or vitamin d or vitamin e or vitamin k or thiamin* or riboflavin* or niacin* or vitamin b6 or vitamin b 6 or folate* or folacin* or folic* or folic acid* or vitamin b12 or vitamin b 12 or pantothenic acid* or biotin* or choline* or copper* or fluoride* or iodine* or iron* or magnesium* or manganese* or molybdenum* or chromium* or calcium* or phosphorus* or selenium* or zinc* or sodium* or potassium* or chloride* or cobalamin* or oligosaccharide*).ti,ab,kw,kf.	4,836,211
48	composition*.ti,ab,kw,kf.	339,088
49	or/6-48	5,275,963
50	Case Reports/	1,967,885

51	Editorial/	457,886
52	Comment/	768,658
53	or/50-52	3,025,027
54	5 and 49	19,902
55	54 not (Animals/ not (Animals/ and Humans/))	19,341
56	55 not 53	18,361
57	56	18,361
58	limit 57 to (english language and yr="1970-Current")	15,558

Search Topic: Nutrient Composition of Human Milk
Database: Embase (Ovid)
Search Date: January 8, 2020

Search No.	**Syntax**	**Results**
1	breast milk/	26,501
2	breast feeding/	50,656
3	breast milk expression/	327
4	(human milk or breast milk or breastmilk).ti,ab,kw.	26,937
5	or/1-4	75,040
6	nutrient/	38,413
7	vitamin/	38,188
8	mineral/	40,297
9	lactose/	19,602
10	milk protein/	10,974
11	fatty acid/	105,682

12	linoleic acid/	22,165
13	docosahexaenoic acid/	20,337
14	vitamin D/	72,536
15	thiamine/	17,046
16	riboflavin/	14,639
17	folic acid/	56,821
18	pantothenic acid/	2,791
19	biotin/	20,951
20	choline/	23,433
21	copper/	109,462
22	fluoride/	28,452
23	iodine/	25,664
24	iron/	151,276
25	magnesium/	73,292
26	manganese/	49,756
27	molybdenum/	14,156
28	chromium/	42,809
29	calcium/	272,031
30	phosphorus/	66,006
31	selenium/	37,047
32	zinc/	108,584
33	sodium/	95,918

34	potassium/	94,324
35	chloride/	40,669
36	oligosaccharide/	24,333
37	(nutrient* or micronutrient* or macronutrient* or vitamin* or mineral* or lactose* or protein* or fat* or lipid* or linoleic acid* or alpha linolenic acid* or eicosapentaenoic acid* or docosahexaenoic acid* or vitamin a or vitamin c or vitamin d or vitamin e or vitamin k or thiamin* or riboflavin* or niacin* or vitamin b6 or vitamin b 6 or folate* or folacin* or folic* or folic acid* or vitamin b12 or vitamin b 12 or pantothenic acid* or biotin* or choline* or copper* or fluoride* or iodine* or iron* or magnesium* or manganese* or molybdenum* or chromium* or calcium* or phosphorus* or selenium* or zinc* or sodium* or potassium* or chloride* or cobalamin* or oligosaccharide*).ti,ab,kw.	6,486,556
38	composition*.ti,ab,kw.	480,433
39	or/6-38	7,004,824
40	case report/	2,430,557
41	editorial/	625,741
42	note/	745,474
43	conference paper/	751,892
44	or/40-43	4,464,482
45	5 and 39	23,871
46	45 not ((exp animal/ or nonhuman/) not exp human/)	22,161
47	46 not 44	19,600
48	limit 47 to (conference abstract or conference paper or “conference review”)	2,614
49	47 not 48	16,986

50	limit 49 to (pubmed-not-medline or "pubmed/medline")	3,358
51	49 not 50	13,628
52	limit 51 to (english language and yr="1970-Current")	12,575

