# A ANNUAL REVIEWS

# Annual Review of Nutrition Breastfeeding Beyond 12 Months: Is There Evidence for Health Impacts?

#### Kimberly A. Lackey,<sup>1</sup> Bethaney D. Fehrenkamp,<sup>1</sup> Ryan M. Pace,<sup>1</sup> Janet E. Williams,<sup>2</sup> Courtney L. Meehan,<sup>3</sup> Mark A. McGuire,<sup>2</sup> and Michelle K. McGuire<sup>1</sup>

<sup>1</sup>Margaret Ritchie School of Family and Consumer Sciences, University of Idaho, Moscow, Idaho 83844, USA; email: smcguire@uidaho.edu

<sup>2</sup>Department of Animal, Veterinary and Food Sciences, University of Idaho, Moscow, Idaho 83844, USA

<sup>3</sup>Department of Anthropology, Washington State University, Pullman, Washington 99164, USA

Annu. Rev. Nutr. 2021. 41:283-308

First published as a Review in Advance on June 11, 2021

The Annual Review of Nutrition is online at nutr.annualreviews.org

https://doi.org/10.1146/annurev-nutr-043020-011242

Copyright © 2021 by Annual Reviews. All rights reserved

### ANNUAL CONNECT

- www.annualreviews.org
- Download figures
- Navigate cited references
- Keyword search
- Explore related articles
- Share via email or social media

#### **Keywords**

breastfeeding, lactation, prolonged, health, guidance

#### Abstract

Because breastfeeding provides optimal nutrition and other benefits for infants (e.g., lower risk of infectious disease) and benefits for mothers (e.g., less postpartum bleeding), many organizations recommend that healthy infants be exclusively breastfed for 4 to 6 months in the United States and 6 months internationally. Recommendations related to how long breastfeeding should continue, however, are inconsistent. The objective of this article is to review the literature related to evidence for benefits of breastfeeding beyond 1 year for mothers and infants. In summary, human milk represents a good source of nutrients and immune components beyond 1 year. Some studies point toward lower infant mortality in undernourished children breastfed for >1 year, and prolonged breastfeeding increases interbirth intervals. Data on other outcomes (e.g., growth, diarrhea, obesity, and maternal weight loss) are inconsistent, often lacking sufficient control for confounding variables. There is a substantial need for rigorous, prospective, mixed-methods, cross-cultural research on this topic.

#### Contents

INTRODUCTION	284
DEFINITION OF PROLONGED BREASTFEEDING	
BREASTFEEDING DURATION: A COMPARATIVE PERSPECTIVE	286
HUMAN MILK PRODUCED AFTER 1 YEAR POSTPARTUM	
AS A SOURCE OF ENERGY AND NUTRIENTS	287
Milk Volume	287
Milk Composition	288
EVIDENCE FOR ASSOCIATION BETWEEN PROLONGED	
BREASTFEEDING AND INFANT OUTCOMES	289
Infant Nutritional Status, Including Physical Growth	289
Prolonged Breastfeeding and Appetite	
Infant Infection Risk	291
Childhood Mortality	292
Infant Gastrointestinal Microbiome	292
Infant Immunity, Including Asthma, Food Sensitization, and Leukemia	293
Prolonged Breastfeeding and Dental Caries	295
Childhood Overweight/Obesity	
Prolonged Breastfeeding, Cognition, and School Success	296
EVIDENCE FOR IMPACT OF PROLONGED BREASTFEEDING	
ON MATERNAL HEALTH OUTCOMES	297
Maternal Body Weight	
Maternal Bone Health	298
Lactational Amenorrhea, Anovulation, and Interbirth Intervals	299
Other Maternal Outcomes	300
SUMMARY OF EVIDENCE FOR A BENEFIT OF PROLONGED	
BREASTFEEDING	300
LIMITATIONS OF AVAILABLE STUDIES	301

#### **INTRODUCTION**

Breastfeeding is widely considered the optimal mode of nutrition for infants (3, 74, 138, 140), in part because milk produced by well-nourished, healthy women can provide complete nutrition in the first 6 months of life. Breastfeeding also reduces primary malnutrition, especially in settings plagued by poverty, unsanitary conditions, and food insecurity (62); is associated with lower incidence of infections (13, 57); reduces infant mortality (109), sudden infant death syndrome (62), dental malocclusions (98), and obesity later in life (56); and may improve intelligence (56). For women, breastfeeding prolongs lactational amenorrhea; may reduce breast and ovarian cancers and type 2 diabetes (5, 25); and may facilitate postpartum weight loss (91). There appears to be a dose-response relationship such that these effects are strengthened with exclusive and increased duration of any breastfeeding—at least within the first year of life. In the United States, exclusive breastfeeding is generally recommended for 4–6 months with continued breastfeeding for up to one year. Internationally, recommendations are generally centered on exclusive breastfeeding for 6 months and then continued breastfeeding for up to one year and, in some cases, even longer. Despite these guidelines, how long women should continue breastfeeding is unclear.

More specifically, the American Academy of Pediatrics (3) recommends that mothers continue breastfeeding until the infant is 1 year old, after which time breastfeeding can be continued if "mutually desired by mother and infant" (p. e827). Similarly, a committee convened by the US National Academy of Sciences recommended that adults who work with infants should promote and support exclusive breastfeeding for 6 months and continuation of breastfeeding for 1 year or more (61). The Academy of Nutrition and Dietetics (74) states that "exclusive breastfeeding provides optimal nutrition and health protection for the first 6 months of life, and that breastfeeding pattern for infants" (p. 444). Whereas the aforementioned references regarding prolonged breastfeeding provide little to no justification for their recommendations, they all cite the World Health Organization (WHO), which recommends that infants receive nutritionally adequate and safe complementary foods while breastfeeding continues for up to 2 years of age or beyond (136, 140). In a subsequent report written jointly by the WHO and the Pan American Health Organization (PAHO) (138), guidelines for prolonged breastfeeding are justified as follows (references cited are those cited in the report).

- 1. Human milk provides substantial amounts of energy, micronutrients, and lipids to a breastfed infant's diet (36, 104, 139).
- 2. Breastfeeding provides enhanced benefits during periods of childhood illness, resulting in the prevention of dehydration and the provision of nutrients needed to recover from infections (20).
- 3. Breastfeeding has a potential impact on maternal fertility and birth spacing.
- 4. Breastfeeding reduces child morbidity and mortality in disadvantaged populations (89, 141).
- 5. Breastfeeding may improve infant appetite and growth (96, 114), although the WHO and PAHO recognized that data were mixed (23, 54).
- 6. Associations exist between longer periods of breastfeeding and reduced risk of childhood illnesses (31) and obesity (21) as well as improved cognition (105).

Of note, aside from a potential impact on maternal fertility and birth spacing (for which there was no citation provided), implications for maternal health do not appear to have been considered. Nonetheless, breastfeeding for  $\geq 2$  years is a common international recommendation based on this and other reports (see the sidebar titled Socioeconomic Status and Prolonged Breastfeeding Trends for global prolonged breastfeeding rates), and in some circumstances, guidance for prolonged breastfeeding is expanded to "frequent, on-demand breastfeeding until 2 years of age or beyond" (138, p. 36).

But what is the scientific evidence that breastfeeding beyond 1 year confers benefits to mothers and/or infants? Answering this question is important for a variety of reasons, including the desire

#### SOCIOECONOMIC STATUS AND PROLONGED BREASTFEEDING TRENDS

Data from 153 countries compiled by Victora and colleagues and published as part of the *Lancet* breastfeeding series (127) suggest that the proportion of infants still breastfed at 20–23 months of life is highest (~64%) in low-income countries and lowest (~17%) in upper- to middle-income countries. Whereas it is likely that rates are even lower in high-income countries, data regarding prolonged breastfeeding in these nations are often not available. National time trends reported between 1993 and 2013 suggest that although the overall rates of prolonged breastfeeding are highest in the poorest countries and lowest in the wealthiest countries, rates in the former are decreasing whereas those in the latter are increasing. The authors raise the concern that poor mothers may move toward breastmilk substitutes after 1 year postpartum as their incomes increase.

#### Prolonged

breastfeeding: any breastfeeding that occurs beyond 1 year postpartum (women) or beyond the first year of life (children)

#### Breastfeeding:

nursing at the breast and the provision of human milk through other devices to optimize maternal and infant health. Here, we provide a comparative perspective on the duration of breastfeeding/lactation across great apes and critically evaluate the literature describing benefits, risks, or neutral outcomes associated with breastfeeding beyond 1 year in humans—focusing primarily on reevaluating justifications used in the 2003 WHO & PAHO (138) report but also including other available research as appropriate. Our intent is not to provide an exhaustive review of the literature; rather, our goal is to present the most relevant publications on a variety of issues related to this topic, often citing recent critical reviews when possible.

#### **DEFINITION OF PROLONGED BREASTFEEDING**

Herein, the term prolonged breastfeeding refers to breastfeeding beyond 1 year postpartum. Only literature that specifically examined associations between breastfeeding after 1 year postpartum and maternal and/or infant health has been considered (not the overall association between breastfeeding and health). Because details are often not specified in the literature, we consider breastfeeding to include nursing at the breast and the provision of human milk through other devices.

#### **BREASTFEEDING DURATION: A COMPARATIVE PERSPECTIVE**

In contrast to much of the literature discussed herein, evolutionary anthropologists and primatologists approach the question of breastfeeding and/or lactation duration and maternal/child health from a comparative ethological perspective. Once situated into its evolutionary history, breastfeeding for >1 year in humans cannot actually be interpreted as extended since human breastfeeding duration is shorter in comparison with our closest relatives, particularly considering human ontogeny (126).

The introduction of complementary foods in humans occurs at approximately the same time as that for other great apes ( $6 \pm 2$  months) (43, 110). Yet, the human pattern diverges after 6 months in notable ways. Unlike other great apes whose initial solid foods are generally limited to those they can self-collect, humans accomplish food supplementation via parental and allomaternal provisioning and processing of nutritious weaning foods (126). Despite providing for energetically costly offspring (59), humans maintain breastfeeding at a relatively limited and decreasing cost across lactation (22), enabled via supplementation. In comparison, other great apes continue to rely primarily on lactation to supply nutrients, and their offspring do not enter a feeding transition period, during which they continue to breastfeed but acquire more calories from self-foraging than milk, until approximately 2–3 years of age (43, 80). Human infants have a variable feeding transition period, but data from human populations suggest it occurs within the second year of life—substantially earlier than in other apes (see discussion below in this section).

All apes continue to lactate for months to years beyond the feeding transition, with mothers' milk possibly serving as a buffer in resource-challenged environments (43). Emery Thompson & Sabbi (43) note that differences among nonhuman apes in available weaning foods that require little processing or learning to acquire help explain variation in the timing of breastfeeding termination in chimpanzees, bonobos, gorillas, and orangutans. For humans, who provide consistent weaning foods for their infants (126), the potential costs of earlier lactation cessation may be further reduced. Hunter-gatherer populations terminate breastfeeding at  $\sim$ 2.5 years, and other small-scale societies cease breastfeeding at  $\sim$ 20–24 months (110, 126); these time points are enabled via comparatively abundant and accessible foods for young children.

