QUANTIFYING THE BENEFITS OF BREASTFEEDING: A SUMMARY OF THE EVIDENCE

Food and Nutrition Program/
Health Promotion and Protection Division
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Quantifying the Benefits of Breastfeeding: A Summary of the Evidence

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FOREWORD

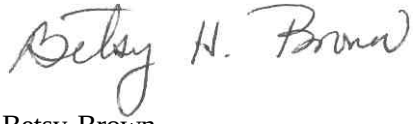
Each year new evidence contributes to our knowledge of breastfeeding's role in the survival, growth, and development of a child as well as the health and well-being of a mother. *Quantifying the Benefits of Breastfeeding: A Summary of the Evidence* provides scientific and epidemiological evidence in support of the World Health Organization's and UNICEF's Global Strategy for Infant and Young Child Feeding.

The Global Strategy for Infant and Young Child Feeding states, "Appropriate evidence-based feeding practices are essential for attaining and maintaining proper nutrition and health. Inappropriate feeding practices and their consequences are major obstacles to sustainable socioeconomic development and poverty reduction." The strategy calls on governments, civil society, and the international community "to renew their commitment to promoting the health and nutrition of infants and young children and to work together for this purpose."

As part of their commitment, the Pan American Health Organization (PAHO) and The LINKAGES Project—a 10-year breastfeeding program supported by the United States Agency for International Development (USAID)—collaborated in the development of this publication. Documentation of the evidence of breastfeeding's impact on health outcomes is particularly important at this time, when concerns about transmission of HIV through breastmilk threaten to erode support for breastfeeding programs. For the vast majority of infants and young children throughout the world, breastfeeding saves lives, prevents morbidity, promotes optimal physical and cognitive development, and reduces the risk of some chronic diseases. Evidence of the benefits of breastfeeding for mothers is growing as well.

We commend this publication to policy makers, program planners, breastfeeding advocates, researchers, and journalists. This summary of the evidence makes a powerful case for protecting, promoting, and supporting a life-saving resource that ensures the best start in life for newborns.

Sir George Alleyne
Director
Pan American Health Organization



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LIST OF ABBREVIATIONS AND ACRONYMS

ALL	acute lymphoblastic leukemia
ALRI	acute lower respiratory infection
AML	acute myeloid leukemia
AOM	acute otitis media
ARI	acute respiratory infection
BF	breastfeeding/breastfed
BMI	body mass index
CI	confidence interval
DTU	Diarrhoea Treatment Unit
EBF	exclusive breastfeeding/exclusively breastfed
FF	formula feeding/formula fed (includes nonbreastfed children)
GI	gastrointestinal
HI	*Haemophilus influenzae*
HPN	Food and Nutrition Program
HPP	Health Promotion and Protection
IDDM	insulin-dependent diabetes mellitus
IDR	incidence density ratio
MR	mortality rate
NCHS	National Center for Health Statistics
NIDDM	noninsulin-dependent diabetes mellitus
OM	otitis media
OME	otitis media with effusion
OR	odds ratio
PAHO	Pan American Health Organization
PBF	partial breastfeeding
RI	respiratory infection
RR	relative risk
SES	socioeconomic status
TSB	total serum bilirubin
UR	upper respiratory
USAID	United States Agency for International Development
WHO	World Health Organization

INTRODUCTION

This annotated bibliography summarizes the published literature on the following six topics related to the benefits of breastfeeding:

- Infant morbidity because of diarrhea, acute respiratory infections, otitis media and ear infections, and other infectious diseases
- Infant mortality because of diarrhea, acute respiratory infection, and all causes
- Child development
- Chronic diseases, particularly obesity, diabetes, and cancer
- Maternal health effects, with special emphasis on breast and ovarian cancers
- Economic benefits

Articles on the association between breastfeeding and health and developmental outcomes are reviewed with respect to four major criteria: 1) avoidance of detection bias and reverse causality through use of an adequate study design, 2) adequate control for confounding factors through statistical analysis, 3) clear definition of breastfeeding, and 4) clear definition of outcome measure(s). Articles are presented chronologically, with the most recent first.

Where sufficient quantitative data are available, tables summarizing the key findings are provided. These tables are available for topics relating to infant morbidity, infant mortality, child development, chronic diseases, and maternal health effects.

Search Methods

The databases Medline and Popline were searched between February 26 and March 6, 1997; between July 24 and August 3, 2001; and in January 2002 for keywords related to the six topics. These keywords, identified in italics for each topic, are as follows:

- Infant morbidity: *breastfeeding, lactation, diarrhea, acute respiratory infection, morbidity*
- Infant mortality: *breastfeeding, lactation, infant mortality*
- Child developmental and adult outcomes: *breastfeeding, lactation, cancer, intelligence, cognitive, motor development, diseases*
- Chronic diseases: *breastfeeding, lactation, obesity, diabetes, chronic diseases, cardio-vascular disease*
- Maternal health effects: *breastfeeding, lactation, maternal health, breast cancer, ovarian cancer, anemia, hemorrhage, maternal depletion*
- Economic benefits: *breastfeeding, lactation, economic benefits, health costs*

This search was limited to articles published in English and, except for the topics on the economic benefits of breastfeeding, to articles available in the Library of Medicine of the National Institutes of Health and on the Web. Because the searches identified few published articles on the economic and environmental benefits of breastfeeding, the review of these effects included unpublished papers.

The search strategy resulted in numerous articles, only some of which were relevant to the specific topic under investigation. For example, the search on infant mortality yielded 783 articles. To narrow the search, article titles and keywords were reviewed for relevance to the topic. In addition, where recent review articles were available, the references were checked against the search to ensure that all relevant articles were

identified. This review process often identified additional relevant literature. Ultimately, 188 articles were reviewed and are summarized here.

Epidemiological Methods

Evidence of the advantages of breastfeeding over alternatives comes from several main lines of research. One deals with the unique constituents and properties of human milk known to be important for optimal growth and development. Examples include nutrients in precisely the right form and balance for the infant and antibodies that are specific to the disease experience of the mother. Another line of research uses animal models to provide evidence that may be relevant to humans. Although the evidence provided by these lines of research can be extremely important in leading to new hypotheses and in helping to understand biological mechanisms, neither is reviewed here.

The line of research summarized in this review uses epidemiological methods to provide information on the functional consequences of breastfeeding human infants compared with alternative infant feeding methods.

In epidemiological research, the type of study that can offer the most conclusive evidence of a causal link between breastfeeding and any functional consequence of interest is the ***randomized controlled trial***, in which different feeding methods are randomly assigned to different infants, themselves randomly selected from the population of interest. Ethical objections aside, this type of study is almost never feasible for breastfeeding because few mothers are willing to accept random assignment of feeding method for their infants.

Most epidemiological evidence, therefore, comes from observational case-control and cohort studies. In ***case-control studies*** the infant feeding strategies of "cases" (infants with an illness or other problem) are compared with those of "controls" (infants without the problem). In ***cohort studies***, the outcomes of infants fed differently are compared instead of the infant feeding methods for infants with different outcomes. For obvious reasons, case-control studies tend to be retrospective and cohort studies prospective.

Although there are many variants of these basic observational designs, all are flawed by the mother's simple act of choosing an infant feeding method. As long as the feeding method is not randomly assigned, like placebos and real medicine in clinical trials, there is a good chance that other characteristics of the mother (such as her education or income) or of the infant (such as a pre-existing illness) are associated with the chosen method of infant feeding or may have actually caused it. Then it becomes difficult to know what is responsible for the association between breastfeeding and the outcome of interest.

For example, if more educated mothers tend to breastfeed, a positive association between breastfeeding and health or intellectual development may be due in part to the direct effect of the mother's education. In statistics this is known as ***confounding***.

Another example is the common observation that breastfed infants stop breastfeeding when they become very ill or are switched to an alternative method of feeding in an effort to make them better. In this case, the illness, or the death that eventually may result, is the cause rather than the consequence of not breastfeeding. This is known as ***reverse causality***.

In our assessment of these studies, frequent mention is made of confounding and reverse causality because these are always threats when observational methods are used. Although these threats can be reduced using statistical methods or more sophisticated

study designs, none of these methods is perfect. Therefore, no single study is as conclusive as a randomized controlled trial could be. However, as the epidemiological evidence favoring breastfeeding is generally derived from multiple studies in a variety of situations, the evidence is in sum, convincing.

Another line of support comes from being able to document a ***"dose-response" relationship***. This term, borrowed from clinical trials, refers to a relationship in which the response (say, the observed benefit of breastfeeding) is proportional to or appears to be a function of the dose (the amount, duration, exclusiveness, etc.). A dose-response relationship is taken to suggest a causal link between the dose and the response. The reviews provided here frequently identify dose-response relationships.

The Benefits of Breastfeeding

The work described here attests to the enormous benefits of breastfeeding in terms of infant health, intellectual and motor development, later chronic disease risk, and maternal health. As the research base expands, and as understanding of this subject grows, the superiority of breastfeeding over alternative feeding methods for all of these outcomes becomes ever clearer. These benefits come not at a price, but with additional economic benefits for the household, the health system, employers, and society.

Morbidity and Mortality

The greatest and most obvious benefits of breastfeeding are for the immediate health and survival of the infant. Rates of diarrhea, respiratory tract infections, otitis media, and other infections, as well as deaths due to these diseases, are all lower in breastfed than in nonbreastfed infants. During the first six months, the rates are lower for exclusively breastfed than for partially breastfed infants.

These benefits, resulting from stronger immunity and reduced exposure to infectious agents, are greatest in younger infants and where hygiene and sanitation are poor. However, the research described here also suggests that these health and survival benefits extend beyond infancy and to well-off Western populations.

Intellectual and Motor Development

Many studies reviewed here confirm that children who are breastfed do better on tests of intellectual and motor development than children who are not breastfed. When potential confounders are taken into account, these differences are often smaller but nevertheless persist, indicating that not all of the observed effect is due to confounding. The consistency of the observed differences across time and space and the observed dose-response relationship further suggest that this effect is real and has a biological basis.

Finally, although the mechanisms are not well understood, there are plausible biological explanations for a causal link between breastfeeding and intellectual development. Unlike breastmilk substitutes, breastmilk contains long-chain polyunsaturated fatty acids known to be important for brain growth and development. Both human and animal studies have documented a correlation between serum levels of these nutrients and test scores. The unique physical contact between mother and infant provided by breastfeeding also is thought to provide psychosocial stimulation and bonding that may have developmental benefits.

Chronic Diseases

Associations between infant feeding and a number of chronic or noncommunicable diseases have been observed in the literature reviewed here. These include allergies, obesity, diabetes, hypertension, cancer, and Crohn's disease. The small number of observational studies on any single outcome suggests cautious interpretation at this time. However, the broad range of chronic diseases that may be attributed to suboptimal breastfeeding, and the enormous impact of many of these conditions on health and the costs of medical care, suggest that more research along these lines is urgently needed. In the meantime, reduction of chronic disease risk can be promoted as an additional potential benefit of breastfeeding.

Maternal Health

Initiation of breastfeeding immediately after delivery stimulates the release of oxytocin, a hormone that helps to contract the uterus, expel the placenta, and reduce postpartum bleeding. Breastfeeding also delays the return of fertility, thus reducing exposure to the maternal health risks associated with short birth intervals. In the longer term, mothers who breastfeed tend to be at lower risk of premenopausal breast cancer and ovarian cancer.

Economics

The analyses reviewed here show clearly that apart from being the safest and healthiest infant feeding method, breastfeeding is also the least expensive. For many poor households, the prohibitive cost of breastmilk substitutes puts this option completely out of reach. For others, the impact of formula purchases on the household budget can be crippling. This is especially true when the unanticipated additional cost of health care for the sick infant takes its toll.

When the cost of medical care is borne by the health system or insurers, the economic impact is felt at that level. When infant illness requires mothers to miss work, employers and the economy are also affected. Although the economic costs of not breastfeeding generally are considered to be greatest for poor households and poor countries, the evidence summarized here suggests that the impact in developed countries is also serious.

1. EFFECT OF BREASTFEEDING ON MORBIDITY

The published literature on breastfeeding's effect on infant morbidity is summarized below. Papers described cover diarrheal, respiratory, ear, and other infections among breastfed and non-breastfed infants.

1.1 Effect of Breastfeeding on Diarrheal Morbidity

Kramer MS, Chalmers B, Hodnett ED, et al. Promotion of Breastfeeding Intervention Trial (PROBIT): A randomized trial in the Republic of Belarus. JAMA 2001;285(4):413–20.

COUNTRY: Belarus

SETTING: Urban and rural

DESIGN: Multicenter randomized control trial using cluster randomization

BREASTFEEDING DEFINITION: Exclusively breastfed (EBF) if child received no solids, non-breastmilk or water, or other liquids for 3-6 months; predominantly breastfed (PBF) if child received no solids or non-breastmilk; juices, water, teas, and other liquids were permitted in this category

OUTCOME MEASURE: The primary outcome measure was the risk of ≥ 1 episode of gastrointestinal (GI) tract infection. The secondary outcomes included risk of ≥ 2 episodes of respiratory tract infection, atopic eczema, ≥ 2 episodes of recurrent wheezing, ≥ 2 upper respiratory (UR) tract infections, prevalence of breastfeeding at 3, 6, 9, and 12 months, and prevalence of EBF and PBF at 3 and 6 months.

RESULTS: The proportion of women EBF at 3 and 6 months was 7 and > 12 times higher, respectively, in the experimental group than in the control group. Furthermore, BF promotion significantly reduced the risk of GI tract infections by 40% and the occurrence of atopic eczema by 46%. No differences were observed regarding respiratory and UR tract infections between the intervention and control groups. It is worth pointing out that while there was 1 death due to sudden infant death syndrome in the intervention groups, there were 5 deaths in the control group ($p = 0.12$ by unpaired *t* test).

METHODOLOGICAL ISSUES: All children in the study received breastmilk for at least 3 months (including the control group infants). Adjusted odds ratios and 95% confidence intervals were used to report findings. Co-variates for multiple regression for the BF outcomes, as well as GI and respiratory tract infections and atopic eczema and other rashes, were included in the analyses.

Clemens J, Elyazeed RA, Rao M, Savarino S, Morsy BZ, Kim Y, et al. Early initiation of breastfeeding and risk of infant diarrhea in rural Egypt. Pediatrics 1999;104: e3.

COUNTRY: Egypt

SETTING: Rural

DESIGN: Prospective birth cohort of 198 infants through the first 6 months of life

BREASTFEEDING DEFINITION: Exclusive breastfeeding if only breastmilk and no other liquids or foods, partial breastfeeding if breastmilk constituted any portion of the child's

diet. Early initiation was defined as having initiated breastfeeding within the first 3 days of life, and late initiation was defined as initiating breastfeeding after the 3rd day of life.

OUTCOME MEASURE: Risk of diarrhea measured through twice-weekly home visits. Diarrhea was defined as 1) passage of 3 or more loose or liquid stools in any 24-hour period (for breastfed infants, this also required the mother to state that stools were different from normal), or 2) passage of at least 1 loose or liquid stool with visible blood in a 24-hour period. An episode of diarrhea was defined as having been bounded by 3 or more consecutive days without diarrhea.

RESULTS: The results showed that infants who initiated breastfeeding within the first 3 days of life had a 26% lower rate of diarrhea during the first 6 months of life (adjusted rate ratio 0.74, 95% CI: 0.56–0.98) compared with infants who initiated after 3 days. Timing of initiation of breastfeeding and diet at follow-up were independently predictive of the rate of diarrhea. Early initiation also was associated with a longer duration of exclusive breastfeeding. There was no relation between early initiation and risk of diarrhea in the second 6 months of life.

METHODOLOGICAL ISSUES: The authors recognized that early initiation is likely to be associated with a longer duration of exclusive breastfeeding, which is also predictive of reduced risk of diarrhea. Therefore, they examined the independent effect of each on the risk of diarrhea. They also controlled for many possible confounding factors, which is particularly important since maternal education is associated positively with early initiation and reduced risk of infant diarrhea.

Nacify AB, Abu-Elyazeed R, Holmes JL, et al. Epidemiology of rotavirus diarrhea in Egyptian children and implications for disease control. Am J Epidemiol 1999;150(7):770–7.

COUNTRY: Egypt

SETTING: Rural (Abu Homos and vicinity villages)

DESIGN: Prospective population-based study design of children < 3 years of age (n = 178) followed for 1 year

BREASTFEEDING DEFINITION: Any breastfeeding compared to no breastfeeding in children aged < 1 year or ≥ 1 year

OUTCOME MEASURE: Rotavirus diarrheal infection. A diarrhea day was defined as the occurrence of at least 3 nonformed stools in a 24-hour period. A diarrhea episode was defined as the duration of diarrhea after at least 3 consecutive days free from diarrhea. A rotavirus episode was defined as a diarrhea episode in which rotavirus was detected in fecal specimen.

RESULTS: Breastfeeding was significantly associated with the incidence of rotavirus diarrheal episodes in children aged < 1 year, but not in older children. The adjusted hazards ratio during the first year of life in infants receiving any breastmilk, compared to those who were not breastfed, was 0.30 (95% CI: 0.11–0.80), p = 0.02.

METHODOLOGICAL ISSUES: The analysis controlled for a variety of potentially confounding factors including season, household size, latrine availability, water source and maternal education.

Meremikwu MM, Asindi AA, Antia-Obong OE. The influence of breast feeding on the occurrence of dysentery, persistent diarrhoea and malnutrition among Nigerian children with diarrhoea. WAJM 1997;16(1):20–3.

COUNTRY: Nigeria

SETTING: Diarrhoea Treatment Unit (DTU) in Calabar

DESIGN: Case-control study of children with diarrhea attending the DTU (n = 1,133)

BREASTFEEDING DEFINITION: Breastfed or not breastfed

OUTCOME MEASURE: Persistent diarrhea defined as diarrhea lasting 14 or more days, dysentery defined as presence of blood in the stool, and underweight defined as weight lower than 2 standard deviations below the reference median (<-2 Z-scores)

RESULTS: Chi-square and Fisher's exact test were used to examine the relationship between morbidity and breastfeeding mode. No significant differences were found in the frequency of dysentery between breastfed and nonbreastfed children. Persistent diarrhea was significantly ($p < 0.05$) less common in breastfeeding children than in those who had stopped breastfeeding (0.4% and 1.9%, respectively). Similarly, underweight was significantly more prevalent in children who did not breastfeed than in those who did (49.6% and 35.9%, respectively).

METHODOLOGICAL ISSUES: Socioeconomic factors, such as income and maternal education, were not controlled for.

Scariati PD, Grummer-Strawn LM, Fein SB. A longitudinal analysis of infant morbidity and extent of breastfeeding in the United States. Pediatrics 1997;99:e5.

COUNTRY: United States

SETTING: Nationwide

DESIGN: Longitudinal data analysis: n = 2,615 mother-infant pairs, infants aged 2–7 months

BREASTFEEDING DEFINITION: Breastmilk only (100% breastmilk), mixed feeding (breast and formula milk), formula only (0% breastmilk). Mixed feeding was separated into high, middle and low mixed feeding, representing 89–99%, 58–88% and 1–57%, respectively, of feedings as breastmilk.

OUTCOME MEASURE: Episodes of diarrhea and ear infection

RESULTS: A dose-response association was found between breastfeeding and the development of diarrhea and ear infections. As the amount of breastmilk an infant received decreased, the risks for diarrhea and ear infection increased. When compared with exclusively breastfed infants, those fed only formula showed an 80% increase in the risk of developing diarrhea and a 70% increase risk of developing an ear infection.

METHODOLOGICAL ISSUES: Information on mode of infant feeding and health status was collected through mailed questionnaires at the time the infants were 2, 3, 4, 5, 6, and 7 months old. Diarrhea, but not ear infection, was predefined. Logistic regression was used to model the effect of co-variates on the odds of experiencing diarrhea and ear infection.

Mølbalk K, Jensen H, Ingholt L, Aaby P. Risk factors for diarrheal disease incidence in early childhood: A community cohort study from Guinea-Bissau. Am J Epidem 1997;146:273–2.

COUNTRY: Guinea-Bissau

SETTING: Peri-urban

DESIGN: Three-year cohort study of children < 4 years of age. N = 1,314 children from 301 randomly sampled households. The median follow-up period per child was 242 days. Weight and length were obtained at intervals of approximately 3 months. Information on child morbidity and feeding patterns was obtained by weekly household interviews.

BREASTFEEDING DEFINITION: 1. Exclusive breastfeeding versus partial breastfeeding versus no breastfeeding, 2. Partial breastfeeding versus no breastfeeding

OUTCOME MEASURE: Risk of diarrhea

RESULTS: Results of the bivariate analysis show that compared with exclusive breastfeeding, both partial breastfeeding and no breastfeeding are significant risk factors for diarrhea (rate ratio 1.23; 95% CI: 1.08–1.40 for partial breastfeeding and 1.62; 95% CI: 1.37–1.91 for no breastfeeding). In the multivariate analysis, only the comparison between exclusive breastfeeding and no breastfeeding was significant (rate ratio 1.34; 95% CI: 1.00–1.79). No breastfeeding was also a risk factor for persistent diarrhea. The authors note that breastfeeding also may be an effect modifier of other risk factors for diarrhea in that there was no association between breastfeeding and socioeconomic status or environmental variables or between maternal education and diarrhea as long as children were breastfed. In contrast, among weaned children, there were strong and independent associations among several socioeconomic, demographic, and environmental variables. The authors conclude that promotion of breastfeeding is a major preventive measure against diarrhea in developing countries.

METHODOLOGICAL ISSUES: Although the study was longitudinal, and diarrhea and breastfeeding practices were carefully defined, it is not clear that the sequential nature of the data was used to ensure that feeding practice always preceded the outcome of interest. The analysis did not include age-specific estimates.

Heinig MJ, Dewey KG. Health advantages of breast feeding for infants: A critical review. Nutr Res Rev 1996;9:89–110.

COUNTRY: U.S. and other industrialized countries

SETTING: Rural and urban

DESIGN: Review article of studies published since 1970

BREASTFEEDING DEFINITION: Variable depending on the study

OUTCOME MEASURES: Physiological and behavioral development, morbidity (acute infectious diseases, gastrointestinal disease, necrotizing enterocolitis, respiratory diseases, otitis media, bacteremia and meningitis, infant botulism, urinary tract infections, chronic illness, insulin-dependent diabetes mellitus, Crohn's disease and ulcerative colitis, childhood cancer, allergy), and mortality

RESULTS: This is a review of the literature on the association between infant feeding mode and a large number of outcome measures. Overall it found that breastmilk is associated with small though consistent differences in cognitive tests, diarrheal disease, lower respiratory disease, and otitis media. It found that breastfeeding may be associated with a number of other outcomes, but the evidence is incomplete. This is an excellent review with a comprehensive list of references on the relationship between breastfeeding and specific disease outcomes.

Mondal SK, Sen Gupta PG, Gupta DN, Ghosh S, et al. Occurrence of diarrhoeal disease in relation to infant feeding practices in a rural community in West Bengal, India. Acta Paediatr 1996;85:1159–62.

COUNTRY: India

SETTING: Rural

DESIGN: Community-based prospective study of 148 infants ages 0 to 2 years who were followed for 12 months

BREASTFEEDING DEFINITION: Exclusively breastfed, predominantly breastfed (includes water and water-based drinks), partially breastfed, not breastfed

OUTCOME MEASURES: Incidence of diarrhea
RESULTS: This prospective community-based study examined the relationship between diarrhea and infant feeding patterns. The results show that although most infants are breastfed for more than 1 year, the duration of exclusive breastfeeding is short. Study infants were divided into 2 groups: those who were breastfed exclusively for 4 months or more were termed "weaned late," and those infants other than exclusively breastfed were termed "weaned early." Infants who received complementary foods at or before the age of 3 months, termed "weaned early," had an incidence rate ratio for diarrhea of 3.02 (95% CI: 1.04–8.80). This shows that early complementary feeding (< 3 months) was associated with 3 times the risk of diarrhea.

METHODOLOGICAL ISSUES: The authors use the term, "weaned," to describe infants who are being fed complementary foods.

Bohler E, Aalen O, Bergstrom S, Halvorsen S. Breast feeding and seasonal determinants of child growth in weight in East Bhutan. Acta Paediatr 1995;84:1029–34.

COUNTRY: Bhutan

SETTING: Rural

DESIGN: Prospective cohort (n = 113) followed for 32 months

BREASTFEEDING DEFINITION: Partially breastfed versus not breastfed. Infant feeding practices were recorded monthly.

OUTCOME MEASURES: Incidence of diarrhea, respiratory tract infection, and weight gain. Only results related to diarrhea are reported here.

RESULTS: The relationship among breastfeeding practices, morbidity, and child nutritional status in relation to seasonal rainfall was studied in a cohort of 113 children who were followed monthly for 32 months. The analysis focused only on children from 12 to 36 months of age. Breastfeeding between 12 and 36 months of age was associated with reduced risk of diarrhea. The odds ratio was 0.51 (95% CI: 0.34–0.78). Breastfed children also gained significantly more weight during the monsoon season, and breastfeeding protected children against weight loss due to diarrhea. This is one of the few studies to show a protective effect of breastfeeding after infancy.

METHODOLOGICAL ISSUES: The authors did not provide socioeconomic characteristics of the families of breastfeeding versus nonbreastfeeding children, nor did they control for potentially confounding variables, which may have biased the results.

Dewey KG, Heinig MJ, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. J Pediatr 1995;126:696–702.

COUNTRY: United States

SETTING: Urban

DESIGN: Prospective: n = 45 breastfed infants and n = 41 formula fed infants followed for first 24 months of life

BREASTFEEDING DEFINITION: Human milk was the major form of milk for breastfeeding infants throughout the first year of life. The formula-fed group included infants who had never breastfed and infants who had breastfed < 3 months.

OUTCOME MEASURES: Respiratory infection, diarrhea, acute otitis media, other symptoms as measured by weekly maternal recall. Medical records were reviewed as well. Only those results pertaining to diarrhea are reported here. See Sections 1.2 and 1.3 for the study's other findings.

RESULTS: Statistical comparisons between groups were made for 2 12-month intervals (birth–12 months and 12–24 months). Incidence was calculated as the number of episodes per 100 days at risk. Prevalence was calculated as the number of days the child was ill during each interval. During the first year of life, the incidence of diarrhea was twice as high among formula-fed infants as among breastfed infants (adjusted incidence/100 days at risk = 0.14 for breastfed infants and 0.31 for formula-fed infants). Diarrheal morbidity during the second year of life did not differ between the 2 groups. The authors suggest that breastfeeding protects against diarrheal disease, even in affluent, highly educated populations.

METHODOLOGICAL ISSUES: Day care use was positively associated with both formula feeding and diarrheal disease and was controlled in the analysis. The data were analyzed conservatively with the child rather than each day of observation as the unit of analysis. Both breastfeeding and the outcome measures were clearly defined.

Al-Mazrou YY, Khan MU, Aziz KMS, Farag MK. Role of social factors in the prevalence of diarrhoeal diseases in under-five Saudi children. J Trop Pediatr 1995;41 (suppl 1):45–51.

COUNTRY: Saudi Arabia

SETTING: Urban/rural

DESIGN: Cross-sectional: n = 4,756 children < 5 years

BREASTFEEDING DEFINITION: Exclusively breastfed, breastfed and bottle-fed, bottle-fed only, other food only

OUTCOME MEASURE: Prevalence of diarrhea defined according to WHO criteria

RESULTS: The prevalence of diarrhea was 18.5%, 23.3%, 17.7%, and 13% for children exclusively breastfed, breastfed and bottle-fed, bottle-fed only, and receiving other food only, respectively. The prevalence of diarrhea is significantly higher in infants in the breastfeeding and bottle category than in the other categories.

METHODOLOGICAL ISSUES: The data are not adjusted for age, which is unfortunate, because breastfeeding practices and risk of diarrhea are age-related. Study does not control for socioeconomic status: the authors state that breastfeeding is more common among noneducated rural mothers, and most women who only bottle-fed are educated and employed. Thus there is the potential for large biases in reported associations because of confounding by age and socioeconomic status.

Long KZ, Wood JW, Gariby EV, Weiss KM, Mathewson JJ, de la Cabada FJ, et al. Proportional hazards analysis of diarrhea due to Enterotoxigenic Escherichia coli and breastfeeding in a cohort of urban Mexican children. Am J Epidem 1994;139:193–205.

COUNTRY: Mexico

SETTING: Urban

DESIGN: Prospective: n = 98 mother/infant pairs followed for the first 3–50 weeks of the infants' life

BREASTFEEDING DEFINITION: Exclusively breastfed, partially breastfed, not breastfed

OUTCOME MEASURES: Incidence and duration of diarrhea

RESULTS: Nonbreastfed infants fed only formula had an incidence of diarrhea more than 3 times higher than exclusively breastfed infants and twice as high as partially breastfed infants. Of particular interest is the finding that infants colonized with enterotoxigenic *Escherichia coli*-producing heat-labile toxin (LT-ETEC) have a lower risk of diarrhea when breastfed, specifically by the amount of pathogen-specific secretory antibody the infant is receiving per day via the mother's breastmilk, and by the provision of medicinal teas. The risk of LC-ETEC is associated with the introduction of high-carbohydrate weaning foods. This study shows that the introduction of complementary foods increases the risk of pathogen colonization, and that the symptomatic expression of infection depends on the amount of protective antibody the infant receives via breastmilk.

METHODOLOGICAL ISSUES: This is an excellent study that shows, through laboratory measures, that breastfeeding protects infants against diarrhea through 2 long-hypothesized mechanisms: 1) reduced risk of pathogens from contaminated complementary foods, and 2) the transfer of antibodies through breastmilk.

Mølbak K, Gottschau A, Aaby P, Hojlyng N, Ingholt L, de Silva APJ. Prolonged breast feeding, diarrhoeal disease, and survival of children in Guinea-Bissau. Br Med J 1994;308:1403–6.

COUNTRY: Guinea-Bissau

SETTING: Urban

DESIGN: Community-based cohort study (n=849) of children under 3 years of age

BREASTFEEDING DEFINITION: Exclusively breastfed, partially breastfed, weaned

OUTCOME MEASURES: Incidence and duration of diarrhea

RESULTS: Weaning was significantly associated with increased risk of diarrhea. Among children aged 12 to 24 months, the relative risk of diarrhea was 1.41 for weaned children (95% CI: 1.29–1.62), compared with children still being breastfed. The mean duration of diarrhea was also significantly longer in weaned children than in breastfed children (6.6 versus 5.3 days) ($p < 0.001$). Among children aged 24 to 36 months, the relative risk of diarrhea was 1.67 (95% CI: 1.29–2.15) for weaned children, compared with children still breastfed. A similar increase in risk of diarrhea was found when the rate and duration were compared 1 month before and 1 month after weaning for each child. These results, independent of age of weaning, show that the protective effect of breastfeeding on diarrhea is unlikely to be confounded by unknown factors associated with both infant feeding practices and risk of diarrhea. The longitudinal analysis also shows that children with low weight-for-age were breastfed longer than the better-nourished children ($p < 0.02$). Paired analysis showed no improvement in nutritional status after weaning. This finding suggests that mothers tend to wean poorly nourished children later than they do well-nourished children, and that the association between prolonged breastfeeding and poor nutritional status is explained by maternal behaviors regarding children who are doing poorly rather than a negative effect of breastfeeding on child growth.

METHODOLOGICAL ISSUES: This is one of the few studies to show a protective effect of breastfeeding on risk of diarrhea among children aged 12–36 months. It is methodologically strong in that it controls for potential confounding in the relationship between infant feeding practices and risk of diarrhea by conducting within-child analyses.

VanDerslice J, Popkin B, Briscoe J. Drinking-water quality, sanitation, and breastfeeding: Their interactive effects on infant health. Bull WHO 1994;72:589–601.

COUNTRY: Philippines

SETTING: Peri-urban

DESIGN: Prospective: data presented for first 6 months of life only, n = 2,355

BREASTFEEDING DEFINITION: 1) exclusively breastfed and breastfed with non-nutritive liquids, 2) mixed-fed, and 3) completely weaned

OUTCOME MEASURE: Diarrhea incidence and prevalence as assessed by maternal recall for previous 7 days

RESULTS: Using a large cohort followed prospectively, this study examined the effect of various feeding modes on risk of diarrhea. Only infants < 6 months of age are included in the present analysis. The infant feeding categories of exclusive breastfeeding and breastfeeding with only the addition of non-nutritive liquids are combined for the regression analysis. The authors hypothesize that the protective effect of breastfeeding is greatest when drinking water is contaminated and environmental sanitation is inadequate. The results show that exclusive breastfeeding and full breastfeeding with uncontaminated water were associated with the lowest risk of diarrhea. Supplementing breastfeeding infants with small amounts of contaminated water nearly doubled the risk of diarrhea, from 0.08 to 0.15. Full breastfeeding protected against diarrhea in communities with both good and bad sanitation; however, the magnitude of the effect was twice as high in areas of poor sanitation as in those with good sanitation.

METHODOLOGICAL ISSUES: Instrumental variables were used in the analysis to avoid the problem of endogeneity in the dependent variables. The results are consistent and biologically plausible with a dose-response in the relationship between degrees of breastfeeding and risk, and with infants in less clean environments deriving a greater benefit from breastfeeding.

Clemens J, Rao M, Ahmed R, et al. Breast-feeding and risk of life-threatening rotavirus diarrhea: Prevention or postponement? Pediatrics 1993;92:680–5.

COUNTRY: Bangladesh

SETTING: Rural

DESIGN: Case-control: cases (n = 102) infants and children < 24 months with clinically severe rotavirus diarrhea; controls (n = 2,587) were selected randomly from the community

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding measured at the time of presentation for care (cases) and at the time of visits to homes during surveys (controls)

OUTCOME MEASURE: Life-threatening rotavirus diarrhea defined as at least 3 loose or liquid stools passed in any 24-hour period, where fecal rotavirus was detected

RESULTS: This study examined the association between breastfeeding and the risk of life-threatening rotavirus diarrhea among infants/children younger than 24 months of age. No breastfeeding was used as the reference category for calculation of risk. Among infants, exclusive breastfeeding and partial breastfeeding were associated with reduced risk of life-threatening rotavirus diarrhea. The adjusted relative risk for exclusive breastfeeding was 0.06, suggesting that exclusive breastfeeding was associated with a 94% reduction in severe infection. Partial breastfeeding also was associated with reduced risk with an adjusted relative risk of 0.44. After adjusting for potentially confounding variables, the trend for increasing protection against severe rotavirus diarrhea in infants by feeding mode was significant and in the expected direction (exclusive breastfeeding >

breastfeeding > no breastfeeding). In the second year of life, breastfeeding was not associated with a protective effect. In fact, the relative risk for breastfeeding compared with no breastfeeding was elevated (relative risk = 2.85; 95% CI: 0.37–21.71), indicating increased risk among breastfed infants, but it failed to reach statistical significance because of the large confidence intervals surrounding the estimate. Because of this trend toward increased risk in the second year of life, there was no overall protective effect of breastfeeding in the first 2 years of life. The authors argue that breastfeeding may postpone the occurrence of severe rotavirus infection to a later age, and that breastfeeding may not have any overall effect on life-threatening rotavirus infection. Although the authors do not discuss this issue, it is important to consider the risk to the infant of a life-threatening infection in the context of infant age. Although breastfeeding may only delay the risk of infection, it is likely that the consequences of such an infection would be greater for a younger infant than for a toddler.

METHODOLOGICAL ISSUES: Almost all subjects in the study were breastfed, which may have limited statistical power to detect a significant protective effect in the second year of life. However, a posteriori calculations argue against insufficient power as an explanation. For example, the type II error of missing a true level of protection of only 10% (a relative risk of 0.9) was < 0.01. Life-threatening rotavirus infection appears to be rare and to constitute only a small proportion of total diarrheal cases.