Search Topic: Nutrient Composition of Human Milk
Database: PubMed
Search Date: January 8, 2020
((“human milk”[Title/Abstract] OR breastfeed[Title/Abstract] OR breastfeeding[Title/Abstract] OR “breast feed”[Title/Abstract] OR “breast feeding”[Title/Abstract] OR “breast fed”[Title/Abstract] OR breastfed[Title/Abstract] OR “breast milk”[Title/Abstract] OR breastmilk[Title/Abstract]) AND (nutrient[Title/Abstract] OR nutrients[Title/Abstract] OR micronutrient[Title/Abstract] OR micronutrients[Title/Abstract] OR macronutrient[Title/Abstract] OR macronutrients[Title/Abstract] OR vitamin[Title/Abstract] OR vitamins[Title/Abstract] OR mineral[Title/Abstract] OR minerals[Title/Abstract] OR lactose[Title/Abstract] OR protein[Title/Abstract] OR proteins[Title/Abstract] OR fat[Title/Abstract] OR fats[Title/Abstract] OR lipid[Title/Abstract] OR lipids[Title/Abstract] OR “linoleic acid”[Title/Abstract] OR “alpha linolenic acid”[Title/Abstract] OR “eicosapentaenoic acid”[Title/Abstract] OR “docosahexaenoic acid”[Title/Abstract] OR “vitamin a”[Title/Abstract] OR “vitamin c”[Title/Abstract] OR “vitamin d”[Title/Abstract] OR “vitamin e”[Title/Abstract] OR “vitamin k”[Title/Abstract] OR thiamin[Title/Abstract] OR riboflavin[Title/Abstract] OR niacin[Title/Abstract] OR “vitamin b6”[Title/Abstract] OR folate[Title/Abstract] OR folacin[Title/Abstract] OR folic[Title/Abstract] OR “folic acid”[Title/Abstract] OR “vitamin b12”[Title/Abstract] OR “pantothenic acid”[Title/Abstract] OR biotin[Title/Abstract] OR choline[Title/Abstract] OR copper[Title/Abstract] OR fluoride[Title/Abstract] OR iodine[Title/Abstract] OR iron[Title/Abstract] OR magnesium[Title/Abstract] OR manganese[Title/Abstract] OR molybdenum[Title/Abstract] OR chromium[Title/Abstract] OR calcium[Title/Abstract] OR phosphorus[Title/Abstract] OR selenium[Title/Abstract] OR zinc[Title/Abstract] OR sodium[Title/Abstract] OR potassium[Title/Abstract] OR chloride[Title/Abstract] OR cobalamin[Title/Abstract] OR oligosaccharide[Title/Abstract] OR oligosaccharides[Title/Abstract] OR composition[Title/Abstract])) AND pubmednotmedline[sb]
Language: English
Exclude Article Type: Case Reports, Comment, Editorial
Results: 695

Search Topic: Nutrient Composition of Human Milk
Database: Scopus
Search Date: January 8, 2020
TITLE-ABS-KEY((“human milk” OR breastfeed* OR “breast feed*” OR “breast fed” OR breastfed OR “breast milk” OR breastmilk) AND (nutrient* OR micronutrient* OR macronutrient* OR vitamin* OR mineral* OR lactose OR protein* OR fat* OR lipid* OR “linoleic acid” OR “alpha linolenic acid” OR “eicosapentaenoic acid” OR “docosahexaenoic acid” OR “vitamin A” OR “vitamin c” OR “vitamin d” OR “vitamin e” OR “vitamin k” OR

thiamin OR riboflavin OR niacin OR "vitamin b6" OR folate OR folacin OR folic OR "folic acid" OR "vitamin b12" OR "pantothenic acid" OR biotin OR choline OR copper OR fluoride OR iodine OR iron OR magnesium OR manganese OR molybdenum OR chromium OR calcium OR phosphorus OR selenium OR zinc OR sodium OR potassium OR chloride OR cobalamin OR oligosaccharide* OR composition)) AND (INDEXTERMS(human*) OR TITLE-ABS-KEY(human*)) AND NOT INDEX(medline) AND PUBYEAR AFT 1969
Language: English
Exclude Document Type: Conference Paper, Note, Editorial
Results: 4,432

Search Topic: Volume of Human Milk
Database: Medline (Ovid)
Search Date: December 12, 2019

Search No.	Syntax	Results
1	Milk, Human/	18,742
2	Breast Feeding/	36,452
3	Breast Milk Expression/	278
4	(human milk* or breastfeed* or breast feed* or breast fed or breastfed or breast milk or breastmilk).ti,ab,kw,kf.	49,854
5	or/1-4	64,505
6	"Infant Nutritional Physiological Phenomena"/	14,784
7	(production or produc* or yield* or consumption* or consum* or amount* or intake* or volume* or output*).ti,ab,kw,kf.	410,7677
8	or/6-7	4,119,082
9	Case Reports/	1,963,775
10	Editorial/	456,019
11	Comment/	764,287
12	or/9-11	3,015,432
13	5 and 8	18,189
14	13 not (Animals/ not (Animals/ and Humans/))	17,655

15	14 not 12	17,031
16	limit 15 to english language	15,111
17	16	15,111
18	Limit 17 to yr="1970-Current"	14,820

Search Topic: Volume of Human Milk
Database: Medline (Ovid)
Search Date: January 9, 2020

Search No.	Syntax	Results
1	Milk, Human/	18,805
2	Breast Feeding/	36,599
3	Breast Milk Expression/	280
4	(human milk* or breastfeed* or breast feed* or breast fed or breastfed or breast milk or breastmilk).ti,ab,kw,kf.	50,108
5	or/1-4	64,782
6	"Infant Nutritional Physiological Phenomena"/	14817
7	(production or produc* or yield* or consumption* or consum* or amount* or intake* or volume* or output*).ti,ab,kw,kf.	4,125,658
8	or/6-7	4,137,080
9	Case Reports/	1,968,968
10	Editorial/	458,542
11	Comment/	769,999
12	or/9-11	3,027,733
13	5 and 8	18,263
14	13 not (Animals/ not (Animals/ and Humans/))	17,727
15	14 not 12	17,098