Early and sustained supplementation and comparatively early breastfeeding cessation in humans are attributed to several unique life history characteristics, including humans' comparatively shorter interbirth intervals (IBIs), simultaneous rearing of multiple dependents, and relatively high fertility (43, 59). For instance, IBIs of hunter-gatherers average 3–5 years (68), and total fertility is ~5.4 live births (55). In comparison, wild gorilla populations have average IBIs ranging from 4 to 5 years (on the lower end), while wild orangutan populations have IBIs of 6–8 years (on the upper end). It is noteworthy that, for wild orangutans, because death frequently occurs during females' reproductive span, fertility only nears replacement levels (43). The human breastfeeding pattern and duration are supported by our prosocial, cooperative nature. Specifically, our willingness to support supplementation for our altricial infants and dependent young children and through cooperative breeding, where allomothers provision infants and reduce maternal energy expenditure during critical reproductive periods, lowers the energetic cost of human reproduction (59, 77, 86). This perspective is particularly important to consider when evaluating the evidence of benefit (or detriment) arising from prolonged lactation in humans.

#### HUMAN MILK PRODUCED AFTER 1 YEAR POSTPARTUM AS A SOURCE OF ENERGY AND NUTRIENTS

The WHO & PAHO (138) report suggests that human milk provided to children after 1 year of age is a valuable source of energy and nutrients. In this section, we examine alterations in milk volume and nutrient composition after 1 year and evidence that human milk necessarily and/or uniquely contributes to infant health and well-being during this time.<sup>1</sup>

#### Milk Volume

Measurements of milk volume after 1 year vary greatly across studies, and this variation is likely influenced by geographic location, cultural norms, and other context-specific factors. For instance, Dewey (35) reports that children 12–23 months of age consume ~448 mL/day of milk, which contributes ~29% of their overall energy needs. Later, Dewey & Brown (36) studied another group of US women with high breastfeeding rates beyond 1 year postpartum and found that human milk accounted for ~40% of daily energy requirements of children 1–2 years of age. Data compiled from multiple multinational cohorts by the WHO & UNICEF (139) suggested that the overall energy needs of children in this age bracket are roughly 20% higher than the estimates of Dewey & Brown (36); in this case, human milk would account for only ~31% of the daily energy needs of children between 1 and 2 years of life (139). Data from another small US cohort (n = 6) suggest that milk production at 1 year is ~600 mL/day, decreasing to ~400 mL/day of milk at 16 months (see figure 4B in 92). Kent and colleagues (67) reported that Australian women (n = 3) produced only 109 g/day of milk at 18 months postpartum.

Estimates from developing nations are equally variable. For instance, data from Indonesia suggest that women (n = 8) between 13 and 23 months postpartum produced 190–460 mL/day of milk, corresponding to 17–54% of total energy needs (10). In another, larger (n = 120) study from this region, milk consumption was 460 and 190 mL/day at 12 and 34 months postpartum, respectively (11). In India, milk intake was estimated to be 480 and 345 mL/day at 37 and 48 months, respectively (7), and in New Guinea, milk intake decreased from 330 to 130 mL/day between 13 and 18 months postpartum (6).

In summary, estimates across populations indicate that children breastfeeding for >1 year consume from  $\sim$ 100 to 600 mL/day of human milk and that human milk can (but does not always) provide a substantial amount of energy to infants during this time. These data do not address

<sup>&</sup>lt;sup>1</sup>Note that milk consumption, rather than capacity for milk production, is the variable of interest in this context.

whether human milk is uniquely important in terms of providing energy and nutrients to infants after 1 year of life and provide little insight as to contexts in which it might be particularly necessary for infant growth, development, and survival.

#### **Milk Composition**

In addition to decreasing in volume after 1 year, milk composition also changes. For example, Czosnykowska-Łukacka and colleagues (27) reported that, compared with milk produced before 12 months, concentrations of protein and lipids were higher and carbohydrates lower in milk produced after 18 months. Later, these researchers demonstrated that protein concentration increased after 1 year and was even higher after 2 years in milk produced by 116 Polish mothers (28). In a similar study, Mandel and colleagues (76) evaluated total energy and lipid contents of milk produced by 27 women between 2 and 6 months compared with that produced by 34 women after >1 year. Both fat and total energy concentrations were higher in the milk produced after 1 year. Perrin et al. (99) evaluated composition of 33 pooled milk samples created from milk produced by 51 women  $\leq 1$  year postpartum and compared those samples with milk collected longitudinally from 19 women between 11 and 17 months. When the milk produced before 1 year was compared with that produced between 11 and 17 months, the milk produced after 1 year was found to have more protein and less zinc, calcium, iron, and oligosaccharides than the milk pools. Between 11 and 17 months, protein, oligosaccharides, and sodium concentrations continued to increase. Conversely, zinc and calcium concentrations decreased, with no changes in lactose, lipids, iron, and potassium. Karra and colleagues (65) found that between 7 and 25 months, concentrations of zinc, calcium, vitamin B<sub>6</sub>, vitamin C, and magnesium (only after 18 months) decreased. Neville et al. (92) reported that sodium, lactose, and protein in milk produced by US women increased after 1 year postpartum. These increases were statistically significant but small, and their physiologic importance is unknown. Other studies have reported no changes in milk's macronutrient concentrations >1 year postpartum. For example, Boediman and colleagues (11) reported no differences in protein, lipids, and lactose in milk produced by Indonesian women in their first, second, or third year postpartum. They did, however, report increased vitamin A concentrations from the first to the second year. Dewey and colleagues (37) evaluated 116 milk samples produced by 46 women between 7 and 20 months postpartum. Compared with women at 4-6 months postpartum, lipid, sodium, and iron were higher; magnesium and calcium were lower; and lactose and protein were unchanged.

In summary, human milk remains a source of macronutrients and micronutrients for children >1 year old, although there is substantial variation in milk volume and nutrient concentrations, likely due to changing infant demand and dilution effects. While estimates suggest that a sizable proportion of energetic needs is contributed to older nurslings' diets in the United States, estimates from Australia suggest a much lower proportion. Similar variations are also reported from developing nations, where data from Indonesia suggest upward of 50% of daily energy requirements is supplied through breastfeeding, compared with New Guinea, where infants only consume a quarter of the amount of milk and thus a quarter of the energy. These data suggest that these differences are not simply explained by development level or socioeconomic status (SES) of the population. Rather, there are clearly additional substantive, nuanced factors contributing to the importance of milk components, particularly energy-yielding nutrients, provided by human milk after the first year across global regions. While it is also clear that there are changes in milk composition after 1 year postpartum, these changes have merely been described and not linked to important factors such as bioavailability, food hygiene, the child's nutritional status, or other infant health outcomes.

#### EVIDENCE FOR ASSOCIATION BETWEEN PROLONGED BREASTFEEDING AND INFANT OUTCOMES

Most studies evaluating short- and long-term infant outcomes associated with breastfeeding focus on breastfeeding as a dichotomous (yes/no) variable, exclusive breastfeeding for 4–6 months, and/or breastfeeding for  $\leq 1$  year. This literature is robust, demonstrating myriad benefits to infants, including promotion of sensory and cognitive development, protection against infectious and chronic disease, and reduction of infant mortality (137). However, this literature generally does not explore associations with prolonged breastfeeding (>1 year) and infant health and wellbeing. Here, we specifically review the literature relating prolonged breastfeeding to infant health, growth, and development during the second year of life and, in some cases, beyond.

#### Infant Nutritional Status, Including Physical Growth

The effect of prolonged breastfeeding on child growth is difficult to address given the complexities of obtaining data needed for its evaluation. Three reviews (33, 42, 50) summarize most of the primary literature (**Table 1**) in this regard and note the challenges related to potential reverse causality and confounding that affect interpretation of each dataset examined. The experimental design for most studies is cross-sectional, with either an absence of or poor control for factors such as SES, availability of supplemental foods, and hygiene. Generally, the cross-sectional approaches (15, 19, 23, 45, 78, 88, 93, 94, 113, 114, 119, 130, 131) identified poorer growth and nutritional status in children breastfeeding for >1 year. Conversely, Taren & Chen (120) detected greater height for age, weight for age, and weight for height in Chinese children breastfed for >1 year compared with those breastfed for <1 year. Prolonged breastfeeding was also related to improved length and weight gain in Kenyan children, although weight for height and weight for age were reduced (96). Longitudinal studies generally agree with cross-sectional studies, associating prolonged breastfeeding with malnutrition (18, 89), although Fawzi and colleagues (45) failed to detect differences in weight or height gains between breastfed or weaned children from 1 to 3 years in Sudan.

Two case-control studies have explored the relationship between prolonged breastfeeding and child growth. In Ethiopia, Thorén et al. (122) reported an elevated risk of malnutrition in children breastfed for >1 year in both cases (diarrhea) and healthy children of similar social background (controls). Cousens et al. (26) matched children hospitalized for clinical malnutrition with neighborhood controls. Prolonged breastfeeding combined with supplementation was associated with a 70% reduction in the risk of clinical malnutrition from ages 1 to 3 years.

A concern with the hypothesis that prolonged breastfeeding causally affects nutritional status in all of these studies is the potential for reverse causality, given that the choice to breastfeed or wean is not controlled. Caulfield and colleagues (23) addressed this possibility with data from 19 developing countries and concluded that the decision to wean was related to child size; however, this was not consistent across cohorts. Additionally, the decision to wean after 1 year was related to availability and acceptance of other foods (112). Many factors could contribute to the decision to wean or extend breastfeeding, including maternal/child illness, food availability, and pregnancy. More in-depth discussion of reverse causality can be found in the reviews of Grummer-Strawn (50) and Elsom & Weaver (42), the papers by Caulfield et al. (23) and Marquis et al. (78), and commentaries by Mølbak et al. (90) and Martin (79).