Ahmed F, Clemens JD, Rao MR, Sack DA, Khan MR, Haque E. Community-based evaluation of the effect of breast-feeding on the risk of microbiologically confirmed or clinically presumptive shigellosis in Bangladeshi children. Pediatrics 1992;90(3):406–11.

COUNTRY: Bangladesh

SETTING: Matlab surveillance area

DESIGN: Case-control: cases (n = 269) were children < 3 years of age with culture-confirmed or clinically presumptive shigellosis; controls (n = 819) were children who lived near cases and presumably were exposed to the same pathogens but did not have shigellosis or other invasive diarrhea

BREASTFEEDING DEFINITION: Exclusive breastfeeding (which included fully breast-feeding children), partial breastfeeding, no breastfeeding

OUTCOME MEASURE: Risk of shigellosis

RESULTS: This study examined the effect of infant feeding mode on shigellosis. Any breastfeeding is strongly associated with the risk of disease. No breastfeeding is used as the reference category to calculate risk. The adjusted odds ratio for any breastfeeding was 0.48, which indicates that breastfeeding was associated with a 52% reduction in risk. The strength of the effect was greatest for infants and decreased with age, but was still significant during the 3rd year of life. For example, breastfeeding was associated with a reduction in risk of 90%, 60%, and 40% for infants aged 0–11 months, 12–23 months, and 24–35 months, respectively. Of particular importance was the finding that breastfeeding was associated with a significant protective effect against strains that were resistant to conventional antibiotic treatment (adjusted odds ratio 0.40). The protective effect of breastfeeding was also greater for children who were more stunted: (for Z-score

< -3.0, the adjusted odds ratio was 0.30). Overall, approximately two-thirds of the expected shigellosis episodes were apparently prevented by breastfeeding.

METHODOLOGICAL ISSUES: All controls were in close contact with a case child; hence, the association between breastfeeding and risk of disease is unlikely to be confounded by differences in exposure. Breastfeeding also was defined conservatively as any breastmilk. All odds ratios were adjusted for known potentially confounding factors.

Hossain MM, Radwan MM, Arafa SA, Habib M, DuPont Hl. Prelacteal infant feeding practices in rural Egypt. J Trop Pediat 1992;38:317–22.

COUNTRY: Egypt

SETTING: Rural

DESIGN: Prospective: n = 157 infants followed from birth to 12 months

BREASTFEEDING DEFINITION: The key independent variable in this study is prelacteal feeding, defined as the administration of any food or drink to the infant before the first breastfeed. Hence, infants are categorized according to prelacteal feeding status (prelacteals versus no prelacteals). The relationship between prelacteal status and breastfeeding practices is not presented clearly, which is an important limitation in that the negative effect of prelacteals on diarrhea may be through the effect of prelacteals on the subsequent mode of infant feeding. For example, the following two conflicting statements on this relationship are presented: 1) "Age specific prevalence of exclusive breastfeeding or partial breastfeeding did not differ significantly by prelacteal feeding status," and 2) "prelacteally-fed infants...were significantly less likely to be exclusive breastfeeding..."

OUTCOME MEASURE: Risk of diarrhea

RESULTS: Prelacteal feeding was associated positively though not statistically with diarrhea. Prelacteal feeding was negatively associated with exclusive breastfeeding in infants < 12 months, but had no effect on breastfeeding mode in infants 12–23 and 24–47 months. Although not significant, this study suggests that prelacteal feeding may have a negative effect on diarrhea independent of its relationship to infant feeding mode.

METHODOLOGICAL ISSUES: Small sample size may limit statistical power, and a posteriori type II error calculations were not performed. The relationship between prelacteal feeds and subsequent breastfeeding practices is not described clearly.

Morrow AL, Reves RR, West MS, et al. Protection against infection with Giardia Lamblia by breast-feeding in a cohort of Mexican infants. J Pediatr 1992;121:363–70.

COUNTRY: Mexico

SETTING: Urban

DESIGN: Prospective: n = 197 followed from birth to 18 months.

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding

OUTCOME MEASURE: Risk of *Giardia* infection

RESULTS: Breastfeeding was significantly associated with both symptomatic and asymptomatic *Giardia* infection. Compared to exclusively breastfed infants, partially breastfed infants had a risk ratio of 3, and infants who were not breastfed had a risk ratio of 5. Breastfeeding was not associated with the duration of *Giardia* infection. This article shows that breastfeeding is highly and negatively associated with risk of *Giardia* infection in a dose-response manner. However, once infection is established, breastfeeding is not associated with the severity of infection, as measured by duration of illness.

METHODOLOGICAL ISSUES: The study addressed the problem of reverse causality, controlled for other potentially confounding factors, and examined risk in relation to both first infection and all infections. Breastfeeding and outcome measures were clearly defined.

Ruuska T. Occurrence of acute diarrhea in atopic and nonatopic infants: The role of prolonged breast-feeding. J Pediatr Gastro Nutr 1992;14:27–33.

COUNTRY: Finland

SETTING: Urban

DESIGN: Prospective: n = 336 infants followed for a total of 717 child-years

BREASTFEEDING DEFINITION: 1) breastfeeding < 6 months; 2) breastfeeding 7–12 months; 3) breastfeeding 13–24 months

OUTCOME MEASURE: Episodes of diarrhea stratified by whether the child also had gastrointestinal allergy, atopic eczema, or was nonatopic

RESULTS: In this study, 83% of infants were breastfed for at least 3 months, and 71% were breastfed for 6 months. The incidence of diarrheal disease was relatively low. The effect of breastfeeding on risk of diarrhea was variable and associated with the atopic status of the child. Breastfeeding for more than 6 months was associated with reduced risk of diarrhea in the first year, with the effect being greater in nonatopic infants than in atopic infants. The authors report that during the second year of life, breastfeeding was associated with increased risk of diarrhea, so there was no overall effect on the incidence of diarrhea during the first 2 years of life. However, they do not show data to support this assertion.

METHODOLOGICAL ISSUES: This is a confusing study that does not control adequately for the time-dependent nature of the protective effect of breastfeeding on diarrhea. For example, the authors show that infants aged 0 to 6 months who are breastfed for more than 6 months have fewer episodes of diarrhea than infants who are breastfed for < 6 months. This analysis ignores the fact that infant feeding mode after 6 months cannot affect risk of diarrhea before 6 months.

Howie HP, Forsyth JS, Ogston SA, Clark A, du V Florey C. Protective effect of breast feeding against infection. Br Med J 1990;300:11–16.

COUNTRY: Scotland

SETTING: Community setting in Dundee

DESIGN: Prospective until 24 months of age (n = 674 mother/infant pairs)

BREASTFEEDING DEFINITION: Breastfeeding duration categorized as follows: 1) full breastfeeding (> 13 weeks with only water and juice, n = 97); 2) partial breastfeeding (> 13 weeks with addition of solids and/or formula, n = 130); 3) weaned early (< 13 weeks breastfeeding, n = 180); and 4) bottle feeders (n = 267).

OUTCOME MEASURE: Prevalence of gastroenteritis. See Section 1.2 for effect on respiratory infection.

RESULTS: The results show that, after adjustment for potentially confounding factors (social class, maternal age, and parental smoking), breastfeeding for 13 weeks or more was associated with a significantly reduced risk of diarrheal incidence in the intervals 14–26 weeks, 27–39 weeks, and 40–52 weeks. The effect during the 14–26 week interval was particularly strong, with a reduction in incidence of between 6.6% and 16.8%. Infants breastfeeding < 13 weeks had a rate of illness similar to that of bottle-fed infants. No effect of the timing of introduction of complementary foods on gastroenteritis was observed. This was one of the few studies to show that the protective effect of breastfeeding was maintained beyond the period of weaning.

METHODOLOGICAL ISSUES: This study adjusted for all known potentially confounding factors. Both breastfeeding and outcome measures were clearly defined. Multiple logistic regression was used to determine the relation of illness to several explanatory variables, and the logarithmic odds of disease incidence were expressed as a linear function of these variables.

Ketsela T, Asfaw M, Kebede D. Patterns of breast feeding in western Ethiopia and their relationship to acute diarrhoea in infants. J Trop Pediat 1990;36:180–3.

COUNTRY: Ethiopia

SETTING: Rural

DESIGN: Cross-sectional: n = 331 infants < 6 months of age, cluster sample at the community level

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding

OUTCOME MEASURES: Acute diarrhea

RESULTS: Exclusive breastfeeding compared with partial breastfeeding was associated with reduced risk of diarrhea in 2 of the 3 age intervals examined (2–4 and 4–6 months). The lack of effect between birth and age 2 months is due to the low prevalence of diarrhea in this age group. At 2–4 months of age, the relative risk of partially breastfed compared with exclusively breastfed infants was 5.42 (95% CI: 2.10, 14.1). At 4–6 months of age, the relative risk among partially breastfed compared with exclusively breastfed infants was 5.00 (95% CI: 1.53, 16.0).

METHODOLOGICAL ISSUES: This study does not control for reverse causality or potentially confounding factors, but it does control for age. Both breastfeeding and outcome measures are clearly defined.

Megraud F, Bourdraa G, Bessaoud K, Bensid S, Dabis F, Soltana R, et al. Incidence of Campylobacter infection in infants in Western Algeria and the possible protective role of breastfeeding. Epidemiol Infect 1990;105:73–8.

COUNTRY: Algeria

SETTING: Urban/rural

DESIGN: Case-control: cases (n = 411) are infants who presented at a clinic with diarrhea associated with campylobacter infection; controls (n = 217) are infants who came to the clinic for immunizations and did not have diarrhea in the previous 2 weeks

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding

OUTCOME MEASURE: Incidence of diarrhea associated with campylobacter infection

RESULTS: Exclusive breastfeeding compared with partial breastfeeding significantly protects infants < 6 months of age from campylobacter-related diarrhea. The odds ratio was 0.1, which suggests a 90% reduction in infection. Overall, the odds ratio for infants (< 12 month) was 0.3, which suggests a 70% reduction.

METHODOLOGICAL ISSUES: The authors state that only infants < 6 months were breastfed, which makes it impossible to study the role of breastfeeding in risk of campylobacter infection among older infants. Reverse causality was not addressed. Data were not adjusted for socioeconomic status. Controls were from a clinic setting rather than the community, which may limit the external validity of the study.

Popkin BM, Adair L, Akin JS, et al. Breast-feeding and diarrheal morbidity. Pediatrics 1990;86(6):874–82.

COUNTRY: Philippines

SETTING: Urban and rural, results presented separately

DESIGN: Prospective: n = more than 3,300 infants

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastmilk and non-nutritive liquids only, breastmilk and nutritive foods, no breastmilk

OUTCOME MEASURE: Risk of diarrhea

RESULTS: Risk of diarrhea was associated with infant feeding mode in both urban and rural samples. Exclusively breastfed infants were used as the reference category. Among urban infants < 6 months of age, breastfeeding with the addition of non-nutritive liquids only resulted in a relative risk of 2 to 3, or 2 to 3 times the risk of diarrhea (depending on the specific 2-month age interval). The use of nutritive foods with breastmilk resulted in a relative risk of 11 to 13 (depending on the specific 2-month age interval). Infants < 6 months of age who were not breastfed had a relative risk of 13 to 17 (depending on the age interval). Compared with exclusive breastfeeding, rural infants < 6 months of age

given non-nutritive liquids only in addition to breastmilk had a relative risk of about 2, or twice the risk of diarrhea. Infants < 6 months of age given breastmilk and nutritive foods had a relative risk of 4 to 6 (depending on the specific 2-month age interval). Infants < 6 months of age who were not breastfed had a relative risk of about 5. After 8 months of age, the association between infant feeding mode and diarrhea declined considerably. There was a slight protective effect of breastfeeding compared with no breastfeeding in urban areas only.

METHODOLOGICAL ISSUES: The prospective design addresses the problem of reverse causality, and numerous control variables were included to control for various biological and behavioral variables that affect susceptibility to illness and exposure to diarrheal pathogens (e.g., birth weight, weight velocity, sex, household use of soap, etc.). Breastfeeding and the outcome measure were clearly defined.

Rubin DH, Leventhal JM, Krasilnikoff PA, et al. Relationships between infant feeding and infectious illness: A prospective study of infants during the first year of life. Pediatrics 1990;85:464–71.

COUNTRY: Denmark

SETTING: Urban

DESIGN: Prospective for first year of child's life (n = 500). Of the monthly questionnaires mailed to mothers, the overall response rate was 73%. Mothers were blind to the study objectives.

BREASTFEEDING DEFINITION: 1) exclusive breastfeeding; 2) breastfeeding > formula feeding; 3) breastfeeding = formula feeding; 4) breastfeeding < formula feeding; and, 5) formula feeding only. The breastfeeding group was defined as categories 1 and 2 and the formula-feeding group as categories 3, 4, and 5.

OUTCOME MEASURE: Four outcome measures were used, one of which, gastroenteritis, pertains to diarrheal disease.

RESULTS: The authors used child-months of observation as the unit of analysis. After adjustment for major co-variates (birth weight, social class, number of children in the family, day care, other illnesses in the family), no significant relationships were found between infant feeding category and risk of gastroenteritis. The authors conclude that breastfeeding does not provide substantial protection against gastroenteritis during infancy in a middle-income population in a developed country.

METHODOLOGICAL ISSUES: Measurement error is a potential problem in this study, particularly with respect to the two mixed-feeding groups identified as "breast feeding > formula feeding" and "formula feeding > breast feeding." Infant feeding mode was based on maternal recall, and the potential for misclassification among mothers of mixed-fed infants is substantial. For the majority of the analyses, the formula-fed infants were grouped with the exclusively breastfed infants if they consumed more breastmilk than formula. Thus, misclassification may have biased the findings toward the null. The overall response rate was 73%, ranging from 92% at month 1 to 44% at month 12. Mothers were blind to the study objectives. Child-months were used as the unit of analysis without adjusting for within-child correlation.

Brown KH, Black RE, de Romana GL, de Kanashiro Hc. Infant-feeding practices and their relationship with diarrheal and other diseases in Huascar (Lima), Peru. Pediatrics 1989;83:31–40.

COUNTRY: Peru

SETTING: Urban

DESIGN: Prospective: n = 153 infants

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastfeeding and other liquids, breastfeeding and artificial milk, breastfeeding and solids, no breastfeeding

OUTCOME MEASURE: Risk of diarrhea, acute respiratory infection, and skin infections. Only those outcomes pertaining to diarrhea are reported here. See Sections 1.2 and 1.3 for other findings.

RESULTS: Risk of diarrhea was significantly associated with infant feeding mode in the expected direction. Exclusively breastfed infants were used as the reference category. Infants < 6 months of age given non-nutritive liquids only in addition to breastmilk had a relative risk of about 2. Infants < 6 months of age given breastmilk and artificial milk had a relative risk of 1.6 to 2.4 (depending on the specific 2-month age interval). Infants < 6 months of age given breastmilk and solids had a relative risk of 2.6 to 3.4 (depending on the specific 2-month age interval). Infants < 6 months of age who were not breastfed had a relative risk of 3.4 to 5.5 (depending on the age interval). Partial breastfeeding was also protective of diarrhea for infants 6–11 month, compared with infants who received no breastmilk. For this comparison, the relative risk for infants 6–8 months was 1.7, and for infants 9–11 months was 1.5.

METHODOLOGICAL ISSUES: The design addresses the problem of reverse causality. This study controlled for several biological and behavioral variables that affect susceptibility to illness and exposure to diarrheal pathogens. Breastfeeding and the outcome measures were well defined.

Jalil F, Karlberg J, Hanson LA, Lindblad BS. Growth disturbance in an urban area of Lahore, Pakistan related to feeding patterns, infections and age, sex, socio-economic factors and seasons. Acta Paediatr 1989;350:44–54.

COUNTRY: Pakistan

SETTING: Urban slum

DESIGN: Prospective: n = 910 infants followed every 3 months from birth to 24 months of age

BREASTFEEDING DEFINITION: Inadequate. "Age at weaning" was used to examine the relationship between infant feeding mode and morbidity. However, this term was never defined, and it cannot be determined whether this indicated the age at which other foods were introduced or when breastfeeding ceased.

OUTCOME MEASURE: Risk of diarrhea; however, diarrhea was not defined. See findings on acute respiratory infections in Section 1.2.

RESULTS: The study did not find an association between "age at weaning" and diarrheal morbidity.

METHODOLOGICAL ISSUES: Infant feeding mode was poorly defined. No definitions of upper or lower respiratory infections or of diarrhea were given.

Mahmood DA, Feachem RG, Huttly SRA. Infant feeding and risk of severe diarrhoea in Basrah City, Iraq: A case-control study. Bull WHO 1989;67(6):701–6.

COUNTRY: Iraq

SETTING: Urban

DESIGN: Case-control: cases (n = 597) were infants hospitalized with diarrhea at local health clinics; controls (n = 723) were infants brought in for routine immunizations with no recent history of hospitalization

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding. Breastfeeding practices were those prior to onset of illness.

OUTCOME MEASURE: Risk of hospitalization with diarrhea

RESULTS: Diarrhea was affected significantly by infant feeding mode. Exclusive breastfeeding was used as the reference category. Infants aged 2–3 months who were partially breastfed had a relative risk of 6.2, and infants who were not breastfed had a relative risk of 36.7. Infants aged 3–4 months who were partially breastfed had a relative risk of 2.9, and infants who were not breastfed had a relative risk of 23.8. Sterilization of bottles as opposed to no sterilization had no effect on hospitalization for diarrhea. Among older infants, partial breastfeeding was used as the reference category. The relative risk of hospitalization for nonbreastfed infants aged 6–7 months was 3.9. Among infants 8–11 months, there was no protective effect of breastfeeding.

This study also examined whether previous breastfeeding protected infants from diarrhea. Previous breastfeeding was defined in two different ways: 1) infants who had stopped breastfeeding 2 months before hospitalization, and 2) infants who had stopped breastfeeding within 2 months before hospitalization. Previous breastfeeding had no protective effect on hospitalization for diarrhea for either measure.

It was estimated that 60% of all cases of hospitalized diarrhea could be prevented if optimal infant feeding practices were observed (e.g., exclusive breastfeeding for all infants < 6 months of age and partial breastfeeding and food thereafter).

METHODOLOGICAL ISSUES: The study addressed the problem of reverse causality, controlled for a number of other potentially confounding variables, and calculated population attributable risk. Breastfeeding and outcome measures were clearly defined.

Campbell CE, Latham MC. Infant feeding and morbidity among poor migrant squatters in Hermosillo, Sonora, Mexico. Nutr Res Rev 1988;8:969–79.

COUNTRY: Mexico

SETTING: Rural

DESIGN: Prospective: n = 105 poor migrant women and infants < 8 months

BREASTFEEDING DEFINITION: Breasfed versus not breastfed; frequency of breastfeeding

OUTCOME MEASURE: Incidence of diarrhea as assessed by maternal recall for prior 2-week period

RESULTS: The study was divided into 3 rounds of data collection, 4 weeks apart. Regression analysis showed that any breastfeeding versus no breastfeeding was significantly associated with reduced risk of diarrhea illnesses only during the first round of data collection but that a higher frequency of breasfeeding was associated with reduced risk of diarrhea at all 3 rounds.

METHODOLOGICAL ISSUES: No clear definition of diarrhea or respiratory infection is provided. The data on risk of illness and infant feeding are not presented in a manner that permits the exact effect to be quantified. The analysis contolled for potentially confounding factors but not for reverse causality.

Oyejide CO, Fagbami AH. An epidemiologic study of rotavirus diarrhoea in a cohort of Nigerian infants: II Incidence of diarrhoea in the first two years of life. Int J Epidem 1988;17:908–12.

COUNTRY: Nigeria

SETTING: Urban

DESIGN: Prospective: n = 131 infants followed every 3 months from birth to 24 months of age

BREASTFEEDING DEFINITION: Inadequate, not well defined with respect to outcome measure

OUTCOME MEASURES: Incidence of acute diarrhea and rotavirus diarrhea, neither well defined

RESULTS: The focus of this study was to examine the epidemiology of rotavirus infection during the first 2 years of life. Information on breastfeeding appears to be secondary to the main focus of the study. The authors report that breastfeeding was common, but that exclusive breastfeeding was rare: within the first month of life, nearly 90% of infants also were being bottle-fed. No association between infant feeding mode and rotavirus infection was found. However, the breastfeeding definitions and methods used to test this association were not reported, making it difficult to assess the validity of the finding.

METHODOLOGICAL ISSUES: Infant feeding mode was poorly defined.

Unni JC, Richard J. Growth and morbidity of breast-fed and artificially-fed infants in urban South Indian families. J Trop Pediatr 1988;34:179–81.

COUNTRY: India

SETTING: Urban

DESIGN: Prospective (clinic based): n = 271 infants followed from birth to 22 weeks; however, only 60 infants completed the study

BREASTFEEDING DEFINITION: Group 1 = exclusive breastfeeding or breastfeeding 5 or more times per day; Group 2 = breastfeeding fewer than 4 times per day or artificially fed

OUTCOME MEASURES: Diarrheal morbidity

RESULTS: At 6 weeks, 2% of the exclusively breastfed (EBF) infants had diarrhea, compared with 24% of partially breastfed (PBF) infants. At 14 weeks, 0% of the EBF infants had diarrhea, compared with 7.5% of the PBF infants. The relationship between feeding mode and diarrhea was only significant at 6 and 14 weeks.

METHODOLOGICAL ISSUES: There is potential for a large degree of misclassification between infant feeding modes. No infants were exclusively breastfed; attrition was extremely high (only 60 of the 271 infants completed the study); and the study did not control for reverse causality or potentially confounding factors.

Clemens JD, Stanton B, Stoll B, Shahid NS, Banu H, Chowdhury AKML. Breastfeeding as a determinant of severity in Shigellosis. Amer J Epidemiol 1986;123(4):710–20.

COUNTRY: Bangladesh

SETTING: Rural

DESIGN: Case-control: n = 53 cases and 487 controls; all children were < 36 months of age

BREASTFEEDING DEFINITION: Breastfed versus nonbreastfed

OUTCOME MEASURE: Severe shigellosis versus nonsevere shigellosis

RESULTS: The adjusted odds ratio for severe infection was 0.38 ($p < 0.001$) for breastfed children, suggesting that breastfeeding was protective of severe infection. This protective effect held for all age groups studied (< 12 months, 12–24 months, 24–36 months). This is one of the few studies to show a protective effect of breastfeeding among children older than 12 months.

METHODOLOGICAL ISSUES: Cases were children with severe shigellosis infection, and controls were children with nonsevere cases of shigellosis infection. Results report the reduction in severity of infection because of any breastfeeding.

Duffy LC, Tyers TE, et al., The effects of infant feeding on rotavirus-induced gastroenteritis: A prospective study. Amer J Public Health 1986;76:259–63.

COUNTRY: United States

SETTING: Urban

DESIGN: Prospective: n = 197 infants followed from birth to about 9 months of age

BREASTFEEDING DEFINITION: Exclusive breastfeeding to 4 months, combination breast and bottle feeding (partial breastfeeding), initial breastfeeding and converted to complete bottle feeding before 4 months, exclusive bottle feeding

OUTCOME MEASURE: Risk of nonspecific gastroenteritis and rotavirus infection

RESULTS: This study followed a cohort of low-socioeconomic-status infants from birth through the winter rotavirus season, which occurred when the infants were between 6 and 9 months of age. Infants were categorized by infant feeding mode at birth (exclusive

breastfeeding, partial breastfeeding, bottle feeding) and again at 4 months of age. Infants exclusively breastfed through 4 months of age had the lowest attack rate of nonspecific gastroenteritis; the relative risk for this group was 0.29, compared with infants who were either partially or fully bottle-fed. There was no evidence of a protective effect of breastfeeding for rotavirus infection. However, breastfed infants did have less severe forms of infection.

METHODOLOGICAL ISSUES: This is a methodologically strong study, which controlled for many potentially confounding factors.

Scott-Emuakpor MM, Okafor UA. Comparative study of morbidity and mortality of breast-fed and bottle-fed Nigerian infants. East African Med J 1986;63(7):452–57.

COUNTRY: Nigeria

SETTING: Urban

DESIGN: Retrospective: n = 401 mothers (who had a total of 414 children aged 0 to 24 months) attending various clinics, and who were questioned about infant feeding practices and child illnesses and mortality

BREASTFEEDING DEFINITION: Exclusively breastfed, partially breastfed, formula fed

OUTCOME MEASURES: Diarrheal morbidity

RESULTS: The risk of diarrheal illness was significantly lower in exclusively breastfed children than in partially breastfed or bottle-fed children. Thirty-five percent of the exclusively breastfed infants had diarrheal disorder alone or in combination with vomiting during the first 24 months of life, compared with 76% of the partially breastfed infants and 74% of the formula-fed infants.

METHODOLOGICAL ISSUES: The data are not age-adjusted, which would tend to bias the analyses in favor of a protective effect of exclusive breastfeeding on morbidity.

Feachem RG, Koblinsky MA. Interventions for the control of diarrhoeal diseases among young children: Promotion of breast-feeding. Bull WHO 1984;62(2):271–91.

COUNTRY: Developed and developing countries

SETTING: Various settings

DESIGN: Review of 35 studies from 14 countries

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding

OUTCOME MEASURES: Diarrheal morbidity and mortality. Only those outcomes related to diarrheal morbidity are reported here.

RESULTS: This study reviewed the literature on the relationship between infant feeding mode and the relative risk of diarrheal morbidity in the following age categories: 0–3 months, 3–5 months, 6–8 months, 9–11 months, and 12–23 months. A dose-response relationship in the association between infant feeding mode and relative risk of diarrheal

morbidity was found, with exclusively breastfed infants having the lowest risk, partially breastfed infants an intermediate risk, and bottle-fed infants the highest risk. At 0–3 months of age, the relative risk for nonbreastfed versus exclusively breastfed infants was 3.5; for partially breastfed versus exclusively breastfed infants, the relative risk was 2.6, and for nonbreastfed versus partially breastfed infants, the relative risk was 1.8. The association between infant feeding mode and risk is also related to infant age in a dose-response manner, with younger infants deriving the greatest benefit. The relative risk for exclusively breastfed versus nonbreastfed infants is 3 for infants aged 0–3 months and 2.4 for infants aged 3–5 months. The relative risks for partially breastfed and nonbreastfed infants are 1.3–1.5 for infants aged 6–8 and 9–11 months. After 1 year of age, no association between infant feeding mode and risk of diarrheal disease was found. Also, no association was found between breastfeeding and risk of diarrheal disease once breastfeeding had ceased, indicating that the protective effect of breastfeeding lasted only while breastfeeding continued.

Concerning the risk for diarrheal mortality, partially breastfed infants less than 6 months of age had a relative risk of 8.6, compared with exclusively breastfed infants. Infants who did not receive any breastmilk had a relative risk for diarrheal mortality of 25, compared with exclusively breastfed infants, and a relative risk of 3, compared with partially breastfed infants.

METHODOLOGICAL ISSUES: The quality of the studies used in the analysis varied considerably. Many of the calculations of relative risk are not adjusted for other factors that influence both infant feeding mode and diarrhea. No tests of significance or confidence intervals are provided.

Kovar MG, Serdula MK, Marks JS, Fraser DW. Review of the epidemiologic evidence for an association between infant feeding and infant health. Pediatrics 1984;74(4 Pt 2 suppl):615–38.

COUNTRY: United States and other industrialized countries

SETTING: Various settings

DESIGN: Review article of studies published since 1970

BREASTFEEDING DEFINITION: Depends on the study

OUTCOME MEASURE: Mortality and morbidity patterns, allergic diseases, malnutrition, psychological and intellectual development. Only those outcomes related to diarrheal morbidity are reviewed here.

RESULTS: This study reviewed the literature on the association between infant feeding mode and a number of outcome measures. The number of postneonatal deaths attributable to suboptimal infant feeding is not trivial. However, evidence was not available to determine the actual association between feeding methods and postneonatal mortality. With respect to diarrheal morbidity, the authors found that, although most of the studies had significant methodological shortcomings, they showed an association between breastfeeding and reduced risk of infection.

Clavano NR. Mode of feeding and its effect on infant mortality and morbidity. J Trop Pediatr 1982;28:287–93.

COUNTRY: Philippines

SETTING: Urban

DESIGN: Cross-sectional: infants (n = 9,886) born in hospital with infant feeding mode recorded on medical record

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding, and unknown infant feeding mode

OUTCOME MEASURE: Risk of diarrhea and mortality in the early neonatal period

RESULTS: Mode of infant feeding in the hospital was significantly related to risk of diarrhea. Of the 138 infants with diarrhea, 90% were formula fed, 6% were partially breastfed, and 4% were exclusively breastfed. Mode of infant feeding was also significantly related to mortality. Of the 67 infants who died, 96% were formula-fed, 1% were partially breastfed, and 3% were exclusively breastfed. The study covers a period of 4 years, during which rooming-in and formal breastfeeding policies were introduced. After rooming-in and formal breastfeeding policies were introduced, the proportion of infants exclusively breastfeeding increased by 135%, and the incidence of death among clinically infected newborns dropped by 95.3%.

METHODOLOGICAL ISSUES: Reverse causality was not controlled, which is a major limitation given that the risk of death in the early neonatal period is significant and is likely to affect infant feeding mode as well.

Paine R, Coble RJ. Breast-feeding and infant health in a rural US community. Am J Dis Child 1982 Jan;136(1):36–8.

COUNTRY: United States

SETTING: Rural

DESIGN: Retrospective: n = 106 less than 12 months of age

BREASTFEEDING DEFINITION: Group A1: exclusive breastfeeding (solids may have been fed); A2: breastfeeding with bottle supplement; A3: bottle feeding with previous breastfeeding; B: exclusive bottle feeding

OUTCOME MEASURES: Upper and lower respiratory tract symptoms, otitis media, conjunctivitis, gastrointestinal disturbances, urinary tract infection, rash, and fever of unknown origin

RESULTS: During the first month, breastfed infants had statistically significantly fewer illness-related medical visits than did bottle-fed infants. For the first 6 months of life, exclusively and mainly breastfed infants (groups A1 and A2 combined) had fewer months with illness than did bottle-fed infants (groups A3 and B). No significant differences were observed between feeding groups for the second 6 months of life.

METHODOLOGICAL ISSUES: Exclusive breastfeeding definition included the possible intake of solids, and age of initiation was not taken into account in assigning infants to feeding groups.

Kumar V, Kumar L, Diwedi P. Morbidity related to feeding pattern in privileged urban and under privileged rural infants. Indian Pediatr 1981;18:743–49.

COUNTRY: India

SETTING: Urban and rural community-based

DESIGN: Prospective: n = 170 infants from upper-socioeconomic-status urban families, and n = 109 infants from lower-socioeconomic-status rural families

BREASTFEEDING DEFINITION: Exclusive breastfeeding for first 4 months without supplementation, mixed-fed (breastfed for first 4 months with supplementation), bottle-fed (not breastfeeding or breastfeeding < 4 months)

OUTCOME MEASURES: Diarrhea, upper respiratory tract infection, fever, otitis media, skin infections. Only those results pertaining to diarrhea are presented here. See Section 1.2 for respiratory infection results.

RESULTS: The results show that among upper-socioeconomic infants, mixed or bottle feeding was associated with twice the risk of total illness, compared with exclusive breastfeeding during the first 4 months of life. Most of this association was explained by the association between feeding mode and diarrhea: a 4-fold difference was found between exclusively breastfed and mixed- or bottle-fed infants with respect to risk of diarrhea. The association between exclusive breastfeeding versus mixed or bottle feeding and total illness was less strong, though still significant, between 5 and 12 months of age. Among the poor rural infants, partial breastfeeding was associated with a 4-fold risk of diarrhea during the first 4 months of life, compared with exclusive breastfeeding. (No infants were weaned, so no comparisons for this infant feeding mode could be made.)

METHODOLOGICAL ISSUES: This is really two separate studies: one examining the association between infant feeding mode and illness among upper-socioeconomic urban infants and the other examining the same relationships among lower-socioeconomic rural infants. Apart from stratification by economic status, the study does not control for potentially confounding factors that may be associated with infant feeding practices and risk of illness or reverse causality.

Fergusson DM, Horwood LJ, Shannon FT, Taylor B. Infant health and breast-feeding during the first 16 weeks of life. Aust Paediatr J 1978 Dec;14(4):254–8.

COUNTRY: New Zealand

SETTING: Urban

DESIGN: Prospective cohort of 1,210 infants followed up to their 4th month of life

BREASTFEEDING DEFINITION: Exclusively breastfed, almost exclusively breastfed (includes administration of cow's milk on an irregular basis), partially breastfed (breastmilk and cow's milk on a regular basis), formula-fed (no breastmilk)

OUTCOME MEASURES: Gastrointestinal (GI) disturbances, including vomiting and diarrhea (not defined) and other health outcomes, such as respiratory infection (cough, coryza, bronchitis, bronchiolitis, pneumonia, and/or otitis media) and skin eruptions (spots and rashes of all types). See Section 1.2 for results on respiratory infections.

RESULTS: Of the 10 infants hospitalized with GI disturbances, 4 were formula fed, 1 was almost exclusively breastfed, and 5 were exclusively breastfed (EBF). A significant

relationship was found between GI disturbance and diet, with formula-fed infants having close to 4 times the risk of medical consultation and 5 times the risk of symptoms of GI disturbance than EBF infants. These risks remained significant after controlling for possible confounding variables.

METHODOLOGICAL ISSUES: Mothers who chose to breastfeed also took their infants for routine checkups more often than mothers who bottle-fed their infants. Diet tended to be associated with the amount of well-baby care received by the infant as well as the risk of early illness.

Cunningham AS. Morbidity in breast-fed and artificially fed infants. J Pediatr 1977;90(5):726–9.

COUNTRY: United States

SETTING: Rural medical center

DESIGN: Retrospective: n = 253 infants less than 1 year of age

BREASTFEEDING DEFINITION: Breastfeeding if received any breastmilk, formula feeding

OUTCOME MEASURES: Episodes of significant illness (otitis media, lower respiratory disease), vomiting, or diarrhea

RESULTS: Overall morbidity was uncommon in breastfed infants. The development of significant illness was delayed in infants who were breastfed beyond 6 weeks of age. The first year incidence of illness in infants given limited breastfeeding (less than 6 weeks) or formula was approximately double that of breastfed infants.

METHODOLOGICAL ISSUES: There were no data on exclusively breastfed infants. Data were not corrected for age.

1.2 Effect of Breastfeeding on Respiratory Infection Morbidity

César JA, Victora CG, Barros FC, et al. Impact of breastfeeding on admission for pneumonia during postneonatal period in Brazil: Nested case-control study. Br Med J 1999;318:1316–20.

COUNTRY: Brazil

SETTING: Pelotas, southern Brazil

DESIGN: Nested case-control: This study examined the relationship between breastfeeding and risk of respiratory infection to determine if this relationship varied by infant age. The study population consisted of a systematic sample of newborn infants from all infants born in the city of Pelotas in 1993 who were visited in their homes at 1, 3, and 6 months of age. Cases (n = 152) were infants admitted to hospital for pneumonia. Age-matched controls (n = 2,391) were drawn from nonhospitalized infants of the same age encountered during the home visits.

BREASTFEEDING DEFINITION: Type of milk consumed, which could include breastmilk alone; breast and formula milk or other fluids; formula milk or any other liquid except

breastmilk (this group was considered fully weaned). The use of fluid supplements excluding formula milk and the use of solid and semisolid foods also were considered.

OUTCOME MEASURE: Cases of pneumonia were identified through daily visits to the city's hospitals. Only children born in 1993 and aged 28–364 days were considered for inclusion as cases. Pneumonia was diagnosed from the presence of difficult or rapid breathing, chest indrawing, and, when available, laboratory radiological tests.