16	15	17,098
17	limit 16 to (english language and yr="1970-Current")	14,885

Search Topic: Volume of Human Milk
Database: Embase (Ovid)
Search Date: January 9, 2020

Search No.	Syntax	Results
1	breast milk/	26,509
2	breast feeding/	50,668
3	breast milk expression/	327
4	(human milk or breast milk or breastmilk).ti,ab,kw.	26,945
5	or/1-4	75,056
6	(production or produc* or yield* or consumption* or consum* or amount* or intake* or volume* or output*).ti,ab,kw.	5,958,104
7	case report/	2,430,838
8	editorial/	625,893
9	note/	745,603
10	conference paper/	751,905
11	or/7-10	4,465,056
12	5 and 6	17,154
13	12 not ((exp animal/ or nonhuman/) not exp human/)	15,808
14	limit 13 to (conference abstract or conference paper or "conference review")	3,044
15	13 not 14	12,764
16	limit 15 to (pubmed-not-medline or "pubmed/medline")	2,570

17	15 not 16	10,194
18	17	10,194
19	limit 18 to (english language and yr="1970-Current")	9,462

Search Topic: Volume of Human Milk
Database: Scopus
Search Date: January 21, 2020
TITLE-ABS-KEY((“human milk” OR breastfeed* OR “breast feed*” OR “breast fed” OR breastfed OR “breast milk” OR breastmilk) AND (production OR produc* or yield* or consumption* or consum* or amount* or intake* or volume* or output*)) AND (INDEXTERMS(human*) OR TITLE-ABS-KEY(human*)) AND NOT INDEX(medline) AND PUBYEAR AFT 1969
Document Type: Exclude: Conference Paper, Note, Editorial
Language: English
Results: 3,161

Search Topic: Volume of Human Milk
Database: PubMed
Search Date: January 21, 2020
((“human milk”[Title/Abstract] OR breastfeed[Title/Abstract] OR breastfeeding[Title/Abstract] OR “breast feed”[Title/Abstract] OR “breast feeding”[Title/Abstract] OR “breast fed”[Title/Abstract] OR breastfed[Title/Abstract] OR “breast milk”[Title/Abstract] OR breastmilk[Title/Abstract]) AND (Production[Title/Abstract] OR produce[Title/Abstract] OR producing[Title/Abstract] OR produces[Title/Abstract] OR produced[Title/Abstract] OR yield[Title/Abstract] OR yielding[Title/Abstract] OR consumption[Title/Abstract] OR consume[Title/Abstract] OR consumed[Title/Abstract] OR consuming[Title/Abstract] OR amount[Title/Abstract] OR amounts[Title/Abstract] OR intake[Title/Abstract] OR intakes[Title/Abstract] OR volume[Title/Abstract] OR output[Title/Abstract] OR outputs[Title/Abstract])) AND pubmednotmedline[sb]
Date: 1970-2020
Language: English
Results: 572

D

Revised Search Criteria

TABLE D-1 Specified Inclusion and Related Exclusion Criteria for Milk Composition Reports

Inclusion Criteria	Related Exclusion Criteria
Healthy Study Population	
Adult women (≥ 18 years old)	Not adult women
Mother generally healthy: e.g., not suffering from acute or chronic illness that might influence milk composition and/or production; living in a high- or middle-income country during the study;[a] include obese women unless they have comorbidities	Mother not healthy: e.g., suffering from acute or chronic illness that might influence milk composition and/or production; living in a low-income country during the study
Full-term singleton infant (defined as ≥ 37 weeks gestation length)	Preterm, twins
Infant generally healthy	Infant not healthy
Infant/child ≤ 12 months old	Infant/child > 12 months old
Nutrients of Interest Included	
Milk nutrients of interest: vitamins A, C, D, E, K, thiamin, riboflavin, niacin, B6, folate, B12, pantothenic acid, biotin, choline, copper, fluorides, iodine, iron, magnesium, manganese, molybdenum, chromium, calcium, phosphorus, sodium, selenium, zinc, potassium, chlorides, total milk protein, lactose, total milk fat, fatty acids (linoleic, alpha linolenic, eicosapentaenoic, docosahexaenoic acids)	No nutrients of interest; this would include such things as human milk oligosaccharide; milk protein fractions (e.g., whey proteins, caseins); fatty acid classes that do not include triglycerides (e.g., phospholipids, cholesteryl esters, free fatty acids)
No oligosaccharides	Contains only data on human milk oligosaccharides
Publication Appropriate	
Published on or after 1980 (revised date)[b]	Published before 1980 (revised date)
Peer-reviewed, primary data	Non-peer-reviewed editorial, commentary, or abstract from conference; review or meta-analysis (no original data)
Study Design and Methods	
Sample size ≥10	Sample size <10
Reported values include a measure of central tendency (mean or median) and a measure of variance (SE, SD, 95% CI, or IQR); values reported in text or tabular form	Reported values do not include a measure of central tendency and variance; values only reported graphically
Study participants not consuming maternal vitamin/mineral supplements or galactagogues, except for OTC prenatal vitamins or general vitamin/mineral usage	Women taking supplements or galactagogues (that would not be considered OTC prenatal vitamins or general vitamin/mineral usage) as part of intervention study