#### **Prolonged Breastfeeding and Appetite**

The WHO & PAHO (138) report acknowledged the fact that there are conflicting data with respect to whether prolonged breastfeeding impacts infant appetite. However, and as addressed by Habicht (54), few studies have evaluated this, and none has specifically evaluated appetite as

# Table 1 Summary of published studies examining the association of prolonged breastfeeding and child growth, nutritional status, and survival

Reference	Country	Sample size	Association with growth	Association with nutritional status	Controlled for confounders	Survival
15	Ghana	202	Lower WH, WA, HA	Malnutrition	No	NR
18	Bangladesh	1,087	Reduced WA	Malnutrition	No	Improved
19	Bangladesh	4,612	Slight increase in mean arm circumference	No association	No	Improved for severely under- nourished children
23	19 developing countries	26,615	Reduced WA and HA	Malnutrition	Yes	NR
26	Burkina Faso	304	HA similar for chronically undernourished given solid food	Reduced risk of malnutrition for those eating solid foods up to 36 months	Case control of undernour- ished children; partly covered	NR
45	Sudan	28,753	No association	No association	Yes	NR
78	Peru	134	Reduced gain in length with low complementary food intake or diarrhea	NA	Yes	NR
88	Botswana	20,908	Reduced WA	Malnutrition	No	NR
89	Guinea-Bissau	849	Reduced WA	Greater relative risk or malnutrition at 21–23 and 27–29 months	No	Improved
93	Zambia	394	Greater HA	No association	Yes	NR
94	Ghana	$\sim$ 500	NA	Reduced malnutrition	Yes	NR
96	Kenya	264	Improved length and weight gain; lower WH and WA; similar HA	No association	Yes	NR
113	Senegal	4,515	Reduced HA and WH	Increased malnutrition	Yes	NR
114	Senegal	443	Greater HA and gain in length	No relationship with weight or arm circumference	Yes	NR
119	Pakistan	1,072	NR	Stunting	Yes	NR
120	China	2,148	Greater HA, WA, and WH	Less malnutrition	Yes	NR
122	Ethiopia	249	NR	More malnutrition	Case control of social background	NR
129	Brazil	4,923	No association	NA	Yes	NR
130	Brazil	802	Reduced HA and WH	NA	Yes	NR
131	Thailand	197	Reduced WA	NA	No	NR
144	Turkey	1,666	No association	No association	Yes	NR

Abbreviations: WA, weight for age; WH, weight for height; HA, height for age; NR, not reported; NA, not applicable.

a primary outcome variable. Another study cited in the WHO & PAHO (138) report, the one by Caulfield et al. (23), also did not evaluate data on infant appetite for any of the 19 cohorts included in the study; nonetheless, the authors hypothesized that a delay in the introduction of complementary foods may be related to a preference for breastmilk over other foods/textures, thus creating an appetite preferential for milk in older children. Of the other references in the WHO & PAHO (138) report related to appetite, one (96) contains no reference to appetite. The other  $(112^2)$  utilized family interviews of 485 rural Senegalese children to explore why children were ultimately weaned before or after 2 years of age. The authors found that of the 120 mothers who continued to breastfeed for >2 years, the most cited reason for continued breastfeeding was that the child was perceived as "little and weak" (112, p. 478). In 59% of these cases, the mothers concurrently reported that the child had low or no appetite for family foods. Independently, low appetite for family foods was the second-most cited reason for breastfeeding for  $\geq 2$ years. The authors caution interpretation of their findings to suggest that prolonged breastfeeding causes reduced appetite, noting that reverse causality is possible. Similarly, Dettwyler (34) reported that mothers in Mali claimed that many children preferred breastmilk to other foods, would consume family foods only when they were extremely hungry, and in some instances completely refused to consume anything but breastmilk, even well after 1 year of age (34).

Brakohiapa and colleagues (15) evaluated 202 breastfed, Ghanaian infants and concluded that "prolonged breastfeeding adversely affects acceptance of food and thus nutritional status" (15, p. 417) and "when breastfed children who are over 12 months old show reluctance to take supplementary foods, they should be weaned completely to enhance their food intake" (15, p. 418). However, the authors provided no empirical data to support these claims. Similarly, Boediman and colleagues (11) reported comparable claims from Indonesian mothers, but again provided no supporting empirical evidence. Nonetheless, they concluded that weaning at 1 year is inappropriate but that solid foods should be offered prior to nursing infants after this time. Bentley and colleagues (9) evaluated acceptance of food in Peruvian children (n = 40, ages 4– 36 months) with diarrhea during the episode and during their recovery. Breastmilk offered in a 12-h period was negatively associated with appetite, whereas higher volumes of milk were associated with reduced appetite for other foods. Together, these studies suggest that maternal decisions related to duration of lactation are at least in part driven by child growth and appetite for other foods, although it is likely that these are multidirectional, complex interactions.

#### **Infant Infection Risk**

Substantial research has shown that breastfeeding in the first year of life reduces the risk of infant infection (71). However, what is the evidence that this protection continues with prolonged breastfeeding? In Guinea-Bissau, Mølbak and colleagues (89) evaluated the association between prolonged breastfeeding and the risk and duration of diarrhea in 849 infants <3 years of age; the median age of weaning was 22 months, and 25% of the children were still breastfed at 27 months. They found that weaned children had significantly more diarrheal episodes than children still receiving human milk after 1 year (relative risks were 1.41 and 1.67 in 1- and 2-year-old children, respectively). At 1 and 2 years of age, the duration of diarrheal episodes was 1 day longer in weaned children compared with those still breastfed. Children weaned between 16 and 19 months were at 2.55 times higher risk of increased diarrheal episodes in the 30 days following weaning compared with the 30 days before; this relationship was not present in children weaned at other ages. When all the weaned children were considered together, an increased risk of diarrhea in the month following weaning was found, compared with the month prior to weaning. Conversely, in 264 Kenyan infants (mean age at enrollment 14.1 months), there were no differences in infections or markers of infection (e.g., fever, low energy, low appetite, or upper respiratory tract infection)

<sup>&</sup>lt;sup>2</sup>The authors of the WHO & PAHO (138) report cited a 2001 paper by Simondon et al. (114) as evidence for mixed effects of prolonged breastfeeding on child appetite. This paper does not support this reference, and we believe it was cited in error. Rather, we believe the correct reference was a different 2001 paper by Simondon et al. (112), which does contain data on infant appetite and prolonged breastfeeding. The latter is discussed here.

among infants weaned at enrollment (n = 14), those who were weaned during the 6-month study period (n = 77), and those breastfed throughout the duration of the study (n = 173) (96).

Størdal and colleagues (118) also evaluated the relationship between breastfeeding duration and the risk of infant infection in Norwegian children  $\leq 18$  months of age. Compared with infants who received breastmilk for <6 months, those who were breastfed for  $\geq 1$  year were less likely to be hospitalized for any infection by 18 months of age. However, the risk of hospitalization in infants breastfed for  $\geq 1$  year was not different from that of those breastfed for 6 to 11 months. This relationship was similar for all infection types evaluated. Conversely, work by Gulick (52) in US infants did not find a relationship between the risk of infant illness and the duration of breastfeeding during the toddler period, although this study did not specify the age at which an infant becomes a toddler.

In summary, while an abundance of evidence exists regarding infectious outcomes as they relate to breastfeeding for  $\leq 1$  year, there is limited evidence related to similar impacts after 1 year. It is noteworthy that the paper cited in the 2003 WHO & PAHO (138) report related to the impact of prolonged breastfeeding on the risk of infant infection (20) did not evaluate breastfeeding for >1 year. Available evidence, therefore, allows no concrete conclusions to be made for a protective effect of breastfeeding for >1 year against infectious disease.

#### **Childhood Mortality**

The document (136) cited as evidence in the 2003 WHO & PAHO (138) report relating reduction in child mortality with prolonged breastfeeding also did not evaluate breastfeeding for >1 year. Nonetheless, there is limited evidence for such an association. For instance, while cause of death in breastfed children versus weaned children between 12 and 35 months of age did not differ, children who were not breastfed during this time experienced 2.6 times higher mortality than those who were breastfed (89). This risk increased to 3.5 times after researchers controlled for cofounding factors. This trend was independent of the age of wearing, but in this cohort >90% of the 849 children were still breastfed at 15 months. Similarly, in Bangladeshi children >18 months of age, those not breastfed during the month of evaluation were twice as likely to die than children who were breastfed (19). Relative risk of death associated with not breastfeeding was 22.1 in children with upper arm circumferences <111 mm, suggesting an interaction between feeding mode and chronic nutritional status in this regard. In this study, breastfed children were more likely to have larger upper arm circumferences than weaned children when adjusted for age, indicating that breastfeeding patterns may have played multiple roles in mediating child health and well-being. The same research group (18) also found that among similarly malnourished children matched for age (12–35 months; n = 1,087), the risk of dying was six times higher in nonbreastfed children compared with breastfed children. Importantly, the findings presented here are likely highly dependent on the specific environment and other context-specific variables; how translatable these findings are to other populations or environments, therefore, is unclear. In summary, while data are sparse, some evidence suggests that prolonged breastfeeding is associated with lower childhood mortality, at least in some contexts where malnutrition is common. To adequately address this, additional well-powered, case-control, longitudinal studies that collect specific breastfeeding and weaning data, and that follow children well into adolescence, would be needed. This area of research is perhaps the most critical of those identified in this review, given the potential impact of lowering childhood mortality on global child health and well-being.

#### Infant Gastrointestinal Microbiome

It is well established that myriad factors influence the development of an infant's gastrointestinal (GI) microbiome during the first 1,000 days of life (117). However, most studies have focused

on the infant's first year of life and were not designed to evaluate the impact of breastfeeding for >1 year. For example, in a study with 48 healthy Australian children, Matsuyama and colleagues (81) explored the association between a child's diet during the second year of life and the fecal microbiome. Although multiple associations between the children's dietary patterns and variation in the fecal microbiome were found, no strong relationships were observed with breastfeeding except at study commencement when children were 1 year of age. The authors suggest that after 1 year, consumption of other foods has a stronger effect on the fecal microbiome than does breastfeeding. Although they observed three bifidobacteria that clustered with human milk intake, there was no association with duration of breastfeeding beyond 1 year on overall fecal Bifidobacterium community structure. In The Environmental Determinants of Diabetes in the Young (TEDDY) study, three phases of infant GI microbiome progression were described: a developmental phase (3-14 months), a transitional phase (15-30 months), and a stable phase (31-46 months) (116). The authors found that breastfeeding was the most significant factor associated with the microbiome structure from 3 to 14 months. However, only 10% of infants continued breastfeeding after 14 months, making it difficult to evaluate the amount of variation in the fecal microbiome explained by breastfeeding. It was noted that Bifidobacterium was more dominant in breastfed infants than in nonbreastfed infants at all time points. In summary, data are limited with respect to the potential impacts of prolonged breastfeeding on the infant GI microbiome, and no broad conclusions can be made.

#### Infant Immunity, Including Asthma, Food Sensitization, and Leukemia

Human milk not only serves as an adaptive nutritional source for the growth needs of the infant but also provides an array of immunomodulatory components. Most studies directly related to infant immune development and breastfeeding duration are limited to examining the first 6 months postpartum. Nonetheless, here we attempt to evaluate changes in immune components in milk produced >1 year postpartum and critically evaluate existing evidence that prolonged breastfeeding is related to infant immune development.

**Immune components in milk.** There is consistency in the literature demonstrating increased concentrations of milk-borne immune components in late lactation, specifically secretory immunoglobulin A (sIgA), total IgA, lactoferrin, and lysozyme. For instance, Goldman and colleagues (48) investigated sIgA, lactoferrin, and lysozyme in milk produced by five women at 12, 13-15, and 16-24 months postpartum; they found that sIgA, IgA, and lactoferrin increased over time and lysozyme peaked at 13-15 months postpartum. The findings were supported by the work of Czosnykowska-Łukacka and colleagues (28), who demonstrated that milk produced by 116 mothers after 1 year had increased IgG and sIgA; concentrations were even higher after 2 years postpartum. The same research group demonstrated that lactoferrin concentration was lowest in the first year postpartum and increased until 18 months postpartum before leveling off (29). While we could identify no studies specifically examining the association between milk's immune composition and infant immune development or immunocompetence, and these types of studies are nearly impossible to conduct for ethical reasons, it is interesting to speculate on the relationship between these changes and the immunological dependence of the infant. Nonetheless, breastfeeding for >1 year continues to provide children with immunological support, although it remains unclear what level of protection this would provide in the older, more developed child. Additional research is needed to understand putative relationships among breastfeeding duration (especially >1 year), immune development, and immunocompetence in the infant.