RESULTS: Compared with infants receiving breastmilk alone, the adjusted odds ratio (OR) of pneumonia for children of all ages not breastfed was 16.7. Younger children were particularly vulnerable to the effects of not breastfeeding. At age 1–2.9 months, the adjusted OR among children who received only formula was 61.1. For children aged 3–6 months, the OR dropped to 10.1, and at 6–11.9 months, to 9.2. For children receiving breastmilk and formula milk, the ORs at 1–2.9, 3–6 and 6–11.9 months were 2.9, 3.4, and 3.7 respectively, but these estimates were not statistically significant.

METHODOLOGICAL ISSUES: Referees were used to avoid diagnostic misclassification bias. Reverse causality was avoided by using breastfeeding status up to 2 months before admission. Recall bias was assessed and found not to influence results unduly. A variety of potential confounders were controlled in multiple logistic regression analysis. At 6–11.9 months, exclusively breastfed infants were used as the comparison group, although exclusive breastfeeding is not recommended for this age group.

Levine OS, Farley M, Harrison LH, et al. Risk factors for invasive pneumococcal disease in children: A population-based case-control study in North America. Pediatrics 1999;103(3):e28.

COUNTRY: United States and Canada

SETTING: Urban (metropolitan Atlanta, Ga.; five counties in Tennessee; metropolitan Baltimore, Md.; Toronto-Peel region, Ontario, Canada)

DESIGN: Case-control: n = 187 cases and 280 controls

BREASTFEEDING DEFINITION: Breastfeeding was determined to be current if it occurred in the preceding 2 weeks. No distinction was made between exclusive breastfeeding and mixed breastfeeding.

OUTCOME MEASURE: Risk factors for invasive pneumococcal disease (day care attendance, ear infection, recent use of antibiotics, current breastfeeding) in infants 2–23 months old

RESULTS: Breastfeeding had a strong protective effect against invasive pneumococcal disease among infants 2–11 months old. Other associations found included 1) day care attendance and increased risk of disease caused by *Streptococcus pneumoniae*, 2) antecedent antibiotic use and penicillin-resistant invasive pneumococcal disease, and 3) recent ear infections and invasive pneumococcal disease.

METHODOLOGICAL ISSUES: Standard telephone questionnaires were used to obtain information from the children's primary caregivers. Age adjusted odds ratios were determined for each age group (2–11, 12–23, and 24–59 months), and logistic regression was used to determine the independent effect of risk factors.

Perera BJC, Ganesan S, Jayarasa J, Ranaweera S. The impact of breastfeeding practices on respiratory and diarrhoeal disease in infancy: A study from Sri Lanka. J Trop Pediatr 1999;45:115–8.

COUNTRY: Sri Lanka

SETTING: Urban

DESIGN: Hospital-based descriptive recall study: cases (n = 58) were infants admitted to the hospital and control infants (n = 285), not ill at the time of the study, were identified from immunization clinics and well-baby clinics

BREASTFEEDING DEFINITION: Exclusively breastfed for 3 months or less, exclusively breastfed for 4 months or more, and never breastfed.

OUTCOME MEASURE: The timing of the first respiratory infection and the first admission for respiratory illness.

RESULTS: Infants exclusively breastfed for 4 or more months had significantly fewer respiratory infections than infants exclusively breastfed for 3 or fewer months. Infants who were never breastfed had the highest risk of hospital admission for an acute respiratory infection.

METHODOLOGICAL ISSUES: Case-control studies can be affected by a number of biases, which have not been controlled for in the analysis. Of particular concern is that reverse causality (e.g., illness leading to a change in breastfeeding pattern rather than infant feeding pattern leading to changes in risk of illness) was not controlled for.

Silfverdal SA, Bodin L, Olcén P. Protective effect of breastfeeding: An ecologic study of Haemophilus influenzae (HI) meningitis and breastfeeding in a Swedish population. Int J Epidem 1999;28:152–6.

COUNTRY: Sweden

SETTING: Örebro County in south central Sweden (urban and rural)

DESIGN: Ecologic study using aggregated data on a population level

BREASTFEEDING DEFINITION: None given

OUTCOME MEASURE: Incidence of *Haemophilus influenze* (HI) infection 5–10 years after receiving breastmilk

RESULTS: There was a strong (negative) correlation between breastfeeding and incidence of HI infection 5–10 years later.

METHODOLOGICAL ISSUES: The aim of the study was to examine the relationship between breastfeeding and incidence of HI infection in the same population where a previous case-control study found breastfeeding to be a protective factor against HI infection. Incidence rates were calculated in 5-year periods. Patients ranged in age from 1 month to 16 years. This study was descriptive and exploratory, rather than explanatory. Control for confounders was minimal.

Nafstad P, Jaakkola JJK, Hagen JA, et al. Breastfeeding, maternal smoking and lower respiratory tract infections. Eur Respir J 1996;9:2623–9.

COUNTRY: Norway

SETTING: Urban (Oslo)

DESIGN: Prospective cohort study of children less than 1 year of age (n = 3,238)

BREASTFEEDING DEFINITION: Any breastfeeding, no breastfeeding, and breastfeeding duration of 0-6 months or > 6 months

OUTCOME MEASURE: Episode of lower respiratory tract infections (LRTIs) as defined by pneumonia, bronchitis, or bronchiolitis as determined by a physician

RESULTS: The adjusted odds ratio (OR) of LRTIs increased on average by a factor of 1.05 (95% CI: 1.02–1.08) per 1-month decrease in duration of breastfeeding. No breastfeeding increased the adjusted OR of LRTIs to 1.7 (95% CI: 1.2–2.5), compared with 12 months of breastfeeding. For children who were breastfed for more than 6 months, maternal smoking had no effect on the risk of LRTIs (adjusted OR = 1.1, 95% CI: 07–1.6). Breastfeeding had a protective effect on infections in children of smoking mothers. Short-term breastfeeding (0–6 mo) combined with maternal smoking was related to an adjusted OR of 2.2 (95% CI: 1.6–3.1) for all infections, and 4.6 (95% CI: 2.5–8.3) for hospitalized infections, compared with long-term breastfeeding (> 6 mo) and no maternal smoking.

METHODOLOGICAL ISSUES: Although children were followed for 1 year, only 2 interviews were administered (at 6 and 12 months), limiting the possibility of finding effects. Mothers of breastfed infants tended to be older, have more years of education, and were less likely to smoke.

Cushing AH, Samet JM, Lambert WE, Skipper BJ, Hunt WC, Young SA, et al. Breastfeeding reduces the risk of respiratory illness in infants. Am J Epidemiol 1998;147:863–70.

COUNTRY: United States

SETTING: Urban

DESIGN: Prospective cohort study of 1,202 healthy infants followed for the first 6 months of life; daily occurrence of respiratory symptoms and breastfeeding status reported by mothers every 2 weeks

BREASTFEEDING DEFINITION: Full breastfeeding, partial breastfeeding, no breast-feeding

OUTCOME MEASURE: Incidence of respiratory infection (2 or more consecutive days with runny or stuffy nose, dry cough, or trouble breathing) and lower respiratory infection (2 or more consecutive days of any upper respiratory symptom and either wet cough or wheezing or both). Duration was also reported for each illness. At least 2 symptom-free days separated illness episodes.

RESULTS: After adjusting for potentially confounding factors, full breastfeeding was associated with a reduction in lower respiratory illness risk (odds ratio = 0.81, 95% CI: 0.68–0.96). The median duration of all respiratory illnesses was 5 days for fully breastfed

infants and 6 days for nonbreastfed or partially breastfed infants. The authors conclude that the pattern of reduced incidence of lower respiratory infections and shorter duration of all respiratory illnesses suggests that breastfeeding reduces the severity of such infections during the first 6 months of life.

METHODOLOGICAL ISSUES: The authors used the longitudinal nature of the data to examine the effect of breastfeeding status at the beginning of an interval on illness during that interval. They also attempted to control biases related to detection and definition of outcome, definition of breastfeeding, and potentially confounding factors.

Lopez-Alarcón M, Villalpando S, Fajardo A. Breast-feeding lowers the frequency and duration of acute respiratory infection and diarrhea in infants under six months of age. J Nutr 1997;127:436–43.

COUNTRY: Mexico

SETTING: Urban

DESIGN: Prospective study of 170 healthy newborns followed for 6 months

BREASTFEEDING DEFINITION: Fully breastfed, partially breastfed, or formula-fed. Information on feeding practices was collected every 2 weeks.

OUTCOME MEASURE: Acute respiratory infection was defined as the presence of runny nose or cough for at least 2 consecutive days.

RESULTS: The probability of having an episode of acute respiratory infection was higher for formula-fed than for fully breastfed infants during the first 4 months of life, but not thereafter. The risks for partially breastfed infants fell between those of formula-fed and fully breastfed infants, suggesting a dose-response effect of breastfeeding on risk of respiratory infection. The prevalence of respiratory infection was also higher for formula-fed than for breastfed infants.

METHODOLOGICAL ISSUES: Infant feeding mode at the beginning of the illness interval was used to avoid the problem of reverse causality. Of the 216 mother-infant pairs initially recruited to the study, only 170 (79%) completed the 6-month follow-up period. However, the characteristics of those mother-infant pairs who dropped out were similar to those who completed the study, suggesting that this did not bias the results. Community-based surveillance avoided the problem of detection bias.

Scariati PD, Grummer-Strawn LM, Fein SB. A longitudinal analysis of infant morbidity and extent of breastfeeding in the United States. Pediatrics 1997;99:e28.

SEE: Study description and results, Section 1.1, page 7

Silfverdal SA, Bodin L, Hugosson S, Garpenholt O, Werner B, Esbjorner E, et al. Protective effect of breastfeeding on invasive Haemophilus influenzae infection: A case-control study in Swedish preschool children. Int J Epidem 1997;26:443–50.

COUNTRY: Sweden

SETTING: One county

DESIGN: Prospective case-control study conducted between 1987 and 1992, with 54 cases of invasive *Haemophilus influenzae* (HI) infection and 139 matched controls (3 per case)

BREASTFEEDING DEFINITION: Duration of exclusive and partial breastfeeding in weeks. Short duration of exclusive breastfeeding was defined as 0–12 weeks, long duration was defined as >13 weeks. Short duration of partial breastfeeding was defined as 0–20 weeks, long duration was defined as >21 weeks.

OUTCOME MEASURE: Clinical findings consistent with invasive *Haemophilus influenzae* (HI) infection with a positive culture

RESULTS: Using multivariate analysis, the risk of HI associated with a short duration of exclusive breastfeeding was nearly 4 times that associated with a long duration of exclusive breastfeeding (odds ratio for 0–12 weeks: 3.79; 95 % CI: 1.6–8.8). The odds ratios for the duration of partial breastfeeding were generally lower than those for exclusive breastfeeding. The authors' findings support a long-lasting protective effect of breastfeeding against invasive HI infection in a dose-response manner, with the risk of HI reduced by 5% for each week of breastfeeding.

METHODOLOGICAL ISSUES: The reported duration of exclusive and partial breastfeeding was checked against clinic records, and good agreement was found. Multivariate analysis controlled for other sources of potential bias was reviewed and discarded as possibly explaining the findings. The study population may have been too small to determine the relevance of socioeconomic status or passive smoking in the incidence of HI infection.

Zaman K, Baqui AH, Yunus MD, Bateman OM, Chowdhury HR, Black RE. Acute respiratory infections in children: A community-based longitudinal study in rural Bangladesh. J Trop Pediatr 1997;43:133–7.

COUNTRY: Bangladesh

SETTING: Rural

DESIGN: Community-based cohort study of 696 children aged 0–59 months followed prospectively. A total of 575 children were recruited at the beginning of the study, and 10–12 newborns were recruited monthly. Of these, 512 children were followed for a full year, and 559 were followed for 6 months or longer.

BREASTFEEDING DEFINITION: Exclusively breastfed for 3 months or less, exclusively breastfed for 4 months or more, and never breastfed

OUTCOME MEASURE: Data on symptoms suggesting acute respiratory infection, such as fever, cough, or nasal discharge, were collected for the preceding 3 days by recall. Upper respiratory infection was defined as the presence of fever with cough and/or nasal

discharge. Acute lower respiratory infection was defined as the presence of cough and respiratory rate in excess of 50 per minute with or without indrawing chest. A new episode was defined when a child was free of symptoms for at least 1 week.

RESULTS: Infants exclusively breastfed for 4 or more months had significantly fewer respiratory infections than infants exclusively breastfed for 3 or fewer months. Infants who were never breastfed had the highest risk of hospital admission for an acute respiratory infection.

METHODOLOGICAL ISSUES*:* Seventy-five percent of the infants had a weight-for-age Z-score and a height-for-age Z-score of <–2, while 25% had a weight-for-height Z-score of <–2. The immunization rate was very low. Physical exams were performed by trained field workers.

Beaudry M, Dufour R, Marcoux S. Relation between infant feeding and infections during the first six months of life. J Pediatr 1995;126:191–7.

COUNTRY: Canada

SETTING: New Brunswick

DESIGN: Retrospective cohort study to assess the effect of infant feeding mode on infectious illnesses during the first 6 months of life (n = 776)

BREASTFEEDING DEFINITION: Breastfeeding was defined as the period of breastfeeding from birth until the infant was totally weaned, even if other foods were offered. The breastfeeding group included those who received no other liquid or food, i.e., those exclusively breastfed, and those who received other liquids or foods, i.e., those who were partially breastfed. Bottle-feeding referred to use of infant formula or cow's milk and no breastfeeding.

OUTCOME MEASURE: Infectious illnesses included gastrointestinal illness (diarrhea, colic, vomiting, gastroenteritis, or gastric influenza) and respiratory illness (otitis, ear infection, cold, influenza, pneumonia, bronchopneumonia, chest cold, bronchitis, throat infection, pharyngitis, tonsilitis, whooping cough, or any illness accompanied by wheezing).

RESULTS: Incidence density ratios (IDRs) were calculated to compare the rates of illness in breastfed and bottle-fed infants, accounting for potentially confounding variables related both to the infant and the mother. Crude IDR analyses indicated a significant protective effect of breastfeeding against total illness during the first 6 months of life (IDR = 0.67; 95% CI: 0.54–0.82). After adjustment for potential confounders, the protective effect of breastfeeding on respiratory illnesses persisted (adjusted IDR = 0.78; 95% CI: 0.61–1.00). Moreover, the adjusted IDR for the probability of hospital admission during the first 6 months of life of breastfed infants compared with bottle-fed infants was 0.32 (95% CI: 0.14–0.72).

METHODOLOGICAL ISSUES: The population under study was predominantly white; therefore, results may not be generalizable to the entire population. Since no exclusively breastfed infants were studied, the protective effects of breastfeeding may be diluted by partial breastfeeding. Breastfed infants came from higher socioeconomic status and had older mothers than did the bottle-fed infants. Smoking may have been a confounder since mothers who bottle-fed tended to smoke more cigarettes than those who breastfed. Data

about the infants' feeding modes and morbidity were collected retrospectively 6 months after birth, which may have introduced recall bias and error.

Bohler E, Aalen O, Bergstrom S, Halvorsen S. Breast feeding and seasonal determinants of child growth in weight in East Bhutan. Acta Paediatr 1995;84:1029–34.

SEE: Study description, Section 1.1, page 9

OUTCOME MEASURES: Incidence of diarrhea, respiratory tract infection, and weight gain. Only those results related to respiratory tract infection are reported here.

RESULTS: Breastfeeding between 12 and 36 months of age was associated with reduced risk of respiratory tract infection. The odds ratio was 0.63 (95% CI: 0.40–0.99). Breastfed children also gained significantly more weight during the monsoon season. This is one of the few studies to show a protective effect of breastfeeding after infancy.

Dewey KG, Heinig MJ, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. J Pediatr 1995;126:696–702.

SEE: Study description, Section 1.1, page 10

OUTCOME MEASURES: Respiratory infection, diarrhea, acute otitis media, other symptoms as measured by weekly maternal recall and medical records. Only those findings pertaining to respiratory infection are reported here. See Sections 1.1 and 1.3 for other findings.

RESULTS: Statistical comparisons between groups were made for 12-month intervals (birth–12 months and 12–24 months). Incidence was calculated as the number of episodes per 100 days at risk. Prevalence was calculated as the number of days the child was ill during each interval. Day care use was positively associated with risk of respiratory infection in the formula-fed group, but not in the breastfed group.The number of siblings was positively associated with incidence of respiratory infection in the breastfed group, but not in the bottle-fed group. Controlling for these factors (day care and siblings), no association was found between the incidence of respiratory infection and infant feeding mode during either the first or second year of life.

Wright AL, Holberg CJ, Taussig LM, Martinez FD. Relationship of infant feeding to recurrent wheezing at age 6 years. Arch Pediatr Adolesc Med 1995;149:458–63.

COUNTRY: United States

SETTING: Urban

DESIGN: Prospective for first 6 years of the child's life; a total of 1,246 infants enrolled in the study with both infant feeding data and data on wheezing at 6 years of age available

BREASTFEEDING DEFINITION: Duration of any breastfeeding categorized by 1-month intervals

OUTCOME MEASURE: Recurrent wheezing, defined as 4 or more episodes in the past year as assessed by parental questionnaire. Atopic skin disease was assessed by skin prick tests.

RESULTS: This study investigated two hypotheses: 1) breastfeeding for any length of time is associated with lower rates of recurrent wheezing at 6 years of age, and 2) the apparent protective effect of breastfeeding against recurrent wheezing is attributable to the fact that breastfed children are less likely to have had wheezing lower respiratory infections early in life. The results show that when potentially confounding factors are included in a multivariate model, nonatopic children who had not been breastfed were 3 times as likely to experience recurrent wheezing (odds ratio = 3.03). The authors conclude that 11% of recurrent wheezing among nonatopic children could be attributed to not breastfeeding. Breastfeeding duration did not affect this relationship: the same degree of protection was afforded by 1 month of breastfeeding as by 6 months. Breastfeeding had no effect on wheezing among atopic children.

METHODOLOGICAL ISSUES: Although the authors controlled for many potentially confounding factors, because of the different characteristics of families of breastfed and nonbreastfed children, it is possible that other factors related to both breastfeeding and wheezing may explain the associations found.

Douglas RM, Woodward A, Miles H, Buetow S, Morris D. A prospective study of proneness to acute respiratory illness in the first two years of life. Int J Epidemio 1994;23(4):818–26.

COUNTRY: Australia

SETTING: Urban

DESIGN: Prospective for first 24 months of child's life

BREASTFEEDING DEFINITION: Duration of partial breastfeeding

OUTCOME MEASURE: Two outcome measures were used: 1) "proneness score" developed by adding together the percent of days with a cold, dry cough or wheezy/noisy breathing, and 2) episodes of acute respiratory infection. Outcome information was recorded by the mother.

RESULTS: Increased duration of breastfeeding was associated with an increase in episodes of respiratory infection and a higher "proneness score" in the second year of life. Children exposed to passive smoke had fewer episodes than children not exposed. Both findings are contrary to other published reports showing breastfeeding to be protective of respiratory illness and passive smoke exposure to be positively associated with respiratory illness.

METHODOLOGICAL ISSUES: Poor definition of breastfeeding and the extremely high dropout rate (35%) limits the credibility of the study. No information is given about the possibility of decreasing breastmilk intake during illness. It is possible that mothers who do not breastfeed under-report children's illness in the face of publicity emphasizing the health benefits of breastfeeding.

Pisacane A, Graziano L, Zona G, Granata G, Dolezalova H, Cafiero M, et al. Breast feeding and acute lower respiratory infection. Acta Paediatr 1994;83:714–8.

COUNTRY: Italy

SETTING: Not specified

DESIGN: Case-control: two groups of infants were studied. The first group (n = 73) were infants < 6 months of age hospitalized with pneumonia or bronchiolitis. The second group (n = 88) were infants < 12 months of age hospitalized with pertussis-like illness. Controls were infants admitted to the same ward with a nonrespiratory illness-related diagnosis and matched on age and month of admission.

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, and no breastfeeding

OUTCOME MEASURE: Hospitalization for pneumonia or bronchiolitis or with pertussis-like illness

RESULTS: Infants < 6 months of age with pneumonia or bronchiolitis were less likely to have been breastfed than controls. The odds ratio (OR) was 0.42 (95% CI: 0.19–0.90). The protective effect of breastfeeding was stronger for those infants who were breastfed at the time of admission (OR = 0.22; 95% CI: 0.09–0.55). Infants who had stopped breastfeeding more than 2 weeks before admission were no longer protected by breastfeeding: infants in this category had similar risks for hospitalization as infants who had never been breastfed. Breastfeeding was also significantly protective of more serious illness. There was no effect of breastfeeding among infants with pertussis-like illness.

METHODOLOGICAL ISSUES: The study controlled for most known potentially confounding factors and ruled out reverse causality. The use of hospital-based controls may have introduced unknown bias.

Howie HP, Forsyth JS, Ogston SA, Clark A, du V Florey C. Protective effect of breast feeding against infection. Br Med J 1990;300:11–16.

SEE: Study description, Section 1.1, page 17

OUTCOME MEASURE: Prevalence of respiratory infections; hospitalization for respiratory infection. See Section 1.1 for effect on diarrhea

RESULTS: After adjustment for potentially confounding factors (social class, maternal age, and parental smoking), breastfeeding was associated with a small protective effect against respiratory infection at 0–13 and 40–52 weeks. During the first 13 weeks of life, the adjusted rate of respiratory infection in bottle-fed infants was 37%, compared with about 25% for both partially and fully breastfed infants. There was no relationship between infant feeding mode and infections of the ear, mouth, or eye; colic; eczema; or diaper rash.

Launer LJ, Habicht J-P, Kardjati S. Breast feeding protects against illness and weight loss due to illness. Am J Epidemiol 1990;131(2):322–31.

COUNTRY: Indonesia

SETTING: Rural

DESIGN: Prospective: n = 33 infants 3–12 months of age

BREASTFEEDING DEFINITION: Infants were categorized into four groups according to the amount of time (measured in minutes) spent breastfeeding during the observation periods. None were exclusively breastfeeding.

OUTCOME MEASURE: Acute respiratory infection, including nasal discharge, cough, and wheezing, with or without fever (defined as an increase in body temperature, detected by maternal palpation of the child's forehead)

RESULTS: Measured diarrheal prevalence was too low to assess its relationship to breastfeeding. The effect of breastfeeding on fever was not significant. There was a significant decrease in the number of days ill from acute respiratory infection as time spent breastfeeding increased. Breastfeeding also prevented weight loss because of acute respiratory infection.

METHODOLOGICAL ISSUES: Small sample size and low prevalence of illness reduced statistical power to detect significant differences. Also, exclusive breastfeeding was not practiced in this setting. Differences in specific infant feeding modes were not examined.

Rubin DH, Leventhal JM, Krasilnikoff PA, et al. Relationships between infant feeding and infectious illness: A prospective study of infants during the first year of life. Pediatrics 1990;85:464–71.

SEE: Study description, Section 1.1, page 19

OUTCOME MEASURE: Of the four outcome measures, two pertain to respiratory infections: 1) upper respiratory infection and 2) lower respiratory illness.

RESULTS: After adjustment for major co-variates (birth weight, social class, number of children in the family, day care, other illnesses in the family), no significant relationships were found between infant feeding category and any of the illnesses examined. The authors conclude that breastfeeding does not provide substantial protection against common childhood illnesses during infancy in a middle-income population in a developed country.

Brown KH, Black RE, de Romana GL, de Kanashiro HC. Infant-feeding practices and their relationship with diarrheal and other diseases in Huascar (Lima), Peru. Pediatrics 1989;83:31–40.

COUNTRY: Peru

SETTING: Urban

DESIGN: Prospective: n = 153 infants, aged 0–12 months

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastfeeding and other liquids, breastfeeding and artificial milk, breastfeeding and solids, no breastfeeding

OUTCOME MEASURE: Risk of diarrhea, acute respiratory infection, and skin infections. Only those outcomes pertaining to acute respiratory infection are reported. See Sections 1.1 and 1.3 for other findings.

RESULTS: Risk of acute respiratory infection was significantly associated with infant feeding mode in the expected direction. Exclusively breastfed infants were used as the reference category. Infants < 6 months of age who received other liquids in addition to breastmilk had a relative risk of 1.8. No breastfeeding was associated with a relative risk of 4.1.

METHODOLOGICAL ISSUES: Infants included in the exclusively breastfed category may have consumed other liquids/foods irregularly. This is a well-conceived and strongly designed study.

Jalil F, Karlberg J, Hanson LA, Lindblad BS. Growth disturbance in an urban area of Lahore, Pakistan related to feeding patterns, infections and age, sex, socio-economic factors and seasons. Acta Paediatr suppl 1989;350:44–54.

SEE: Study description, Section 1.1, page 20

OUTCOME MEASURE: Number of episodes of upper and lower respiratory infections and diarrhea in 3-month periods

RESULTS: No association was found between "age at weaning" and acute respiratory infection.

Wright AL, Holberg CJ, Martinez FD, Morgan WJ, Taussig LM. Breast feeding and lower respiratory tract illness in the first year of life. Br Med J 1989;299:946–9.

COUNTRY: United States

SETTING: Urban children enrolled in a health maintenance organization

DESIGN: Prospective ascertainment of illness during infancy; retrospective ascertainment of breastfeeding

BREASTFEEDING DEFINITION: Duration of any breastfeeding categorized as 0–1 month, 1–4 months, and > 4 months

OUTCOME MEASURE: Type of lower respiratory tract illness (wheezing and non-wheezing) at different age intervals during infancy

RESULTS: This study investigated the effect of any breastfeeding on lower respiratory tract infection during infancy. Breastfeeding was associated with reduced risk of wheezing illness only during the first 4 months of life. The adjusted odds ratio was 1.7. Nonwheezing illnesses were not associated with infant feeding mode. An interactive effect between breastfeeding, sharing a room, and wheezing illness was found: infants who shared a room and were not breastfeeding had a 3 times greater risk of a wheezing illness than infants who were exposed to only 1 of these risk factors. The authors

conclude that breastfeeding protects against wheezing respiratory tract illness only in the first 4 months of life, and that these effects are particularly strong when other risk factors, such as sharing a room, are present.

METHODOLOGICAL ISSUES: Only illnesses that were observed when the child was considered to be under the care of 1 of the pediatricians were included in the analysis. The study only focused on respiratory illness associated with wheeze and did not include other conditions. Authors suggest an association with ethnicity and socioeconomic status and morbidity outcome. Data were controlled for potential confounders with multivariate techniques and stratification.

Chen Y, Yu S, Li W-X. Artificial feeding and hospitalization in the first 18 months of life. Pediatrics 1988;81:58–62.

COUNTRY: China

SETTING: Not specified

DESIGN: Community-based retrospective study of 1,163 children from birth to 18 months of age

BREASTFEEDING DEFINITION: Breastfed at any time during the first 18 months of life, never breastfed

OUTCOME MEASURE: Risk of hospitalization for respiratory infection

RESULTS: This study examined the association between hospitalization during the first 18 months of life and infant feeding patterns. Data were adjusted for infant sex, birth weight, paternal education, and household smoking status. Breastfeeding was associated with lower socioeconomic status: children whose fathers had a university education were significantly more likely to be bottle-fed than children whose fathers had less education. Thus, to the extent that risk of hospitalization is inversely associated with socioeconomic status, the results would be biased against finding an effect because of breastfeeding. The rate of hospitalization for a first episode of respiratory infection was 18% for artificially fed children and 11% for children who had ever been breastfed. Children who had never received any breastmilk had twice the risk of hospitalization for respiratory infection. The adjusted odds ratio for method of feeding and risk of hospitalization with respiratory infection was 2.11 (95% CI: 1.34–3.30).

METHODOLOGICAL ISSUES: Estimates are likely to be conservative, given the manner in which breastfeeding was defined and the potential for random error in recall. This is a methodologically strong study that adds considerably to the evidence that breastfeeding protects against respiratory infection.

Forman MR, Graubard BI, Hoffman HJ, Harley EE, Bennett P. The Pima infant feeding study and respiratory infections during the first year of life. Int J Epidem 1984;13:447–53.

COUNTRY: U.S., population of Native Americans

SETTING: Rural

DESIGN: Retrospective: n = 571 infants

BREASTFEEDING DEFINITION: Infants were categorized into three feeding groups: 1) bottle-fed only, 2) partially breastfed and bottle-fed, and 3) exclusively breastfed for 5 months and then mixed breastmilk and other foods (about 25% also received a bottle during the period of mixed feeding).

OUTCOME MEASURE: First episode of upper respiratory infection for which treatment was sought at a hospital

RESULTS: Compared with partially breastfed or bottle-fed infants, exclusively breastfed infants had significantly lower rates of first respiratory infection between birth and 4 months of age. The adjusted odds ratio for this association was 0.61 ($p = 0.05$). The adjusted odds ratio between 5 and 8 months of age was 0.48 ($p = 0.02$). There was no association between infant feeding mode and risk of respiratory infection between 9 and 12 months of age. Overall, the adjusted odds ratio of an upper respiratory infection during the first year of life among exclusive breastfeeding infants was 0.63 ($p = 0.06$). Infant feeding mode was not associated with risk of pneumonia. Partial breastfeeding was associated with an increased risk of otitis media, compared with exclusive breastfeeding or bottle feeding.

METHODOLOGICAL ISSUES: Only first episodes that resulted in a hospital visit were included. Episodes that occurred at home were not recorded and were presumed to be less severe. This may have resulted in an overestimation of the age at diagnosis of first episode. The data were insufficient to determine effects of reverse causality (if any).

Campbell CE, Latham MC. Infant feeding and morbidity among poor migrant squatters in Hermosillo, Sonora, Mexico. Nutr Res Rev 1988;8:969–79

SEE: Study description, Section 1.1, page 21

OUTCOME MEASURE: Incidence of respiratory infection as assessed by maternal recall for prior 2-week period

RESULTS: The study was divided into three rounds of data collection, 4 weeks apart. Regression analysis showed that any breasfeeding versus no breasfeeding was not significantly associated with respiratory infection in any of the three rounds of data collection but that a higher frequency of breastfeeding was associated with reduced risk of respiratory infection during the last two rounds.

Kumar V, Kumar L, Diwedi P. Morbidity related to feeding pattern in privileged urban and under privileged rural infants. Indian Pediatr 1981;18:743–9.

SEE: Study description, Section 1.1, page 27

OUTCOME MEASURES: Diarrhea, upper respiratory tract infection, fever, otitis media, skin infections. Results pertaining to upper respiratory infection are reported here.

RESULTS: The authors use child-months as the unit of analysis. Infant feeding mode was not associated with upper respiratory infection or otitis media in the first 4 months of life in either the urban high socioeconomic group or the rural low socioeconomic group. Between 5 and 12 months in the urban high socioeconomic group, exclusive

breastfeeding compared with mixed or bottle-feeding was associated with a significantly lower risk for upper respiratory infection (8.9% for exclusively breastfed infants versus 19% for mixed and 15.4% for bottle-fed infants). For the rural lower socioeconomic group, exclusive breastfeeding compared with mixed feeding was associated with a lower risk for upper respiratory infection (7.6% for exclusively breastfed infants versus 16% for mixed-fed infants). There were no significant differences in the risk of otitis media.

Fergusson DM, Horwood LJ, Shannon FT, Taylor B. Infant health and breast-feeding during the first 16 weeks of life. Aust Paediatr J 1978 Dec;14(4):254–8.

SEE: Study description, Section 1.1, page 27

RESULTS: Of the 13 infants hospitalized with respiratory infections, 5 were formula-fed, 4 were almost exclusively breastfed, and 4 were exclusively breastfed. After controlling for confounding variables, no significant associations were found between feeding mode and hospitalization for respiratory infection or risk of respiratory infection symptoms.

Cunningham AS. Morbidity in breast-fed and artificially fed infants. J. Pediatr 1977;90(5):726–9.

SEE: Study description and results, Section 1.1, page 28

1.3 Effect of Breastfeeding on Otitis Media and Ear Infection

Daly KA, Brown JE, Lindgren BR, Meland MH, Le CT, Giebink GS. Epidemiology of otitis media onset by six months of age. Pediatrics 1999; 103:1158–66.

COUNTRY: United States

SETTING: Rural

DESIGN: Community-based cohort study of 596 children aged 0–59 months followed prospectively for 6 months or longer

BREASTFEEDING DEFINITION: Exclusively breastfed for 3 months (or not), exclusively breastfed for 6 months (or not)

OUTCOME MEASURE: Early acute otitis media, defined as a physician-diagnosed episode of otits media during follow-up from birth to 6 months

RESULTS: Univariate and multivariate models were used to assess associations between breastfeeding and otitis media. In the univariate model, infants exclusively breastfed for 6 months had significantly fewer episodes of early acute otitis media than infants not exclusively breastfed this long (relative risk: 0.7; 95% CI: 0.5–0.98). For infants breastfed exclusively for more than 3 months, the relative risk was 0.8 (95% CI: 0.6–0.96). In the multivariate model, these effects were not statistically significant.

METHODOLOGICAL ISSUES: The study was prospective with a low withdrawal rate. However, the manner in which exclusive breastfeeding status was measured was not described. Exclusive breastfeeding was only one of many risk factors examined and may not have been given adequate emphasis in the design and analysis. For example, the inclusion of respiratory infection as a co-variate in the multivariate model, itself known to be causally associated with breastfeeding, likely would have reduced the ability to detect an independent relationship between breastfeeding and otitis media.

Duffy LC, Faden H, Wasielewski R, et al. Exclusive breastfeeding protects against bacterial colonization and cay care exposure to otitis media. Pediatrics. 1997;100:e7.

COUNTRY: United States

SETTING: Suburban pediatric practices

DESIGN: Prospective cohort study: n = 306 infants followed monthly for the first 6 months, then at months 8, 10, 12, 15, 18, 21, and 24.

BREASTFEEDING DEFINITION: Feeding groups consisted of exclusively breastfed infants, partially breastfed infants, and exclusively formula-fed infants.

OUTCOME MEASURE: Frequency of episodes of otitis media (OM) as acute otitis media (AOM) and otitis media with effusion (OME)

RESULTS: Rates of OM episodes were expressed as cumulative incidence rates. Logistic regression models were used to test relative effect of independent factors on OM episodes. Cox proportional hazard analyses were performed to examine the mediating influence of breastfeeding and age on OM. Peak incidence of OM was inversely related to breastfeeding rates beyond 3 months. At 6 months, the cumulative incidence of OM for exclusively breastfed children was < 30%, compared with > 50% for infants who never received any breastmilk. First episodes of AOM were significantly higher in children who were formula-fed from birth to 3 months, compared with those who were exclusively breastfed for the same period. For longer duration (≥ 6 months), the risk of first episode of AOM or OME was approximately 2-fold in the formula-fed infants, compared with the exclusively breastfed ones. Although not statistically significant, formula-fed infants showed higher risk for recurrent episodes of AOM and OME. Formula feeding was the best predictor of OM episodes at 3, 6, and 12 months of life.

METHODOLOGICAL ISSUES: Ninety-nine percent of the subjects were Caucasian. Day care outside the home was an important risk factor; however, other factors that might influence the infection incidence and rate (such as the number of children in day care, the number of days per week attending this type of day care, and the sanitary conditions of the day care facilities) were not taken into consideration. Socioeconomic and educational levels of the subjects' households were not considered.

Dewey KG, Heinig MJ, Nommsen-Rivers LA. Differences in morbidity between breast-fed and formula-fed infants. J Pediatr 1995;126:696–702.

SEE: Study description, Section 1.1, page 10

OUTCOME MEASURES: Respiratory infection, diarrhea, acute otitis media, and other symptoms as measured by weekly maternal recall and medical records. Only those

findings pertaining to otitis media are reported here. See Sections 1.1 and 1.2 for the study's other findings.