Eligible study design: RCT, observational prospective cohort study	Ineligible study design: case study, inadequate control group, donor or pooled milk
Adequate milk collection and storage methods used for outcome of interest: e.g., complete breast expression for total lipids	Inadequate milk collection and storage methods used for outcome of interest: e.g., not complete breast expression for total lipids
Adequate analysis methods used for outcome of interest: e.g., milk protein values adjusted for nonprotein nitrogen.	Inadequate analysis methods used for outcome of interest: e.g., milk protein values not adjusted for nonprotein nitrogen
Adequate units of measure in reported values of nutrients and/or classes of nutrients: e.g., absolute values (mg/mL milk) for lipids	Inadequate units of measure in reported values of nutrients and/or classes of nutrients: e.g., relative amounts of fatty acids based on only identified fatty acids (%wt:wt)

NOTE: CI = confidence interval; IQR = interquartile range; mg = milligram; mL = milliliter; OTC = over-the-counter; RCT = randomized, double-blind, placebo-controlled trial; SD = standard deviation; SE = standard error; wt:wt = weight:weight.

[a] The committee made the decision to go beyond the United States and Canada to accept data from countries that were ranked high-income or high middle-income by the World Bank. The committee used its own judgment to decide whether to exclude reports from high middle-income countries that would have not been in this classification when the investigation was done. The committee chose to use these two groups of countries as they helped it to distinguish environments that might produce results for milk volume and composition that would be similar to those obtained among contemporary American women.

[b] Original search date was 1970.

TABLE D-2 Specified Inclusion and Related Exclusion Criteria for Milk Volume Reports

Inclusion Criteria	**Related Exclusion Criteria**
Healthy Study Population	
Adult women (≥ 18 years old)	Not adult women
Mother generally healthy: e.g., not suffering from acute or chronic illness that might influence milk production; no mention of lactation insufficiency or difficulty; living in a high- or middle-income country during the study; include obese women unless they have comorbidities	Mother not healthy: e.g., suffering from acute or chronic illness that might influence milk production; lactation insufficiency or difficulty; living in a low-income country during the study
Full-term, singleton infant (defined as ≥ 37 weeks gestation length)	Preterm, twins, etc.
Infant generally healthy	Infant not healthy
Infant/child ≤ 6 months old	Infant/child > 6 months old
Exclusive breastfeeding	Nonexclusive breastfeeding
Outcome of Interest	
Milk consumption over a period of ≥ 24 hours	Milk consumption over a period of < 24 hours; milk output/synthesis rather than consumption measured
Publication	
Published on or after 1980 (revised date)	Published before 1980 (revised date)
Peer-reviewed, primary data	Non-peer-reviewed editorial, commentary, or abstract from conference; review or meta-analysis (no original data)
Study Design and Methods	
Sample size ≥10	Sample size <10

Reported values include a measure of central tendency (mean or median) and a measure of variance (SE, SD, 95% CI, or IQR); values reported in text or tabular form	Reported values do not include a measure of central tendency and variance; values only reported graphically
Study participants not consuming galactagogues (to our knowledge)	Women taking galactagogues as part of intervention study
Eligible study design: RCT, observational prospective cohort study	Ineligible study design: case study, inadequate control group
Adequate method used:[a] 24-hour infant test-weighing; deuterium dilution (note that the committee is *not* excluding studies that did not correct for insensible water loss)	Inadequate method used: weighing mother rather than infant; not directly measuring milk intake during night
Adequate units of measure in reported values of milk intake: e.g., mL/24 hour	Inadequate units of measure in reported values of milk intake: e.g., mL/kg/24 hour, mL/kg, mL/24 hour/breast, mL/feed

NOTE: CI = confidence interval; IQR = interquartile range; kg = kilogram; mL = milligram; RCT = randomized, double-blind, placebo-controlled trial; SD = standard deviation; SE = standard error.

[a] To measure milk volume, infant intake is assessed, not maternal weight change or total production which can be higher because infants leave milk in the breast. Weighing the infant before and after a feed underestimates the volume consumed because of insensible water loss (sweat that has evaporated and exhaled water). Because very few reports corrected for these losses and often without having estimated the amount lost, the committee did not use correction for insensible water loss as an exclusion criterion.