**Respiratory outcomes, eczema, and atopy.** Demonstrating the categorical aggregate inconsistencies within the literature, data from two cohorts (Swedish and Australian) originally reporting

conflicting results were methodologically harmonized and reevaluated to determine the relationship between breastfeeding duration and wheezing at 4–5 and 8 years of age. Brew and colleagues (17) expanded upon the previous analyses by utilizing six categories for the duration of breastfeeding (<1, 1–4, 4–7, 7–10, 10–13, and >13 months) instead of the two utilized previously (<3 versus >3 months, or <6 versus >6 months). They found that longer breastfeeding duration was associated with lower asthma risk in early childhood: Every additional 3 months was positively associated with reduced risk. However, this effect was greater in the Swedish cohort (in which breastfeeding duration was longer and infants were recruited from the general population) compared with the Australian cohort (which comprised infants with a family history of asthma). It is also important to note the highest category of breastfeeding duration was >13 months, and therefore little extrapolation can be made on the protective effects beyond one year.

A dose-response relationship between breastfeeding duration and respiratory outcomes was also examined by Silvers and colleagues (111), who reported that each additional month of breastfeeding was associated with a 7–8% reduction of risk of asthma and wheezing in New Zealand infants at 15 months of age. In this large cohort (n = 987), approximately one-third of infants were still breastfeeding at 1 year; however, no further delineation of breastfeeding duration was examined or can be determined, and therefore examinations of protective effects beyond 1 year are limited. Of interest is that this study showed that the duration of exclusive breastfeeding was a stronger predictor of respiratory illness than the duration of any breastfeeding, but the researchers found no association with breastfeeding (exclusive or duration) and risk of eczema or atopy at 15 months. Watanabe and colleagues (133) reported that, compared with a duration of breastfeeding of <10 months, durations of 10–14, 14–19, and >19 months were inversely associated with asthma in a Japanese cohort. However, the odds ratios were very similar across the groups with durations of >10 months (0.69, 0.73, and 0.67, respectively). Unfortunately, the authors did not statistically compare the odds ratios among these longer-duration groups.

One case-control study (100) conducted in India examined wheezing as a primary outcome. Cases were defined as children who presented with wheezing or received a nebulizer treatment; a family history of asthma was not reported for cases or controls. Infants breastfed for <1 year had a higher incidence of wheezing than did controls; it was not until breastfeeding duration was >1 year that the protective effects of breastfeeding associated with a lower risk of wheezing were demonstrated. Infants breastfed for 2 years had an even lower incidence of wheezing. In summary, while studies are limited, the literature seems to support a protective effect of breastfeeding for >1 year in relation to some respiratory outcomes. Further studies are needed, especially in low-to middle-income countries where the prevalence and severity of asthma are increasing.

**Food allergies.** The protective effect of breastfeeding on the development of food allergies remains controversial, and only one study that examined this relationship was identified. van Ginkel and colleagues (125) found that each additional month of breastfeeding was associated with a reduced risk of clinical food allergies to any food by  $\sim 4\%$ . Of note, out of 492 participants, only 48 (9.8%) reported breastfeeding for >1 year. This study reported a higher prevalence of bovine milk allergy among infants breastfed for >1 year compared with formula-fed infants, but this association was confounded by atopy in the mothers, suggesting the possibility of reverse causation whereby atopic mothers purposefully breastfeed their infants for longer.

**Leukemia.** Childhood leukemia is the most common cancer in children and is intimately associated with infant immune development, although its etiology remains largely unknown. Rudant and colleagues (108), reporting results from a retrospective study conducted in France, found that compared with no breastfeeding, breastfeeding for >1 year was associated with a 40% lower risk of acute lymphoblastic leukemia but was not protective against acute myeloblastic leukemia. A marked increase in the risk of acute myeloblastic leukemia was seen in infants breastfed for 6-11 months compared with those breastfed for >12 months. Breastfeeding for >12 months provided an additional 10% reduction in the risk of acute lymphoblastic leukemia compared with breastfeeding for 6-11 months. To our knowledge, this is the only study available evaluating the association of breastfeeding duration for >1 year and immune-related cancers in children.

#### **Prolonged Breastfeeding and Dental Caries**

The relationship between prolonged breastfeeding and dental caries has been the subject of considerable recent debate. Adding to this controversy, in 2018 the British Society of Paediatric Dentistry (14) published a recommendation that women who continue to breastfeed their infants after 1 year of age work closely with their health practitioners to minimize the risk of dental decay and consider reducing on-demand and nighttime feedings. The society also recommended that after 1 year of age, the last breastfeeding session of the day take place before toothbrushing so that the last substance on the child's teeth before bedtime is fluoridated toothpaste. Although this continues to be a highly charged issue, a review of the topic by Branger et al. (16) (see the sidebar titled Prolonged Breastfeeding and Dental Health) concluded that breastfeeding beyond 1 year of age is associated with an increased risk of caries and that breastfeeding until 2 years is associated with a greater severity of caries in primary teeth, independent of sugar consumption. Nonetheless, the authors concluded that it is nearly impossible to assess causality in the currently published studies because none has adequately controlled for confounding factors. A similar conclusion was reached by Tham et al. (121).

#### Childhood Overweight/Obesity

Pediatric overweight/obesity is a growing international public health crisis. Not only are overweight and obese children more likely to be obese as adults, but obesity is also strongly correlated with other chronic diseases (e.g., diabetes). Breastfeeding is considered protective against obesity, as breastfed children generally have a decreased incidence of obesity when compared with formula-fed children (145). While most studies have focused on the first 6 months, several research groups have examined obesity in the context of prolonged breastfeeding and identified an inverse relationship between longer overall breastfeeding and decreasing incidence of overweight/obesity in pediatric populations. For example, in a German cohort (n = 2,108; mean age 9.6 years), Liese et al. (75) found that longer breastfeeding duration was associated with a lower risk of being overweight. Compared with nonbreastfed children, children breastfeed for 6 months to >1 year were less likely to be overweight. A subanalysis of 1,754 children who were never breastfeed showed an

#### PROLONGED BREASTFEEDING AND DENTAL HEALTH

In its 2018 position paper, the British Society of Pediatric Dentistry (14) called for (*a*) high-quality research designed to assess the relationship between prolonged breastfeeding and dental caries risk, controlling for confounding factors, and (*b*) reconsideration by the World Health Organization to revise their guidelines on breastfeeding to consider the relative importance of continued breastfeeding beyond 1 year in developing versus developed nations. Largely because development of early childhood caries represents a multifaceted infectious disease and risks of prolonged breastfeeding must be weighed against benefits, these recommendations were challenged by a variety of organizations. This remains a highly charged debate, as reviewed by Branger and colleagues (16). even stronger association. Compared with children breastfed for <6 months, children breastfed for >1 year were considerably less likely to be overweight, suggesting a dose-response-like pattern for the relationship between breastfeeding duration and risk of overweight.

In a US cohort (n = 12,587; mean age 4 years), Grummer-Strawn & Mei (51) found that breastfeeding for  $\geq 1$  year was associated with a decreased prevalence of overweight. As did Liese et al. (75), they found that the duration of breastfeeding showed a dose-response-like protective relationship. However, this effect was largely confounded by race/ethnicity and, when stratified by race/ethnicity, the protective effect of breastfeeding was limited to Caucasian, non-Hispanic children.

Fallahzadeh et al. (44) examined the association between breastfeeding for >1 year and the risk of obesity in a cohort of 800 Iranian children (mean age 12.1 years). Compared with children breastfed for <1 year, and after adjusting for age, sex, gravida, and parental education, those breastfed for 12–23.9 months had a similar risk of becoming obese, but those still breastfed at 2 years were 44% less likely to become obese. An important limitation of this study is that it did not control for diet and physical activity in the children. In a Kenyan cohort (n = 1,443; mean age 3.8 years), Gewa (47) also found that, compared with children breastfed for <1 year (and after adjusting for SES, maternal body mass index, birth weight, and child's current stunting status), children breastfed for 1–2 years were not at lower risk for overweight/obesity, but those breastfed for >2 years were 45% less likely to be overweight/obese.

Taken together, several (but not all) studies have demonstrated that prolonged breastfeeding may be associated with a decreased risk of childhood overweight/obesity. However, this appears to vary by race/ethnicity and population. A limitation of this body of literature is that almost all studies failed to capture or account for the intake of human milk, the exclusivity of breastfeeding, and the child's typical overall diet and activity level.

#### Prolonged Breastfeeding, Cognition, and School Success

Breastfeeding is largely considered beneficial for cognitive development and education attainment (4, 128), and many milk-borne nutrients and biologically active factors (e.g., docosahexaenoic acid) have been proposed as important mediators of this relationship. Nursing at the breast (as opposed to receiving human milk from a bottle) may also provide benefits (97). Less is known about the relationship between prolonged breastfeeding and cognitive development and/or educational attainment, although a small number of studies support the general finding that breastfeeding is beneficial. In a Filipino cohort (n = 1,984), Daniels & Adair (30) found that prolonged breastfeeding was associated with improved cognitive development. Using a nonverbal intelligence test of fluid abilities (i.e., children were tasked with discriminating differences among five pictures on a set of 100 cards) administered at 8.5 and 11.5 years of age, they compared children of both healthy and low birthweights that breastfed for 0 to 6 months with those breastfed for 6–12 months, 12–18 months, 18–24 months, and  $\geq$ 2 years. Overall, the mean scores were 51.4 at 8.5 years of age and 69.1 at 11.5 years of age. In a model adjusted for various parental and SES factors, breastfeeding for 12-18 months was associated with increases in nonverbal intelligence test scores of 1.6 and 9.8 points at 8.5 years of age in healthy and low birthweight children, respectively. While no significant association was observed for breastfeeding for 18-24 months or  $\geq$ 2 years in healthy birthweight children, improved cognitive development was observed in low birthweight children breastfed for 18-24 months (6.6-point increase) and >2 years (7.1-point increase). In both healthy and low birthweight children, the beneficial association with prolonged breastfeeding remained at 11.5 years of age, although mostly weakened, with improved cognitive development observed only in healthy birthweight children breastfed for 12 to <18 months

(1.4-point increase, a decrease of 0.2 points from 8.5 years of age). In a Brazilian population-based birth cohort (n = 3,493), Victora et al. (127) found that, compared with children breastfed for <1 month, children breastfed for  $\geq$ 12 months had higher intelligence quotient scores (3.76 points) and education attainment at 30 years of age after adjusting for confounders. Conversely, Horta & Victora (57) conducted a pooled meta-analysis of five global birth cohorts (n = 10,082) and found no association between prolonged breastfeeding and educational attainment in any cohort, although prolonged breastfeeding was positively associated with completion of  $\geq$ 12 years of school. In summary, prolonged breastfeeding may be associated with improvements in cognition and education attainment during childhood and extending into adulthood. However, while a lack of controlling for confounders remains plausible, differences in cognition have been observed on the basis of the extent of prolonged breastfeeding, which should be further explored.