RESULTS: Statistical comparisons between groups were made in 12-month intervals (birth–12 months and 12–24 months). Incidence was calculated as the number of episodes per 100 days at risk. Prevalence was calculated as the number of days the child was ill during each interval. During the first year of life, the incidence of acute otitis media was significantly higher among formula-fed infants than among breastfed infants (adjusted incidence/100 days at risk = 0.45 for breastfed infants and 0.53 for formula-fed infants). The number of episodes/year was also higher among formula-fed infants than among breastfed infants (adjusted estimates: 1.53 versus 1.78). The prevalence, defined as the number of days ill/year, was also higher among formula-fed infants (adjusted estimates: 10 versus 15.8). Risk of acute otitis media during the second year of life did not differ between the two groups. However, the duration of episodes was significantly greater among formula-fed infants than among breastfed infants in both the first and second year of life. The authors suggest that breastfeeding is protective against otitis media disease even in affluent, highly educated populations.

Aniansson G, Alm B, Andersson B, Hakansson A, Larsson P, Nylen O, et al. A prospective cohort study on breast-feeding and otitis media in Swedish infants. Pediatr Infect Dis J 1994;13:183–8.

COUNTRY: Sweden

SETTING: Urban

DESIGN: Prospective: n = 400 infants followed from birth to 12 months

BREASTFEEDING DEFINITION: Exclusively breastfed, partially breastfed, and weaned. All infants had been breastfed for at least a short amount of time.

OUTCOME MEASURE: Acute otitis media

RESULTS: The frequency of acute otitis media was significantly lower among breastfed infants at the 3 different age intervals examined: 1–3, 4–7, and 8–12 months. In the 1 to 3 month-old age group, infants who were partially breastfed experienced significantly more episodes than did the exclusively breastfed infants ($p < 0.05$). The difference between exclusively breastfed infants and weaned infants was not significant; however, only 36 infants fell into the weaned category, and the power to detect a difference was probably low. During the 2 intervals, 4–7 months and 8–12 months, weaned infants experienced significantly more episodes than did partially breastfed infants ($p < 0.05$). The age at which the first episode occurred was associated with breastfeeding duration. The authors conclude that breastfeeding protects against acute otitis media.

METHODOLOGICAL ISSUES: The exact manner in which infants were classified in an infant feeding category was not clear, given that within age intervals, infants likely would change categories. No effect sizes were reported, only percentages and significance.

Duncan B, Ey J, Holberg CJ, Wright AL, Martinez F, Taussig LM. Exclusive breastfeeding for at least 4 months protects against otitis media. Pediatrics 1993; 91:867–72.

COUNTRY: United States

SETTING: Urban

DESIGN: Observational, based on retrospective review of medical records of 1,220 infants using a health maintenance organization

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding and partial breastfeeding was categorized as follows: 1) no breastfeeding (n = 169); 2) breastfeeding < 4 months (n = 269); 3) breastfeeding > 4 months with supplemental formula or foods (n = 200); 4) breastfeeding > 4 months with supplemental foods beginning between 4 and 6 months (n = 199); and 5) exclusive breastfeeding for 6 months or more (n = 154).

OUTCOME MEASURE: This study examined the effect of infant feeding mode during infancy on 2 outcomes: 1) acute otitis media and 2) recurrent otitis media (defined as 4 or more episodes of acute otitis media in a 6-month period or 4 episodes in a 12-month period).

RESULTS: From birth to 6 months of age and from 6 months to 12 months of age, the mean number of episodes of acute otitis media decreased significantly with increased duration and exclusivity of breastfeeding. Infants who were exclusively breastfed > 4 months had half the mean number of acute otitis media episodes of infants who were not breastfed at all, and 40% fewer episodes than infants whose diets had been supplemented before 4 months. Infants breastfed < 4 months had similar levels of acute otitis media as infants who were not breastfed. Infants exclusively breastfed for 6 or more months had similar levels of acute otitis media as infants who were exclusively breastfed for 4 months. There was no effect of feeding mode on age at first episode of acute otitis media.

With respect to recurrent otitis media, both longer duration and exclusivity of breastfeeding were protective. As with acute otitis media, rates were similar for those not breastfed or breastfed < 4 months, and these groups were combined for further analysis to form the reference group. Recurrent otitis media rates in infants exclusively breastfed for more than 6 months was 10%, compared with 20.5% for those in the reference group. Potentially confounding factors included marital status, family history of allergy, gender, ethnicity, number of siblings in the home, number of persons sharing a room with the infant, use of day care, maternal smoking, and the number of cigarettes the mother smoked per day.

METHODOLOGICAL ISSUES: Although the authors controlled for most known potentially confounding factors, there may have been uncontrolled factors that affected both breastfeeding and risk of illness.

1.4 Effect of Breastfeeding on Other Aspects of Infant Health

Bertini G, Dani, C, Tronchin M, Rubaltelli FF. Is breastfeeding really favoring early neonatal jaundice? Pediatrics 2001;107:c41.

COUNTRY: Italy

SETTING: Florence metropolitan area

DESIGN: Prospective study (n = 2,174 infants) for 72 hours after birth

BREASTFEEDING DEFINITION: Infants were exclusively breastfed if they received only breastmilk on demand every 1–3 hours with no supplementation of water or formula at any time. Infants were considered partially breastfed if they were breastfed and received additional formula supplements. Infants exclusively formula-fed received only formula.

OUTCOME MEASURE: Jaundice, as indicated by a total serum bilirubin (TSB) level >12.9 mg/dL

RESULTS: Breastfeeding showed a negative correlation with TSB. Furthermore, a positive statistically significant relationship was observed between TSB > 12.9 mg/dL and partially breastfed. A subpopulation of breastfed newborns showed high serum bilirubin peaks, which was not present in formula-fed infants; however, most of these infants were partially breastfed.

METHODOLOGICAL ISSUES: Mothers of formula-fed infants included those with pathological conditions that contraindicated breastfeeding. Of the 112 infants identified as having jaundice, only 30 (26.6%) were formula-fed, and, for 65 of them (58.0%), the authors were unable to find a cause of jaundice. There was a subpopulation of exclusively breastfed infants with very high serum bilirubin peaks.

Oddy WH, Holt PG, Sly PD, et al. Association between breast feeding and asthma in 6 year old children: Findings of a prospective birth cohort study. Br Med J 1999; 319:815–9.

COUNTRY: Australia

SETTING: Western Australia (Perth)

DESIGN: Prospective birth cohort study of 2,187 children followed from birth to 6 years of age

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding (child's age at introduction of other milks)

OUTCOME MEASURE: Asthma as diagnosed by a doctor, wheeze 3 or more times since age 1 year, wheeze in the past year, sleep disturbance due to wheeze in the past year, and objective atopy defined by skin prick test

RESULTS: Unconditional logistic regression analyses were performed to obtain adjusted odds ratios for the association of duration of breastfeeding and exclusive breastfeeding and the mentioned outcomes. There was a positive association with all the outcomes mentioned in children who were introduced to other milks before the age of 4 months. The adjusted odds ratios for children aged 6 years who stopped being exclusively breastfed by age 4 months were: for asthma, 1.25 (95% CI: 1.02–1.52); for wheezing ≥ 3 times since age 1 year, 1.41 (95% CI: 1.14–1.76); for wheeze in the past year, 1.31 (95% CI: 1.05–1.64); for sleep disturbance due to wheeze in the past year, 1.42 (95% CI 1.07–1.89); and for positive skin prick test, 1.30 (95% CI: 1.04–1.61). If other milk was introduced before 4 months, the cumulative incidence of both asthma and wheeze was higher as well.

METHODOLOGICAL ISSUES: Although co-variate analyses included preterm babies, subjects were recruited primarily through a tertiary obstetric hospital and included a small excess of mothers with preterm babies. Subjects were followed prospectively, which decreases recall bias.

Raisler J, Alexander C, O'Campo P. Breast-feeding and infant illness: A dose-response relationship? Am J Public Health. 1999;89:25–30.

COUNTRY: United States

SETTING: Nationwide

DESIGN: Retrospective design using data from the 1988 National Maternal and Infant Health Survey: n = 7,092 infants aged < 6 months

BREASTFEEDING DEFINITION: Breastfeeding was divided into 5 categories depending on the ratio of breastfeeding to other foods and liquids in the infant's diet. "Full breastfeeding" referred to breastmilk alone, "most" referred to more breastmilk than other foods and liquids, "equal" referred to equal amounts of breastmilk and other, "less" referred to less breastmilk than other, and "none" referred to only other (no breastfeeding).

OUTCOME MEASURE: Number of sick-baby medical visits and months of illness with diarrhea, cough or wheeze, ear infection, runny nose or cold, fever, vomiting, or pneumonia

RESULTS: All exclusively breastfed infants had lower odds ratios (ORs) of diarrhea (OR = 0.54, 95% CI: 0.43–0.66), cough/wheeze (OR = 0.83, 95% CI: 0.70–1.00), vomiting (OR = 0.71, 95% CI: 0.56–0.91), and lower mean ratios (MRs) of total illness (MR = 0.78, 95% CI: 0.72–0.85) months and any illness in a month (MR = 0.73, 95% CI: 0.66–0.80). Infants who were mostly breastfed also showed protection against diarrhea (OR = 0.83, 95% CI: 0.69–0.99) and cough/wheeze (OR = 0.81, 95% CI: 0.68–0.96). Feeding infants equal amounts of breastmilk and other foods or liquids only provided protection against cough/wheeze (OR = 0.68, 95% CI: 0.51–0.92). There was no protective association for children receiving less breastmilk than other foods or liquids in any of the illness outcomes. Infants without siblings and who were exclusively breastfed were also protected against ear infection (OR = 0.49, 95% CI: 0.36–0.66), runny nose/cold (OR = 0.69, 95% CI: 0.57–0.84), and fever (OR = 0.71, 95% CI: 0.57–0.87). Infants who were mostly breastfed and had no siblings were protected against ear infection (OR = 0.74, 95% CI: 0.59–0.95) and runny nose/cold (OR = 0.76, 95% CI: 0.62–0.93), and infants who received equal amounts of breastmilk and other foods or liquids and had no siblings also were protected against ear infection (OR = 0.55, 95% CI: 0.34–0.89).

METHODOLOGICAL ISSUES: Differences between breastfeeding and not breastfeeding mothers and their infants may have introduced confounding variables. For example, infants who breastfed for at least one month had higher mean birth weights and were less likely to be of low birth weight. Breastfeeding mothers were more likely to be older, more educated, maried and non-Black, and to have health insurance and higher incomes. They were also more likely to enroll early in prenatal care and attend childbirth classes.

Wilson AG, Forsyth S, Greene SA, Irvine L, Hau C, Howie PW. Relation of infant diet to childhood health: Seven year follow-up of cohort of children in Dundee infant feeding study. Br Med J. 1998;316:21–5.

COUNTRY: United Kingdom (Scotland)

SETTING: Urban, industrialized society

DESIGN: Longitudinal, follow-up cohort study: n = 545 children aged 7 years

BREASTFEEDING DEFINITION: Three milk groups were defined: 1) only breastmilk for at least 15 weeks; 2) partial breastfeeding for 15 weeks; and 3) bottle-feeding for 15 weeks. Within each group, infants were divided further by whether they received their first solids before or after 15 weeks of age.

OUTCOME MEASURE: Respiratory illness (including one or more symptoms, such as persistent cough, wheeze, or breathlessness); measurements of growth, body composition and blood pressure

RESULTS: Children who received only breastmilk for 15 weeks or more had consistently less probability of having respiratory illnesses than those who were exclusively breastfed for less than 15 weeks and those who received other types of infant feeding. Premature introduction of solids was associated with an increased probability of wheeze (21% for children receiving solids before 15 weeks, compared with 9.7% for children receiving solids after 15 weeks). In addition, longer duration of breastfeeding was associated with reduced probability of having had or currently having respiratory illness. Infants who received solids before 15 weeks were significantly heavier and had a greater percentage of body fat than those who were given solids after 15 weeks. Children who only received formula had higher systolic blood pressure than those who were partially or exclusively breastfed. Furthermore, a longer duration of breastfeeding was associated with a reduction in systolic blood pressure in children. The associations indicated a dose-response effect.

METHODOLOGICAL ISSUES: There was greater loss to follow-up among the lower social classes, who also tended to bottle-feed more. All analyses were adjusted for co-variates, but there was no information on or control for diet during the intervening period, so it is possible that subsequent dietary patterns differed between the groups in a manner that also would explain the findings. The effect of infant feeding on respiratory illness was analyzed using logistic regression. The effect of infant feeding on growth and body composition of children was analyzed using multiple regression analyses.

Wright AL, Bauer M, Naylor A, et al. Increasing breastfeeding rates to reduce infant illness at the community level. Pediatrics 1998;101:837–44.

COUNTRY: United States

SETTING: Navajo Reservation at Shiprock, New Mexico

DESIGN: Prospective cohort population-based study of 977 infants before exclusive breastfeeding promotion and 858 infants after promotion

BREASTFEEDING DEFINITION: Exclusive breastfeeding (never formula-fed), exclusive breastfeeding for any period of time (postponed formula feeding), and formula-fed from birth (never breastfed)

OUTCOME MEASURE: Illness occuring within the first year of life, mainly otitis media, recurrent otitis media, gastroenteritis, bronchiolitis, pneumonia, bronchitis, croup, nasopharyngitis, and sepsis

RESULTS: The promotion of exclusive breastfeeding increased the proportion of women who exclusively breastfed for some period of time from 16.4% to 54.6% and decreased the proportion of infants being formula-fed from birth from 83.6% to 45.5%. An inverse relationship was observed between the amount of breastfeeding and the incidence of most illnesses, including otitis media (relative risk = 0.70; 95% CI: 0.56–0.88), gastroenteritis (relative risk = 0.52; 95% CI: 0.32–0.86), bronchiolitis (relative risk = 0.39; 95% CI: 0.19–0.79), nasopharyngitis (relative risk = 0.77; 95% CI: 0.60–0.98), and fevers > 100.4^{o}F (relative risk = 0.65; 95% CI: 0.52–0.81). Furthermore, the incidence rates of pneumonia, bronchitis, and gastroenteritis were reduced by 32%, 72%, and 15%, respectively. Overall, infants who were never formula-fed had half the incidence of lower respiratory tract illness of those receiving formula.

METHODOLOGICAL ISSUES: There is substantial seasonal and annual mobility within the Navajo families, which may have influenced illness rates for some infants. Information on possible confounding variables, such as maternal education, was not available.

Chandra RK. Five-year follow-up of high risk infants with family history of allergy who were exclusively breast-fed or fed partial whey hydrolysate, soy, and conventional cow's milk formulas. J Pediatr Gastro Nutr 1997;24:380–8.

COUNTRY: Canada

SETTING: Newfoundland hospitals

DESIGN: Prospective randomized double-blinded design (n = 288 infants) for first 5 years of age

BREASTFEEDING DEFINITION: Exclusively breastfed for 4 months or longer (no definition of exclusively breastfed provided) and formula-fed with whey hydrolysate, soy, or cow's milk commercial formulas (Good Start, Isomil, and Similac, respectively) for the first 6 months of life

OUTCOME MEASURE: Incidence of atopic disease (eczema, asthma, or allergic rhinitis) and food allergy in high-risk infants with family history of atopy

RESULTS: Of the three formula groups, whey hydrolysate produced the lowest incidence of atopic disease. Differences between the exclusively breastfed group and the whey hydrolysate formula-fed group were not significant for atopic eczema, eczema score, incidence of asthma, or prevalences of eczema and asthma at age 18–60 months. The authors performed a cost-benefit analysis of the 4 different feeding modes. Although total whey hydrolysate formula produced the fewest allergic reactions, it is also the most expensive and least palatable. Partial whey hydrolysate, on the other hand, is well tolerated and costs approximately the same as conventional formulas. However, the cost of prevention and management until age 5 of all children with atopy is lowest if children exclusively breastfeed rather than receive whey hydrolysate, soy, or cow's milk formulas ($326,000 versus $928,000; $1,155,000; and $1,244,000, respectively).

METHODOLOGICAL ISSUES: Because only high-risk infants were studied, the possible benefit of exclusive breastfeeding may be underestimated. None of the breastfed infants was in day care until the age of 6 months, but this was not the case among formula-fed infants.

Wang YS, Wu SY. The effect of exclusive breastfeeding on development and incidence of infection in infants. J Hum Lact 1996;12:27–30.

COUNTRY: China

SETTING: Xu Hui District, Shanghai

DESIGN: Prospective population-based study design of infants aged less than 1 year born in the International Peace Maternity and Child Health Hospital (n = 145)

BREASTFEEDING DEFINITION: Exclusive breastfeeding for at least 4 months and partial breastfeeding (including no breastfeeding) for the first 4 months of life

OUTCOME MEASURE: Physical development determined by weight and height, development assessment measured using the Denver Developmental Screening Test, and cumulative incidence of infectious diseases, including respiratory, gastrointestinal, and skin infections

RESULTS: Infants who were exclusively breastfed had significantly higher mean body weight at 4 months than those who were not exclusively breastfed (7.46 ± 0.74 versus 7.18 ± 0.89 kg, $p < 0.05$). The mean cumulative incidence of infectious diseases during the first year of life was lower in the exclusively breastfed infants than in the nonexclusively breastfed infants (2.58 ± 1.38 versus 3.10 ± 1.65, $p < 0.05$).

METHODOLOGICAL ISSUES: No comparison was provided between the mothers of the infants who were exclusively breastfed and the mothers of those who were partially breastfed.

Brown KH, Black RE, de Romana GL, de Kanashiro HC. Infant-feeding practices and their relationship with diarrheal and other diseases in Huascar (Lima), Peru. Pediatrics 1989;83:31–40.

COUNTRY: Peru

SETTING: Urban

DESIGN: Prospective: n=153 infants

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastfeeding and other liquids, breastfeeding and artificial milk, breastfeeding and solids, no breastfeeding

OUTCOME MEASURE: Diarrhea, acute respiratory infection, and skin infections. Only those outcomes pertaining to skin infections are reported here. See also Sections 1.1 and 1.2 for other findings.

RESULTS: Breastfeeding was protective against skin infections. Compared with exclusive breastfeeding, infants < 6 months of age who received other liquids in addition to breastmilk had a relative risk of 3.8. Breastfeeding and artificial milk was associated with a relative risk of 1.9, and breastfeeding and solids was associated with a relative risk of 2.8. Among infants aged 6–11 months, no breastfeeding was associated with a relative risk of 5.7 compared with any breastfeeding.

METHODOLOGICAL ISSUES: The design addresses the problem of reverse causality. Compared with the study by Popkin et al., this study controlled for fewer biologic and behavioral variables that affect susceptibility to illness and exposure to diarrheal pathogens. Breastfeeding and outcome measures were well defined.

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2. EFFECT OF BREASTFEEDING ON INFANT MORTALITY

The most important benefit of breastfeeding is the infant's immediate survival. Literature on breastfeeding's effect on infant mortality from diarrheal infection, respiratory infection, and other causes is summarized below.

2.1 Effect of Breastfeeding on Diarrheal Mortality

Arifeen S, Black RE, Antelman G, Baqui A, Caulfield L, Becker S. Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. Pediatr 2001;108:e67.

COUNTRY: Bangladesh

SETTING: Urban slums

DESIGN: Prospective n = 1,677 infants enrolled at birth and visited at home at 1, 3, 6, 9, and 12 months

BREASTFEEDING DEFINITION: Exclusively breastfed, predominantly breastfed, partially breastfed, and not breastfed, during the first 4 months, based on 7-day recall at each visit

OUTCOME MEASURES: Deaths due to specific causes, including diarrhea, based on verbal autopsy at the subsequent visit

RESULTS: There were 180 infant deaths (107 per 1,000 live births), 26 (14%) due to diarrhea and another 10 (6%) due to diarrhea plus acute respiratory infections. Proportional hazards regression was used to relate infant feeding method at the previous visit (up to month 3) to subsequent infant diarrheal death, adjusting for birth weight and parity. Many other confounding variables were tested for significance and excluded. Infants who were partially breastfed or not breastfed had a risk of diarrheal death 3.94 times greater (95% CI: 1.47–10.57) than exclusively breastfed infants. The risk of death due to diarrhea among predominantly breastfed infants was also higher but not statistically different from that of exclusively breastfed infants (hazard ratio: 2.22; CI: 0.67–7.37).

METHODOLOGICAL ISSUES: Appropriate definition of breastfeeding, control for a variety of potentially confounding variables, and efforts to control for reverse causality by excluding deaths near birth make this a methodologically strong study. The failure to find a protective effect of exclusive breastfeeding relative to predominant breastfeeding is explained as a problem of small sample size.

Betran AP, Onis M, Lauer JA, Villar J. Ecological study of effect of breast feeding on infant mortality in Latin America. Br Med J 2001;323:1–5.

COUNTRY: Latin America and the Caribbean (LAC)

SETTING: Urban and rural

DESIGN: Ecological study

BREASTFEEDING DEFINITION: Exclusive breastfeeding means the child receives no liquids or solids other than breastmilk, except vitamins, mineral supplements, or medicines. Partial breastfeeding means the child receives some breastmilk, regardless of how much.

OUTCOME MEASURE: Mortality rates due to diarrheal disease and acute respiratory infections during the first year of life

RESULTS: In Latin America and the Caribbean, exclusive breastfeeding for the first 3 months of life and partial breastfeeding for the remainder of the first year, can prevent 55% of infant deaths related to diarrheal disease and acute respiratory infection. Among infants aged 0–3 months, 66% of the deaths from both diseases were prevented by exclusive breastfeeding, while 32% of deaths among those aged 4–11 months were prevented by partial breastfeeding. Overall, 13.9% of all-causes infant mortality in Latin America and the Caribbean (approximately 52,000 deaths a year) could be prevented by exclusive breastfeeding for the first 3 months of life and partial breastfeeding for the remainder of infancy. Overall Latin American and Caribbean estimates of preventable mortality from diarrheal disease for infants 0–3 months and 4–11 months were 0.78 and 0.33, respectively, and the estimates from acute respiratory infection were 0.57 and 0.31 for infants aged 0–3 months and 4–11 months, respectively. In Latin America and the Caribbean, 7.1% and 6.8% of deaths of infants aged 0–11 months caused by diarrheal disease and acute respiratory infection, respectively, could be prevented by exclusive breastfeeding for at least the first 3 months and partial breastfeeding thereafter for the remainder of the first year.

METHODOLOGICAL ISSUES: To study the potential of exclusive breastfeeding during the first 4 months of life and partial breastfeeding thereafter, infants were divided into 2 age groups: 0–3 months and 4–11 months. Exclusive breastfeeding, partial breastfeeding, and no breastfeeding were considered for the first age group, and partial breastfeeding and no breastfeeding were considered for the second age group. Attributable risks derived from the published literature were used to calculate the fraction of deaths from diarrheal disease and acute respiratory infection that could be prevented by exclusive or partial breastfeeding. Simple least squares regressions were used to predict cause-specific mortality at 4 months of age. Sensitivity analyses were performed on a series of variables to allow for possible errors in estimation or modeling assumptions.

WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: A pooled analysis. Lancet 2000;355:451–5.

COUNTRIES: Brazil, Pakistan, Philippines

SETTING: Urban and rural

DESIGN: Meta-analysis of case-control and prospective studies

BREASTFEEDING DEFINITION: Breastfeeding versus not breastfeeding

OUTCOME MEASURE: All-cause infant mortality and mortality from diarrhea or acute respiratory infection

RESULTS: During infancy, data were available from only three countries (Brazil, Pakistan, and the Philippines) because the vast majority of women in the African studies breastfed throughout the first year of life. In the first 6 months of life, the odds ratio (OR) for mortality from infectious disease among nonbreastfed infants was 3.5 (95% CI: 2.4–5.0). Risk of mortality from diarrhea was substantially greater (OR 6.1, 95% CI: 4.1–9.0) compared with acute respiratory infection (OR 2.4, 95% CI: 1.6–3.5). In the second 6

months of life, similar levels of protection were observed against both causes of death. The OR for mortality from diarrhea was 1.9 (95% CI: 1.2–3.1), and for acute respiratory infection, it was 2.5 (95% CI: 1.4–4.6). Therefore, while the protective effect of breastfeeding against diarrhea declined with age, the protective effect against acute respiratory infection remained constant. The protective effect during the second year of life was not consistent. The largest effect was seen in Ghana (OR 7.9, 95% CI: 1.2–53.2), but was based on only 7 deaths. In Senegal, the OR was 2.0 (95% CI: 1.4–3.1). None of the other ORs was significant. Data were not available for Brazil, which only had data on infancy.

METHODOLOGICAL ISSUES: The authors addressed confounding and reverse causality by excluding all deaths in the first week of life and excluding from most analyses deaths not due to infectious diseases. In the case-control studies, breastfeeding status 7 days before death was used for cases.

Yoon PW, Black RE, Moulton LH, Becker S. Effect of not breastfeeding on the risk of diarrhea and respiratory mortality in children under 2 years of age in Metro Cebu, The Philippines. Amer J Epidemiol 1996;143:1142–8.

COUNTRY: The Philippines

SETTING: Urban

DESIGN: Prospective: n = 9,942 children followed from birth to 24 months

BREASTFEEDING DEFINITION: Total months breastfed, breastfeeding status immediately prior to the illness that led to death; breastfeeding status during the 2 months before death

OUTCOME MEASURES: Diarrhea alone, acute lower respiratory infection alone, combined diarrhea and acute lower respiratory infection. Only those findings related to diarrheal mortality are reported here.

RESULTS: To determine if risk changed with age, data were analyzed in three age groups (0–5 months, 6–11 months, and 12–23 months). Risk of death was significantly greater among infants than among children 12–23 months. Potentially confounding factors included those associated with both mortality and major risk factors, including maternal education, type of toilet facility, and length of previous birth interval. There was a strong relationship between breastfeeding and previous birth interval: children who were born 18 months or less after a sibling were much less likely to be breastfed. Proportional hazards models were used to investigate the association between not breastfeeding and diarrheal mortality. In the first 6 months of life, there was a strong association between breastfeeding and diarrheal mortality. Failing to initiate breastfeeding or ceasing to breastfeed was associated with a 10-fold increase in diarrheal mortality (adjusted rate ratio = 9.7). There were no significant associations among the older age groups. The associations were greatest for low birth weight infants and infants whose mothers had little formal education.

METHODOLOGICAL ISSUES: This is a methodologically strong study. Only infants > 4 days old are included to avoid deaths in the early neonatal period that were unlikely to be related to infant feeding mode. The analysis addressed the problem of reverse causality and controlled for many important confounding factors. Risks are analyzed by age.

Victora CG, Huttly SR, Fuchs SC, et al. Deaths due to dysentery, acute and persistent diarrhoea among Brazilian infants. Acta Paediatr suppl 1992;381:7–11.

COUNTRY: Brazil

SETTING: Urban

DESIGN: Population-based case-control study: cases (n = 227) infants (< 12 months of age) who had died from dysentery, acute diarrhea, or persistent diarrhea. Two neighborhood controls were used for each case.

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastfeeding, and no breastfeeding

OUTCOME MEASURES: Mortality from acute diarrhea, persistent diarrhea, and dysentery

RESULTS: This study examined the epidemiology of death from 3 causes: acute diarrhea, persistent diarrhea, and dysentery in 2 urban areas in Brazil. Persistent diarrhea accounted for 62% of deaths, acute diarrhea for 28% of deaths, and dysentery for 10% of deaths. The greatest number of deaths occurred between 3 and 5 months of age, which is when weaning occurred most often. Infant feeding mode was strongly associated with risk of death for both acute and persistent diarrhea. Using exclusive breastfeeding as the reference category, the age-adjusted relative risks of death due to acute diarrhea were 4.0 and 21 for any breastfeeding and no breastfeeding, respectively. The age-adjusted relative risks of death due to persistent diarrhea were 4.3 and 10.0, for any breastfeeding and no breastfeeding, respectively. The age-adjusted relative risk for dysentery failed to reach statistical significance.

METHODOLOGICAL ISSUES: The study was restricted to infants between the ages of 7 days and 364 days to avoid including neonatal deaths that were not likely related to infant feeding mode. Infant feeding mode was the one before the onset of fatal illness to avoid the problem of reverse causality. Because of small sample size for each of the 3 outcomes examined, risks were only adjusted for age and not for other potentially confounding factors.

Sachdev HPS, Kumar S, Singh KK, Puri RK. Does breastfeeding influence mortality in children hospitalized with diarrhoea? J Trop Pediatr 1991;37:275–279.

(The results of this study were the same as the one cited below; therefore, we chose only to summarize one of the articles while making reference to both).

Sachdev HPS, Kumar S, Singh KK, Satyanarayana L, Puri RK. Risk factors for fatal diarrhea in hospitalized children in India. J Pediatr Gastro Nutr 1991;12:76–81.

COUNTRY: India

SETTING: Urban

DESIGN: Prospective: n = 309 children < 18 months of age

BREASTFEEDING DEFINITION: Breastfeeding status (yes or no) before onset of illness

OUTCOME MEASURES: Death from diarrhea

RESULTS: This study examined the association between infant feeding mode (breastfeeding versus no breastfeeding) on mortality risk of children < 18 months of age hospitalized with diarrhea. Infant feeding mode in the 36 children who died was

compared to that of 273 children who survived and were discharged from the hospital in satisfactory condition. Results are adjusted for 5 potentially confounding factors, which were not specified in the paper. The adjusted odds ratio (OR) was 2.7 ($p < 0.001$). Stratified multivariate analyses were performed to estimate the association between infant feeding mode and mortality as a function of age, nutritional status, and duration of diarrhea. The results show that the protective effect of breastfeeding was greatest among younger children, though it was still significant among older children. The adjusted ORs were 6.0, 2.6, and 1.8 for children aged 0–6 months, 7–12 months, and 13–18 months, respectively. The protective effect of breastfeeding was also greater for more malnourished children. The adjusted ORs for weight-for-age ≤ 50% and > 50% of the National Center for Health Statistics (NCHS) median were 5.7 and 2.2, respectively. For children of low height-for-age, the adjusted ORs for height-for-age < 85% and > 85% of the NCHS median were 4.3 and 2.4, respectively. Breastfeeding also was more protective for children with protracted diarrhea. The adjusted ORs for diarrhea > 14 days and < 14 days were 4.5 and 2.5, respectively.

METHODOLOGICAL ISSUES: The authors control for reverse causality, and risk analyses are stratified by age, nutritional status, and duration of disease. Inferences that can be made from this study may be limited because hospitalized populations are not representative of the general population.

Victora CG, Smith PG, Patrick J, et al. Infant feeding and deaths due to diarrhea: A case-control study. Amer J Epidemiol 1989;129:1032–41.

COUNTRY: Brazil

SETTING: Urban

DESIGN: Matched case-control: cases (n = 170) were infants who had died from diarrhea, and controls (n = 340) with a similar age distribution were selected from the community. A second comparison group consisted of 106 infants who were presumed to have died from noninfectious causes.

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastfeeding and powdered milk, breastfeeding and cow's milk, powdered milk only, cow's milk only

OUTCOME MEASURES: Diarrheal mortality

RESULTS: This study examined the association between infant feeding mode and diarrheal mortality in two urban areas of Brazil. Exclusive breastfeeding was the reference group. Breastfeeding was associated in a dose-response manner with risk of mortality with the lowest risk among exclusively breastfed infants, intermediate risk among partially breastfed infants, and the greatest risk among nonbreastfed infants. Compared with exclusive breastfeeding, partial breastfeeding was associated with 4.2 times the risk of death, and no breastfeeding was associated with 14.2 times the risk of death, after adjusting for age and other potentially confounding factors.

Risks were strongest for youngest infants: among infants < 2 months, those who received no breastmilk were 23.3 times more likely to die from diarrhea. After 2 months of age, the odds ratio dropped to 5.3.

METHODOLOGICAL ISSUES: The study was restricted to infants between the ages 7 days and 364 days to avoid including neonatal deaths that were unlikely to be related to infant feeding mode. The infant feeding mode studied was the one before the onset of fatal

illness to avoid the problem of reverse causality. Many potentially confounding variables were controlled. The study also was strengthened by using a second control group of infants who had died from noninfectious diseases.

Feachem RG, Koblinsky MA. Interventions for the control of diarrhoeal diseases among young children: Promotion of breast-feeding. Bull WHO 1984;62(2):271–91.

COUNTRY: Review article with results from many countries

SETTING: Specific to the country of study. Some studies included only lower socioeconomic groups, and some included all socioeconomic groups

DESIGN: Review of 35 studies from 14 countries; however, only 9 studies from 5 countries have data on mortality, and these are summarized here

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding

OUTCOME MEASURES: Only that outcome related to diarrheal mortality is reported here.

RESULTS: This review article examines the relationship between infant feeding mode and risk of death from diarrheal disease. Infant age is broken into several different categories, depending on the specific infant feeding mode comparisons being made. A dose-response relationship between infant feeding mode and risk of death from diarrheal disease was found, with exclusively breastfed infants having the lowest risk, partially breastfed infants an intermediate risk, and bottle-fed infants the highest risk. For example, among infants aged 0–5 months, the relative risk of death for nonbreastfed versus exclusively breastfed infants was 25; for partially breastfed versus exclusively breastfed infants, it was 8.6; and for nonbreastfed versus partially breastfed infants, it was 3.5. The association between infant feeding mode and risk is also related to infant age in a dose-response manner, with younger infants deriving the greatest benefit. The relative risk for exclusively breastfed compared with nonbreastfed is 25 for infants aged 0–2 months and 11 for infants aged 6–8 months. Results are reported for risks after 1 year of age. The relative risk of death from diarrhea is 2 to 6 times greater than the risk of illness from diarrhea. This suggests a difference in the case-fatality ratio by feeding mode, whereby breastfed infants benefit from increased protection from death given illness, compared with formula-fed infants.

METHODOLOGICAL ISSUES: The results reported here are old, all but one from before 1947, and limited in quality. Many do not control for potentially confounding factors that could be related to both infant feeding method and risk of death from diarrhea. The formula-fed children were not receiving modern formulas, which may have increased their risk of death, compared with infants today who are being fed formula.

Robinson M. Infant morbidity and mortality: A study of 3266 infants. Lancet 1951(April 7):788–94.

COUNTRY: England

SETTING: Urban and rural

DESIGN: Review of hospital records: n = 3,266 infants that had been followed between 1 and 7 months of age

BREASTFEEDING DEFINITION: Exclusive breastfeeding (n = 971), partially bottle-fed (n = 1,441), bottle-fed (n = 854)

OUTCOME MEASURES: Mortality and morbidity. Only those results pertaining to diarrheal mortality are reported here.

RESULTS: This study examined the association between infant feeding mode and mortality among a large cohort of children who had medical records available for the period 1 month to 7 months of age. The study population consisted of infants attending the same clinic between 1936 and 1942. A dose-response relationship was found with respect to exclusive breastfeeding, partial bottle feeding, and full bottle feeding and mortality from all causes as well as from diarrhea specifically. The unadjusted overall mortality rate per 1,000 was 10.2 for exclusively breastfed, 25.7 for partially breastfed, and 57.3 for bottle-fed infants. The unadjusted diarrhea mortality rate per 1,000 was 0 for exclusively breastfed, 2.0 for partially breastfed, and 7.0 for bottle-fed infants.

METHODOLOGICAL ISSUES: The results in this study are not adjusted for potentially confounding factors that may be associated with both infant feeding method and risk of mortality. However, the author did exclude from the analysis infants who died within the first 2 weeks of life or who died from causes not associated with infant feeding method (birth anomalies, accidents). The author also controlled for reverse causality by using the infant feeding method before the onset of fatal illness rather than the feeding mode at the time of death.

2.2 Effect of Breastfeeding on Respiratory Infection Mortality

Arifeen S, Black RE, Atbeknab G, Baqui A, Caulfield L, Becker S. Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. Pediatrics 2001;108(4):e67.