TABLE D-3 Analytical Methods for Sampling and Analysis of Human Milk Relevant to the Specified Inclusion and Exclusion Criteria

Nutrient	Sampling	Analysis	Reference(s)
Total fat	Full-breast expression;[a] 24-hour collection or weighted combined aliquots of fore- and hindmilk from one breast at each pumping over 24 hours; standardize by time of day, collection mode, collection breast and time since last feed/expression	Solvent extraction (Folch method or HPLC); creamatocrit is "not accurate for database development"	Committee opinion; Jensen et al., 1985; Leghi et al., 2020; Wu et al., 2018
Fatty acids	See total fat	To determine the amount in milk both total fat and the amount of the fatty acid (as wt%) are required	Committee opinion; Jensen et al., 1985; Leghi et al., 2020
Total protein	Fore-, mid- or hindmilk are adequate; standardized by time of day, collection mode, collection breast, and time since last feed/expression	Kjeldahl with correction for nonprotein nitrogen by acid precipitation	Atkinson et al., 1980; Leghi et al., 2020; Wu et al., 2018
Lactose	Fore-, mid- or hindmilk are adequate; standardized by time of day, collection mode, collection breast, and time since last feed/expression	"LC-MS or HPLC are superior to enzymatic methods"; Miris analyzer reports lower values (excluded by committee opinion)	Leghi et al., 2020; Sprenger et al., 2017; Wu et al., 2018

Vitamin A	As for total fat (presumably); no circadian variability	HPLC (coupled with UV, fluorescence, and MS detection) has been the dominant method	Hampel et al., 2017, 2018
Vitamin D	As for total fat (presumably)	"HPLC and CPBA or LC-MS/MS should be applied"	Hampel et al., 2018
Vitamin E	As for total fat (presumably); no circadian variability	"HPLC coupled with fluorescence or UV detection is a well-studied and suitable technique for quantifying vitamin E; LC-MS/MS is a valid alternative"	Hampel et al., 2017, 2018
Vitamin K	As for total fat (presumably)	"HPLC-FLD is the preferred method; alternatively, LC-MS/MS provides the needed sensitivity"	Hampel et al., 2018
Thiamin	Morning and evening sample combined; avoid fasting or soon after supplement ingestion; afternoon and evening samples are preferred	Thiochrome method; recent methods use chromatographic separation before fluorescence detection; among the microbiological assays, "only *L. viridescens* provides results comparable to the thiochrome assay"	Hampel and Allen, 2016; Hampel et al., 2017, 2018
Riboflavin	See thiamin; afternoon and evening samples are preferred	Microbiological approaches are susceptible to error; Preferred: HPLC separation followed by fluorescence detection (current infant AI is based on UV detection and fluorometric measurements after HPLC separation)	Hampel et al., 2017, 2018
Niacin	See thiamin; afternoon and evening samples are preferred	A microbiological assay with *L. arabinosus* "continues to be a suitable choice;" LC-MS/MS can also be used	Hampel et al., 2017, 2018
Vitamin B6	See thiamin; afternoon and evening samples are preferred	Usually assessed with LC-based methods of *Saccharomyces uvarum*; HPLC methods provide "a more robust and rapid approach"	Hampel et al., 2017, 2018
Vitamin B12	See thiamin; afternoon and evening samples are preferred	*L. leichmanii* has been used in the past but may overestimate the vitamin; preferred method is competitive chemiluminescence enzyme immunoassays	Hampel et al., 2017, 2018
Folate	See thiamin	Method of choice: microbiological assay with *L. casei*	Hampel et al., 2018

Pantothenic acid	See thiamin	"The majority of analyses have been conducted via microbiological assays, but chromographic separation followed by UV or MS/MS detection may be beneficial"	Hampel et al., 2018
Biotin	See thiamin	Microbiological assays (*L. arabinosus* and *L. plantarum*) are commonly used; novel LC-MS/MS are being developed	Hampel et al., 2018
Choline	Unknown	"LC-MS/MS provides validated results with only minimal sample preparation without possible radiation exposure;" older methods include RIA and GC-MS analysis	Hampel et al., 2018
Vitamin C	See thiamin	"HPLC methods should be used;" note that the current AI is based on colorimetric assays	Hampel et al., 2018
Iron	Use trace-element free supplies	"Both AAS and inductively coupled argon plasma spectroscopy are suitable"	Hampel et al., 2018
Copper	Use trace-element free supplies	"AAS, ICP-AES, and ICP-MS are valid approaches"	Hampel et al., 2018
Zinc	Use trace-element free supplies	Same as for copper	Hampel et al., 2018
Iodine	Use trace-element free supplies	"ICP-MS is the preferred approach;" older studies used colorimetric approaches and have some analytic bias; iodide is analyzed differently	Hampel et al., 2018
Selenium	Use trace-element free supplies	AAS (less sample handling and no radiation step compared to other methods)	Hampel et al., 2018
Flouride(s)	Unknown	Fluoride-specific electrode	D. Hampel (personal communication)
Magnesium	Unknown	ICP-MS	Method used by Daniels et al., 2019
Molybdenum	Use trace-element free supplies	ICP-MS (based on official analysis method for infant formula)	AOAC, 2011
Chromium	Use trace-element free supplies	ICP-MS (based on official analysis method for infant formula)	AOAC, 2011
Calcium	Unknown	ICP-MS	Method used by Daniels et al., 2019