#### EVIDENCE FOR IMPACT OF PROLONGED BREASTFEEDING ON MATERNAL HEALTH OUTCOMES

In addition to providing acute and long-lasting benefits to infants, breastfeeding also impacts maternal health. For instance, breastfeeding immediately after birth helps a woman recover from the process of childbirth (106). Lactation also inhibits ovulatory activity and thus fertility, although the duration of postpartum anovulation varies greatly (39, 66, 84). Risks of some cancers are lower in women who breastfeed (64, 85, 134, 146), and although data are mixed, there is some evidence that breastfeeding modulates weight loss during the immediate postpartum period (38, 40). Most of the research on the impacts of breastfeeding on maternal health, however, focuses on what can be considered the dichotomous nature of breastfeeding and/or investigates dose-response associations between the duration of exclusive breastfeeding or any breastfeeding during the first year postpartum. Here, we evaluate the literature as it relates to the association between prolonged breastfeeding and maternal health and well-being.

#### **Maternal Body Weight**

With obesity an international health crisis and the well-documented association between parity and obesity risk, there is substantial interest in determining whether prolonged breastfeeding can help women maintain healthy body weights. Conversely, in some low-resource settings, repeated pregnancies can lead to maternal depletion-particularly when they overlap with breastfeeding (87). In these cases, there is a concern that prolonged lactation might exacerbate maternal undernutrition. In a study conducted by Mazariegos and colleagues (83), the relationship between breastfeeding duration and long-term body weight was evaluated in 75,421 Mexican women. For each live birth, the study participants reported if they had breastfed and the duration of breastfeeding. The total number of months of breastfeeding reported was divided by the number of live births to estimate the mean duration of lactation for each child. Important covariates, such as gestational weight gain, diet, and physical activity, were controlled for. Data suggest that, compared with women who did not breastfeed, those who breastfed for  $\sim$ 3–6 months per child had a modest but significantly lower weight gain. Additional months of breastfeeding, however, were not associated with additional weight loss or gain. Similar findings were reported by Dewey and colleagues (38), who studied relatively healthy, matched cohorts of US women who breastfed for <3 months (n = 39) or >1 year (n = 46).

In contrast, Adair & Popkin (1) studied 375 rural and 1,245 urban lactating Filipino women who were generally malnourished. Women were studied 2 years following parturition. For the urban women, each 100 days of breastfeeding was associated with a loss of 0.117 kg of body weight over the 2-year period. For rural women, the negative impact of lactation began to accrue after  $\sim$ 13.5 months postpartum; women who breastfed for 2 years lost an average of 1.0 kg. Older women in both urban and rural settings were at increased risk of weight loss with prolonged breastfeeding and were less likely than younger women to replenish their energy reserves over the period of the study.

In summary, data suggest that prolonged breastfeeding either does not impact maternal body weight or might exacerbate maternal depletion in chronically malnourished women. However, it is possible that reverse causality (i.e., women living in regions of chronic malnutrition purposefully breastfeed for longer periods of time) might be at least in part driving the latter relationship.

#### Maternal Bone Health

Lactation represents a homeorhetic period during which calcium absorption, usage, and excretion are systematically shifted to support milk production (8), with secretion of 240–320 mg of calcium into milk daily during peak lactation (70, 103). As such, it is reasonable to assume that lactation might lead to higher risk of bone loss, osteopenia, and osteoporosis, and some but not all studies support this assumption (e.g., 2, 49, 72), although it appears that bone remineralization occurs somewhat successfully after weaning (101). However, most studies on this topic do not examine the relationship between prolonged breastfeeding and maternal bone health. Nonetheless, Gur et al. (53) evaluated the association of cumulative breastfeeding duration (as opposed to duration of breastfeeding per child) and bone mass in 509 postmenopausal, osteoporotic Turkish women. They compared bone mineral density in several locations among women who never breastfed, breastfed for <96 months, or breastfed for  $\geq$ 96 months. Overall, they found that bone mineral density at the trochanter site was highest in women who never breastfed; those women who breastfed for  $\geq$ 96 months (~19 months of breastfeeding per child) had lower bone mineral density at this site than those who breastfed for <96 months. Among the oldest women (60–80 years), breastfeeding duration was inversely correlated with bone mineral densities of the spine and Ward's triangle.

In a study of 1,486 postmenopausal Turkish women, Dursun and colleagues (41) reported that women who had breastfed (cumulatively) for <1 year had higher lumbar spine bone mineral density than those who had breastfed (cumulatively) for 1-2 years, 2-5 years, and >5 years. Similar results were found for femoral neck bone mineral density. They concluded that their data suggest a possible negative impact of long-term breastfeeding as a risk factor for postmenopausal osteoporosis. Okyay and colleagues (95) studied 542 Turkish women and found that those who had, on average, breastfed each of their children for >1 year had the highest risk for osteoporosis (odds ratio 12.92).

Conversely, Feldblum and colleagues (46) explored whether breastfeeding duration was related to bone density in 352 relatively healthy, postmenopausal US women (40–54 years). Participants were categorized as having never breastfed, having breastfed for 1–11 months, or having breastfed for  $\geq$ 1 year. After adjusting for age at first lactation and recentness of the last lactation, they found no consistent trends in bone mineral density related to having breastfed for >1 year. In a study of 501 postmenopausal Turkish women, Cavkaytar et al. (24) also found no clear relationship between prolonged breastfeeding and risk of osteopenia or osteoporosis. Rojano-Mejía et al. (107) also studied the association between cumulative duration of breastfeeding and risk of osteoporosis in 567 postmenopausal Mexican mestizo women and found similar risk in women breastfeeding for a total of >3 years (roughly equivalent to 10 months/child) and those breastfeeding for a total of >4 years (about 14 months/child).

In summary, although data are conflicting and studies do not always characterize the duration of breastfeeding in a way that allows direct translation into prolonged breastfeeding, there is some evidence for a negative association between prolonged breastfeeding and maternal bone health. It should be noted that inadequate dietary consumption of calcium does not appear to drive lactation-related bone loss, and calcium supplementation during this period might have unintended negative impacts on overall maternal calcium homeostasis and bone health (102). As such, more research is needed to understand the complex interaction among diet, lactation, and bone health, including an appreciation for the likely importance of maternal vitamin D status (32). These studies should include and evaluate important contextual variables such as chronic and acute calcium and vitamin D consumption, seasonality, maternal physical activity patterns, and breastfeeding intensity beyond 1 year of life.

#### Lactational Amenorrhea, Anovulation, and Interbirth Intervals

Myriad studies have found that breastfeeding duration lengthens lactational amenorrhea (LA) (e.g., 12, 58, 143). However, women display tremendous heterogeneity in breastfeeding behavior and LA duration (132, 142). Cultural norms for postpartum sexual behavior, contraceptive use, maternal nutrition, infant supplementation, breastfeeding structure, parity, and health are also likely contributors to LA duration, but such factors are difficult to tease apart (58, 132, 142).

Understanding the factors that influence the relationships among breastfeeding duration, LA, and IBI in women breastfeeding for >1 year suffers additional challenges. Frequently, studies focus on the transition period from full breastfeeding ( $\leq 6$  months) to 12 months postpartum. Studies that report LA data beyond 1 year postpartum often condense data, present broad summaries, and leave associations between breastfeeding and LA beyond 1 year to be inferred from 12-month data and/or visually interpreted from figures. Additionally, these studies are frequently conducted in rural populations, have small sample sizes, and do not simultaneously collect behavioral observations on nursing behavior, nutritional data, social norms/behaviors, and biomarkers, which would allow findings that address the biosocial nature of LA. Therefore, here, we provide a broad review of the trends in LA and IBI studies and brief overviews of studies that have investigated proximate factors contributing to variation in postpartum infertility in women who breastfeed for >1 year.

Lactational amenorrhea. Studies conducted on natural fertility populations were among the first to call attention to the relationship between breastfeeding and LA and provided early evidence of behavioral impacts on maternal physiology (reviewed in 12). For instance, Konner & Worthman (69) studied 17 !Kung mother-infant dyads and concluded that the !Kung breastfeeding pattern suppressed ovarian function through a prolactin-meditated effect of frequent nipple stimulation. However, as shown by similar studies on breastfeeding and LA (e.g., 135), other proximate factors are also likely contributors to LA duration (e.g., nutrition) (69). Numerous additional studies, although frequently lacking biomarker or behavioral data, continued to identify an association between prolonged breastfeeding and LA duration (e.g., 60, 73). For instance, Bongaarts & Potter (12) indicated in their review that mean/median LA duration exceeded 12 months in populations with breastfeeding durations of >18 months.

A more recent effort to understand the role that LA serves in regulating fertility has focused on the metabolic load hypothesis, which integrates nursing intensity and maternal nutrition to assess maternal energetic stress (123, 124). Valeggia & Ellison (123) found that well-nourished Toba women (n = 113) resumed menses following a period of positive energy balance, a finding that helps to explain why comparable nursing-intensive populations can have substantial differences in LA duration.

**Interbirth interval.** Breastfeeding beyond 1 year is also repeatedly associated with longer IBIs. Jain & Bongaarts (63) performed a study utilizing data from the World Fertility Survey conducted with breastfeeding women in Bangladesh, Indonesia, Sri Lanka, Jordan, Peru, Guyana, Colombia,

and Panama and found that breastfeeding continues to be associated with increasing IBI into the second and third year postpartum. Mattison et al. (82) conducted a study in Kilimanjaro, Tanzania, in which they specifically tested whether breastfeeding beyond 2 years was associated with IBI, and their results indicated that children who breastfed for  $\geq 2$  years were significantly more likely to experience a longer IBI between their birth and their subsequent sibling's birth.

In summary, breastfeeding during the second year postpartum is associated with longer durations of LA, which in turn lengthens IBI and impacts fertility. As in studies focused primarily on earlier stages of lactation (142), evidence that breastfeeding structure, nursing intensity, and duration influence LA and fertility regulation continues to exist for women breastfeeding for >1 year. However, population and individual variations suggest that cross-cultural and individual factors play critical roles (115).

#### **Other Maternal Outcomes**

Despite anecdotal suggestion, we were unable to find scientific data regarding putative associations between prolonged breastfeeding and other maternal outcomes, such as effects on the maternal GI microbiome, chronic disease, risk of cancer, all-cause morbidity, immunity, and increased life expectancy. This lack of information highlights the need for such research to provide sciencebased evidence to make informed decisions and provide guidance for prolonged breastfeeding.

# SUMMARY OF EVIDENCE FOR A BENEFIT OF PROLONGED BREASTFEEDING

Here, we have summarized the data within the framework of that used in the 2003 WHO & PAHO (138) document, in addition to emerging evidence for health impacts of prolonged breastfeeding. With regard to the premise that human milk can contribute substantially to the nutrient (and energy) requirements of the infant, and acknowledging that milk does not represent sole-source nutrition for toddlers and volume varies greatly, there is solid evidence to support this rationale for prolonged breastfeeding. Nonetheless, whether the nutrients contributed by human milk are necessarily superior in terms of bioavailability or bioactivity (e.g., immune-related proteins such as lactoferrin) to those available from other foods is unclear. Moreover, in the situation of breastfeeding/pregnancy overlap, there might be a negative impact on milk consumption by the younger child. The importance of prolonged breastfeeding for provision of nutrients in humans likely depends on the availability of nutritious weaning and/or complementary foods and also on their accessibility and safety. This also raises relevant concerns when the intent is not to wean breastfeed children but to complement human milk intake at various ages.