SEE: Study description, Section 2.1, page 52

OUTCOME MEASURES: Deaths due to specific causes, including acute respiratory infections (ARIs), based on verbal autopsy at the subsequent visit

RESULTS: There were 180 infant deaths (107 per 1,000 live births), 39 (22%) due to ARI and another 10 (6%) due to ARI plus diarrhea. Proportional hazards regression was used to relate infant feeding method at the previous visit (up to month 3) to subsequent infant ARI death, adjusting for birth weight, income, education, and parity. Many other confounding variables were tested for significance and excluded. Infants who were partially breastfed or not breastfed had a risk of ARI death 2.40 times greater (95% CI: 1.14–5.04) than exclusively breastfed infants. The risk of death due to ARI among predominantly breastfed infants was not statistically different from that of exclusively breastfed infants.

Betran AP, Onis M, Lauer JA, Villar J. Ecological study of effect of breast feeding on infant mortality in Latin America. Br Med J 2001;323:1–5.

SEE: Study description, Section 2.1, page 52

WHO Collaborative Study Team on the role of breastfeeding on the prevention of infant mortality. Lancet 2000;355:451–5.

SEE: Study description, Section 2.1, page 53

Victora CG, Kirkwood BR, Ashworth A, et al. Potential interventions for the prevention of childhood pneumonia in developing countries: Improving nutrition. Am J Clin Nutr 1999;70:309-320.

COUNTRY: Brazil, the Philippines, Tanzania

SETTING: Various settings

DESIGN: Review

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding (breast-milk and nonbreastmilk) or no breastfeeding

OUTCOME MEASURES: Mortality from acute lower respiratory infection (ALRI) and relationship to a number of different nutritional factors, such as low birth weight, protein-energy malnutrition, and lack of breastfeeding

RESULTS: The weighted average of the relative risk of pneumonia deaths due to lack of breastfeeding was 2.0. Data from a population-based study from Brazil showed that children < 12 months who were not breastfed had a relative risk of dying from ALRI of 3.6; infants who were partially breastfed had a relative risk of 1.6. Data from a community-based cohort study in the Philippines failed to show an association between breastfeeding and ALRI mortality in children < 24 months, but a case-control study from Tanzania showed a relative risk of 1.7 for nonbreastfed children, aged 0–59 months. Furthermore, in Rwanda, a study reported that nonbreastfed children were twice as likely to die from pneumonia than were breastfed children. In addition, low birth weight and malnutrition (underweight) are also important risk factors for pneumonia and ALRI morbidity and mortality in the developing world.

METHODOLOGICAL ISSUES: The review was limited to developing countries or low-income populations from developed countries. Many studies reviewed here are limited by reverse causality, confounding, and self-selection bias.

Yoon PW, Black RE, Moulton LH, Becker S. Effect of not breastfeeding on the risk of diarrhea and respiratory mortality in children under 2 years of age in Metro Cebu, The Philippines. Amer J Epidemiol 1996;143:1142–8.

SEE: Study description, Section 2.1, page 54

OUTCOME MEASURES: Death due to diarrhea alone, acute lower respiratory infection alone, combined diarrhea and acute lower respiratory infection. Only those findings related to acute lower respiratory infection alone and combined diarrhea and acute lower respiratory infection are reported here.

RESULTS: Proportional hazards models were used to investigate the association between not breastfeeding and acute lower respiratory infection or combined diarrhea and acute

lower respiratory infection. There was no effect of nonbreastfeeding on risk of death from acute lower respiratory infection. However, among infants aged 0–5 months, the rate of mortality associated with both acute lower respiratory infection and diarrhea was increased nearly 6 times by not breastfeeding (rate ratio = 5.7). There was no effect of nonbreastfeeding on the risk of death from combined diarrhea and acute lower respiratory infection in the older age group.

Victora CG, Smith PG, Barros FC, Vaughan JP, Fuchs SC. Risk factors for deaths due to respiratory infections among Brazilian infants. Int J Epidem 1989;918–25.

COUNTRY: Brazil

SETTING: Urban

DESIGN: Matched case-control: cases (n = 170) infants who had died from diarrhea. Two neighborhood controls were used for each case. Those chosen were the first neighbor aged 7 to 364 days and the next closest neighbor aged 7 to 182 days.

BREASTFEEDING DEFINITION: Exclusive breastfeeding, breastfeeding and powdered milk; breastfeeding and cow's milk, powdered milk only, cow's milk only

OUTCOME MEASURES: Mortality from respiratory infection and diarrhea. Only those results for respiratory mortality are summarized here. See results for diarrheal mortality in Section 2.1, page 55.

RESULTS: This study examined the association between infant feeding mode and mortality from respiratory infection in 2 urban areas in Brazil. Exclusive breastfeeding was the reference group. Breastfeeding was associated with a reduced risk of death from respiratory infections; however, the magnitude of the association was smaller than for diarrhea-related deaths. Compared with exclusive breastfeeding, the relative risk for any breastfeeding was 1.6. However, the confidence intervals span 1, so the finding was not statistically significant. In contrast, compared with exclusive breastfeeding, the relative risk of no breastfeeding was 3.6 and statistically significant. The risks were greatest for those infants under 2 months of age.

METHODOLOGICAL ISSUES: The study was restricted to infants between the ages 7 and 364 days to avoid including neonatal deaths that were unlikely to be related to infant feeding mode. Infant feeding mode was that before the onset of fatal illness to avoid the problem of reverse causality. Potentially confounding variables were controlled.

Victora CG, Vaughan JP, Lombardi C, et al. Evidence for protection by breast-feeding against infant deaths from infectious diseases in Brazil. Lancet 1987 (August 8):319–21

(The results of this study were the same as the one reported above; therefore, we chose to summarize only one of them, while making reference to both.)

Robinson M. Infant morbidity and mortality: A study of 3266 infants. Lancet 1951(April 7):788–94.

SEE: Study description, Section 2.1, page 57

OUTCOME MEASURES: Mortality and morbidity. Only those results pertaining to mortality from respiratory infections are reported here.

RESULTS: A dose-response relationship was found with respect to exclusive breastfeeding, partial bottle-feeding, and full bottle-feeding and mortality from all causes as well as specifically from respiratory infections. The unadjusted overall mortality rate per 1,000 was 10.2 for exclusive breastfeeding, 25.7 for partial breastfeeding, and 57.3 for bottle-fed infants. The unadjusted mortality rate from respiratory infection per 1,000 was 8.2 for exclusively breastfed, 15.9 for partially breastfed, and 31.6 for bottle-fed infants. For otitis media, the unadjusted overall mortality rate per 1,000 was 0 for exclusive breastfeeding, 2.0 for partial breastfeeding, and 8.1 for bottle-fed infants.

2.3 Effect of Breastfeeding on All-Cause Infant Mortality

Arifeen S, Black RE, Antelman G, Baqui A, Caulfield L, Becker S. Exclusive breastfeeding reduces acute respiratory infection and diarrhea deaths among infants in Dhaka slums. Pediatr 2001;108:e67.

SEE: Study description, Section 2.1, page 52

OUTCOME MEASURES: Deaths due to all causes up to 12 months, based on verbal autopsy at the subsequent visit

RESULTS: There were 180 infant deaths (107 per 1,000 live births), including 60 neonatal deaths and 120 postneonatal. Proportional hazards regression was used to relate infant feeding method at the previous visit (up to month 3) to subsequent infant death, adjusting for birth weight, mother's height and parity, household income and religion, and father's education. Other confounding variables were tested for significance and excluded. Infants who were partially breastfed or not breastfed had a risk of death 2.23 times greater (95% CI: 1.45–3.44) than exclusively breastfed infants. The risk of death among predominantly breastfed infants was not statistically different from that of exclusively breastfed infants (hazard ratio: 1.13; CI: 0.65–1.97).

Manda SOM. Birth intervals, breastfeeding and determinants of childhood mortality in Malawi. Social Sci & Med 1999;48:301–12.

COUNTRY: Malawi

SETTING: Nationwide

DESIGN: Retrospective study design using the 1992 Malawi Demographic and Health Survey of 4,838 singleton births of 2,911women aged 15–49 years

BREASTFEEDING DEFINITION: Breastfeeding duration captured in a series of dummy (yes/no) variables to indicate, for children in each of 2 age groups (0–11 months and 12–59 months), if: still breastfed, stopped breastfeeding due to illness, stopped breastfeeding due to other reasons, or breastfeeding information is missing.

OUTCOME MEASURES: Infant mortality (0–11 months) and child mortality (12–59 months)

RESULTS: Proportional hazards model based on Cox were used to determine the association between selected variables and infant and child mortality. Children who had never breastfed or had stopped breastfeeding because of illness (theirs or their mothers') were 4.3 times more likely to experience infant mortality than children who continued to breastfeed. Stopping breastfeeding because of weaning or maternal pregnancy during the subject's first 12 months significantly increased infant mortality by a factor of 8.26. The effects of breastfeeding on child mortality were less notable.

METHODOLOGICAL ISSUES: Nearly all children were breastfed during the first year, unless they died or were ill (depending on the type of illness). This produces an almost perfect correlation between breastfeeding and child survival, especially during infancy. Therefore, estimates of the effects of stopping breastfeeding for other reasons are based on small numbers and may be unstable.

Terra de Souza AC, Cufino E, Peterson KE, et al. Variations in infant mortality rates among municipalities in the state of Ceará, Northeast Brazil: An ecological analysis. Int J Epidem 1999;28:267–75.

COUNTRY: Brazil

SETTING: Urban and rural

DESIGN: Ecological design comparing 140 municipalities

BREASTFEEDING DEFINITION: Exclusive breastfeeding for the first 4 months of life

OUTCOME MEASURES: Infant mortality rate defined as the ratio of infant deaths to live births in the 30-month study period

RESULTS: Crude analyses show an inverse association with the percentage of infants who were exclusively breastfed for the first 4 months of life and average infant mortality rate ($\beta = -0.62$, $p = 0.0005$, $R^2 = 9.3$). The association was not affected after controlling for the percentage of infants with adequate weight gain. In the adjusted analysis, a 10-point increase in percent of infants exclusively breastfed would result in 5.9 fewer infants deaths per 1,000 live births. Forty-one percent of the variance in municipality-level infant mortality rates was explained by percent of exclusively breastfed infants, up-to-date prenatal care, low household income, female illiteracy rate, inadequate water supply, urbanization, and per capita gross national product.

METHODOLOGICAL ISSUES: Low birth weight, which can affect infant mortality risk and, therefore, be a confounding variable, was not taken into account. A strength of the study is that the unit of analysis (the municipalities) is the same as the unit of potential interventions, thus providing an understanding of the determinants of infant mortality that work at the ecological level.

Augustine T, Bhatia BD. Early neonatal morbidity and mortality pattern in hospitalized children. Indian J Mat Child Health 1994;5(1):17–19.

COUNTRY: India

SETTING: Hospital-based

DESIGN: Retrospective review of medical records of newborns < 7 days old (n = 169) admitted to a neonatal intensive care unit

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding, no breastfeeding, not yet fed

OUTCOME MEASURE: Mortality

RESULTS: This study examined the association between infant feeding mode and mortality among infants admitted to the hospital in the first 7 days of life. Exclusive breastfeeding was associated with the lowest rate of mortality (29%), compared with infants not yet fed (64%) or those receiving sugar water or cow's milk with or without breastfeeding (43%). Statistics on the significance of these differences were not reported.

METHODOLOGICAL ISSUES: The study does not control for reverse causality, the possibility that infant health determined infant feeding practices. This problem is particularly acute in this study, given the very young age of the study population. It is likely that many newborns who had not yet been fed upon admission to the hospital were too ill to initiate breastfeeding.

Hanson LA, Ashraf R, Zaman S, et al. Breast feeding is a natural contraceptive and prevents disease and death in infants, linking infant mortality and birth rates. Acta Paediatr 1994;83:3–6.

COUNTRY: Pakistan

SETTING: Urban and rural

DESIGN: Review article

BREASTFEEDING DEFINITIONS: Not provided

OUTCOME MEASURES: Mortality

RESULTS: This article is a review of the relationships between the contraceptive effect of breastfeeding and the protective effect of breastfeeding on child morbidity. It describes how breastfeeding links infant mortality to birth rates as well as the effect of changing patterns of breastfeeding.

METHODOLOGICAL ISSUES: No definition of breastfeeding (exclusive or partial) is given, and no new data are presented. A strong argument is made for promotion of breastfeeding as a mechanism to reduce both mortality and birth rates.

Mølbak K, Gottschau A, Aaby P, Højlyng N, Ingholt L, da Silva APJ. Prolonged breast feeding, diarrhoeal disease, and survival of children in Guinea-Bissau. Br Med J 1994;308:1403–6.

COUNTRY: Guinea-Bissau

SETTING: Urban

DESIGN: Community-based cohort study (n = 691) of children under 3 years of age

BREASTFEEDING DEFINITION: Exclusively breastfed, partially breastfed, weaned

OUTCOME MEASURES: All-cause mortality

RESULTS: During a period of follow-up of 840 child-years, 48 deaths occurred. Weaned children had 2.6 times the risk of death of breastfed children (95% CI: 1.1–6.2). The risk of death increased to 3.5 times (95% CI: 1.4–8.3) when analyses were adjusted for maternal education and ethnic group. The excess mortality was independent of age at weaning. Thus, although breastfed children tended to have lower nutritional status than weaned children, they were more likely to survive. This is one of the few studies to show a protective effect of breastfeeding on risk of mortality among children 12 to 36 months of age.

METHODOLOGICAL ISSUES: This study controls for many factors that may confound the relationships under study. It also analyzes the data in a number of different ways, which demonstrates the robustness of the findings.

Shahidullah M. Breast-feeding and child survival in Matlab, Bangladesh. J Biosoc Sci 1994;26:143–54.

COUNTRY: Bangladesh

SETTING: Rural

DESIGN: Prospective: n = 2,990 children followed from birth until 5 years of age

BREASTFEEDING DEFINITION: Duration of unsupplemented and supplemented breast-feeding. Unsupplemented and supplemented breastfeeding were not clearly defined, though it appears from one table that supplementation refers to food supplementation.

OUTCOME MEASURES: All-cause childhood mortality

RESULTS: A discrete hazard model approach was used to evaluate the effect of infant feeding mode and birth interval on mortality risk. Important demographic and socioeconomic indicators were also included as control variables: parity, sex of child, maternal education, and preceding birth interval. Other things being equal, the mortality risk of a child who has received complementary food is 2.1 times greater than that of a child who has not received complementary food. Short subsequent birth interval had the greatest impact. If the mother became pregnant again, the index child was 4.4 times more likely to die than a child whose mother did not become pregnant again. The combined effects of complementary feeding and subsequent pregnancy were particularly important: a child who experienced both of these events had nearly 9 times the risk of death as a child who had not experienced these events. Overall, it was not the duration of any breastfeeding but the duration of unsupplemented breastfeeding that was the important determinant of childhood mortality.

METHODOLOGICAL ISSUES: The definition of breastfeeding was not clear, and the analysis does not take into account the fact that an infant feeding practice that is appropriate for one age, such as unsupplemented breastfeeding, may be inappropriate at another, older age. The authors state that 11 discrete age intervals were created for the analysis, but the results are not presented by age.

Srivastava SP, Sharma VK, Jha SP. Mortality patterns in breast versus artificially fed term babies in early infancy: A longitudinal study. Indian Pediatr 1994;31:1393–6.

COUNTRY: India

SETTING: Urban

DESIGN: Hospital-based follow-up of 1,000 term infants, half of whom were breastfed and half were bottle-fed

BREASTFEEDING DEFINITION: Breastfed versus artificially fed

OUTCOME MEASURES: All-cause mortality

RESULTS: Self-diagnosed "lactation failure" or "poor lactation" was the most common reason for artificial feeding. Sepsis was the major cause of early neonatal mortality among low birth weight infants and artificially fed infants. Diarrhea was the main cause of mortality during the 1- to 6- month period. Mortality was higher in both low birth weight and artificially fed infants; however, tests of significance were not provided.

METHODOLOGICAL ISSUES: Infants who changed from breastfeeding to bottle feeding were excluded from the analysis, which would bias the study toward finding a positive effect of breastfeeding on mortality. The authors state that they followed 1,000 term infants of whom half were breastfed and half were bottle-fed, but provided no other information about the selection criteria.

Singh K, Srivastava P. The effect of colostrum on infant mortality: Urban rural differentials. Health and Population 1992;15(3&4):94–100.

COUNTRY: India

SETTING: Urban and rural

DESIGN: Cross-sectional survey: n = 826 infants

BREASTFEEDING DEFINITIONS: Knowledge and feeding of colostrum

OUTCOME MEASURES: Neonatal and postneonatal mortality

RESULTS: Total neonatal mortality was 6.6%; total postneonatal mortality was 5.1%. Knowledge and use of colostrum was significantly related to setting. More than half of urban mothers did not know about or feed colostrum to their newborns. In contrast, in rural areas, nearly three-quarters of mothers knew about or fed colostrum to their newborns. To examine the association between colostrum and mortality, the data were stratified by 3 socioeconomic groups (high, medium, and low) in each of two settings (urban and rural). In the urban high socioeconomic group, no neonatal deaths were found in the group that received colostrum, and 4.26% of neonates died in the group that did not receive colostrum. Comparable postneonatal deaths were 1.67% and 5.32%. In the rural, high socioeconomic group, no neonatal deaths were found among the group that received colostrum, and 8.2% of neonates died in the group that did not receive colostrum. Comparable postneonatal deaths were 0% and 1.64%.

In the urban middle socioeconomic group, 2.17% of neonates died in the group that received colostrum, compared with 5.69% of neonates in the group that did not receive

colostrum. Comparable postneonatal deaths were 4.35% and 7.32%. In the rural middle socioeconomic group, 3.7% of neonates died in the group that received colostrum, compared with 4.91% of neonates who did not receive colostrum. Comparable postneonatal deaths were 3.7% and 4.29%. In the urban low socioeconomic group, 10% of neonates died in the group that received colostrum, compared with 17.39% of neonates in the group that did not receive colostrum. Comparable postneonatal deaths were 0 and 13.04%. In the rural low socioeconomic group, none of the neonates who received colostrum died, compared with 11.36% of neonates who did not receive colostrum. Comparable postneonatal deaths were 0% and 3.41%. Tests of significance were not provided. As a general conclusion, 1.72% of urban neonates and 2.59% of urban postneonates who received colostrum died, compared with 6.25% and 7.08% who did not receive colostrum. Comparable rural neonatal and postneonatal deaths were 1.69% and 1.69%, respectively, for infants who received colostrum, and 7.37% and 3.53%, respectively, for infants who did not receive colostrum.

METHODOLOGICAL ISSUES: The authors failed to control for reverse causality. Little information is provided about how mortality data were collected. Although analyses were stratified by socioeconomic status, other potentially confounding factors were not controlled. For various reasons, information about colostrum use could not be obtained from 8.3% of urban mothers and 10.7% of rural mothers.

Awathi S, Malik GK, Misra PK. Mortality patterns in breast versus artificially fed term babies in early infancy: A longitudinal study. Indian Pediatr 1991;28:243–8.

COUNTRY: India

SETTING: Urban

DESIGN: Prospective: n = 507 term infants of whom approximately half (n = 273) were breastfed and approximately half (n = 234) were not breastfed. Infants were matched for socioeconomic status, divided into two groups (normal birth weight and low birth weight), and followed for 6 months

BREASTFEEDING DEFINITION: Breastfed versus artificially fed

OUTCOME MEASURES: Neonatal mortality and postneonatal mortality (1–6 months only)

RESULTS: This study examined the association between infant feeding mode (breastfeeding versus formula feeding) and neonatal and postneonatal morbidity (through 6 months only) among normal and low birth weight infants. Results are not adjusted for potentially confounding factors or reverse causality, which may be a particular problem among low birth weight infants. The percentage of neonates > 2.5 kg dying was 0.47 and 1.1 for the breastfed and artificially fed groups, respectively ($p < 0.05$). The comparable figures among the low birth weight neonates were 6.94 and 12.96 ($p < 0.001$). For postneonatal mortality, the percentage of infants > 2.5 kg dying was 0 for both breastfed and artificially fed infants. For low birth weight infants, the percentage dying was 2.78 for the breastfed group and 3.70 for the formula-fed group ($p < 0.001$).

METHODOLOGICAL ISSUES: The authors report significant loss to follow-up, with only 334 (66%) infants studied for the entire 6 months. Moreover, they also excluded breastfed infants who switched into the formula-feeding category during the study.

Briend A, Bari A. Breastfeeding improves survival, but not nutritional status, of 12–35 months old children in rural Bangladesh. Eur J Clin Nutr 1989;43:603–8.

COUNTRY: Bangladesh

SETTING: Rural

DESIGN: Prospective: n=1,087 children aged 12–35 months followed monthly for 2 years

BREASTFEEDING DEFINITION: Breastfed versus weaned

OUTCOME MEASURE: Mortality

RESULTS: This study examined the association among infant feeding mode, nutritional status, and mortality among children. It is one of the few studies identified that looks at children beyond 1 year of age. The unit of analysis was child-months. Children who were breastfed had a significantly lower weight for age than children who were weaned. However, despite their better nutritional status, weaned children had a relative risk of dying of 2.6, compared with breastfed children. The estimated prevented fraction of deaths was 38%.

Age-adjusted relative risks were 6.1, 4.5, 3.7, and 3.1 for children aged 12–17 months, 18–23 months, 24–29 months, and 30–36 months, respectively. Malnourished children (weight-for-age < 60%) who were weaned had a relative risk of 6.0, compared with similarly malnourished children who were breastfed. Although the estimates were not adjusted for potentially confounding factors, the authors argue that the results are not likely to be spurious. The tendency for mothers to wean their better-nourished children earlier, and the reported higher frequency of breastfeeding among the poorest women, should have resulted in an underestimation of the strength of the association.

METHODOLOGICAL ISSUES: The study does not control for reverse causality—the possibility that the infant's health determined infant feeding practices. Although the authors argue that the poorest mothers breastfed the longest, so the unadjusted relative risks are likely to be an underestimate, the analysis does not control for potentially confounding factors.

Molteno CD, Kibel MA. Postneonatal mortality in the Matroosberg Divisional Council area of the Case Western Health Region. South African Med J 1989;75:575–8.

COUNTRY: South Africa

SETTING: Urban

DESIGN: Case-control: cases (n = 49) were black infants who died within a 12-month period. The selection of controls was not clearly presented.

BREASTFEEDING DEFINITION: None

OUTCOME MEASURES: Mortality

RESULTS: Of the infants who died, 33% had not been breastfed, compared with 7% of controls ($p < 0.001$). However, these figures were not adjusted for reverse causality or potentially confounding factors. Cases were more likely to have had a number of problems that were associated with risk of mortality, such as low birth weight, a larger family size, a father with less education, a father in prison, an incomplete immunization

record, or a family with social problems. They also were less likely to have belonged to a nuclear family.

METHODOLOGICAL ISSUES: This study does not control for many factors that may be related to both infant feeding mode and risk of mortality, nor does it take steps to avoid reverse causality.

Retherford RD, Choe MK, Thapa S, Gbuhaju BB. To what extent does breastfeeding explain birth-interval effects on early childhood mortality? Demography 1989; 26(3):439–50.

COUNTRY: Nepal

SETTING: Urban and rural

DESIGN: Cross-sectional survey: data from the World Fertility Survey, n = 4,050 ever-married women aged 15–49

BREASTFEEDING DEFINITION: Duration of breastfeeding

OUTCOME MEASURES: All-cause childhood mortality

RESULTS: This paper examines the extent to which breastfeeding explains the birth-interval effect on early childhood mortality. Two age categories are used: birth to 18 months and 18 to 60 months. No breastfeeding is used as the reference category. Among children aged < 18 months, the effect of breastfeeding on mortality was significant and large. The relative risk associated with any breastfeeding is 0.19, which suggests an 81% mortality reduction. Subsequent birth interval also has a large and significant effect on mortality of the index child. Analysis of both the effects of breastfeeding and subsequent birth interval suggests that the effects of the subsequent birth interval on infant mortality of the index child are explained almost entirely by breastfeeding. Between 18 and 60 months, the effect of breastfeeding is smaller though still significant, with an adjusted relative risk of 0.45. Unlike the case for mortality up until 18 months, breastfeeding only partly explains the effect of the subsequent birth interval on the mortality risk of the index child. Thus, between the ages of 18 and 60 months, breastfeeding is only one of several factors through which following birth interval affects child mortality. The results also show that fathers' literacy has no effect on infant mortality, but it does have a substantial effect on child mortality. The authors interpret this finding to indicate that as long as a child is breastfed, he or she receives adequate nourishment and is not dependent on the father's ability to provide (as assessed indirectly through the relationship between paternal literacy and socioeconomic status). However, after weaning, the ability of the family to provide adequate food is determined by socioeconomic status.

METHODOLOGICAL ISSUES: Although the analysis controls for many potentially confounding factors, it does not adjust for the problem of reverse causality.

Habicht J-P, DaVanzo J, Butz WP. Mother's milk and sewage: Their interactive effects on infant mortality. Pediatrics 1988;81(3):456–61.

COUNTRY: Malaysia

SETTING: Urban and rural

DESIGN: Retrospective: n = 1,262 women and their 5,141 infants

BREASTFEEDING DEFINITION: Breastfed versus not breastfed

OUTCOME MEASURES: All-cause mortality

RESULTS: This study examined the relationships among breastfeeding, piped water, toilets and infant mortality. Breastfeeding was highly protective. Compared with breastfeeding, the adjusted relative risks of death due to not breastfeeding were 5.2 if the household had neither a toilet nor piped water, 2.67 if the household had a toilet only, and 2.51 if the household had both a toilet and piped water. The authors calculate that 21% of all deaths in this sample were due to not breastfeeding.

METHODOLOGICAL ISSUES: Deaths in the first week of life were excluded to prevent reverse causality. Analyses were adjusted for a number of potentially confounding factors.

Thapa S, Short RV, Potts M. Breast feeding, birth spacing and their effects on child survival. Nature 1988;335;679–82.

COUNTRY: 29 countries that had World Fertility Surveys

SETTING: Urban and rural

DESIGN: Cross-sectional: n = 150,000 women

BREASTFEEDING DEFINITION: Duration of breastfeeding

OUTCOME MEASURES: All-cause childhood mortality

RESULTS: This paper quantifies the total fertility rate. It estimates the number of potential births currently inhibited by breastfeeding and by modern forms of contraception in 29 countries and by three regions: Africa, Asia, and America. The paper provides estimates of the increase in the total fertility rate if breastfeeding duration were to decline by 25% and 50%. It also includes estimates of the increase in contraceptive prevalence that would be required to offset these declines in breastfeeding duration. For example, the paper estimates that, in Senegal, a 25% decline in breastfeeding duration would require almost a tripling in contraceptive prevalence. It also discusses the effect of birth intervals on child survival using estimates from other studies. The authors estimate that if all mothers could space their births at least 2 years apart, the result would be a 20% reduction in mortality in the first year of life. This reduction corresponds to about a half-million lives saved.

METHODOLOGICAL ISSUES: This paper does not provide estimates of the risk of mortality by different infant feeding modes but, rather, an argument as to the effect of breastfeeding on the total fertility rate and, by inference, to the effect on mortality through birth spacing. The much greater direct effects of breastfeeding on under-5 mortality are not considered. The estimates of reduced infant mortality with increased birth spacing could be the result of reverse causality, with neonatal death leading to an early postpartum pregnancy.

Habicht J-P, DaVanzo, J, Butz WP. Does breastfeeding really save lives, or are apparent benefits due to biases? Amer J Epidemiol 1986;123(2):279–90.

COUNTRY: Malaysia

SETTING: Urban and rural

DESIGN: Retrospective: n = 1,262 women and their 5,357 infants

BREASTFEEDING DEFINITION: Total duration of exclusive breastfeeding and breastfeeding

OUTCOME MEASURE: Infant mortality

RESULTS: The effects of breastfeeding on infant mortality are reported for three subperiods of infancy: 8–28 days, 29 days–6 months, and 7–12 months. Logistic regression was used to estimate the effect of infant feeding mode on mortality. The authors investigated the sensitivity of the association between infant feeding mode and mortality by estimating the effect for all live births, excluding cases where the length of breastfeeding was equal to the length of life, or when death occurred on the first day of life, or where breastfeeding stopped because of fatal illness. This sensitivity analysis showed that although the associations remained significant and in the expected direction, the magnitude was reduced, compared with analyses using the entire sample. Multivariate analysis, which controlled for a number of factors associated with both infant feeding mode and risk of mortality, showed a dose-response relationship in the expected direction for full and partial breastfeeding and risk of death. As expected, risks were also greater for younger infants. For example, the reductions in deaths per 1,000 infants per added month of full breastfeeding were 68.6, 24.9, and 3.4 for the periods, 8–28 days, 29 days–6 months, and 7–12 months, respectively. The reduction in deaths per 1,000 infants per added month of partial breastfeeding were 21.9, 11.2, and 1.7 for the three time periods.

METHODOLOGICAL ISSUES: This study controlled for reverse causality and for many potentially confounding factors. Age-related factors having to do with both mortality risk and infant feeding mode were addressed as well.

Butz WP, Habicht J-P, DaVanzo J. Environmental factors in the relationship between breastfeeding and infant mortality: The role of sanitation and water in Malaysia. Amer J Epidemiol 1984;119(4):516–25.

COUNTRY: Malaysia

SETTING: Urban and rural

DESIGN: Retrospective: n = 1,262 women and their 5,471 infants

BREASTFEEDING DEFINITION: Duration of supplemented and unsupplemented breastfeeding

OUTCOME MEASURE: All-cause mortality

RESULTS: This study examines the effect of breastfeeding, water, and toilet sanitation on infant mortality. Infancy is divided into three time periods: 8–28 days, 2–6 months, and 7–12 months. Breastfeeding is significantly associated with mortality, especially in early infancy. Infants who were fully breastfed throughout their first week of life have 16/1,000 fewer deaths during the first month than those not fully breastfed. The estimated

risk difference between unsupplemented breastfeeding the entire first 4 weeks and not breastfeeding at all is 25/1,000 deaths during the interval 2–6 months. In the last 6 months of infancy, infants who were fully breastfed through their first 6 months had 20/1,000 fewer deaths than those not breastfed at all. An interaction among breastfeeding, toilet sanitation, and mortality was found: the risk of death due to not breastfeeding increases in households with poor sanitation.

METHODOLOGICAL ISSUES: This is a methodologically strong study, which controlled for many potentially confounding factors.

Plank SJ, Milanesi ML. Infant feeding and infant mortality in rural Chile. Bull WHO 1973;48:203–10.

COUNTRY: Chile

SETTING: Rural

DESIGN: Cross-sectional survey of n = 1,712 women

BREASTFEEDING DEFINITION: Exclusive breastfeeding, any breastfeeding, bottle feeding

OUTCOME MEASURES: All-cause childhood mortality

RESULTS: This paper examines the association between infant feeding and mortality in rural Chilean infants. Breastfeeding declined significantly as maternal education and paternal income increased. Postneonatal deaths were significantly associated with infant feeding mode. Mortality rates are provided for 3 overlapping age groups: 1–12 months, 3–12 months, and 6–12 months. In the 1–12 months age group, the mortality rates for exclusive breastfeeding, breastfeeding plus bottle, and bottle only were 29.2, 56.0, and 60.5, respectively. Thus, using exclusive breastfeeding as the reference category, the unadjusted relative risk for bottle feeding was 2. In the 3–12 months age group, the mortality rates for exclusive breastfeeding, breastfeeding plus bottle, and bottle only were 13.8, 37.5, and 38.7, respectively. In the 6–12 months age group, the mortality rates for exclusive breastfeeding, breastfeeding plus bottle, and bottle only were 10.0, 14.0, and 19.9, respectively. Tests of statistical significance were not provided.

The authors note that some of the higher mortality associated with bottle feeding was an artifact because of the inclusion of low birth weight infants for whom supplementary milk was prescribed medically. The results also showed that those infants given bottles in addition to being breastfed had mortality rates similar to those who received only a bottle. Once bottle feeding began, breastfeeding appeared to offer no protection against mortality. There was an inverse association among infant mortality, family income, environmental factors, and medical care: families with higher incomes, better household sanitation, and greater access to medical care also were more likely to use bottles and had greater mortality risks. This suggests that the differences in infant mortality observed were attributable to bottle feeding and inappropriate use of supplementary foods.

METHODOLOGICAL ISSUES: Neonatal deaths and living children under 4 weeks of age were excluded to avoid some of the bias caused by reverse causality. Risk ratios were likely biased downward because there was no adjustment for the confounding postive association of bottle feeding with higher family income and maternal education. Tests of statistical significance were not provided.

3. EFFECT OF BREASTFEEDING ON INTELLECTUAL AND MOTOR DEVELOPMENT

The studies described below explore the link between breastfeeding and children's development. Studies cover differences in test results between breastfed and non-breastfed children and possible biological explanations for a causal link between breastfeeding and intellectual and motor development.

Mortenson EL, Michaelsen KF, Sanders SA, Reinisch JM. The association between duration of breastfeeding and adult intelligence, JAMA 2002;287:2365-2371.

COUNTRY: Denmark

SETTING: Urban (Copenhagen)

DESIGN: Prospective birth cohort; comprising 2 samples: 1) 973 men and women and 2) 2280 men

BREASTFEEDING DEFINITION: 5 categories of breastfeeding duration assessed by physician interview at 1 year: ≤1, 2–3, 4–6, 7–9, and >9 months.

OUTCOME MEASURE: Test scores on the Danish version of the Wechsler Adult Intelligence Scale (WAIS), including Verbal, Performance and Full scales (sample 1) and the Børge Priens Prøve (BPP) (sample 2). The BPP is an intelligence test administered at the compulsary registration of all Danish males for the military draft at age 18.

RESULTS: After adjusting for a variety of factors, there was a dose-response relationship between breastfeeding duration and all IQ measures (Verbal, Performance and Full scales of the WAIS and the BPP). This duration effect appeared to be non-linear with individuals in the last two duration categories (7–9 and >9 months) having similar test results. The adjusted difference between test scores of individuals breastfed for <1 months and those breastfed for 7–9 months was 6.6 points for the Full Scale WAIS and 2.1 points for the BPP, representing one half and one fifth of a standard deviation, respectively.

METHODOLOGICAL ISSUES: The regression analysis adjusted for a wide variety of potentially confounding variables, interactions and non-linear effects.

Dewey KG, Cohen RJ, Brown KH, et al. Effects of exclusive breastfeeding for four versus six months on maternal nutritional status and infant motor development: Results of two randomized trials in Honduras. J Nutr 2001;131:262–7.

COUNTRY: Honduras

SETTING: Maternity hospitals in San Pedro Sula

DESIGN: Prospective observational study for the first 4 months of life, followed by a randomized intervention trial from 4 to 6 months and a follow-up period for the second half of the first year. Trial 1 consisted of 141 infants of women from low socioeconomic status; Trial 2 consisted of 119 low birth weight infants. All infants were exclusively breastfed (EBF) from birth to 4 months and then randomized to EBF until 6 months or to introduction of solid foods at month 4.

BREASTFEEDING DEFINITION: Exclusive breastfeeding defined as receiving only breastmilk

OUTCOME MEASURE: Maternal body mass index, duration of lactational amenorrhea, and infant motor development (following 10 motor milestones)

RESULTS: Infants who only received breastmilk for the first 6 months of life crawled sooner and were more likely to walk by 12 months of age than infants who received solid foods starting at 4 months. Infants in the EBF group also were marginally (but significantly) able to sit earlier than those who received solids by 4 months of age.

METHODOLOGICAL ISSUES: All groups in both studies were exclusively breastfed until 4 months and continued to receive some amount of breastmilk past 6 months. Since neither study had a formula-only group, it can be assumed that the developmental differences observed would be stronger in situations where the differences in infant feeding practices are less subtle.