Phosphorus	Unknown	ICP-MS	Method used by Daniels et al., 2019
Sodium	Unknown	ICP-MS flame atomic emission spectrometry; ICP-MS is a branch of AAS Flame photometry (aka flame atomic emission spectrometry) is another branch of AAS that is acceptable for metal ions (Na, K)	Method used by Daniels et al., 2019
Chloride(s)	Unknown	Chloridometer or colorimetric titration by chloride counter; potentiometric method	D. Hampel (pers. comm.); Wack et al., 1997
Potassium	Unknown	ICP-MS is a branch of AAS Flame photometry (aka flame atomic emission spectrometry) is another branch of AAS that is acceptable for metal ions (Na, K)	Method used by Daniels et al., 2019

NOTE: AAS = atomic absorption spectrometry; AI = Adequate Intake; CPBA = competitive protein-binding assay; GC-MS = gas chromatography–mass spectrometry; HPLC = high-performance liquid chromatography; HPLC-FLD = high-performance liquid chromatography with fluorescence detection; ICP-AES = inductively coupled plasma-atomic emission spectrometry; ICP-MS = inductively coupled plasma–mass spectrometry; LC-MS/MS = liquid chromatography-tandem mass spectrometry; MS = mass spectrometry; MS/MS = tandem mass spectrometry; RIA = radioimmunoassay; UV = ultraviolet; wt = weight.

[a] A number of authors claimed that fatty acids do not change within a feed and used this as their rationale for not using a complete breast expression as their sample. However, the fatty acids are part of the lipid component of milk, which varies throughout the feed. If the proportion of fatty acids is the only objective, less than a full expression may be sufficient. For estimating an infant's needs, however, the total amount of a fatty acid actually delivered is required. Total fatty acid is the product of the total lipid in the entire feed with the proportion of the fatty acid.

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E

Data Abstraction Spreadsheet

To facilitate the final screening and data abstraction process, the committee constructed an online spreadsheet using Google Sheets. A snapshot of this spreadsheet is provided below.

	CITATION INFORMATION									
ID	category	Authors	Title	Full Text	PRIMARY SCREENER	VALIDATOR	VALIDATOR AGREES WITH PRIMARY SCREENER	REASON FOR DISAGREEMENT	INCLUDE PAPER IN FINAL REPORT?	REASON FOR EXCLUSION
				Link to PDF in Dropbox	*Select your initials*	*Select your initials*	*Check if yes; if no, add reason in next column*	*State reason for disagreement*	*Check if yes*	*if paper should not be included, cite reason for exclusion*
207	mineral	Ortega, R. M.; Martine	Calcium levels in maternal milk:				☐		☐	
208	mineral	Ozdemir, H. S.; Karadas	The selenium levels of mothers a				☐		☐	
209	mineral	Pearce, E. N.; Leung, A.	Breast milk iodine and perchlora				☐		☐	
210	mineral	Prentice, A.; Yan, L.; Ja	Vitamin D status does not influer				☐		☐	
211	mineral	Qian, L.; Wang, B.; Tan	Polymorphisms of SLC30A2 and				☐		☐	
212	mineral	Rodriguez Rodriguez, E	Concentrations of selenium in hu				☐		☐	
213	mineral	Rossipal, E.; Krachler, M	Pattern of trace elements in hum				☐		☐	
214	mineral	Sabatier, M.; Garcia-Ro	Longitudinal changes of mineral				☐		☐	
215	mineral	Salmenpera, L.; Perhee	Low zinc intake during exclusive				☐		☐	
216	mineral	Salmenpera, L.; Perhee	Cu nutrition in infants during pro				☐		☐	
217	mineral	Sener, Yagmur; Tosun,	Fluoride levels of human plasma				☐		☐	
218	mineral	Severi, C.; Hambidge, M	Zinc in plasma and breast milk in				☐		☐	
219	mineral	Silvestre, D.; Martinez-	Copper, iron, and zinc contents ir				☐		☐	
220	mineral	Silvestre, M. D.; Lagard	A study of factors that may influe				☐		☐	
221	mineral	Snoj Tratnik, J.; Falnoga	Results of the first national huma				☐		☐	
222	mineral	Taghipour, S.; Nikniaz, I	Synbiotic supplementation is not				☐		☐	
223	mineral	Tamari, Y.; Chayama, K.	Longitudinal study on selenium c				☐		☐	
224	mineral	Tamari, Y.; Kim, E. S.	Longitudinal study of the dietary				☐		☐	
225	mineral	Taravati Javad, M.; Vah	Analysis of aluminum, minerals a				☐		☐	
226	mineral	Urzica, D.; Gales, C.; Za	The influence of oral steroidal co				☐		☐	
227	mineral	Valent, F.; Horvat, M.; I	Maternal diet and selenium conc				☐		☐	
228	mineral	Vuori, E.; Makinen, S. M	The effects of the dietary intakes				☐		☐	
229	mineral	Wack, R. P.; Lien, E. L.;	Electrolyte composition of huma				☐		☐	