In the 2003 WHO & PAHO (138) report, prolonged breastfeeding was also justified as providing benefits during periods of childhood illness, although the cited reference (20) does not actually evaluate breastfeeding for >1 year in this regard. Nonetheless, several research teams (e.g., those mentioned in 89) have provided evidence that prolonged breastfeeding is associated with decreased child mortality, despite the fact that prolonged breastfeeding is often associated with reduced child growth and inconsistent effects on infectious disease. The potential importance of provision of human milk, as opposed to the avoidance of contaminated food and water common in areas where hygiene is difficult and clean water unavailable, is also notable and requires further study. Moreover, emerging data (e.g., 128), although inconsistent (e.g., 57), support a relationship between prolonged breastfeeding and improvements in cognition and education attainment during childhood and possibly into adulthood. This line of research also warrants further investigation to determine if these relationships hold true across the SES spectrum and are not better explained by confounders.

For the mother, substantial research supports an association of prolonged breastfeeding with reduced maternal fertility and increased birth spacing, although the physiologic mechanisms underpinning this effect are unclear. If lower fertility and increased birth spacing are desired, these effects appear to be a clear benefit of breastfeeding for >1 year. However, the potential negative impacts on maternal depletion and bone health, particularly in chronically undernourished women, should be further investigated.

In evaluating the published literature related to whether prolonged breastfeeding impacts maternal and infant health, it is important to consider both the mother and the infant and objectively weigh benefits against possible risks coupled with the real possibilities of confounding and reverse causality complicating the interpretation of study findings. Indeed, as described by Grummer-Strawn (50), the potential for an external factor (e.g., poverty) to cause both prolonged breastfeeding and an outcome of interest (e.g., infant malnutrition) may lead to spurious correlations in observational studies. As such, and because conducting controlled intervention studies would be wholly unethical, research in this area must account for these confounders. Child feeding decisions, such as whether to continue breastfeeding beyond 1 year, can also be driven by child size, growth, and overall health. This reality can result in reverse causality unless longitudinal data (including qualitative data assessing caregiver decision making) are simultaneously evaluated. In addition, there are likely important interactions among duration of breastfeeding, cultural norms, and SES on health outcomes in both mothers and infants. As such, it is possible that effects seen in some locations would be different from those expected in others. Clearly, there is no one-size-fitsall guidance regarding the optimal duration of breastfeeding. Nonetheless, this topic is of great importance to both public health and public interest, and guidance based on the current state of the science should be provided to populations and families as much as possible.

#### LIMITATIONS OF AVAILABLE STUDIES

The most pressing limitation related to available evidence examining the impact of prolonged breastfeeding on maternal/infant health is the inadequate nature of the available literature specifically and rigorously examining these associations. In addition, it is to be expected that these relationships vary by context, with different outcomes anticipated on the basis of location and culture. To our knowledge, no multicohort studies have examined the interactions among prolonged breastfeeding, population, and maternal and/or infant health. Prospective studies that adequately collect data regarding relevant biological, abiotic, environmental, and psychosocial confounders are needed to evaluate whether breastfeeding beyond 1 year impacts maternal and/or infant health. These studies should be designed in such a way that adequate sample sizes of maternal-infant dyads who continue to breastfeed after 1 year postpartum are included. When possible, researchers should collect and analyze milk for its nutritional and immunologic components so that contributions to the child's diet and immune competence can be evaluated; evaluate overall maternal and infant nutrient consumption; and quantify anthropometric, biochemical, and clinical indices of maternal and infant nutritional status. Qualitative data should be longitudinally collected to help elucidate maternal decision-making patterns related to continuation and discontinuation of breastfeeding, including availability and affordability of other age-appropriate, hygienic, and nutritious food sources. These studies should encompass, if possible, multiple cohorts representing different socioeconomic and cultural realities.

#### **DISCLOSURE STATEMENT**

The authors are not aware of any affiliations, memberships, funding, or financial holdings that might be perceived as affecting the objectivity of this review.

#### ACKNOWLEDGMENTS

Although there was no funding obtained specifically for this article, the authors would like to acknowledge the following funding mechanisms, which provided us with funding during the time period in which this article was written: the National Institutes of Health (R01HD092297), the Bill and Melinda Gates Foundation (INV-016943), the National Science Foundation (IOS-BIO 2031753 and 2031715), and the USDA National Institute of Food and Agriculture (Hatch project IDA01643).

#### LITERATURE CITED

- Adair LS, Popkin BM. 1992. Prolonged lactation contributes to depletion of maternal energy reserves in Filipino women. *J. Nutr.* 122(8):1643–55
- Aloia JF, Vaswani AN, Yeh JK, Ross P, Ellis K, Cohn SH. 1983. Determinants of bone mass in postmenopausal women. Arch. Intern. Med. 143(9):1700–4
- 3. Am. Acad. Pediatr. 2012. Breastfeeding and the use of human milk. Pediatrics 129(3):e827-41
- Anderson JW, Johnstone BM, Remley DT. 1999. Breast-feeding and cognitive development: a metaanalysis. Am. J. Clin. Nutr. 70(4):525–35
- Aune D, Norat T, Romundstad P, Vatten LJ. 2014. Breastfeeding and the maternal risk of type 2 diabetes: a systematic review and dose-response meta-analysis of cohort studies. *Nutr. Metab. Cardiovasc. Dis.* 24(2):107–15
- Bailey KV. 1965. Quantity and composition of breastmilk in some New Guinean populations. J. Trop. Pediatr. Afr. Child Health 11(2):35–49
- Banik ND. 1975. Breast feeding and weaning practices of pre-school children in urban community in Delhi. *Indian Pediatr.* 12(7):569–74
- Bauman DE, Currie WB. 1980. Partitioning of nutrients during pregnancy and lactation: a review of mechanisms involving homeostasis and homeorhesis. *J. Dairy Sci.* 63(9):1514–29
- Bentley ME, Stallings RY, Fukumoto M, Elder JA. 1991. Maternal feeding behavior and child acceptance of food during diarrhea, convalescence, and health in the central Sierra of Peru. Am. J. Public Health 81(1):43–47
- Blankhart DM. 1962. Measured food intakes of young Indonesian children. J. Trop. Pediatr. Afr. Child Health 8(1):18–21
- Boediman D, Ismail D, Iman S, Ismangoen Ismadi SD. 1979. Composition of breast milk beyond one year. J. Trop. Pediatr. Environ. Child Health 25(4):107–10
- 12. Bongaarts J, Potter RG. 1983. Fertility, Biology, and Behavior: An Analysis of Proximate Determinants. New York: Academic
- Bowatte G, Tham R, Allen KJ, Tan DJ, Dai X, et al. 2015. Breastfeeding and childhood acute otitis media: a systematic review and meta-analysis. *Acta Paediatr: Suppl.* 104(467):85–95
- 14. Br. Soc. Paediatr. Dent. 2018. Position statement on infant feeding. Br. Soc. Paediatr. Dent., London
- Brakohiapa LA, Bille A, Quansah E, Kishi K, Yartey J, et al. 1988. Does prolonged breastfeeding adversely affect a child's nutritional status? *Lancet* 2(8608):416–18
- Branger B, Camelot F, Droz D, Houbiers B, Marchalot A, et al. 2019. Breastfeeding and early childhood caries. Review of the literature, recommendations, and prevention. *Arch. Pediatr.* 26(8):497–503. Erratum. 2020. *Arch Pediatr.* 27(3):172
- Brew BK, Kull I, Garden F, Almqvist C, Bergström A, et al. 2012. Breastfeeding, asthma, and allergy: a tale of two cities. *Pediatr. Allergy Immunol.* 23(1):75–82
- Briend A, Bari A. 1989. Breastfeeding improves survival, but not nutritional status of 12–35 months old children in rural Bangladesh. *Eur. J. Clin. Nutr.* 43(9):603–8
- Briend A, Wojtyniak B, Rowland MG. 1988. Breastfeeding, nutritional state, and child survival in rural Bangladesh. Brit. Med. J. 296(6626):879–82
- Brown KH, Stallings RY, de Kanashiro HC, Lopez de Romaña G, Black RE. 1990. Effects of common illnesses on infants' energy intakes from breast milk and other foods during longitudinal communitybased studies in Huascar (Lima), Peru. Am. J. Clin. Nutr. 52(6):1005–13

- 21. Butte NF. 2001. The role of breastfeeding in obesity. Pediatr. Clin. N. Am. 48(1):189-98
- 22. Butte NF, King JC. 2005. Energy requirements during pregnancy and lactation. *Public Health Nutr*. 8(7A):1010–27
- 23. Caulfield LE, Bentley ME, Ahmed S. 1996. Is prolonged breastfeeding associated with malnutrition? Evidence from nineteen demographic and health surveys. *Int. J. Epidemiol.* 25(4):693–703
- Cavkaytar S, Seval MM, Atak Z, Findik RB, Ture S, Kokanali D. 2015. Effect of reproductive history, lactation, first pregnancy age and dietary habits on bone mineral density in natural postmenopausal women. *Aging Clin. Exp. Res.* 27(5):689–94
- Chowdhury R, Sinha B, Sankar MJ, Taneja S, Bhandari N, et al. 2015. Breastfeeding and maternal health outcomes: a systematic review and meta-analysis. *Acta Paediatr. Suppl.* 104(467):96–113
- Cousens S, Nacro B, Curtis V, Kanki B, Tall F, Traore E, et al. 1993. Prolonged breastfeeding: no association with increased risk of clinical malnutrition in young children in Burkina Faso. *Bull. World Health Org.* 71(6):713–22
- Czosnykowska-Łukacka M, Królak-Olejnik B, Orczyk-Pawiłowicz M. 2018. Breast milk macronutrient components in prolonged lactation. *Nutrients* 10(12):1893
- 28. Czosnykowska-Łukacka M, Lis-Kuberka J, Królak-Olejnik B, Orczyk-Pawiłowicz M. 2020. Changes in human milk immunoglobulin profile during prolonged lactation. *Front. Pediatr.* 8:428
- Czosnykowska-Łukacka M, Orczyk-Pawiłowicz M, Broers B, Królak-Olejnik B. 2019. Lactoferrin in human milk of prolonged lactation. *Nutrients* 11(10):2350
- Daniels MC, Adair LS. 2005. Breast-feeding influences cognitive development in Filipino children. J. Nutr. 135(11):2589–95
- Davis MK. 2001. Breastfeeding and chronic disease in childhood and adolescence. *Pediatr. Clin. N. Am.* 48(1):125–42
- 32. Dawodu A, Zalla L, Woo JG, Herbers PM, Davidson BS, Heubi JE, Morrow AL. 2014. Heightened attention to supplementation is needed to improve the vitamin D status of breastfeeding mothers and infants when sunshine exposure is restricted. *Matern. Child Nutr*: 10(3):383–97
- Delgado C, Matijasevich A. 2013. Breastfeeding up to two years of age or beyond and its influence on child growth and development: a systematic review. *Cad. Saúde Pública* 29(2):243–56
- Dettwyler KA. 1987. Breastfeeding and weaning in Mali: cultural context and hard data. Soc. Sci. Med. 24(8):633–44
- Dewey KG. 2001. Nutrition, growth and complementary feeding of the breastfed infant. *Pediatr: Clin.* N. Am. 48(1):87–104
- Dewey KG, Brown KH. 2003. Update on technical issues concerning complementary feeding of young children in developing countries and implications for intervention programs. *Food Nutr. Bull.* 24(1):5–28
- Dewey KG, Finley DA, Lönnerdal B. 1984. Breast milk volume and composition during late lactation (7–20 months). *J. Pediatr: Gastroenterol. Nutr.* 3(5):713–20
- Dewey KG, Heinig MJ, Nommsen LA. 1993. Maternal weight-loss patterns during prolonged lactation. Am. J. Clin. Nutr. 58(2):162–66
- Díaz S, Cárdenas H, Brandeis A, Miranda P, Salvatierra AM, Croxatto HB. 1992. Relative contributions of anovulation and luteal phase defect to the reduced pregnancy rate of breastfeeding women. *Fertil. Steril.* 58(3):498–503
- 40. Dugdale AE, Eaton-Evans J. 1989. The effect of lactation and other factors on post-partum changes in body-weight and triceps skinfold thickness. *Br. J. Nutr.* 61(2):149–53
- Dursun N, Akin S, Dursun E, Sade I, Korkusuz F. 2006. Influence of duration of total breast-feeding on bone mineral density in a Turkish population: Does the priority of risk factors differ from society to society? Osteoporos. Int. 17(5):651–55
- Elsom R, Weaver L. 1999. Does breastfeeding beyond one year benefit children? *Fetal Matern. Med. Rev.* 11(3):163–74
- 43. Emery Thompson M, Sabbi K. 2020. Evolutionary demography of the great apes. In *Human Evolutionary Demography*, ed. O Burger, RD Lee, R Sear. In press. https://osf.io/d2thj
- 44. Fallahzadeh H, Golestan M, Rezvanian T, Ghasemian Z. 2009. Breast-feeding history and overweight in 11 to 13-year-old children in Iran. *World J. Pediatr.* 5(1):36–41