Horwood LJ, Darlow BA, Mogridge N. Breast milk feeding and cognitive ability at 7-8 years. Arch Dis Child Fetal Neonatal Ed 2001; 84:F23–F27.

COUNTRY: New Zealand

SETTING: Nationwide

DESIGN: Prospective, n=280 survivors of a cohort of 413 very low birth weight infants born in 1986 and assessed at 7-8 years of age

BREASTFEEDING DEFINITION: Not breastfed, breastfed < 4 months, 4-7.9 months, ≥ 8 months

OUTCOME MEASURE: Verbal and performance IQ scores using the revised Wechsler intelligence scale for children

RESULTS: Breastfeeding duration was significantly related to both verbal and performance IQ test scores. Infants breastfed for 8 months or longer had a verbal IQ score 10.2 points higher and a performance IQ score 6.2 points higher on average than those of non-breastfed infants. After adjusting for potentially confounding factors, these advantages were reduced to 6.0 points in the case of verbal IQ and to statistical non-significance in the case of performance IQ.

METHODOLOGICAL ISSUES: A variety of perinatal and household socio-economic and demographic factors were controlled for in multiple regression analysis.

Anderson JW, Johnstone BM, Remley DT. Breast-feeding and cognitive development: A meta-analysis. Am J Clin Nutr 1999;70:525–35.

COUNTRY: Multicountry (United Kingdom, United States, Australia, Germany, New Zealand, and Spain)

SETTING: Urban and rural

DESIGN: Meta-analysis of 20 observational cohort and case-control studies, including low or normal birth weight infants

BREASTFEEDING DEFINITION: Predominantly breastfed versus predominantly formula-fed and breastfed. Breastfed group was pooled for duration into: 4–7, 8–11, 12–19, 20–27, and ≥ 28 wks.

OUTCOME MEASURE: The most commonly used tests of cognitive development were the Bayley Mental Development Index (12 observations), the Peabody Picture Vocabulary Test (6 observations), the General Cognitive Index of the McCarthy Scales of Children's Abilities (5 observations), the Wechsler Child Intelligence Scale (4 observations), and the Stanford-Binet Intelligence Scale (2 observations).

RESULTS: The average unadjusted pooled mean benefit in cognitive development score of breastfeeding, compared with formula feeding, ranged from 5 to 6 points. After adjustment, the difference declined to 3.16 points, but remained significant. The group deriving the greatest benefit from breastfeeding was low birth weight children, with an average adjusted benefit of 5.18 points across the 6 studies available. This was significantly higher than the average adjusted increment of 2.66 points observed for breastfed children born with normal weight. A significant benefit was observed as well for longer breastfeeding duration. The results showed a gradual increase in the magnitude of the benefit in cognitive development correlated to breastfeeding exposure as it increased from 8 to 11 weeks (weighted mean benefit of 1.68 points) to ≥ 28 weeks (weighted mean benefit of 2.91 points).

METHODOLOGICAL ISSUES: Appropriately conducted meta-analysis with careful specificity of criteria for study selection, quality assessment, and control of confounding variables.

Horwood LJ, Fergusson DM. Breastfeeding and later cognitive and academic outcomes. Pediatrics 1998;101(1):e9.

COUNTRY: New Zealand

SETTING: Christchurch urban population

DESIGN: Longitudinal cohort study (n > 1,000 children), studied at birth, 4 months, 1 year, at annual intervals thereafter to 16 years of age, and again at age 18

BREASTFEEDING DEFINITION: Exclusive breastfeeding was defined as receiving breastmilk, to age of 4 months, without any additional cow's milk, milk formula preparation, or solid food. Other categories included not breastfed, breastfed for < 4 months, breastfed for 4–7 months, and breastfed for ≥ 8 months.

OUTCOME MEASURE: Child's cognitive ability and academic achievement (using a variety of tools) from 8 to 18 years of age

RESULTS: Breastfeeding was significantly associated with higher scores of cognitive ability, teacher ratings, standardized achievement tests, and increased high school success. The duration of breastfeeding was positively associated with cognitive ability and academic success levels from middle childhood to school graduation. However, after controlling for social and family differences, the strength of the associations was reduced; suggesting that breastmilk was not the sole factor affecting cognitive ability and academic performance. Nonetheless, small but consistent tendencies were observed for an association between increasing duration of breastfeeding and increased IQ scores, performance on standard achievement tests, teacher ratings, and high school achievement.

Even after statistical adjustment, children who received breastmilk for ≥ 8 months had higher test scores than those who were not breastfed.

METHODOLOGICAL ISSUES: Multiple regression analyses were performed to study associations between duration of breastfeeding and cognitive ability into adulthood, and between breastfeeding and indices of academic achievement. Statistical significance was tested by one-way analysis of variance and the dichotomous measure by χ^2 test of independence. Confounding factors included measures of social, family, and others known to have an association with a mother's decision to breastfeed and/or with cognitive and academic outcomes. Mothers who breastfed tended to have higher socioeconomic status and were less likely to be single parents than mothers who did not breastfeed.

Wang YS,Wu SY. The effect of exclusive breastfeeding on development and incidence of infection in infants. J Hum Lact 1996;12:27–30.

COUNTRY: China

SETTING: Xu Hui District, Shanghai

DESIGN: Prospective population-based study of infants aged less than 1 year (n = 145)

BREASTFEEDING DEFINITION: Exclusive breastfeeding for at least 4 months and partial breastfeeding (including no breastfeeding) for the first 4 months of life

OUTCOME MEASURE: Physical development determined by weight and height, development assessment measured using the Denver Developmental Screening Test and cumulative incidence of infectious diseases including respiratory, gastrointestinal, and skin infections

RESULTS: Infants who were exclusively breastfed had significantly higher mean body weight at 4 months than those who were not exclusively breastfed (7.46 ± 0.74 versus 7.18 ± 0.89 kg, $p < 0.05$). At 1 year, mean Gross Motor Development scores were 47.37 for exclusively breastfed children, compared with 30.68 for nonexclusively breastfed children. Furthermore, 30 exclusively breastfed children had failed the Gross Motor Development Assesment, compared with 61 in the nonexclusively breastfed group ($p < 0.05$).

METHODOLOGICAL ISSUES: No comparison was provided between the mothers of the infants exclusively breastfed and the mothers of those partially breastfed.

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de Andraca I, Uauy R. Breastfeeding for optimal mental development: The alpha and omega in human milk. World Rev of Nutr Diet 1995;78:1–27.

These review articles summarize the results of many of the studies included in this bibliography. They also discuss specific breastmilk components, particularly essential fatty acids and research results that examine possible mechanisms whereby breastmilk may have an effect on later intelligence. The article concludes that all results comparing breastfeeding with bottle feeding need to be interpreted cautiously because of the potential for confounding. The authors suggest that the effects of breastfeeding are

complex and related to both the nutritional properties of breastmilk and the emotional and bonding factors associated with the process of breastfeeding, and their interaction. The article also concludes that the challenge in future studies will be to establish a conceptual framework that enables these separate and interactive effects to be disentangled. They argue further that breastfeeding should be considered best unless proven otherwise, and that it is particularly important in developing countries and among underprivileged communities in developed countries.

Florey CDV, Leech AM, Blackhall AA. Infant feeding and mental and motor development at 18 months of age in first born singletons. Inter J Epidem 1995;S21–6.

COUNTRY: Scotland

SETTING: Dundee (urban)

DESIGN: Population-based prospective/retrospective: n = 592

BREASTFEEDING DEFINITION: Breastfed versus bottle-fed, as assessed from hospital discharge records and home health visits

OUTCOME MEASURE: Bayley Mental and Motor Developmental Indices

RESULTS: The study population consisted of 846 firstborn singletons born during a 1-month period in 1986, of whom 592 were assessed for mental and motor development at 18 months of age. Potentially confounding factors controlled in the analysis included partner's social class; maternal age, height, education, cigarette and alcohol consumption during pregnancy; and the infant's sex, birth weight, gestational age, and placental weight. Unadjusted analyses showed that the whole distribution of scores for mental outcomes for bottle-fed children was lower, which suggests that whatever is influencing scores affects children over the entire range of mental abilities. The unadjusted mean difference was 7.7 points (110.2 for breastfed and 102.5 for bottle-fed children). No consistent difference was found for the motor development indices. Regression analyses, which controlled for potentially confounding factors, showed a significant difference in mental developmental indices of between 3.7 and 5.7 points, depending on the source of the infant feeding data. The feeding data were not completely concordant for all children.

METHODOLOGICAL ISSUES: Breastfeeding is poorly defined, and it is not clear what the duration of breastfeeding was among the breastfed cohort. Nonetheless, these data were not collected as part of the study on mental and motor development but were available from birth and early health records. One psychologist performed all the tests and was blinded to the infant feeding mode.

Greene LC, Lucas A, Livingstone MBE, et al. Relationship between early diet and subsequent cognitive performance during adolescence. Biochem Soc Trans 1995;23:376S.

COUNTRY: England

SETTING: South Tees area

DESIGN: Retrospective: n=432 subjects aged 11–16 years

BREASTFEEDING DEFINITION: Breastfed versus not breastfed as assessed by medical records; duration of breastfeeding (1–12 weeks and > 12 weeks)

OUTCOME MEASURE: Cognitive ability as assessed by the Raven Standard Progressive Matrices and subtests of the Primary Mental Abilities test

RESULTS: This study examined whether breastfeeding was associated with differences in IQ between 11 and 16 years of age. Breastfeeding was positively associated with social class and education. Firstborn children also were significantly more likely to be breastfed. Unadjusted results show breastfeeding to be significantly and positively associated with IQ scores. However, these differences disappeared when analyses were adjusted for potentially confounding factors. In these analyses, social class, birth rank, and maternal age were significant. The effect of breastfeeding duration was also assessed for the following breastfeeding categories: 1) 1–12 weeks and > 12 weeks. No significant differences in birth weight, gestational age, birth rank, child's sex, maternal age, maternal education, and social class were found between the 2 groups. A significant 6-point advantage in verbal IQ and a 5.4-point advantage in reasoning IQ was found after adjustment for potentially confounding factors for infants breastfed for > 12 weeks.

METHODOLOGICAL ISSUES: Authors controlled for many known potentially confounding factors. One strength of the study is that it looks at the relationship between breastfeeding duration and development. Because all mothers in this subanalysis breastfed, this is likely to control better for familial factors associated with maternal decisions to breastfeed and contribute toward child development.

Uauy R, de Andraca I. Human milk and breastfeeding for optimal mental development. J Nutr 1995;125:2278S–2289S.

(The results of this study were the same as *de Andraca I, Uauy R. Breastfeeding for optimal mental development: The alpha and omega in human milk. World Rev Nutr Diet 1995;78:1–27*; therefore, we chose to only summarize one of them, while making reference to both).

Lucas A, Morley R, Cole TJ, Gore SM. A randomized multicentre study of human milk versus formula and later development in preterm infants. Archives Dis Child 1994;70:F141–6.

COUNTRY: England

SETTING: 3 neonatal clinics

DESIGN: Randomized trial: children (n = 502) who were preterm and < 1850 g at birth and followed for 18 months. Two separate studies were conducted, and the results were reported in several articles. In the first 3-center study, infants whose mothers chose not to use their own breastmilk were randomized to receive a special high-protein and calorie preterm formula or banked donor breastmilk (Trial A). Infants whose mothers chose to provide their own expressed breastmilk were randomly assigned to receive the preterm formula or banked donor breastmilk to supplement their own breastmilk as needed (Trial B). In Trial B, the proportion of breastmilk provided by the mother ranged from 0% to 100%, with a median of 53%. There were no differences in the proportion of maternal breastmilk provided between the two treatment groups. In a separate 2-center study, infants whose mothers chose not to breastfeed were randomized to receive a

regular-term formula or the special preterm formula (Trial A). Infants whose mothers chose to provide expressed breastmilk were randomly assigned to receive term formula or preterm formula to supplement maternal breastmilk as needed (Trial B). Thus, within studies, trials A and B can be treated independently or combined to compare the banked brestmilk or term formulas versus the preterm formula as the sole diet or in combination with the mother's own expressed breastmilk.

BREASTFEEDING DEFINITION: Banked breastmilk versus special preterm formula (Trial A) and banked breastmilk and expressed maternal breastmilk versus preterm formula and expressed maternal breastmilk (Trial B). Both treatments were provided to the infants by nasogastric tube.

OUTCOME MEASURE: Bayley psychomotor and mental development indices at 18 months of age

RESULTS: Children who were fed the special preterm formula had better motor and mental development outcomes at 18 months of age than children who received a standard formula (see Lucas et al., 1992). Thus, the formula used in the present study was the "best" available.

There were no significant developmental differences at 18 months between the children receiving the preterm formula and those receiving banked breastmilk as either the sole diet (Trial A) or in combination with the expressed maternal breastmilk (Trial B). Male children who had received preterm formula had a 7.6 point advantage on the Bayley psychomotor development test over male children receiving banked breastmilk, but this difference was not statistically significant. When the children fed banked breastmilk and standard formula were compared (using data from both studies and, hence, breaking the randomized design), children fed banked breastmilk had significantly higher scores. In this nonrandomized comparison, children fed banked breastmilk scored 8.8 points higher on the Bayley index of psychomotor development than those fed standard formula. The differences in mental development favored children fed banked breastmilk over children receiving term formula, but these differences did not reach statistical significance.

METHODOLOGICAL ISSUES: Randomization permits the effect of breastmilk to be evaluated in a manner that is not confounded by social and educational differences between mothers who chose to breastfeed and those who do not. Interviewers who administered the Bayley Developmental Tests were blinded to infant feeding status. Although the design was intended to control for self-selection in choice of infant feeding mode, the most interesting results of the study were the comparisons that broke this design and compared the banked breastmilk to term formula, which were treatments from two different studies. The extent to which results from very low birth weight infants are representative of normal weight infants is unknown.

Pollock JI. Long-term associations with infant feeding in a clinically advantaged population of babies. Develop Med Child Neurol 1994;36:429–40.

COUNTRY: England

SETTING: Nationwide

DESIGN: Prospective/retrospective: n = 3838 children born within a 1-week period in 1970 and assessed at 5 and 10 years of age

BREASTFEEDING DEFINITION: Exclusively breastfed for 3 months or more versus bottle-fed

OUTCOME MEASURES: Health, physical, and developmental assessments through a vocabulary test at 5 years and intellectual assessment through the British Ability Scales test at 10 years

RESULTS: This methodologically rigorous study compares the physical, health, and developmental differences between 2 cohorts of children: those who had been exclusively breastfed for 3 or more months and those who had been bottle-fed, excluding clinically disadvantaged infants. The potentially confounding effect of 76 variables was assessed, and a hierarchical regression procedure was used to identify and include potentially confounding factors in the final model. Adjusted odds ratios and their 99% confidence intervals were presented. Exclusive breastfeeding was positively associated with both maternal and paternal education and maternal attendance at prenatal classes and negatively associated with maternal smoking. At 5 years of age, a total of 22 outcomes related to medical history and physical and mental development were assessed. The 3 intellectual development tests administered were a picture-based vocabulary test, drawing a human figure, and copying a simple design.

The authors estimate that using the 2-tailed threshold for significance, the expected number of chance associations was 0.2. Of the 22 outcomes, only the picture vocabulary test was significantly and positively associated with exclusive breastfeeding. At 10 years of age, a total of 24 medical, 7 physical, and 8 intellectual factors were assessed. The expected number of significant chance associations was 0.4. None of the medical or physical factors was associated with infant feeding mode, but exclusively breastfed children scored significantly higher on 4 of the tests for intellectual development. Linear regression on actual scores showed that exclusively breastfed infants scored 2.6 to 3.5 points higher in a population mean of 100 on the British Ability Scales for word definitions (involving retrieval and application of knowledge), matrices, similarities (involving reasoning skills), and total score (measuring overall perceptual and cognitive ability).

The authors conclude that the study supports the hypothesis that some aspects of intellectual attainment can be demonstrated to be superior among children who were exclusively breastfed for at least 3 months, compared with their bottle-fed counterparts—after early clinically disadvantaged bottle-fed children were excluded from the analysis, and remaining potentially confounding factors were controlled.

METHODOLOGICAL ISSUES: As with the other studies in this area, uncontrolled confounding may at least partly explain the results observed.

Rogan WJ, Gladen BC. Breast-feeding and cognitive development. Early Hum Dev 1993;31:181–93.

COUNTRY: United States

SETTING: North Carolina (hospital and clinic-based)

DESIGN: Prospective: birth cohort of children assessed at different ages up to age 5 years (initial n = 855)

BREASTFEEDING DEFINITION: Breastfeeding duration divided into 4 categories (short, medium, long, very long), bottle feeding

OUTCOME MEASURE: Bayley Scales of Infant Development at 6, 12, 18, and 24 months; subscales of both mental and psychomotor development; McCarthy Scales at 3, 4, and 5 years; report cards at third grade

RESULTS: This study examined whether breastfeeding was associated with differences in mental and motor skills at various age intervals up to 5 years of age and with school performance in third grade. The unadjusted results show that there was a tendency for the Bayley Mental Development Index to be higher among breastfed infants than among bottle-fed infants, and to be higher among those breastfed infants who were breastfed for longer durations. After adjustment for potentially confounding factors, children breastfed the shortest had scores 1 to 3 points lower than those bottle-fed, and 3 to 7 points lower than those breastfed the longest. Differences were significant only at 24 months of age, however.

The results from the Psychomotor Development Index were similar, with a tendency for slightly higher scores among children breastfed for longer durations, and with differences among groups significant only at 24 months. With respect to the McCarthy Scale, children breastfed the longest had a tendency toward higher scores (2 to 4 points) than children breastfed the shortest. These differences were significant at 3 and 4 years, but only marginally so at 5 years. Duration of breastfeeding was marginally associated with both English and math grades at third grade. However, after adjustment for potentially confounding factors, the differences were only marginally significant for English and not significant for math. The difference between children bottle-fed and breastfed the shortest was 0.17 points, and between children breastfed the shortest and breastfed the longest, the difference was 0.06 points.

The authors conclude that there were small but significant advantages for breastfed children on some Bayley and McCarthy subscales at all time points from 2 through 5 years of age. This advantage was more consistent for cognitive than motor skills (which is consistent with other studies).

METHODOLOGICAL ISSUES: Although the authors controlled for many known potentially confounding variables, mothers who chose to breastfeed may have had other characteristics associated with child development that could explain the results.

Lucas A, Morley R, Cole TJ, Lister G, Lesson-Payne C. Breast milk and subsequent intelligence quotient in children born preterm. Lancet 1992;339:261–4.

COUNTRY: England

SETTING: 5 neonatal clinics

DESIGN: Prospective: children (n = 300) who were preterm and < 1850 g at birth and followed for about 8 years

BREASTFEEDING DEFINITION: Maternal expressed breastmilk exclusively, or in combination with formula, versus formula; proportion of total intake provided by maternal breastmilk

OUTCOME MEASURE: Intelligence quotient (IQ) at 7 to 8 years of age

RESULTS: This study examined whether having been fed breastmilk through a nasogastric tube early in life was associated with intelligence quotient at 7 to 8 years of age. Because breastmilk was delivered to the infant by nasogastric tube, the authors were able to examine the effect of breastmilk on subsequent intelligence rather than the actual process of breastfeeding. There was a significant dose-response relationship between the proportion of breastmilk provided to the infant and intelligence ($p < 0.05$). The effect was greatest for the verbal scale, where a 9-point difference was found between those infants who consumed 100 percent breastmilk and those infants who consumed no breastmilk. Children of mothers who chose to provide breastmilk, but were unable to do so, had intelligence quotients similar to children whose mothers did not choose to provide breastmilk. Overall, differences in intelligence quotient between those children who received some breastmilk and those who received none was 8.3 points. The data were adjusted for maternal education, social class, days the infant was on a ventilator, and infant sex, which also were associated with intelligence quotient. The effect of early breastmilk feeding, however, was stronger than any of these factors. The effects of early breastmilk feeding on intelligence quotient in preterm infants are larger than the effects for full-term infants. The authors suggest that preterm infants are especially vulnerable to the effects of early nutrition.

METHODOLOGICAL ISSUES: Mothers who provided breastmilk were of a higher social class and educational level, which may be associated with parenting attributes that are not completely captured by these two measures. The authors state that the results could be explained by differences between the groups in parenting skills or genetics even after adjustment for social class and maternal education.

Morrow-Tlucak M, Haude RH, Ernhart CB. Breastfeeding and cognitive development in the first 2 years of life. Social Sci & Med 1988;26(6):635–9.

COUNTRY: United States

SETTING: Inner city

DESIGN: Prospective: Children (n = 229) at risk for developmental delay

BREASTFEEDING DEFINITION: Duration of breastfeeding as a continuous variable or categorized as follows: 0, < 4 months, > 4 months

OUTCOME MEASURE: Bayley Motor Development Test at 6 months, 1 and 2 years, and the Home Observation for Measurement of the Environment at 1 and 2 years

RESULTS: This study examined whether breastfeeding was associated with differences in mental and motor development during the first 2 years of life. Breastfeeding was associated with significantly increased scores on the Bayley Mental Development Index. At 12 and 24 months, scores were about 2.5 points higher for children breastfed > 4 months than for those breastfed < 4 months ($p < 0.001$). Differences at 6 months favored breastfeeding, but failed to reach statistical significance. Mothers who breastfed were more likely to have more education and be older and married. Because these are also characteristics that might independently and positively influence child development, they were controlled for in the analysis.

METHODOLOGICAL ISSUES: The authors acknowledge that the observed differences may be at least partly due to uncontrolled maternal social factors.

Taylor B, Wadsworth J. Breastfeeding and child development at five years. Dev Med Child Neurol 1984;26:73–80.

COUNTRY: United Kingdom

SETTING: Nationwide

DESIGN: Prospective/retrospective cohort study, n=13,135 children born within a one-week period in 1970 and assessed at five years of age

BREASTFEEDING DEFINITION: Not breastfed, breastfed < 1 month, 1–2.9 months, ≥ 3 months.

OUTCOME MEASURE: The English Picture Vocabulary Test, Copying Designs Score, and the Rutter Child Behavior Score.

RESULTS: The duration of breastfeeding was associated with improved scores on the three tests but, after controlling for potentially confounding factors, the association with the Rutter Score was non-linear and only marginally significant ($p=0.046$). The associations with the other two tests were attenuated but remained significant ($p<0.001$). The authors suggest that despite the statistical significance of the adjusted results the magnitudes of these effects were small.

METHODOLOGICAL ISSUES: The analysis controlled for a variety of potentially confounding factors including socio-economic status and "home furnishings and equipment," maternal age, maternal smoking, and number of siblings. However, by also including other behavioral measures as covariates in the analysis (for example the Rutter Child Behavior Score is cited as a significant covariate in the analysis of the relationship between breastfeeding duration and the vocabulary scores), the true effect of breastfeeding on child development may have been underestimated in the adjusted analysis.

Fergusson DM, Beautrais AL, Silva PA. Breast-feeding and cognitive development in the first seven years of life. Soc Sci & Med 1982;16:1705–8.

COUNTRY: New Zealand

SETTING: Dunedin

DESIGN: Prospective: birth cohort of children assessed at age 3 (n = 1,037), age 5 (n = 997), and age 7 years (n = 954)

BREASTFEEDING DEFINITION: Breastfed > 4 months, breastfed < 4 months, bottle fed

OUTCOME MEASURE: Measures of intelligence at 3, 5, and 7 years. The 3-year-old measure was based on the Peabody Picture Vocabulary Test, the 5-year measure on the Stanford Binet Intelligence Scale, and the 7-year measure on the Weschler Child Intelligence Scale. Language development was also measured at the 3 ages and articulation at ages 5 and 7 years.

RESULTS: This study examined whether breastfeeding was associated with differences in 11 indicators of intelligence and language development at ages 3, 5, and 7 years. The unadjusted results show that there was a tendency for test scores to vary with the duration of breastfeeding among children breastfed 4 months or longer. On tests that had a standard deviation of 10, scores of these children were 1.90 to 5.55 (mean = 3.84) points higher than those of bottle-fed children. Although adjustment for 7 co-variates (maternal intelligence, maternal educational level, maternal training in child rearing, child experience, family socioeconomic status, child's birth weight, and gestational age) attenuated these differences, breastfed children still had significantly higher scores (by 0.82 to 2.71 (mean = 1.89) points). There was no sex-breastfeeding interaction, which indicates that sexes do not respond differently to the effect of breastfeeding on intelligence.

METHODOLOGICAL ISSUES: The authors conclude that breastfeeding may be associated with very small improvements in intelligence and language development. Alternatively, the difference may have been due to the effects of other confounding factors not entered into the analysis.

Rodgers B. Feeding in infancy and later ability and attainment: A longitudinal study. Develop Med Child Neurol 1978;20:421–6.

COUNTRY: England

SETTING: Nationwide

DESIGN: Prospective: survey sample of live births (n = 5,362) followed for 15 years

BREASTFEEDING DEFINITION: Duration of any breastfeeding and duration of bottle-feeding

OUTCOME MEASURE: Tests of picture intelligence and mechanical word reading at 8 years of age and scores for reading attainment, nonverbal ability, and mathematical attainment at 15 years of age

RESULTS: This study examined whether breastfeeding was associated with differences in mental and motor development at 8 and 15 years in a cohort of children followed prospectively from birth. Breastfeeding was found to be more common in families of

higher social class, higher educational levels, and that showed greater interest in the child's primary education. Multivariate analyses were performed to control for these potentially confounding factors. Breastfeeding was associated with significantly increased scores on 4 of the 5 outcomes examined: these included picture intelligence in children 8 years of age (1.76 points), nonverbal ability (1.76 points), mathematics (1.55 points), and sentence completion (1.73 points) in children 15 years of age.

METHODOLOGICAL ISSUES: Although the authors controlled for most known potentially confounding factors, the fact that breastfeeding was associated with other familial attributes that contribute to intellectual development makes it difficult to rule out uncontrolled confounding in the reported associations.

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4. EFFECT OF BREASTFEEDING ON CHRONIC DISEASES

Papers summarized in this section explore associations between infant feeding and chronic or noncommunicable diseases. Some observational studies suggest that suboptimal breastfeeding may be a factor in obesity, diabetes, cancer, and other conditions.

4.1 Effect of Breastfeeding on Obesity

Gillman MW, Rifas-Shiman SL, Carmargo CA Jr., Berkey CS, Frazier AL, Rockett HRH,et al. Risk of overweight among adolescents who were breastfed as infants. JAMA 2001;285:2461–7.

COUNTRY: United States

SETTING: Nationwide

DESIGN: Cohort study using participants from the Growing Up Today Study (on diet, activity, and growth), n = 15,341 (8,186 girls and 7,155 boys) 9–14 years old

BREASTFEEDING DEFINITION: Using a 5-point scale: breastmilk only, more breastmilk than infant formula, both equally, more infant formula than breastmilk, infant formula only

OUTCOME MEASURE: Overweight status defined as body mass index (BMI) exceeding the 95th percentile for age and sex from U.S. national data

RESULTS: There was an inverse association between duration of breastfeeding and risk of overweight; those who were breastfed for ≥ 7 months were 20% less likely to be overweight than those who were breastfed for ≤ 3 months. Similarly, adolescents who received mostly or only breastmilk in the first 6 months had 22% lower risk of being overweight. For mothers, those who exclusively breastfed for the first 6 months had the lowest BMI, and those who breastfed the longest had a lower BMI than mothers who breastfed for shorter periods. Time of introduction of solids had no effect on the outcomes.

METHODOLOGICAL ISSUES: Sex-specific questionnaires were used to collect self-reported information from the participants regarding their age, sex, race/ethnicity, height, weight, sexual maturity, age at menarche, diet, and physical activity. Mothers responded to a supplemental questionnaire with information about the children's birth weight and length, gestational age, childhood medical conditions, and infant feeding practices. Comparisons were made between subjects who were mostly or only breastfed and those who were mostly or only formula-fed, and between subjects who were breastfed ≥ 7 months and those breastfed for ≤ 3 months. Co-variates included sexual maturity, sex, energy intake, total physical activity, hours of TV watching, and mother's body mass index (in 1995). Potential confounders included social and economic factors, including birth weight. All participants were children of registered nurses who participated in the Nurses Health Study II, and 93.6% of them were white.

Hediger ML, Overpeck MD, Kuczmarski RJ, Ruan WJ. Association between infant breastfeeding and overweight in young children. JAMA 2001;285:2453–60.

COUNTRY: United States

SETTING: Nationwide

DESIGN: Data obtained from the cross-sectional National Health and Nutrition Examination Survey III (NHANES III) study: n = 2,685 (1,310 boys and 1,375 girls) 3–5 years old

BREASTFEEDING DEFINITION: Fully breastfed if no liquids other than breastmilk or water were received daily, partially breastfed if daily supplements with formula or milk were received

OUTCOME MEASURE: Body mass index (BMI) between 85th and 94th percentile was considered "at risk" of overweight; body mass index ≥ 95th percentile was considered overweight

RESULTS: Children who were ever breastfed were 37% less likely to be at risk of overweight and 16% less likely to be overweight than children who were never breastfed. There was no clear dose-dependent effect of duration of full breastfeeding with risk of overweight or with overweight. Although there was a slight reduction in child body mass index with duration of full breastfeeding, the difference was not statistically significant. Eleven percent of the children were determined to be at risk of overweight, while 8.2% were classified as overweight. Girls showed a trend toward increasing overweight between 3 and 5 years of age. Ethnic differences were observed regarding ever having been breastfed, with non-Hispanic black infants being the least likely ever to have been breastfed. Maternal BMI influenced breastfeeding patterns: underweight mothers breastfed for shorter periods of time than normal-weight mothers, while overweight and obese mothers were more likely not to breastfeed at all. The strongest predictor of overweight among children was the mother's present BMI; children of overweight and obese women were 3 and 4 times more likely to be at risk of overweight, respectively, than children of normal-weight mothers.

METHODOLOGICAL ISSUES: Ethnically diverse, U.S.-born children 3–5 years old were studied. Weighted sample statistical analyses and standard error estimations were done. Multiple regression was used to estimate the effect of duration of full breastfeeding on child body mass index. Odds and adjusted odds ratios were estimated for risk of overweight and for overweight using normal body mass index as the reference. Confounding variables were taken into account, and unweighted analyses were performed to confirm the significance of the findings.

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von Kries R, Koletzko B, Sauerwald T, et al. Breast feeding and obesity: Cross sectional study. Br Med J 1999;319:147–50.

COUNTRY: Germany

SETTING: Bavaria (southern Germany, rural regions)

DESIGN: Cross-sectional survey: n = 9,357 children aged 5–6 years

BREASTFEEDING DEFINITION: Exclusive breastfeeding was defined as giving no food other than breastmilk to the child.

OUTCOME MEASURE: Body mass index (kg/meter^2); obesity was defined as body mass index > 97th percentile and overweight as body mass index > 90th percentile.

RESULTS: There was a clear dose-response relationship between the duration of breastfeeding and the prevalence of overweight or obesity. Children who had been breastfed for ≥ 6 months were more than 30% less likely to be overweight and more than 40% less likely to be obese.

METHODOLOGICAL ISSUES: Anthropometric data were obtained from mandatory school entrance examinations and dietary habits, and complementary feeding information was gathered from questionnaires sent to parents. Chi-square tests were used to compare children who were and were not breastfed, and logistic regression models were used to assess the impact of variables associated with breastfeeding and being overweight or obese.

4.2 Effect of Breastfeeding on Diabetes

Jones ME, Swerdlow AJ, Gill LE, et al. Pre-natal and early life risk factors for childhood onset diabetes mellitus: A record linkage study. Int J Epidem 1998;27:444–9.

COUNTRY: United Kingdom

SETTING: Urban

DESIGN: Case-control study using data from the Oxford Record Linkage Study (ORLS)

BREASTFEEDING DEFINITION: Breastfed or nonbreastfed infants

OUTCOME MEASURE: Incidence of diabetes mellitus

RESULTS: There was a significant 33% increased risk of diabetes among infants who were not breastfed at discharge. Maternal diabetes was a strong predictor of diabetes in children. Maternal preeclampsia was associated with increased risk for early and later onset of diabetes.

METHODOLOGICAL ISSUES: Conditional logistic regression for matched case-control studies was used for calculating adjusted relative risk of diabetes among 0- to 20-year-olds. Breastfeeding status was obtained before the actual diagnosis of diabetes in the children.

Pettitt DJ, Forman MR, Hanson RL, Knowler WC, Bennett PH. Breastfeeding and the incidence of non-insulin-dependent diabetes mellitus in Pima Indians. Lancet 1997;350:166–8.

COUNTRY: United States

SETTING: Not reported

DESIGN: Longitudinal: breastfeeding data obtained retrospectively but before most of the subjects had developed diabetes

BREASTFEEDING DEFINITION: Exclusive breastfeeding (EBF), partial breast-feeding, exclusive formula-feeding (FF) during the first 2 months of life

OUTCOME MEASURE: Noninsulin-dependent diabetes mellitus (NIDDM) measured by a glucose tolerance test

RESULTS: The rate of NIDDM for those exclusively breastfed was lower than for those who were exclusively bottle-fed. At age 10–19 years, none of the EBF children had developed NIDDM, whereas 3.6% of the FF children had. At ages 20–29 years, 8.6% of the EBF and 14.7% of the FF subjects had developed NIDDM, and at ages 30–39 years, 20% of the EBF and 29.6% of the FF subjects had developed NIDDM. The odds ratio for NIDDM for subjects who were EBF was 0.44 (95% CI: 0.43–0.96).

METHODOLOGICAL ISSUES: Breastfeeding data were collected before the onset of most cases of noninsulin-dependent diabetes. Recall consistency was checked in a subsample, showing that most women were consistent.

Norris JM, Scott FW. A meta-analysis of infant diet and insulin-dependent diabetes mellitus: Do biases play a role? Epidemiology 1996;7:87–92.

COUNTRY: Multicountry (Europe and the United States)

SETTING: Not reported

DESIGN: Meta-analysis of 17 case-control and 2 ecological studies

BREASTFEEDING DEFINITION: Ever having been breastfed compared with never having been breastfed and duration of breastfeeding; age at introduction of breastmilk substitutes (any milks or foods other than breastmilk in the infant's diet).

OUTCOME MEASURE: Insulin-dependent diabetes mellitus (IDDM)

RESULTS: The summary odds ratio of never having been breastfed and IDDM was 1.13 (95% CI: 1.04–1.23). Subjects who were breastfed for less than 3 months compared with those who were breastfed for at least 3 months had a summary odds ratio for IDDM of 1.23 (95% CI: 1.12–1.35). The summary odds ratio showed elevated risks for IDDM associated with age at first introduction of any breastmilk substitute before the age of 6 months. The incident odds ratio for the risk of IDDM associated with exposure to a breastmilk substitute before 3 months of age compared with ≥ 3 months was 1.54 (95% CI: 1.17–2.03).

METHODOLOGICAL ISSUES: Recall bias may be an issue in case-control studies, particularly if the recall time is large.

Samuelsson U, Johansson C, Ludvigsson J. Breast-feeding seems to play a marginal role in the prevention of insulin-dependent diabetes mellitus. Diabetes Research and Clinical Practice 1993;19:203–10.

COUNTRY: Sweden

SETTING: Southeast region

DESIGN: Case-control: cases (n = 297) were diabetic children < 15 years; controls (n = 792) were matched by age, sex, and place of residence

OUTCOME MEASURE: Childhood insulin dependent diabetes

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding and any breast-feeding

RESULTS: There was no significant effect of breastfeeding history on risk of developing diabetes. In a subgroup analysis, it was found that children diagnosed during the winter tended to have older mothers and to have been breastfed for a shorter period of time than controls. The authors suggest that, among these "epidemic" type cases, breastfeeding might have a weak protective effect.