POPULATION CHARACTERISTICS		NUTRIENTS WHOSE CONCENTRATIONS WERE REPORTED												
Paper includes statement that mothers were healthy	**What other information was reported?**	**Specify nutrient #1**	**Was milk sampled by an appropriate method?**	**Was the milk analysis methodology appropriate?**	**Specificy nutrient #2**	**Was milk sampled by an appropriate method?**	**Was the milk analysis methodology appropriate?**	**Specify nutrient #3**	**Was milk sampled by an appropriate method?**	**Was the milk analysis methodology appropriate?**	**Specify nutrient #4**	**Was milk sampled by an appropriate method?**	**Was the milk analysis methodology appropriate?**	**Specify nutrient #5**
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Was milk sampled by an appropriate method?	Was the milk analysis methodology appropriate?	Specify nutrient #6	Was milk sampled by an appropriate method?	Was the milk analysis methodology appropriate?	Specify nutrient #7	Was milk sampled by an appropriate method?	Was the milk analysis methodology appropriate?	Was Volume Measured	Was milk sampled by an appropriate method?	COMMENTS
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Committee Member Biographies

Kathleen M. Rasmussen, Sc.D. (*Chair*) is the Nancy Schlegel Meinig Professor of Maternal and Child Nutrition in the Division of Nutritional Sciences at Cornell University. Dr. Rasmussen is internationally known for her research on maternal and child nutrition, particularly in the areas of pregnancy and lactation. She has served as the program director for Cornell's National Institutes of Health–sponsored training grant in maternal and child nutrition since 1986 and has also directed a training grant in international maternal and child nutrition. Dr. Rasmussen has taught a nationally recognized course in maternal and child nutrition for graduate students since 1980 and has taught a unique course on public health nutrition for undergraduate students since 1998. As part of her commitment to mentoring future leaders in nutrition, Dr. Rasmussen served as the principal faculty member at the Dannon Nutrition Leadership Institute, which she helped to develop, from 1998 until the program ended in 2017. She has received the Excellence in Nutrition Education Award and also the Mentorship Award from the American Society for Nutrition. The American Public Health Association honored her for her research accomplishments related to maternal–fetal nutrition with their Agnes Higgins Award in 2012. The International Society for Research in Human Milk and Lactation honored her for her research accomplishments related to lactation in 2016. Dr. Rasmussen has served as the president of the American Society for Nutritional Sciences and also as the president of the International Society for Research in Human Milk and Lactation. She has been the associate dean and the secretary of the university faculty and served a 4-year term on Cornell's Board of Trustees as one of its faculty-elected members. Dr. Rasmussen has been a member of several expert committees at the Institute of Medicine (IOM) with a focus on pregnancy, lactation, and the Special Supplemental Nutrition Program for Women, Infants, and Children (WIC). She served as the chair of the Committee to Reexamine IOM Pregnancy Weight Guidelines and then as the chair of a committee to disseminate these new guidelines. Most recently, she served as the chair of the Committee to Review the WIC Food Packages. She received her A.B. from Brown University in molecular biology and both her Sc.M. and Sc.D. from Harvard University in nutrition.

Meghan Azad, Ph.D., is an associate professor of pediatrics and child health at the University of Manitoba and a research scientist at the Children's Hospital Research Institute of Manitoba. She holds a Canada Research Chair in Developmental Origins of Chronic Disease and co-directs the new Manitoba Interdisciplinary Lactation Centre (MILC, www.milcresearch.com). Her research program (www.azadlab.ca) is focused on the role of infant nutrition and the microbiome in child growth, development, and resilience. Dr. Azad is directing the new International Milk Composition Consortium that will comprehensively profile human milk from women in diverse low- and middle-income settings, funded by the Bill & Melinda Gates Foundation. She also co-leads the Manitoba site of the CHILD Cohort Study (www.childstudy.ca), a national pregnancy cohort following 3,500 children to understand how early life experiences shape lifelong health to promote or protect against asthma, allergies, and obesity. Dr. Azad directs multiple projects

related to infant feeding practices, human milk composition, and the microbiome in the CHILD cohort and other populations, including preterm neonates receiving donor milk, and Bangladeshi infants at risk of malnutrition. She also leads collaborative projects examining perceptions of breastfeeding on social media and developing methods to improve societal support for breastfeeding through school-based education programs. Dr. Azad received the 2018 International Society for Research in Human Milk and Lactation (ISRHML) Ehrlich-Koldovsky Award. She serves on the ISRHML Executive Council, the Breastfeeding Committee of Canada, and the joint U.S./Canada Human Milk Composition Initiative.