- Fawzi WW, Herrera MG, Nestel P, Amin AE, Mohamed KA. 1998. A longitudinal study of prolonged breastfeeding in relation to child undernutrition. *Int. J. Epidemiol.* 27(2):255–60
- Feldblum PJ, Zhang J, Rich LE, Fortney JA, Talmage RV. 1992. Lactation history and bone mineral density among perimenopausal women. *Epidemiology* 3(6):527–31
- Gewa CA. 2009. Childhood overweight and obesity among Kenyan pre-school children: association with maternal and early child nutritional factors. *Public Health Nutr.* 13(4):496–503
- Goldman AS, Goldblum RM, Garza C. 1983. Immunologic components in human milk during the second year of lactation. *Acta Paediatr. Scand.* 72(3):461–62
- Goldsmith NF, Johnston JO. 1975. Bone mineral: effects of oral contraceptives, pregnancy, and lactation. J. Bone Joint Surg. Am. 57(5):657–68
- Grummer-Strawn LM. 1993. Does prolonged breast-feeding impair child growth? A critical review. Pediatrics 91(4):766–71
- Grummer-Strawn LM, Mei Z. 2004. Does breastfeeding protect against pediatric overweight? Analysis
  of longitudinal data from the Centers for Disease Control and Prevention Pediatric Nutrition Surveillance System. *Pediatrics* 113(2):e81–86
- 52. Gulick EE. 1986. The effects of breast-feeding on toddler health. Pediatr. Nurs. 12(1):51-54
- Gur A, Nas K, Cevik R, Sarac AJ, Ataoglu S, Karakoc M. 2003. Influence of number of pregnancies on bone mineral density in postmenopausal women of different age groups. *J. Bone Miner: Metab.* 21(4):234– 41
- Habicht JP. 2000. The association between prolonged breastfeeding and poor growth. In Short and Long Term Effects of Breast Feeding on Child Health, ed. B Koletzko, KF Michaelsen, O Hernell, pp. 193–200. New York: Kluwer Academic/Plenum Publishers
- 55. Hewlett BS. 1991. Demography and childcare in preindustrial societies. J. Anthropol. Res. 47(1):1-37
- Horta BL, de Mola CL, Victora CG. 2015. Breastfeeding and intelligence: systematic review and metaanalysis. Acta Paediatr: Suppl. 104(467):14–19
- 57. Horta BL, Victora CG. 2013. Short-term effects of breastfeeding: a systematic review of the benefits of breastfeeding on diarrhoea and pneumonia mortality. Rep., World Health Organ., Geneva
- Howie PW, McNeilly AS. 1982. Effect of breast-feeding patterns on human birth intervals. *Reproduction* 65(2):545–57
- 59. Hrdy SB. 2009. Mothers and Others: The Evolutionary Origins of Mutual Understanding. Cambridge, MA: Harvard University Press
- Huffman SL, Ford K, Allen HA Jr., Streble P. 1987. Nutrition and fertility in Bangladesh: breastfeeding and postpartum amenorrhoea. *Pop. Stud.* 41(3):447–62
- 61. Inst. Med. 2011. Early Childhood Obesity Prevention Policies. Washington, DC: Natl. Acad. Press
- Ip S, Chung M, Raman G, Chew P, Magula N, et al. 2007. Breastfeeding and maternal and infant bealth outcomes in developed countries. Evid. Rep. Technol. Assess. 153, U.S. Dep. Health Hum. Serv., Rockville, MD
- Jain AK, Bongaarts J. 1981. Breastfeeding: patterns, correlates, and fertility effects. Stud. Fam. Plan. 12(3):79–99
- John EM, Whittemore AS, Harris R, Itnyre J, Collab. Ovarian Cancer Group. 1993. Characteristics relating to ovarian cancer risk: collaborative analysis of seven U.S. case-control studies. Epithelial ovarian cancer in black women. *J. Natl. Cancer Inst.* 85(2):142–47
- Karra MV, Udipi SA, Kirksey A, Roepke JL. 1986. Changes in specific nutrients in breast milk during extended lactation. *Am. J. Clin. Nutr.* 43(4):495–503
- Kennedy KI, Rivera R, McNeilly AS. 1989. Consensus statement on the use of breastfeeding as a family planning method. *Contraception* 39(5):477–96
- Kent JC, Mitoulas L, Cox DB, Owens RA, Hartmann PE. 1999. Breast volume and milk production during extended lactation in women. *Exp. Physiol.* 84(2):435–47
- Konner M. 2016. Hunter-gatherer infancy and childhood in the context of human evolution. In *Childbood: Origins, Evolution, and Implications*, ed. CL Meehan, AN Crittenden, pp. 123–54. Santa Fe, NM: School for Advanced Research Press
- Konner M, Worthman C. 1980. Nursing frequency, gonadal function, and birth spacing among !Kung hunter-gatherers. Science 207(4432):788–91

- Kovacs CS, Kronenberg HM. 1997. Maternal-fetal calcium and bone metabolism during pregnancy, puerperium, and lactation. *Endocr. Rev.* 18(6):832–72
- Kramer MS, Kakuma R. 2012. Optimal duration of exclusive breastfeeding. *Cochrane Database Syst. Rev.* 2012(8):CD003517
- 72. Kritz-Silverstein D, Barrett-Connor E, Hollenbach KA. 1992. Pregnancy and lactation as determinants of bone mineral density in postmenopausal women. *Am. 7. Epidemiol.* 136(9):1052–59
- Labbok MH, Hight-Laukaran V, Peterson AE, Fletcher V, von Hertzen H, Van Look PF. 1997. Multicenter study of the lactational amenorrhea method (LAM): I. Efficacy, duration, and implications for clinical application. *Contraception* 55(6):327–36
- Lessen R, Kavanagh K. 2015. Position of the Academy of Nutrition and Dietetics: promoting and supporting breastfeeding. J. Acad. Nutr. Diet. 115(3):444–49
- Liese AD, Hirsch T, von Mutius E, Keil U, Leupold W, Weiland SK. 2001. Inverse association of overweight and breast feeding in 9 to 10-y-old children in Germany. Int. J. Obes. Relat. Metab. Disord. 25(11):1644–50
- 76. Mandel D, Lubetzky R, Dollberg S, Barak S, Mimouni FB. 2005. Fat and energy contents of expressed human breast milk in prolonged lactation. *Pediatrics* 116(3):e432–35
- Marlowe FW. 2003. A critical period for provisioning by Hadza men: implications for pair bonding. Evol. Hum. Behav. 24(3):217–29
- Marquis GS, Habicht JP, Lanata CF, Black RE, Rasmussen KM. 1997. Association of breastfeeding and stunting in Peruvian toddlers: an example of reverse causality. *Int. J. Epidemiol.* 26(2):349–56
- Martin RM. 2001. Commentary: Does breastfeeding for longer cause children to be shorter? Int. J. Epidemiol. 30(3):481–84
- Matsumoto T. 2017. Developmental changes in feeding behaviors of infant chimpanzees at Mahale, Tanzania: implications for nutritional independence long before cessation of nipple contact. Am. J. Phys. Anthropol. 163(2):356–66
- Matsuyama M, Morrison M, Cao KL, Pruilh S, Davies PSW, et al. 2019. Dietary intake influences gut microbiota development of healthy Australian children from the age of one to two years. *Sci. Rep.* 9(1):12476
- Mattison SM, Wander K, Hinde K. 2015. Breastfeeding over two years is associated with longer birth intervals, but not measures of growth or health, among children in Kilimanjaro, TZ. Am. J. Hum. Biol. 27(6):807–15
- Mazariegos M, Ortiz-Panozo E, González de Cosío T, Lajous M, López-Ridaura R. 2020. Parity, lactation, and long-term weight change in Mexican women. *Matern. Child Nutr.* 16(3):e12988
- McNeilly AS, Tay CC, Glasier A. 1994. Physiological mechanisms underlying lactational amenorrhea. Ann. N. Y. Acad. Sci. 709:145–55
- McTiernan A, Thomas DB. 1986. Evidence for a protective effect of lactation on risk of breast cancer in young women. Results from a case-control study. Am. J. Epidemiol. 124(3):353–58
- Meehan CL, Quinlan R, Malcom CD. 2013. Cooperative breeding and maternal energy expenditure among Aka foragers. Am. J. Hum. Biol. 25(1):42–57
- Merchant K, Martorell R, Haas J. 1990. Maternal and fetal responses to the stresses of lactation concurrent with pregnancy and of short recuperative intervals. *Am. J. Clin. Nutr.* 52:280–88
- 88. Michaelsen KF. 1988. Value of prolonged breastfeeding. Lancet 2:788-89
- Mølbak K, Gottschau A, Aaby P, Højlyng N, Ingholt L, da Silva APJ. 1994. Prolonged breast feeding, diarrhoeal disease, and survival of children in Guinea-Bissau. *BMJ* 308(6941):1403–6
- Mølbak K, Jakobsen M, Sodemann M, Aaby P. 1997. Letters to the Editor: Is malnutrition associated with prolonged breastfeeding? Int. J. Epidemiol. 26(2):458–59
- Neville CE, McKinley MC, Holmes VA, Spence D, Woodside JV. 2014. The relationship between breastfeeding and postpartum weight change—a systematic review and critical evaluation. *Int. J. Obes.* 38(4):577–90
- 92. Neville MC, Allen JC, Archer PC, Casey CE, Seacat J, et al. 1991. Studies in human lactation: milk volume and nutrient composition during weaning and lactogenesis. *Am. J. Clin. Nutr.* 54(1):81–92
- Ng'andu NH, Watts TEE. 1990. Child growth and duration of breast feeding in urban Zambia. J. Epidemiol. Community Health 44(4):281–85