METHODOLOGICAL ISSUES: The authors examined the data for many different subgroup effects and found a slight association for one of these (winter diagnosis, older mothers, and shorter duration of breastfeeding). They did not discuss the mechanism by which the subgroup with these characteristics might be at greater risk. Overall, this study does little to establish an association between diabetes and breastfeeding.

4.3 Effect of Breastfeeding on Later Risk of Cancer

Shu XO, Linet MS, Steinbuch M, et al. Breast-feeding and risk of childhood acute leukemia. J Natl Cancer Inst 1999;91:1765–72.

COUNTRY: Multicountry (United States, Canada and Australia)

SETTING: Not reported

DESIGN: Case-control study design with 2,200 childhood acute leukemia cases (1,744 cases with acute lymphoblastic leukemia [ALL], and 456 cases with acute myeloid leukemia [AML]) obtained from the Children's Cancer Group and 2,418 controls (1,879 for ALL and 539 for AML) obtained through random digit dialing and matched for age at diagnosis, geographic location, and race. Children in the ALL groups were aged 1–14 years and children in the AML groups were aged 1–17 years.

BREASTFEEDING DEFINITION: Breastfeeding for 6 months or longer, breastfeeding for 1–6 months, or not breastfeeding

OUTCOME MEASURE: Acute lymphoblastic leukemia and acute myeloid leukemia

RESULTS: Overall, there was an inverse association between ever having been breastfed and a reduced risk of childhood acute leukemia, for both ALL (odds ratio = 0.80; 95% CI: 0.69–0.93) and AML (odds ratio = 0.77; 95% CI: 0.57–1.03). A reduction in the risk of childhood acute leukemia was particularly strong among children who were breastfed for more than 6 months. The odds ratio of children who were breastfed for longer was 0.72 (95% CI: 0.60–0.87) for ALL and 0.57 (95% CI: 0.39–084) for AML.

METHODOLOGICAL ISSUES: Mothers of children with acute leukemia were more likely to be nonwhite and, on average, less educated. More ALL cases were from lower-income families or had birth weights greater than 4000 g, than were controls, possibly introducing confounding variables or bias.

Titus-Ernstoff L, Egan KM, Newcomb PA, Baron JA, Stampfer M, Greenberg ER, et al. Exposure to breast milk in infancy and adult breast cancer risk. J Natl Cancer Inst 1998;90:921–4.

COUNTRY: United States

SETTING: Three states: Massachusetts, New Hampshire, Wisconsin

DESIGN: Population-based case-control study of 8,299 women aged 50 or more. A total of 205 cases and 220 controls were premenopausal, and 3,803 cases and 4,071 controls were postmenopausal.

BREASTFEEDING DEFINITION: Ever having been breastfed

OUTCOME MEASURE: Breast cancer

RESULTS: After adjusting for breast cancer risk factors, there was no relationship between having been breastfed as an infant and breast cancer occurrence in either pre- or postmenopausal women.

METHODOLOGICAL ISSUES: The authors discuss a number of sources of bias, such as recall bias, and rule them out.

Potischman N, Brinton LA, Coates RJ, Malone DE, Schoenberg JB. Letter re: Fruedenheim et al., Epidemiology 1995;6(2):198–200.

COUNTRY: United States

SETTING: Georgia, Washington, New Jersey (urban)

DESIGN: Case-control: cases (n = 380) were newly identified with premenopausal breast cancer; controls (n = 311) were selected randomly from the community

BREASTFEEDING DEFINITION: Any breastfeeding (yes, no); breastfeeding histories were obtained from subject's mothers.

OUTCOME MEASURE: Breast cancer

RESULTS: This study examined whether having been breastfed as an infant reduced a woman's risk of premenopausal breast cancer. Having been breastfed as an infant was associated with reduced risk. The magnitude of the reduction in risk was identical to that found in Fruedenheim et al. (1994), for premenopausal women (odds ratio = 0.76; 95% CI: 0.54–1.08).

METHODOLOGICAL ISSUES: The response rate for cases and controls was low.

Freudenheim JL, Marshall JR, Graham S, Laughlin R, Vena JE, Bandera E, et al. Exposure to breastmilk in infancy and the risk of breast cancer. Epidemiology 1994;5:324–1.

COUNTRY: United States

SETTING: Western New York

DESIGN: Case-control: cases (n = 528) were women newly diagnosed with breast cancer; age-matched controls (n = 602) were randomly selected from the community

BREASTFEEDING DEFINITION: Any breastfeeding (yes, no); breastfeeding histories as an infant were obtained from the subjects

OUTCOME MEASURE: Breast cancer

RESULTS: This study examined whether having been breastfed as an infant reduced a woman's risk of breast cancer. Having been breastfed was associated with a significantly decreased risk. The adjusted odds ratio was 0.74 (95% CI: 0.56–0.99). The difference was found for both pre- and postmenopausal women. The authors conclude that being bottle-fed as infants may predispose women to the development of breast cancer.

METHODOLOGICAL ISSUES: The participation of eligible cases and controls was low (about 50%), and only about half of the cases and controls knew whether they had been breastfed as infants. Thus, results may have been biased by low participation and poor recall. The authors controlled for many known confounding factors.

Davis MK, Savitz DA, Graudard BI. Infant feeding and childhood cancer. Lancet 1988;August 13:365–8.

COUNTRY: United States

SETTING: Statewide (Colorado)

DESIGN: Case-control: cases (n = 201) were children diagnosed with childhood cancer; controls (n = 181) of similar age, sex, and area of residence were randomly selected from the community.

BREASTFEEDING DEFINITION: Duration of any breastfeeding categorized as follows: no breastfeeding, breastfed < 6 months; breastfed > 6 months

OUTCOME MEASURE: Childhood cancer

RESULTS: This study examined whether having been breastfed was associated with a decreased risk of childhood cancer. Compared with children who had been breastfed > 6 months, children who were not breastfed or breastfed for < 6 months had significantly higher risk of developing cancer (p = 0.023). Compared with breastfeeding > 6 months, the crude odds ratios for no breastfeeding and breastfeeding < 6 months were 1.8 and 1.9, respectively. Adjusted odds ratios were similar. Increased risk was largely the result of increased risk for lymphoma. Compared with children who had been breastfed > 6 months, children not breastfed or breastfed < 6 months had a 5 to 8 times greater risk of developing lymphoma (unadjusted p value = 0.023). However, when adjusted for maternal education, the p value increased to 0.1.

METHODOLOGICAL ISSUES: Young cases < 1.5 years of age were excluded from the study to avoid the possibility of reverse causality. The small number of cases made it difficult to evaluate the effect of maternal education, which was associated with breastfeeding and cancer risk.

4.4 Effect of Breastfeeding on Other Outcomes

Singhal A, Cole TJ, Lucas A. Early nutrition in preterm infants and later blood pressure: Two cohorts after randomised trials. Lancet 2001;357:413–9.

COUNTRY: United Kingdom

SETTING: Five neonatal units in the UK and follow-up 13–16 years later

DESIGN: Randomized with prospective follow-up of children 13–16 years old born preterm (n = 926). Two parallel studies were conducted: trial 1 consisted of preterm infants randomized to receive either breastmilk (from a breastmilk bank) or preterm formula, and trial 2 consisted of preterm infants receiving either normal-term or preterm formula.

BREASTFEEDING DEFINITION: Banked breastmilk, preterm formula, standard term formula

OUTCOME MEASURE: Systolic, diastolic, and mean arterial blood pressure

RESULTS: Mean arterial and diastolic blood pressure were significantly lower in children aged 13–16 years who received banked breastmilk than in those who received preterm formula. No significant differences were found among infants who received either term or preterm formula. The proportion of enteral intake of breastmilk was significantly related to mean arterial and diastolic blood pressure, even after adjustment for confounding factors, but not to systolic blood pressure. Neither energy nor protein intake was related to mean arterial blood pressure.

METHODOLOGICAL ISSUES: Multiple linear regression analyses were performed for the observational epidemiological data.

Ravelli ACJ, van der Meulen JHP, Osmond C, et al. Infant feeding and adult glucose tolerance, lipid profile, blood pressure, and obesity. Arch Dis Child 2000;82:248–52.

COUNTRY: The Netherlands

SETTING: Urban (Amsterdam)

DESIGN: Population-based observational study: n=625

BREASTFEEDING DEFINITION: Exclusive breastfeeding, partial breastfeeding (PB), exclusive formula feeding (FF)

OUTCOME MEASURE: Glucose tolerance, plasma lipid profile, blood pressure, and body mass in 48- to 53-year-olds

RESULTS: Adults who had been bottle fed (PBF and FF) had higher fasting insulin,

higher LDL cholesterol and apolipoprotein B concentrations (fasted), higher LDL:HDL ratios, and lower HDL concentrations than adults who had been exclusively breastfed in infancy. No effects of infant feeding mode were found for blood pressure, body mass index, or body fat distribution.

METHODOLOGICAL ISSUES: All subjects were born during the Dutch Famine, so they were exposed to malnutrition in utero. Infant feeding methods were separated into exclusive breastfeeding, partial bottle feeding, and exclusive bottle-feeding. Eighty-three percent of the subjects were exclusively breastfed, close to 16% were partially bottle fed, and only 1% were exclusively bottle-fed. Multiple regression was used for analyses of the continuously distributed variables, and logistic regression was used to assess the dichotomous outcome (impaired glucose tolerance). All analyses were adjusted for sex, period of prenatal exposure to famine (early, mid, or late gestation), maternal age, length of hospital stay, maternal characteristics, birth outcomes, and adult characteristics.

Saarinen UM, Kajosarri M. Breastfeeding as prophylaxis against atopic disease: Prospective follow-up study until 17 years old. Lancet 1995 (October 21);346:1065–9.

COUNTRY: Finland

SETTING: Helsinki (southern Finland)

DESIGN: Prospective: n = 236, 150 of whom were followed until 17 years of age

BREASTFEEDING DEFINITION: Breastfeeding duration categorized as follows: > 6 months, 1–6 months, < 1 month or no breastfeeding

OUTCOME MEASURE: Atopic eczema, food allergy, respiratory allergy. A child was considered atopic if any of these 3 measures was diagnosed.

RESULTS: This study examined the association between infant feeding mode and various atopic diseases. Children were followed from birth, seen frequently during infancy and again at ages 1, 3, 5, 10, and 17 years. The prevalence of atopy throughout the follow-up period was significantly higher in the group that had little or no breastfeeding. The prevalence of eczema at ages 1 and 3 years was lowest in the group breastfed the longest. The prevalence of food allergy between 1 and 3 years was highest in the group that had little or no breastfeeding. Respiratory allergy was most prevalent in the group that had little or no breastfeeding. The prevalence of respiratory allergy at 17 years of age for children breastfed the longest was 42%, compared with 65% among children breastfed the shortest or not at all. The authors conclude that breastfeeding protects against atopic disease throughout childhood and adolescence.

METHODOLOGICAL ISSUES: The prevalence of respiratory allergy is very high even among the breastfed children, which the authors do not discuss but which suggests that being born just before the birch pollen season may have contributed to the high prevalence that developed later in the children.

Wingard DL, Criqui MH, Edelstein SL, Tucker J, et al. Is breast-feeding in infancy associated with adult longevity? Amer J Public Health 1994;84(9):1458–62.

COUNTRY: United States

SETTING: Statewide (California)

DESIGN: Prospective population-based: subjects (n = 1,170) were followed more than 65 years and cause-specific mortality was documented

BREASTFEEDING DEFINITION: Duration of breastfeeding categorized as follows: 0, 1–5, 6–11, 12–36 months. Breastfeeding information was obtained from the subject's parents within 10 years of the child's birth.

RESULTS: This study examined whether breastfeeding is associated with increased longevity in adulthood. After adjustment for all known confounding factors, there was a weak association between having been breastfed and increased longevity among men. No association was found among women. Breastfeeding was not associated with death from cardiovascular disease for either sex. Death from accidental injury was inversely associated with breastfeeding and showed a dose-response with duration of breastfeeding in men only. No biologically plausible explanation is offered for why having been breastfed as an infant would reduce risk of death from injury. Overall, the results do not provide strong evidence that breastfeeding is related to adult longevity.

METHODOLOGICAL ISSUES: This sample was restricted to middle-class children with access to health care, so differences in health care are unlikely to explain the findings. The study controlled for many potentially confounding factors.

Koletzko S, Griffiths A, Corey M, Smith C, Sherman P. Infant feeding practices and ulcerative colitis in childhood. Br Med J 1991;302:1580–1.

COUNTRY: Canada

SETTING: Not reported

DESIGN: Case-control: cases (n = 93) were children with ulcerative colitis; controls (n = 138) were unaffected biological siblings

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding and any breast-feeding, and age of introduction of solids

OUTCOME MEASURE*:* Ulcerative colitis

RESULTS: The study examined whether having been breastfed was associated with decreased risk of ulcerative colitis. Infant feeding practices were not associated with risk of disease development.

METHODOLOGICAL ISSUES: The small sample size may have precluded finding meaningful differences; however, the authors did not perform ex post power calculations to determine the power of their study to have detected a significant difference.

Koletzko S, Sherman P, Corey M, Griffiths A, Smith C. Role of infant feeding practices in development of Crohn's disease in childhood. Br Med J 1989;298:1617–8.

COUNTRY: Canada

SETTING: Not reported

DESIGN: Case-control: cases (n = 114) were children < 18 years with Crohn's disease; controls (n = 180) were unaffected biological siblings

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding or any breastfeeding

OUTCOME MEASURE: Crohn's disease

RESULTS: This study examined whether having been breastfed as an infant was associated with the risk of developing Crohn's disease. Lack of breastfeeding was a significant risk factor for disease development. Compared with children who had been breastfed, children who had not been breastfed had 3 times the risk ($p < 0.002$). Having had diarrhea in infancy was an independent risk factor.

METHODOLOGICAL ISSUES: The authors did not control for the possibility of reverse causality, e.g. that the disease could influence infant feeding patterns. Biological siblings were used as controls, and women tend to have similar infant feeding patterns across their children. Thus, the issue of why infants who later became ill were fed differently from their siblings merits investigation and discussion, which was lacking in the article.

5. EFFECT OF BREASTFEEDING ON MATERNAL HEALTH

Breastfeeding brings health benefits for the mother as well as the infant. The effect of breastfeeding on postpartum bleeding, the return of fertility, and mothers' risk of breast and ovarian cancer is described in the papers below.

5.1 Effect of Breastfeeding on Maternal Risk of Breast Cancer

Tryggvadottir L, Tulinius H, Eyfjord JE, Sigurvinsson T. Breastfeeding and reduced risk of breast cancer in an Icelandic cohort study. Am J Epidemiol 2001;154:37–42.

COUNTRY: Iceland

SETTING: Women visiting the Cancer Detection Clinic of the Icelandic Cancer Society

DESIGN: Nested case-control study: n = 10,722 (993 cases, 9,729 matched controls) separated into 3 age groups: < 40 years, 40–55 years, and > 55 years

BREASTFEEDING DEFINITION: Duration of any breastfeeding

OUTCOME MEASURE: Breast cancer incidence

RESULTS: An inverse dose-response relation between breastfeeding duration and risk of breast cancer was observed for women in the youngest age group (< 40 years). Data suggested a decreased risk of breast cancer in women who ever lactated compared with those who never lactated in all 3 age groups.

METHODOLOGICAL ISSUES: Variables used included: age at menarche, age at first birth, number of births, number of children breastfed, average number of weeks breastfeeding each child, use of oral contraceptives, height and weight. Duration of breastfeeding and age at diagnosis were used as variables for the 2 interaction models analyzed. Multiple logistic regression was applied for the multivariate analysis of matched data.

Gao Y-T, Shu X-O, Dai Q, et al. Association of menstrual and reproductive factors with breast cancer risk: Results from the Shanghai Breast Cancer Study. Int J Cancer 2000;87:295–300.

COUNTRY: China

SETTING: Urban Shanghai

DESIGN: Case-control (population-based) study of women between the ages of 25 and 64 years. Cases (n = 1,459) were diagnosed by 2 pathologists, and age-matched controls (n = 1,556) were randomly selected from females permanently living in urban Shanghai.

BREASTFEEDING DEFINITION: Ever having breastfed, never having breastfed, and duration of breastfeeding for each live birth

OUTCOME MEASURE: Breast cancer

RESULTS: Women who ever breastfed had an unadjusted odds ratio for breast cancer lower than those who never breastfed (OR = 0.6; 95% CI: 0.5–0.9). The cumulative duration of breastfeeding was associated with reduced risk of breast cancer. Women who breastfed for longer than 24 months had an odds ratio of 0.9 (95% CI: 0.7–1.4), compared with women who never breastfed. Breastfeeding was associated with reduced risk only among postmenopausal women.

METHODOLOGICAL ISSUES: Cases were slightly older and more likely to have had more years of education than controls.

Lipworth L, Bailey R, Trichopoulos D. History of breast-feeding in relation to breast cancer risk: A review of the epidemiologic literature. J Natl Cancer Inst 2000;92:302–12.

COUNTRY: Multicountry (mainly North America and Europe)

SETTING: Various

DESIGN: Review of studies between 1966 and 1998 that included more than 200 cases overall and explicitly controlled for number of full-term pregnancies and age at first birth

BREASTFEEDING DEFINITION: Ever versus never having breastfed and cumulative duration of breastfeeding

OUTCOME MEASURE: Breast cancer

RESULTS: Overall, the evidence of an inverse association between ever breastfeeding and breast cancer risk remains limited and inconclusive. Relative risks among parous women who have ever breastfed, compared with those who have never breastfed, range from 0.54 to just below 1.0. Regarding the number of children breastfed, the authors conclude that there is no clear trend of decreasing risk with increasing number of breastfed children. Regarding the cumulative effect of breastfeeding, adjusted odds ratios for premenopausal women who breastfed for > 12 months ranged from 0.21 to just under 1.0, compared with parous women who never breastfed.

The authors speculate that the failure of some studies to detect an association may be due to the low prevalence of prolonged breastfeeding, since there appears to be some evidence of the protective effect of extensive cumulative durations of breastfeeding in non-Western societies, which tend to breastfeed longer than women in Western societies. Women who stopped breastfeeding because of "insufficient milk" tended to have significantly elevated risks of breast cancer compared with women who successfully breastfed for at least 2 years (odds ratio ranged from 3.0 to 3.1). Women who ever breastfed were 3 times more likely than those who never breastfed to have estrogen receptor-positive tumors as opposed to estrogen receptor-negative tumors (the latter is more aggressive and less respondent to therapy). Regarding ethnicity, larger effects of increasing total months of breastfeeding and association with decreased risk of breast cancer were seen in African-American women than in Caucasian women (odds ratio = 0.45 and 0.76, respectively). Non-Hispanic white women who breastfed longer than 12 months had an odds ratio of 0.58, while their Hispanic counterparts had an odds ratio of 0.78. With regard to menopausal status, the protective effects of breastfeeding seem to be greatest in or confined to premenopausal women.

METHODOLOGICAL ISSUES: Relatively low prevalence of prolonged breastfeeding in Western populations reduces the ability of studies to detect effects. Inconsistent classification of breastfeeding history across studies presents problems for reviewers.

Zheng T, Duan L, Liu Y, et al. Lactation reduces breast cancer risk in Shandong Province, China. Am J Epidemiol 2000;152:1129–35.

COUNTRY: China

SETTING: Hospital-based population

DESIGN: Case-control study: n = 404 cases and 404 matched controls

BREASTFEEDING DEFINITION: None given

OUTCOME MEASURE: Risk of breast cancer

RESULTS: Later age at menarche, breastfeeding for > 24 months per child, and lifetime duration of breastfeeding of ≥72 months were associated with reduced risk of breast cancer. In addition, nonsignificant lower risk of breast cancer was observed for women who breastfed more than 3 children, for those who were < 25 years old at their first breastfeeding episode, and for women who had more than 1 child and had breastfed for > 72 months. Moreover, later age at menopause and later age at first full-term pregnancy were found to be associated with higher risk of breast cancer.

METHODOLOGICAL ISSUES: Both cases and controls were hospital-based, which may lower the generalizability of the results since authors do not include information about cancer cases that did not attend study hospitals.

Furberg H, Newman B, Moorman P, Millikan R. Lactation and breast cancer risk. Int J Epidem 1999;28:396–402.

COUNTRY: United States

SETTING: Not reported

DESIGN: Case-control, population-based study with data from the Carolina Breast Cancer Study (n = 751 cases, 742 controls)

BREASTFEEDING DEFINITION: Duration of breastfeeding, number of months of breastfeeding without menses. These variables were summed for all live births.

OUTCOME MEASURE: All women between the ages of 20 and 74 years who were diagnosed with a first, invasive breast cancer

RESULTS: Having breastfed was inversely associated with risk of breast cancer among parous women. The adjusted odds ratio for younger women (aged 20–49 years) was 0.8 (95% CI: 0.5–1.1), for older women (aged 50–74 years) was 0.7 (0.5–0.9), and for all women was 0.7 (0.5–0.8). Length of breastfeeding, timing of lactation, number of children breastfed, or number of months without periods while breastfeeding do not appear to influence risk.

METHODOLOGICAL ISSUES: Controls were frequency matched to cases by age and race (white and African-American). Analyses were performed separately according to age

groups; younger women (20–49 years old), older women (50–74 years old), and all women combined. Menopausal status was determined to be a confounding variable and controlled for. Overall response rates differed by case-control status and race of the participants. The authors rule out recall bias; however, they note that nurses who collected the data knew the case status of the participants, but argue that this was unlikely to introduce bias because a standardized questionnaire was used, and lactation history was not a main focus of the interview. Odds ratios were calculated using unconditional logistic regression models to study associations between different breastfeeding aspects (breastfeeding duration, number of children breastfed, ages at first and last lactation, months of amenorrhea, and use of lactation suppressants) and breast cancer. Adjustments of co-variates included age, race, parity, age at last full-term pregnancy, current body mass index, history of breast or ovarian cancer, and menopausal status.

Marcus PM, Baird DD, Millikan RC, et al. Adolescent reproductive events and subsequent breast cancer risk. J Public Health 1999;89:1244–7.

COUNTRY: United States

SETTING: Various counties in North Carolina (central and eastern regions)

DESIGN: Case-control population-based study of women aged 20–74 years. Cases (n = 862) were randomly obtained form the Carolina Breast Cancer Study, and controls (n = 790) were obtained from the Division of Motor Vehicles (for women < 65 years) and from Medicare records (women ≥ 65 years).

BREASTFEEDING DEFINITION: Ever versus never having breastfed and cumulative duration of breastfeeding

OUTCOME MEASURE: Breast cancer

RESULTS: Odds ratios were adjusted for race and age at diagnosis-selection. Breastfeeding before 20 years of age was associated with a significantly reduced risk of disease (OR = 0.2; 95% CI: 0.1–0.6), compared with women with no history of breastfeeding. The relationship persisted for women who breastfed for 1 year or longer and whose first pregnancy occurred before age 20 (OR = 0.1; 95% CI: 0.0–0.8). Multiparous women (greater than 2) produced similar results (data not shown).

METHODOLOGICAL ISSUES: A small number of women reported breastfeeding during their teen years. Results were only significant among premenopausal women.

Newcomb PA, Egan KM, Titus-Ernstoff L, et al. Lactation in relation to postmenopausal breast cancer. Am J Epidemiol 1999;150(2):174–82.

COUNTRY: United States

SETTING: Multicenter; statewide in Massachusetts (excluding Boston), New Hampshire, and Wisconsin

DESIGN: Case-control population-based study of postmenopausal women aged 50–79 years. Cases (n = 3,633) were selected from tumor registries with invasive breast carcinoma confirmed through histologic or cytologic

analyses; controls (n = 3,790) were randomly selected from licensed drivers and Medicare beneficiaries.

BREASTFEEDING DEFINITION: Ever breastfeeding compared to never breastfeeding and cumulative duration of breastfeeding

OUTCOME MEASURE: Invasive breast carcinoma in postmenopausal women

RESULTS: Breastfeeding was associated with a very modest reduction in the risk of breast cancer. Women who breastfed for at least 2 weeks had an adjusted relative risk of 0.87 (95% CI: 0.78–0.96), compared with women who never breastfed. The longer the total duration of breastfeeding in a lifetime, the greater the reduction in risk. Women who breastfed for ≥ 24 months had a relative risk of 0.73 (95% CI: 0.56–0.94). The inverse association between breastfeeding and breast cancer seems to persist throughout the postmenopausal period.

METHODOLOGICAL ISSUES: Retrospective recall bias may be an issue. To maintain blinding, information on the woman's screening practices and her personal and family history of breast cancer was not obtained until the end of the telephone interviews.

Romieu I, Hernandez-Avila M, Lazcano E, Lopez L, Romero-Jaime R. Breast cancer and lactation history in Mexican women. Am J Epidemiol 1996;143(6):543–52.

COUNTRY: Mexico

SETTING: Urban (Mexico City)

DESIGN: Case-control: cases (n = 349) were newly diagnosed with breast cancer; controls (n = 1,005) were selected from the general population. Lactation history was obtained before diagnosis of breast cancer.

BREASTFEEDING DEFINITION: Total duration of breastfeeding, ever breastfed, duration of breastfeeding for first and second live-born children

RESULTS: Breastfeeding was protective against breast cancer for both pre- and postmenopausal women. Parous women who had ever breastfed had a cancer risk of 0.47 (95% CI: 0.30–0.73), compared with parous women who had never breastfed. Duration of lactation was also associated with a reduction in breast cancer risk (test for trend $p < 0.005$). This protective effect was stronger in postmenopausal women. Among premenopausal women, no increase in protection was found after 3 months of breastfeeding. The duration of breastfeeding was particularly important for firstborn children. The duration of breastfeeding for the second child was shorter and significant only among postmenopausal women.

METHODOLOGICAL ISSUES: The high proportions of premenopausal women and long durations of breastfeeding among study subjects resulted in a large degree of statistical power to test the associations of interest.

Brinton LA, Potischman NA, Swanson CA, Schoenberg JB, et al. Breastfeeding and cancer risk. Cancer Causes and Control 1995;6:199–208.

COUNTRY: United States

SETTING: Three geographic regions (Atlanta, Georgia; Seattle, Washington, central New Jersey)

DESIGN: Case-control with a focus on premenopausal women (< 45 years): cases = 1,211 newly diagnosed with breast cancer (86% of eligible cases); controls = 1,120 contacted in the community through random digit dialing (67% of eligible)

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding, any breastfeeding, why breastfeeding discontinued, medications to inhibit breastfeeding

RESULTS: The overall findings are consistent with studies that have shown breastfeeding to be a weak protective factor for breast cancer. The relative risk for > 2 weeks of breastfeeding versus no breastfeeding was 0.87 (95% CI: 0.7–1.0). Longer durations were associated with decreased risk. The relative risk for > 36 months was 0.72 (95% CI: 0.5–1.1). The relative risk for > 72 weeks was 0.67 (95% CI: 0.4–1.1) (p for trend = 0.04). Subjects who were young at first lactation (< 22 years) had the lowest risk. Breastfeeding was associated with a greater reduction in risk among subjects with a family history of breast cancer (p for interaction = 0.03).

METHODOLOGICAL ISSUES: The study lacked statistical power in that durations of breastfeeding were short among most subjects.

Mayberry RM. Age-specific patterns of association between breast cancer and risk factors in Black women, ages 20 to 39 and 40 to 54. Ann Epidemiol 1994;4:205–213.

COUNTRY: United States

DESIGN: Case-control: among women < 40 years of age, cases (n = 177) were compared with controls (n = 137); among women aged 40–54 years cases (n = 313) were compared with controls (n = 348)

BREASTFEEDING DEFINITION: Total months of breastfeeding defined as follows: > 8 months, 4–7 months, and < 4 months

RESULTS: The adjusted odds ratio showed no association between breastfeeding and risk of breast cancer.

METHODOLOGICAL ISSUES: Small sample size may have limited the statistical power to detect an association.

Newcomb PA, Storer BE, Longnecker MP, et al. Lactation and a reduced risk of premenopausal breast cancer. New Eng J Med 1994;330(2):81–7.

COUNTRY: United States

SETTING: Wisconsin, Massachusetts, New Hampshire

DESIGN: Case-control (multicenter study): cases = 6,888 (81% of eligible cases); controls = 8,216 (82% of eligible controls)

BREASTFEEDING DEFINITION: Duration of breastfeeding (before cancer diagnosis), reasons for stopping breastfeeding, medications used to prevent lactation, age at first lactation

RESULTS: Among all parous women who had ever lactated, the estimated relative risk for breast cancer was 0.97, a nonsignificant difference. Among premenopausal women, a history of breastfeeding was associated with a slight decrease in risk of breast cancer. The relative risk is 0.78 (95% CI: 0.66–0.91). Total duration of breastfeeding was associated with a decrease in risk of breast cancer ($p < 0.001$) only among premenopausal women. Compared with women who never lactated, a cumulative total of > 24 months of breastfeeding was associated with a relative risk of 0.72. Age at first lactation had an independent effect on risk of breast cancer. Younger ages at first lactation were associated with a decreased risk (p for trend was 0.003). The authors conclude, "If women who do not breastfeed or who breastfeed for < 3 months were to do so for 4 to 12 months, breast cancer among parous premenopausal women could be reduced by 11 percent, judging from current rates. If all women with children lactated for 24 months or longer, however, then the incidence might be reduced by nearly 25 percent. This reduction would be even greater among women who first lactate at an early age."

METHODOLOGICAL ISSUES: The study had sufficient statistical power to detect differences in risk among premenopausal women.

Kelsey JL, Gammon MK, John EM. Reproductive factors and breast cancer. Epidemiol Reviews 1993;15(1):36–47.

COUNTRY: Multicountry

SETTING: Various

DESIGN: Review article of existing studies

BREASTFEEDING DEFINITION: Varies by study

RESULTS: This review article concludes that breastfeeding may reduce the risk of breast cancer among women under 50 years of age. Of the 10 case-control studies reviewed, 8 found an association between breastfeeding and reduced risk, and 2 failed to show an effect. Five of these studies found a small protective effect of ever breastfeeding but no trend of decreased risk with increased breastfeeding duration. Three studies found decreased risk in both pre- and postmenopausal women. Where a protective effect was found, the adjusted odds ratios ranged from 0.21 to 0.77. Of concern is the fact that 2 large prospective cohort studies have failed to find an association between breastfeeding and breast cancer risk. Although it would have been helpful, the authors do not discuss the difference in findings between case-control and prospective cohort studies. Cohort

studies generally are considered to be stronger than case-control studies, and the fact that 2 have now failed to confirm the protective effect found in case-control studies is troubling.

Thomas DB, Noonan EA, WHO Collaborative Study of Neoplasia and Steroid Contraceptives. Breast cancer and prolonged lactation. Int J Epidem 1993;22(4):619–26.

COUNTRY: Multinational case-control study (Australia, Germany, Israel, Chile, China, Colombia, Kenya, Mexico, Philippines, Thailand)

SETTING: Hospital

DESIGN: Case-control: cases (n = 2,336) were newly diagnosed breast cancer patients; controls (n = 14,900) were hospital patients not admitted for obstetric/gynecological reasons or for any condition associated with use of oral contraceptives

BREASTFEEDING DEFINITION: Duration of breastfeeding; women who breastfed < 3 months were used as the reference group

RESULTS: No significant protective effect of breastfeeding was found for any of the models examined. These models included pre- and postmenopausal women, age of diagnosis, women with different numbers of live births, or mean number of months that women breastfed each child. In premenopausal women and those with two or more live births, most risk estimates indicated a protective effect of breastfeeding > 6 months, compared with women who breastfed < 3 months, but none of these risk estimates was statistically significant.

METHODOLOGICAL ISSUES: The authors used women who had breastfed < 3 months as a reference group to avoid potentially confounding factors associated with unidentified risk factors that might occur if the comparison group consisted of women who had lactation failure. However, to avoid this bias, the authors may have inadvertently minimized their ability to find an effect in that many studies have shown that the protective effect of breastfeeding in premenopausal women occurs with short breastfeeding durations and is not increased with longer durations.

Yoo K-Y, Tajima K, Kuroishi T, Hirose K, et al. Independent protective effect of lactation against breast cancer: A case-control study in Japan. Am J Epidemiol 1992;135(7):726–33.

COUNTRY: Japan

SETTING: Nagoya Aichi Cancer Center Hospital

DESIGN: Case-control: cases = 521 confirmed by histological and clinical exam; controls = 521 women with no history of breast cancer selected from the hospital

BREASTFEEDING DEFINITION: Any breastfeeding, total number of breastfed children, average months of breastfeeding each child

RESULTS: Among parous women, the adjusted odds ratio of breast cancer among women with a positive history of breastfeeding was 0.62 (95% CI: 0.37–1.04) compared with no breastfeeding. A significant trend of decreased risk of breast cancer with increased average months of breastfeeding was observed ($p < 0.05$) among premenopausal women only. Premenopausal women who had lactated for 7–9 months showed the lowest risk of breast cancer (adjusted odds ratio = 0.39, 95% CI: 0.15–0.97).

METHODOLOGICAL ISSUES: Controls were selected from a hospital-based population and hence may not be representative of the community. There was good simultaneous adjustment for age, parity, and menopausal status. The study also restricted the analyses to parous women, which is important because of the importance of age of first pregnancy on risk of breast cancer.

London SJ, Colditz GA, Stampfer MJ, et al. Lactation and risk of breast cancer in a cohort of US women. Am J Epidemiol 1990;132(1):17–26.

COUNTRY: United States

SETTING: Multistate (11 larger US states)

DESIGN: Prospective for cancer outcomes; however, breastfeeding history was obtained retrospectively; n = 89,413 parous female nurses aged 30–55 years

BREASTFEEDING DEFINITION: Never breastfed, breastfed for the following lengths of time: <1 month, 1–3 months, 4–6 months, 7–11 months, 12–17 months, 18–23 months, 24–35 months, 36–47 months, > 48 months, unknown

RESULTS: No association between lactation and risk of breast cancer was found.

METHODOLOGICAL ISSUES: The study controlled for the possibility that breast cancer reduced breastfeeding. Short breastfeeding duration among the population (only 6% breastfed > 24 months) may have reduced the size of the effect.

Layde PM, Webster LA, Baughman AL, et al. The independent associations of parity, age at first full term pregnancy, and duration of breastfeeding with risk of breast cancer. J Clin Epidemiol 1989;42(10):963–73.

COUNTRY: United States

SETTING: Multi-center

DESIGN: Case-control: cases (n = 4,599) were newly diagnosed with breast cancer; controls (n = 4,536) were women of similar age selected at random from the community

BREASTFEEDING DEFINITION: Total duration of breastfeeding

RESULTS: Compared with parous women who never breastfed, breastfeeding was protective against breast cancer. A dose-response relationship was found: the risk of breast cancer decreased with increasing duration of breastfeeding (p for trend < 0.01). The odds ratio for never having breastfed compared with breastfeeding for more than 24 months was 0.67.

METHODOLOGICAL ISSUES: This study controlled for many potentially confounding factors and tested for interactions.

Siskind V, Schofield F, Rice D, Bain C. Breast cancer and breastfeeding: Results from an Australian case-control study. Amer J Epidemiol 1989;130(2):229–36.

COUNTRY: Australia

SETTING: Brisbane and suburbs

DESIGN: Case-control: cases = 459; control = 1,091

BREASTFEEDING DEFINITION: Total duration of breastfeeding, average duration per live-born child, total number of children breastfed, average number of children breastfed, length of time first liveborn child was breastfed

RESULTS: A weak inverse association between history of breastfeeding and breast cancer was found. However, none of the risk estimates or overall tests of association between breastfeeding and breast cancer was statistically significant.

METHODOLOGICAL ISSUES: The study had limited statistical power to detect differences, particularly for premenopausal women.