Lars Bode, Ph.D., is a professor of pediatrics in the Division of Neonatology and the Division of Gastroenterology, Hepatology and Nutrition (http://www.bodelab.com), the Larsson-Rosenquist Chair of Collaborative Human Milk Research, and the director of the Larsson-Rosenquist Foundation Mother-Milk-Infant Center of Research Excellence (MOMI CORE, http://milk.ucsd.edu) at the University of California, San Diego. Dr. Bode received both his M.S. and Ph.D. in nutritional sciences from the Justus-Liebig University in Giessen, Germany, and completed a predoctoral fellowship at the Institute of Child Health at the University College London in the United Kingdom. Following a postdoctoral fellowship at the Sanford Burnham Prebys Medical Discovery Institute in La Jolla, California, Dr. Bode joined the University of California, San Diego, where he is now leading a research program dedicated to investigating human milk oligosaccharide biosynthesis and functions with potential benefits for infant and adult health. Dr. Bode is the recipient of the 2012 Ehrlich-Koldovsky Award from the International Society for Research in Human Milk and Lactation, the recipient of the 2013 Norman Kretchmer Memorial Award in Nutrition and Development from the American Society for Nutrition, and the 2014 Bio Serv Award in Experimental Animal Nutrition from the American Society for Nutrition.

Michelle McGuire, Ph.D., is the director and a professor of nutrition in the Margaret Ritchie School of Family and Consumer Sciences at the University of Idaho. Dr. McGuire received her M.S. in nutritional sciences from the University of Illinois and her Ph.D. in human nutrition from Cornell University. She has a background in human physiology and nutrition, with specific training and expertise in maternal/infant nutrition, human milk composition, nutritional assessment, milk and fecal microbiomes, and lactation physiology. Dr. McGuire has conducted studies related to myriad human milk components, including minerals, hormones, lipids, pesticides, and most recently microbes. She also has a keen interest in understanding the physiologic mechanisms regulating duration of postpartum amenorrhea. Dr. McGuire has overseen a variety of projects related to human nutrition and lactation funded by the Bill & Melinda Gates Foundation, the National Institutes of Health, the National Science Foundation, and the U.S. Department of Agriculture, as well as a variety of industry sources such as the National Cattlemen's Beef Association and United Dairymen of Idaho. She has twice served on the executive committee of the International Society for Research in Human Milk and Lactation (ISRHML), including the roles of secretary and treasurer; and has also served on the executive board of the American Society for Nutrition during which time she was the director of the Research Interest Sections. A seasoned science writer, Dr. McGuire is the author of two college-level introductory nutrition textbooks. In 2002 she received the Ehrlich-Koldovsky Award from ISRHML, and in 2018 she received the Excellence in Nutrition Education Award from the American Society for Nutrition.

Laurie Nommsen-Rivers, Ph.D., R.D., IBCLC, is an associate professor of nutrition and the Ruth Rosevear Endowed Chair of Maternal and Child Nutrition at the University of Cincinnati. Dr. Nommsen-Rivers is a Registered Dietitian since 1990 and an International Board Certified Lactation Consultant since 1993. She served as the associate editor of the *Journal of Human Lactation* from 1997 to 2006. After receiving her master's degree in nutrition from the University of California (UC), Davis, she spent 18 years working with hundreds of mother–infant dyads as a research associate at UC Davis. Between 2009 and 2016 Dr. Nommsen-Rivers was an assistant professor of pediatrics in the Division of Neonatology at Cincinnati Children's Hospital Medical Center. Dr. Nommsen-Rivers has co-authored more than 70 research publications related to the breastfeeding dyad with a focus on barriers that impede lactation success. Her current work focuses on physiologic factors that influence milk production in lactating mothers.

Ian J. Saldanha, M.B.B.S., M.P.H., Ph.D., is an assistant professor of health services, policy, and practice and an assistant professor of epidemiology in the Center for Evidence Synthesis in Health at the Brown University School of Public Health. Dr. Saldanha has expertise conducting systematic reviews and meta-analyses, developing and advancing methods to improve their conduct, and teaching methods for their conduct. He has also conducted research into the use of outcomes in clinical research. Dr. Saldanha was the co-principal investigator (PI) of a National Academies of Sciences, Engineering, and Medicine contract to conduct a systematic review of public health emergency preparedness activities. He is the PI of the Agency for Healthcare Research and Quality (AHRQ)-funded systematic reviews of the management of primary headaches during pregnancy and breast reconstruction after mastectomy. Additionally, he is the PI of an AHRQ contract for the development, advancement, and support of the Systematic Review Data Repository. He has been the PI of two subcontracts to Brown University: the National Eye Institute–funded Cochrane Eyes and Vision U.S. Satellite, and the Patient-Centered Outcomes Research Institute–funded Data Abstraction Assistant project. Dr. Saldanha is an elected member of the Society for Research Synthesis Methodology and serves as the associate editor for two journals (*Systematic Reviews* and *Journal of Glaucoma*) and for the AHRQ Effective Healthcare Program. Dr. Saldanha has taught multiple courses and workshops related to systematic reviews, meta-analysis, clinical trials, and epidemiology at the undergraduate, graduate, and professional levels, including at the Centers for Disease Control and Prevention.