- Nubé M, Asenso-Okyere WK. 1996. Large differences in nutritional status between fully weaned and partially breastfed children beyond the age of 12 months. *Eur. J. Clin. Nutr.* 50(3):171–77
- Okyay DO, Okyay E, Dogan E, Kurtulmus S, Acet F, Taner CE. 2013. Prolonged breast-feeding is an independent risk factor for postmenopausal osteoporosis. *Maturitas* 74(3):270–75
- Onyango AW, Esrey SA, Kramer MS. 1999. Continued breastfeeding and child growth in the second year of life: a prospective cohort study in western Kenya. *Lancet* 354(9195):2041–45
- Pang WW, Tan PT, Cai S, Fok D, Chua MC, et al. 2020. Nutrients or nursing? Understanding how breast milk feeding affects child cognition. *Eur. J. Nutr.* 59(2):609–19
- Peres KG, Cascaes AM, Nascimento GG, Victora CG. 2015. Effect of breastfeeding on malocclusions: a systematic review and meta-analysis. *Acta Paediatr: Suppl.* 104(467):54–61
- Perrin MT, Fogleman AD, Newburg DS, Allen JC. 2017. A longitudinal study of human milk composition in the second year postpartum: implications for human milk banking. *Matern. Child Nutr*. 13(1):e12239
- Potharajula S, Kadke AK. 2019. Study of correlation between breast feeding and wheezing in children. Int. J. Contemp. Pediatr. 6(1):191–94
- Prentice A. 2003. Micronutrients and the bone mineral content of the mother, fetus and newborn. J. Nutr. 133(5 Suppl. 2):1693S–99S
- 102. Prentice A. 2011. Milk intake, calcium and vitamin D in pregnancy and lactation: effects on maternal, fetal and infant bone in low- and high-income countries. *Nestlé Nutr: Inst. Workshop Ser. Pediatr: Program* 67:1–15
- 103. Prentice A, Jarjou LM, Cole TJ, Stirling DM, Dibba B, Fairweather-Tait S. 1995. Calcium requirements of lactating Gambian mothers: effects of a calcium supplement on breast-milk calcium concentration, maternal bone mineral content, and urinary calcium excretion. Am. J. Clin. Nutr. 62(1):58–67
- 104. Prentice A, Paul AA. 1990. Contribution of breast-milk to nutrition during prolonged breastfeeding. In Breastfeeding, Nutrition, Infection and Infant Growth in Developed and Emerging Countries, ed. SA Atkinson, LA Hanson, RK Chandras, pp. 87–116. St. John's, Can.: ARTS Biomed. Publ. Distrib.
- 105. Reynolds A. 2001. Breastfeeding and brain development. Pediatr. Clin. N. Am. 48(1):159-72
- 106. Riordan J. 1993. Anatomy and psychophysiology of lactation. In *Breastfeeding and Human Lactation*, ed. J Riordan, KF Auerbach, pp. 81–104. Boston: Jones and Bartlett
- Rojano-Mejía D, Aguilar-Madrid G, López-Medina G, Cortes-Espinosa L, Hernández-Chiu MC, et al. 2011. Risk factors and impact on bone mineral density in postmenopausal Mexican mestizo women. *Menopause* 18(3):302–6
- Rudant J, Orsi L, Menegaux F, Petit A, Baruchel A, et al. 2010. Childhood acute leukemia, early common infections, and allergy: The ESCALE Study. Am. J. Epidemiol. 172(9):1015–27
- Sankar MJ, Sinha B, Chowdhury R, Bhandari N, Taneja S, et al. 2015. Optimal breastfeeding practices and infant and child mortality: a systematic review and meta-analysis. *Acta Paediatr.* 104(467):3–13
- Sellen DW, Smay DB. 2001. Relationship between subsistence and age at weaning in "preindustrial" societies. *Hum. Nat.* 12(1):47–87
- Silvers KM, Frampton CM, Wickens K, Epton MJ, Pattemore PK, et al. 2009. Breastfeeding protects against adverse respiratory outcomes at 15 months of age. *Matern. Child Nutr.* 5(3):243–50
- 112. Simondon KB, Costes R, Delaunay V, Diallo A, Simondon F. 2001. Children's height, health and appetite influence mothers' weaning decisions in rural Senegal. *Int. J. Epidemiol.* 30(3):476–81
- Simondon KB, Simondon F. 1998. Mothers prolong breastfeeding of undernourished children in rural Senegal. Int. J. Epidemiol. 27(3):490–94
- Simondon KB, Simondon F, Costes R, Delaunay V, Diallo A. 2001. Breast-feeding is associated with improved growth in length, but not weight, in rural Senegalese toddlers. *Am. J. Clin. Nutr.* 73(5):959–67
- Stallings JF, Worthman CM, Panter-Brick C. 1998. Biological and behavioral factors influence group differences in prolactin levels among breastfeeding Nepali women. Am. J. Hum. Biol. 10(2):191–210
- Stewart CJ, Ajami NJ, O'Brien JL, Hutchinson DS, Smith DP, et al. 2018. Temporal development of the gut microbiome in early childhood from the TEDDY study. *Nature* 562(7728):583–88
- Stinson L. 2020. Establishment of the early-life microbiome: a DOHaD perspective. J. Dev. Orig. Health Dis. 11(3):201–10

- Størdal K, Lundeby KM, Brantsæter AL, Haugen M, Nakstad B, et al. 2017. Breast-feeding and infant hospitalization for infections: large cohort and sibling analysis. *J. Pediatr. Gastroenterol. Nutr.* 65(2):225– 31
- Syeda B, Agho K, Wilson L, Maheshwari GK, Raza MQ. 2020. Relationship between breastfeeding duration and undernutrition conditions among children aged 0–3 years in Pakistan. *Inter. J. Pediatr. Adolescent. Med.* 8(1):10–17
- Taren D, Chen J. 1993. A positive association between extended breast-feeding and nutritional status in rural Hubei Province, People's Republic of China. Am. J. Clin. Nutr. 58(6):862–67
- 121. Tham R, Bowatte G, Dharmage SC, Tan DJ, Lau MX, et al. 2015. Breastfeeding and the risk of dental caries: a systematic review and meta-analysis. *Acta Paediatr.* 104(467):62–84
- Thorén A, Stintzing G, Michaelsen KF. 1988. Value of prolonged breastfeeding. *Lancet* 332(8614):788– 89
- Valeggia CR, Ellison PT. 2004. Lactational amenorrhea in well nourished Toba women of Argentina. *J. Biosoc. Sci.* 36(5):573–95
- 124. Valeggia CR, Ellison PT. 2009. Interactions between metabolic and reproductive functions in the resumption of postpartum fecundity. Am. J. Hum. Biol. 21(4):559–66
- 125. van Ginkel CD, van der Meulen GN, Bak E, Flokstra-de Blok BMJ, Kollen BJ, et al. 2018. Retrospective observational cohort study regarding the effect of breastfeeding on challenge-proven food allergy. *Eur. J. Clin. Nutr.* 72(4):557–63
- 126. Van Noordwijk MA, Kuzawa CW, Van Schaik CP. 2013. The evolution of the patterning of human lactation: a comparative perspective. *Evol. Anthropol. Issues News Rev.* 22(5):202–12
- 127. Victora CG, Bahl R, Barros AJ, França GV, Horton S, et al. 2016. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *Lancet* 387(10017):475–90
- 128. Victora CG, Horta BL, de Mola CL, Quevedo L, Pinheiro RT, et al. 2015. Association between breastfeeding and intelligence, educational attainment, and income at 30 years of age: a prospective birth cohort study from Brazil. *Lancet Glob. Health* 3(4):e199–205
- Victora CG, Huttly SR, Barros FC, Martines JC, Vaughan JP. 1991. Prolonged breastfeeding and malnutrition: confounding and effect modification in a Brazilian cohort study. *Epidemiology* 2(3):175–81
- Victora CG, Vaughan JP, Martines JC. 1984. Is prolonged breast-feeding associated with malnutrition? *Am. J. Clin. Nutr.* 39(2):307–14
- 131. Viseshakul D. 1976. Growth rate, feeding practices, and dietary intake of Thai infants under two years old in central Bangkok. *J. Hum. Nutr.* 30(2):71–78
- 132. Vitzthum VJ. 1994. Comparative study of breastfeeding structure and its relation to human reproductive ecology. *Am. J. Phys. Antbropol.* 37(S19):307–49
- 133. Watanabe JI, Tanaka K, Nagata C, Furukawa S, Arakawa M, Miyake Y. 2018. Breastfeeding duration is inversely associated with asthma in Japanese children aged 3 years. *J. Asthma* 55(5):511–16
- 134. Whittemore AS. 1993. Personal characteristics relating to risk of invasive epithelial ovarian cancer in older women in the United States. *Cancer* 71(2 Suppl.):558–65
- Wood JW, Lai D, Johnson PL, Campbell KL, Maslar IA. 1985. Lactation and birth spacing in highland New Guinea. *J. Biosoc. Sci. Suppl.* 9:159–73
- 136. World Health Organ. 2001. Infant and young child nutrition. World Health Organ., Geneva
- 137. World Health Organ. 2020. Breastfeeding. World Health Organ., Geneva. https://www.who.int/ maternal\_child\_adolescent/topics/child/nutrition/breastfeeding/en/
- 138. World Health Organ., Pan Am. Health Organ. 2003. Guiding principles for complementary feeding of the breastfed child. World Health Organ., Washington, DC
- 139. World Health Organ., U. N. Intl. Children's Emerg. Fund. 1998. Complementary feeding of young children in developing countries: a review of current scientific knowledge. World Health Organ., Geneva
- 140. World Health Organ., U. N. Intl. Children's Emerg. Fund. 2003. *Global strategy for infant and young child feeding*. World Health Organ., Geneva
- World Health Organ. Collab. Study Team Role Breastfeed. Prev. Infant Mortal. 2000. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet* 355(9202):451–55

- 142. World Health Organ. Task Force Methods Nat. Regul. Fertil. 1998. The World Health Organization multinational study of breast-feeding and lactational amenorrhea. I. Description of infant feeding patterns and of the return of menses. *Fertil. Steril.* 70(3):448–60
- 143. World Health Organ. Task Force Methods Nat. Regul. Fertil. 1998. The World Health Organization multinational study of breast-feeding and lactational amenorrhea. II. Factors associated with the length of amenorrhea. *Fertil. Steril.* 70(3):461–71
- 144. Yalçin SS, Yalçin S, Kurtuluş-Yiğit E. 2014. Determinants of continued breastfeeding beyond 12 months in Turkey: secondary data analysis of the Demographic and Health Survey. *Turkish J. Pediatr*: 56(6):581– 91
- 145. Yan J, Liu L, Zhu Y, Huang G, Wang PP. 2014. The association between breastfeeding and childhood obesity: a meta-analysis. *BMC Public Health* 14:1267
- 146. Yoo KY, Tajima K, Kuroishi T, Hirose K, Yoshida M, et al. 1992. Independent protective effect of lactation against breast cancer: a case-control study in Japan. Am. J. Epidemiol. 135(7):726–33