Rosero-Bixby L, Oberle MW, Lee NC. Reproductive history and breast cancer in a population of high fertility, Costa Rica, 1984–1985. Int J Cancer 1987;40:747–54.

COUNTRY: Costa Rica

SETTING: Nationwide

DESIGN: Case-control: cases (n = 171) were interviewed within 3 years of diagnosis; controls (n = 826) were selected from the general population

BREASTFEEDING DEFINITION: Total duration of breastfeeding

RESULTS: After controlling for parity, the duration of breastfeeding had no association with risk of breast cancer.

METHODOLOGICAL ISSUES: The number of cases was small, which may have limited statistical power to detect an association.

Byers T, Graham S, Rzepka T, Marshall J. Lactation and breast cancer. Amer J Epidemiol 1985;121(5):664–74.

COUNTRY: United States

SETTING: Urban

DESIGN: Case-control: cases = 453 newly diagnosed cases; controls = 1,365 women selected randomly in the community

BREASTFEEDING DEFINITION: Duration of breastfeeding, number of infants breastfed, reasons for stopping breastfeeding

RESULTS: The results show a negative association between breastfeeding and breast cancer among premenopausal women only. The relative risk for 12 months of lactation was 0.6 ($p < 0.01$). A dose-response was detected with increasing durations of breastfeeding (p for trend = 0.07). Women's reports of insufficient milk were associated with increased risk for breast cancer, especially in premenopausal women, but when controlled for in multiple logistic regression, there was only a slight reduction in the association between breastfeeding duration and the risk of breast cancer.

METHODOLOGICAL ISSUES: This is the first study to raise the issue that a third factor may be related to both difficulty in breastfeeding, which is perceived by mothers to be insufficient milk, and breast cancer. If this were the case, then breastfeeding may not be protective of breast cancer, but rather a marker that the third factor related to breast cancer is not present. Many subsequent studies have attempted to address failure to breastfeed as a physiological marker of risk rather than as a behavioral choice.

Raksasook S. The relationship of breast cancer with parity and breast feeding in Thai women. Southeast Asian J Surgery 1985;8(1):23–30.

COUNTRY: Thailand

SETTING: Phyathai area in Bangkok

DESIGN: Case-control: women were divided into 3 groups: normal (n = 825); benign breast disease (n = 162); and breast cancer (n = 109)

BREASTFEEDING DEFINITION: Ever breastfed, duration of breastfeeding

RESULTS: In contrast to all of the other studies reviewed, women with breast cancer were more likely to have breastfed and, among breastfeeding women, to have breastfed longer than controls did, but these associations were not tested for statistical significance.

METHODOLOGICAL ISSUES: Associations were not tested for statistical significance.

Brinton LA, Hoover R, Fraumeni JF. Reproductive factors in the aetiology of breast cancer. Br J Cancer 1983;47:757–62.

COUNTRY: United States

SETTING: Urban

DESIGN: Case-control: cases = 1,362; controls = 1,250

BREASTFEEDING DEFINITION: Any breastfeeding, number of breastfeeding children

RESULTS: The results show no association between breastfeeding history and risk of breast cancer. The adjusted relative risk among women who ever breastfed was 0.94, in comparison with women who never breastfed, but this risk was not statistically significant (95% confidence interval: 0.8–1.1).

METHODOLOGICAL ISSUES: No information on breastfeeding duration was available. Small sample size may have limited statistical power.

MacMahon B, Purde M, Cramer D, Hint E. Association of breast cancer risk with age at first and subsequent births: A study in the population of the Estonian Republic. J Natl Cancer Inst 1982;69(5):1035–8.

COUNTRY: Estonian Republic

SETTING: Urban (Tallinn and Tartu)

DESIGN: Case-control: cases = 362 newly diagnosed cases; controls = 694 women participating in a gynecological screening program

BREASTFEEDING DEFINITION: Duration of breastfeeding categorized as follows: 0, 1–6, 7–12, 13–24, > 25 months

RESULTS: Breastfeeding duration did not have any effect on breast cancer.

METHODOLOGICAL ISSUES: Cases and controls differed in age distributions, with the cases being older than the controls. This study may have lacked statistical power to detect an effect because of the relatively short durations of breastfeeding. Breastfeeding association analyses were restricted to women who had only 1 or 2 live births.

Kalache A, Vessery MP, McPherson K. Lactation and breast cancer. Br Med J 1980 (Jan 26);280(6209):223–4.

COUNTRY: England

SETTING: Eight teaching hospitals in London and Oxford

DESIGN: Case-control of 707 married women aged 16–50 years

BREASTFEEDING DEFINITION: Ever breastfeeding, breastfeeding for more than 16 weeks, and mean duration of breastfeeding

RESULTS: No significant differences in breastfeeding behaviors were found between cases and controls, suggesting no relationship between breastfeeding and the risk of breast cancer.

METHODOLOGICAL ISSUES: No information was provided to compare case and control groups.

Ing R, Ho JHC, Petrakis NL. Unilateral breast-feeding and breast cancer. Lancet 1977 (July 16): 124–7.

COUNTRY: Hong Kong

SETTING: Fishing villages in Southern China

DESIGN: Retrospective (n = 2403): Chinese breast cancer patients, including 73 women who had breastfed from one breast only

BREASTFEEDING DEFINITION: Number of children breastfed, average duration of breastfeeding, history of breastfeeding with only one breast, relative use of both breasts during breastfeeding

RESULTS: The unsuckled breast among women who only breastfed on one side had a 4-fold increase in cancer risk in postmenopausal older women (> 55 years of age).

METHODOLOGICAL ISSUES: Tests of significance are not provided. Only mothers who suckled on one side "for convenience or custom" were included, reducing the likelihood of reverse causality (avoidance of a predisposed breast).

MacMahon B, Lin TM, Lowe CR, et al. Lactation and cancer of the breast: A summary of an international study. Bull WHO 1970;42:185–194.

COUNTRY: Multicountry (United States, England, Greece, Slovenia, Yugoslavia, Brazil, Japan, Taiwan)

SETTING: Hospital-based populations

DESIGN: Case-control: cases (n = 4,395) were newly diagnosed breast cancer patients; controls (n = 12,888) were selected from the hospital

BREASTFEEDING DEFINITION: Number of parous women who never breastfed, mean duration of breastfeeding among those children who breastfed, number of women with long lifetime histories of lactation (the precise cutoff depended on the country)

RESULTS: No consistent differences in duration of lactation were found between women with breast cancer and those without breast cancer, after controlling for parity.

METHODOLOGICAL ISSUES: Use of hospital-based controls may have introduced undetected bias in the study.

Valaoras VG, MacMahon B, Trichopoulos D, Polychronopoulou A. Lactation and reproductive histories of breast cancer patients in greater Athens, 1965–69. Int J Cancer 1969;4:350–63.

COUNTRY: Greece

SETTING: Urban (Athens and Piraeus)

DESIGN: Case-control: cases (n = 799) were newly diagnosed breast cancer patients; controls (n = 2,470) were selected from the hospital

BREASTFEEDING DEFINITION: Number of parous women who never breastfed, mean duration of breastfeeding among those children who breastfed, number of women who breastfed > 24 months

RESULTS: Although the associations are in the direction of a protective effect of breastfeeding, the differences are small and not statistically significant, even for long durations of breastfeeding.

METHODOLOGICAL ISSUES: Substantial differences present between the cases and the control groups on several pertinent variables, such as demographics, marital status, birthplace of the study groups, and number of stillborn children.

MacMahon B, Feinleib M. Breast cancer in relation to nursing and menopausal history. J Nat Cancer Inst 1960;24:733–53.

COUNTRY: United States

SETTING: New York city hospitals (5)

DESIGN: Case-control: cases (n = 340) were selected from current cancer lists; controls (n = 340) were general surgical patients matched for 8 variables

BREASTFEEDING DEFINITION: Total duration of breastfeeding, average duration of breastfeeding per child, proportion of mothers who have never breastfed, proportion of children who have been breastfed

RESULTS: No consistent differences in duration of lactation were found between women with breast cancer and those without breast cancer, after controlling for potentially confounding factors.

METHODOLOGICAL ISSUES: No examinations, other than race, religious tendencies, marital status, and native or foreign born, were presented comparing cases and controls. Moreover, cases and controls were not completely matched for parity.

5.2 Effect of Breastfeeding on Maternal Risk of Ovarian Cancer

Ness RB, Grisso JA, Cottrea C, et al. Factors related to inflammation of the ovarian epithelium and risk of ovarian cancer. Epidemiology 2000;11:111–17.

COUNTRY: United States

SETTING: Delaware Valley area (including counties in eastern Pennsylvania, southern New Jersey, and Delaware)

DESIGN: Case-control population-based study design of 20–69 year old women: cases (n = 767) were identified from 39 hospitals and histologically confirmed as borderline or invasive epithelial ovarian cancer; controls (n =1,367) were selected from the community by random digit dialing and frequency matched by 5-year age groups

BREASTFEEDING DEFINITION: Any breastfeeding, total months of breastfeeding

OUTCOME MEASURE: Ovarian cancer

RESULTS: Breastfeeding for 24 months or more (cumulative) was associated with reduced risk of ovarian cancer. The adjusted odds ratio of women who breastfed ≥ 24 months was 0.6 (95% CI: 0.4–1.0). Other factors associated with reduced risk of ovarian cancer were higher parity and use of oral contraceptives, both of which, like breastfeeding, suppress ovulation.

METHODOLOGICAL ISSUES: Recall bias may be an issue, especially among the older women. Low participation rate (61% response rate), especially among the cases, may be an issue.

Siskind V, Green A, Bain C, Purdie D. Breastfeeding, menopause, and epithelial ovarian cancer. Epidemiology 1997;8(2):188–91.

COUNTRY: Australia

SETTING: Queensland, New South Wales, and Victoria

DESIGN: Case-control study (n > 600 parous ovarian cancer patients, aged 18–79 years; cases (n = 619) were obtained from major oncology treatment centers in the three Australian states; controls (n = 724) were obtained randomly from the electoral rolls.

BREASTFEEDING DEFINITION: Duration of exclusive breastfeeding: full breastfeeding if unsupplemented by formula or solids, partial if supplemented. Only considered full breastfeeding.

OUTCOME MEASURE: Epithelial ovarian cancer registered in oncology treatment centers in the mentioned sites

RESULTS: A modest protective effect of prolonged breastfeeding was found on the risk of epithelial ovarian cancer among premenopausal women (adjusted odds ratio 0.98; 95% CI = 0.95–1.01). No such association was found among postmenopausal women (adjusted odd ratio 1.00; 95% CI = 0.9-–1.01) or between ovarian cancer and the length of time first live-born child was breastfed.

METHODOLOGICAL ISSUES: Authors controlled for parity (live births only) and other potential confounders. Generalizability might be an issue, since cases came from only 3 Australian states.

Rosenblatt KA, Thomas DB, WHO Collaborative Study of Neoplasia and Steroid Contraceptives. Lactation and the risk of epithelial ovarian cancer. Int J Epidem 1993;22:192–7.

COUNTRY: Australia, Chile, China, Israel, Mexico, Philippines, Thailand

SETTING: Hospital patients

DESIGN: Case-control: cases = 393 newly diagnosed cases; controls = 2,565 women hospitalized in the same hospital for digestive or nervous system disorders

BREASTFEEDING DEFINITION: Duration of breastfeeding

OUTCOME MEASURE: Ovarian cancer

RESULTS: Risk of ovarian cancer decreased with increasing duration of breastfeeding, but after adjusting for the number of live births, this trend was not significant. A significant reduction in risk was found for women who breastfed for at least 2 months, but no further reduction was found with longer-term breastfeeding. The findings are consistent with those of a meta-analysis of 12 studies that showed a slight reduction in risk associated with short-term breastfeeding and no further reduction in risk associated with longer term lactation (see Whittemore et al., 1992).

METHODOLOGICAL ISSUES: Analyses were restricted to parous women only, which is important because pregnancy has an independent protective effect on ovarian cancer risk. Potentially confounding factors were controlled as well.

Whittemore AS, Harris R, Itnyre J, Collaborative Ovarian Cancer Group. Characteristics relating to ovarian cancer risk: Collaborative analysis of 12 US case-control studies. Am J Epidemiol 1992;136:1184–1203.

COUNTRY: United States

SETTING: Community and hospital

DESIGN: Case-control: used data from 2,197 ovarian cancer patients and 8,893 controls from 12 case-control studies (6-hospital-based, 6 community-based)

BREASTFEEDING DEFINITION: Duration of breastfeeding

OUTCOME MEASURE: Ovarian cancer

RESULTS: After adjusting for parity and oral contraceptive use, parous women who had ever breastfed had a lower risk than did those who had never breastfed. The odds ratios were 0.73 (95% CI: 0.51–1.0) in the hospital studies and 0.81 (95% CI: 0.68–0.95) in the community-based studies. The percent of risk reduction per month of breastfeeding for the first 6 months after delivery exceeds that for breastfeeding after 6 months. This suggests that part of the protective effect of breastfeeding may be through suppression of ovulation. There was also a trend of decreasing risk with increasing duration of breastfeeding.

METHODOLOGICAL ISSUES: Analyses were restricted to parous women only, which is important because pregnancy has an independent protective effect on ovarian cancer risk. Potentially confounding factors were controlled as well.

Gwinn ML, Lee NC, Rhodes PH, Layde PM, Rubin GL. Pregnancy, breast feeding, and oral contraceptives and the risk of epithelial ovarian cancer. J Clin Epidemiol 1990;43(6):559–68.

COUNTRY: United States

SETTING: Multicenter (Atlanta, Detroit, San Francisco, Seattle, Connecticut, Iowa, New Mexico, Utah)

DESIGN: Case-control: n = 436 cases and 3,833 controls randomly selected from the community

BREASTFEEDING DEFINITION: Any breastfeeding, total months of breastfeeding

OUTCOME MEASURE: Ovarian cancer

RESULTS: Among parous women, breastfeeding was protective against ovarian cancer. The relative risk was 0.6 (95% CI: 0.5–0.9). Further reductions in risk were seen in women who had breastfed for > 24 month. Each month of breastfeeding was associated

with a reduced risk of 2.4 percent. Most of the protection due to breastfeeding occurred with the first exposure.

METHODOLOGICAL ISSUES: The parity variable included live and stillbirths, unlike other studies, which only include live births in the analyses.

Booth M, Beral V, Smith P. Risk factors for ovarian cancer: A case-control study. Br J Cancer 1989;60:592–8.

COUNTRY: England

SETTING: London and Oxford hospitals (13)

DESIGN: Case-control: cases (n=235) and controls (n=451) were selected from the hospital.

BREASTFEEDING DEFINITION: Duration of breastfeeding, ever breastfed

OUTCOME MEASURE: Ovarian cancer

RESULTS: In contrast to the results from the other studies reviewed, women who had breastfed for more than 2 years had 3 times the risk of ovarian cancer of women who never breastfed ($p < 0.05$).

METHODOLOGICAL ISSUES: Controls were selected from the hospital, which may have introduced undetected bias.

Risch HA, Weirs NS, Lyon JL, Daling JR, Lift JM. Events of reproductive life and the incidence of epithelial ovarian cancer. Am J Epidemiol 1983;117(2):128–39.

COUNTRY: United States

SETTING: Washington and Utah (six counties)

DESIGN: Case-control: n = 290 cases (68% of eligible cases), n = 705 controls randomly selected from the community and age-matched

BREASTFEEDING DEFINITION: Total months of breastfeeding, 0–2 months or >3 months

RESULTS: The estimated relative risk for breastfeeding was 0.79 per year of lactation ($p = 0.034$). Breastfeeding more than 3 months, compared with 2 or fewer months, was inversely associated with ovarian cancer: relative risk = 0.694 (95% CI: 0.503–0.959; $p = 0.026$). The authors found that the magnitudes of the diminished risk from lactation and other protective exposures (e.g., pregnancies and oral contraceptives) substantially exceeded those that would have been expected solely on the basis of their inhibition of ovulation. This suggests another mechanism by which these events protect against ovarian cancer.

METHODOLOGICAL ISSUES: Only 67% of eligible cases were included, which suggests that the results may not be representative of women with advanced cases of cancer. The study controlled for many potentially confounding factors.

5.3 Effect of Breastfeeding on Other Maternal Outcomes

Dewey KG, Cohen RJ, Brown KH, et al. Effects of exclusive breastfeeding for four versus six months on maternal nutritional status and infant motor development: Results of two randomized trials in Honduras. J Nutr 2001, 131:262–7.

COUNTRY: Honduras

SETTING: Maternity hospitals in San Pedro Sula

DESIGN: Prospective observational study for the first 4 months of life, followed by a randomized intervention trial from 4 to 6 months and a follow-up period for the second half of the first year

BREASTFEEDING DEFINITION: Exclusive breastfeeding consisted of infants receiving only breastmilk.

OUTCOME MEASURE: Maternal body mass index, duration of lactational amenorrhea, and infant motor development (following 10 motor milestones)

RESULTS: Women who exclusively breastfed 4–6 months experienced small but significantly more postpartum weight loss and longer duration of postpartum amenorrhea than women who introduced solids at 4 months. Moreover, the nutritional burden or nutritional cost of the mothers who were exclusively breastfeeding was only slightly higher than that of women who introduced solid foods at 4 months.

METHODOLOGICAL ISSUES: All groups in both studies were exclusively breastfed until the age of 4 months and continued to receive some breastmilk past 6 months. Since neither study had a formula-only group, it can be assumed that the developmental differences observed would be stronger between the exclusively breastfed and the formula-fed infants.

Gigante D, Victora CG, Barros FC. Breast-feeding has a limited long-time effect on anthropometry and body composition of Brazilian mothers. J Nutr 2001;131:78–84.

COUNTRY: Brazil

SETTING: Urban

DESIGN: Longitudinal study: n = 312

BREASTFEEDING DEFINITION: Not specified, but referred to the breastfeeding patterns classified according to Labbok and Krasovec (Stud Fam Plann 1990; 21:226–30).

OUTCOME MEASURE: Maternal anthropometric measures: body mass index (BMI), waist:hip ratio, waist circumference, percent fat mass, body mass index gain, weight gain, arm fat index, fat mass change after 5–6 years

RESULTS: All anthropometric values tended to be higher for women who breastfed for < 1 month or ≥ 12 months. Women who breastfed 6–11.9 months had the smallest BMI, percent fat mass, and skinfold measurements. Moreover, women who exclusively or predominantly breastfed their infants tended to be thinner than those who breastfed partially or not at all.

METHODOLOGICAL ISSUES: Breastfeeding duration information was collected at 6 and 12 months. Confounding variables, such as income, education, age, parity, and prepregnancy weight and BMI were taken into account during the multivariate analyses. ANOVA bivariate analyses were conducted to compare the mean anthropometric values with breastfeeding duration and pattern.

Michaëlson K, Baron JA, Farahmand BY, et al. Influence of parity and lactation on hip fracture risk. Am J Epidemiol 2001;153(12):1166–72.

COUNTRY: Sweden

SETTING: Nationwide

DESIGN: Population-based case-control among postmenopausal women aged 50–81 years of age: cases (n = 1,328) were determined by mailed questionnaires; controls (n = 3,312) were randomly selected.

BREASTFEEDING DEFINITION: Duration of breastfeeding was divided into 4 categories defined by quartiles of either total duration or mean duration per child (1–5 mo, 6–10 mo, 11–16 mo, > 16 mo total).

OUTCOME MEASURE: Incidence of hip fracture

RESULTS: Long total duration of breastfeeding was associated with a reduction in hip fracture risk, but the association disappeared when adjustments were made. No substantial risk differences were found considering mean duration of breastfeeding per child or among those with their first pregnancy as teenagers or after age 30. Increased parity among nonoral contraceptive users was associated with a modest reduction in risk of hip fracture.

METHODOLOGICAL ISSUES: This study was carried out only on postmenopausal women through mailed and telephone interviews. Possible confounders were age, oral contraceptive use, and parity.

Motil KJ, Shen HP, Kertz BL, et al. Lean body mass of well-nourished women is preserved during lactation. Am J Clin Nutr 1998;67:292–300.

COUNTRY: United States

SETTING: Not reported

DESIGN: Longitudinal: six-week interval observations between 6 and 24 weeks postpartum and at 52 weeks postpartum

BREASTFEEDING DEFINITION: Lactating women exclusively breastfed from birth to 6 months and gradually weaned their infants from 6 to 12 months.

OUTCOME MEASURE: Lean body mass, body weight, dietary protein intakes, milk production, and milk protein output of women in the lactating, nonlactating postpartum, and nulliparous groups

RESULTS: Lactating women had significantly more body fat than the nulliparous women only at the first 3 visits (up to 18 weeks postpartum, but not the fourth [24 weeks]). None

of the skinfold thicknesses differed significantly for the lactating, nonlactating, or nulliparous women at the fifth visit (1 year). Lean body mass was preserved in well-nourished lactating women who exclusively breastfed for the first 6 months of life, but small progressive body weight losses were observed throughout the breastfeeding period.

METHODOLOGICAL ISSUES: Sample size (n = 30) was small. Body composition was determined at all visits, body fat was calculated, dietary consumption was determined with 3-day food records (including 1 weekend day), and milk production was measured for 50 hours by test-weighing. Differences among women were determined with analysis of variance and analysis of co-variance.

6. ECONOMIC BENEFITS OF BREASTFEEDING

This section summarizes literature on the economic value of breastfeeding compared with infant formula from the national, public sector, hospital, household, and environmental perspective. Some of the studies explore the longer-term economic impact of breastfeeding for industrialized as well as developing countries.

Weimer J. The economic benefits of breastfeeding: A review and analysis. ERS Food Assistance and Nutrition Research Report No. 13. USDA Economic Research Service, Washington, D.C. 2001.

COUNTRY: United States

This article reviews the economic benefits of breastfeeding in the United States and provides new estimates of the economic gains from increasing breastfeeding rates from the 1998 level to targets set by the Surgeon General. From virtually all infants being breastfed in 1950, the prevalence of breastfeeding at hospital discharge declined to a low of 25% in 1967, rebounding to hover at around 64% by 1998. At least part of the erosion of breastfeeding in the United States is attributed to the increase in the proportion of women who work outside the home. After reviewing the health benefits of breastfeeding both for infants and mothers, the author examines the few studies that assess the economic benefits of breastfeeding in the United States. The economic benefits of breastfeeding include savings in reduced expenditure on publicly subsidized formula and health care, lower net food cost to households, and lower overall health care costs.

Although each analysis has a different perspective and uses different assumptions, the conclusions are unanimous: It is more expensive to provide formula than to breastfeed, and formula-feeding results in excess illness, which increases the cost of health care. Drawing on epidemiological studies that relate breastfeeding to the risk of otitis media, gastroenteritis, and necrotizing enterocolitis, and estimates of treatment costs, the author estimates that an increase in breatfeeding rates from the 1998 levels (64% at hospital discharge and 29% at 6 months) to the Surgeon General's targets (75% at discharge and 50% at 6 months), would save a minimum of $3.6 billion.

The majority of these savings ($3.1 billion) are attributable to preventing premature deaths due to necrotizing enterocolitis, which cost $8.3 million per death. Savings due to reductions in medical expenses and the cost of parents' time are estimated at $0.5 billion per year. This is considered to be conservative because it does not include a number of expenses related to the 3 conditions examined, nor does it include many other conditions with economic consequences, such as cognitive effects and other childhood, maternal, and chronic illnesses.

Ball TM, Wright AL. Health care cost of formula-feeding in the first year of life. Pediatrics 1999;103:870–6.

COUNTRY: United States and Scotland

SETTING: Small, middle-class cities

DESIGN: Retrospective

BREASTFEEDING DEFINITION: Exclusive breastfeeding < 3 months or ≥ 3 months used to determine 3 feeding categories: exclusively fed if breastfed only for ≥ 3 months, partially breastfed if received formula in the first 3 months of life, and never breastfed if never received breastmilk

OUTCOME MEASURE: Number of office visits and associated costs, days of hospitalization, and purchase of prescription drugs for lower respiratory tract illnesses, otitis media, and gastroenteritis.

RESULTS: After adjustments were made, the never breastfed infants were observed to have had 60 more episodes of lower respiratory tract illness, 580 more episodes of otitis media, and 1,053 more episodes of gastrointestinal illness per 1,000 infants. The total direct cost incurred by never breastfed infants during the first 12 months of life for lower respiratory tract illness, otitis media, and gastrointestinal illnesses was between $331 and $475 per infant. This totaled $331,051 for the cost for medical care of 1,000 never breastfed infants, compared with the infants who were exclusively breastfed for the first 3 months of life.

METHODOLOGICAL ISSUES: Home visits for 617 infants were followed at 2 weeks and at 1-6, 9, and 12 months of age. Costs of care were estimated based on the actual experiences of the largest health management organization in Tucson, Arizona, and generally were lower than those of regular clinic fees. Chi-squared tests and adjusted mean differences were used to assess the relationship between feeding status and illness outcome.

Davis P. Time allocation and infant-feeding pattern: Women's work in the informal sector in Kampala, Uganda. Wellstart International's Expanded Promotion of Breastfeeding Working Paper. Washington, DC. 1996.

COUNTRY: Uganda

This paper describes the relationship between time spent in infant feeding and market work activities among women in the informal sector in Kampala, Uganda. The results show that women spent a large proportion of time breastfeeding their infants. Out of a 14-hour day, an average of 3.7 hours were spent breastfeeding infants of all ages, and 5.4 hours were spent breastfeeding infants under the age of 4 months. In contrast, mothers spent negligible amounts of time feeding other foods, which is explained by the fact that this was usually done by someone other than the mother. The amount of time spent breastfeeding (categorized as high, medium, and low) was inversely and significantly related to the proportion of time spent in market activities. However, the amount of time spent in market activities (categorized as high, medium, and low) was not associated with the proportion of time spent breastfeeding. This is because the proportion of time spent in market activities and breastfeeding varied markedly by specific activity. Also, the amount of time spent on household chores was inversely and significantly related to the proportion of time spent in market activities, which suggests that household work presents more of a constraint on time available for market activities than does breastfeeding.

Gryboski KL. Maternal and non-maternal time-allocation to infant care, and care during infant illness in rural Java, Indonesia. Soc Sci & Med 1996;43:209–19.

COUNTRY: Indonesia

The time costs of breastfeeding and time costs of caring for ill infants have emerged as important considerations in quantifying the economic value of breastfeeding. This paper describes maternal and nonmaternal time allocation to infant care during symptom-free days and ill days. A longitudinal design of repeated household visits and observation was used to record the time spent in daily tasks. The results show that infants were fed by caretakers other than the mother or by caretakers in addition to the mother on one-third of all study days. The paper does not present the data in such a way that the proportion of time spent feeding or devoted to ill infants can be related to feeding mode. There was no significant difference between well and sick days in the amount of time spent breastfeeding or the frequency of breastfeeding, mothers' remunerative work outside or inside the home, or minutes of infant care either by the mother or other caregivers.

Horton S, Sanghvi T, Phillips M, Fiedler J, Perez-Escamilla R, Lutter C, et al. Breastfeeding promotion and priority setting in health. Health Policy and Planning 1996;11(2):156–68.

COUNTRY: Brazil, Honduras, Mexico

This paper examines the cost-effectiveness of hospital-based breastfeeding promotion programs. Effectiveness estimates are based on 3 hospital-based programs in Brazil, Honduras, and Mexico. Costs were determined by estimating the costs associated with training, maternity ward education and support, prenatal and postnatal education, and equipment. Savings were determined by estimating the reductions in purchase of formula and changes in birthing procedures and drug use. Cost-effectiveness calculations were based on estimated reductions in mortality from acute respiratory infections and diarrhea. Based on estimated mortality reductions, the costs per disability-adjusted-life-year gained through increases in breastfeeding were estimated to range from $4 to $19, which were comparable to those gained from reductions in measles and rotavirus infection and less than those for oral rehydration therapy. The cost of breastfeeding promotion per birth ranged from $0.30 to $0.40, when the savings due to eliminating formula were included, and from $2 to $3 when the savings due to eliminating formula no longer could be used to offset the cost of breastfeeding promotion.

Tuttle CR, Dewey KG. Potential cost savings for Medi-Cal, AFDC, Food Stamps, and WIC programs associated with increasing breast-feeding among low-income Hmong women in California. J Am Dietetic Assoc 1996;96:885–90.

COUNTRY: United States

This article calculates the theoretical savings for public welfare costs from less formula use, decreased morbidity, and decreased fertility. The implications for 4 public welfare programs were analyzed for cost: Medicaid in California, Aid to Families with Dependent Children, Food Stamps, and Women, Infants, and Children (WIC). The authors report a substantial savings associated with breastfeeding. The total savings per family over a 7.5-year period range from $3,422 to $4,944, or from $4,475 to $6,060, depending on the discount rate used. Most of the savings are due to decreased fertility in

that the population studied does not use modern contraceptives and has a high fertility rate, with subsequent high public welfare costs. These estimates are conservative because they do not include the cost of maternal perinatal care or delivery or postnatal care associated with increased fertility. The savings due to formula costs are minimal because of rebates the State of California receives from formula makers for formula purchased with WIC vouchers. Also, women who partially breastfeed under the WIC program receive both a full set of vouchers for formula and an enhanced maternal package of food, which increases the cost of partial breastfeeding to the program.

Cohen RJ, Haddix K, Hurtado E, Dewey KG. Maternal activity budgets: Feasibility of exclusive breastfeeding for six months among urban women in Honduras. Soc Sci & Med 1995;41:527–36.

COUNTRY: Honduras

In this study, data from 2 12-hour in-home observations at 19 and 24 weeks postpartum are used to estimate maternal time costs of exclusive breastfeeding versus partial breastfeeding infants 4–6 months of age. Two groups of partially breastfeeding women were considered: those who maintained nursing frequency similar to that of an exclusively breastfeeding woman and those who did not. The results show that the time spent breastfeeding was similar in both groups of women and averaged about 75 minutes per 12-hour period. One exception was that multiparous women in the exclusive breastfeeding group spent more time breastfeeding at 24 weeks than women in the partial breastfeeding group. When total time spent feeding an infant was considered (breastfeeding plus preparing and feeding solids), partially breastfeeding women spent more time than exclusively breastfeeding women, except for multiparous women, at 24 weeks. For example, at 19 weeks, exclusively breastfeeding primiparous women spent 71±27 minutes breastfeeding, compared with 99±40 and 108±38 minutes in the 2 partially breastfeeding groups ($p < 0.01$).

This comparison underestimates the time spent preparing baby food because primiparous women were provided baby food in jars and did not have to make it from scratch. Time spent on other activities shows that both exclusively and partially breastfeeding women spent 2–3 hours per 12-hour period resting, chatting, or watching television. However, mothers expressed a preference for partial breastfeeding because they perceived it to be less time-consuming. The authors conclude that time was not a constraint to exclusive breastfeeding in this population, but that it was perceived to be a barrier. Such perceptions should be addressed in programs to promote exclusive breastfeeding.

Cohen R, Mrtek MB, Mrtek RG. Comparison of maternal absenteeism and infant illness rates among breast-feeding and formula-feeding women in two corporations. Am J Health Promot 1995;10:148–53.

COUNTRY: United States

This study used an observational design to study the effect of infant feeding practices on infant illness and maternal absenteeism over a 1-year period. Two groups of women were studied: those employed at a utility company, and those employed at an aeronautics corporation. Both companies had on-site lactation programs. A total of 101 mother/infant pairs were studied for whom breastfeeding was the feeding mode in 59 of the cases, and bottle-feeding was the feeding mode in 42 cases. Entry into the study was voluntary, so

self-selection may limit validity. Because the associations found did not differ by company, the companies are combined for presentation of results. Breastfeeding mothers had higher levels of education and salaries than the formula-feeding mothers. For example, more than 80% of breastfeeding mothers earned more than $30,000 per year, compared with 40% among the formula-feeding mothers. More than 26% of the breastfeeding mothers earned more than $60,000, compared with 15% of the formula-feeding mothers. Ethnic background was also significantly related to feeding mode: 74% of the formula-feeding mothers were Asian or Hispanic; only 28% of the breastfeeding mothers were Asian or Hispanic.

The results show a significant 6-fold difference in the risk of becoming ill between breastfed and formula-fed infants. A total of 28% (28 out of 101) of the study infants experienced no illness during the study period. This "well-babies" group consisted of 86% breastfed infants (n = 24) and 14% formula-fed infants (n = 4). A total of 205 episodes of illness was reported among the remaining 73 infants. Of these, the rates are significantly different from those expected if there were no association between infant feeding mode and illness. An insignificant difference was found by feeding mode for mild illnesses that did not require mothers to miss work (74% of all episodes for breastfed infants and 57% of all episodes for formula-fed infants). However, of the 40 episodes that caused a 1-day absence, absences were twice as frequent among the formula-feeding mothers than among the breastfeeding mothers (26% versus 11% [$p < 0.05$]). No difference in feeding mode was found for the remaining 26 episodes of serious illness that resulted in significantly longer days of maternal absenteeism.

METHODOLOGICAL ISSUES: This study does not control for other factors that may be related to infant feeding mode, infant illness, and maternal absenteeism, such as household smoking and child care arrangements.

Jarosz LA. Breast-feeding versus formula: Cost comparison. Hawaii Med J 1993;52(1):14–8.

Country: United States

This article compares the cost of 2 months of either exclusive breastfeeding or formula-feeding of a hypothetical healthy, full-term newborn in Hawaii. Calculations are based on several assumptions: 1) infant weight at 1 month and 2 months, which is based on National Center for Health Statistics medians for male infants; 2) dietary energy needs, which are assumed to be similar to and based on requirements set forth by the National Academy of Sciences; 3) the energy content of artificial formula; and 4) the cost of the maternal diet to produce the infant's energy requirements in breastmilk, using an assumed efficiency of converting this food into breastmilk of 80%. Two different food spending plans specified by the U.S. Department of Agriculture were used: a thrifty plan and a moderate plan. Food items were priced, and the lowest-priced brand of each formula type (powder, concentrate, etc.) was used to calculate formula costs. Also, the lowest-priced brand was used to price maternal foods. A total of 36 different artificial milks and 29 maternal foods were priced. The results show that even the moderate maternal dietary plan was 39% less expensive than the cheapest formula. The difference in cost increased substantially when higher-priced formulas were used. For example, the lowest-priced concentrated formula cost twice as much as the moderate food plan and three times as much as the thrifty food plan over the 2-month period.

Huffman S, Steel A, Toure KM, Middleton E. Economic value of breastfeeding in Belize. Nuture: Center to Prevent Childhood Malnutrition. Washington DC, 1992.

Country: Belize

In this working paper, a workbook for assessing the economic value of breastfeeding was used to estimate the economic value of breastfeeding in Belize. The total cost of breastfeeding promotion was $84,000 per year, which did not include the cost of volunteers who work within the program. The costs of bottle-feeding included both the direct costs to households and the public sector in terms of formula and supplies and the indirect costs, which included excess infant morbidity and mortality and maternal fertility that could be averted through optimal breastfeeding practices. The national costs of bottle-feeding were estimated to be $516,750 (assuming that 25% of imported dried milk was used for infant feeding) and $62,000 for interest on the external debt. National-level data on the costs of bottles, teats, and other supplies needed to bottle-feed were not available.

Based on national level infant feeding data and the number of births per year, the direct household costs of purchasing breastmilk substitutes were estimated to be $716,400 for nonbreastfed infants and $489,000 for partially breastfed infants. Estimates of the annual hospital cost of bottle-feeding in the main hospital, where one-third of all births occur, was $175,000. Indirect costs associated with excess morbidity from diarrhea and acute respiratory infection were not estimated. However, national data on the prevalence of these illnesses, the treatment rate/illness episode, and the cost of treatment of each illness suggest substantial costs associated with excess morbidity. Costs associated with reduced fertility and environmental damage were not quantified.

Radford A. The ecological impact of bottle feeding. Baby Milk Action Coalition. 1991. Mimeo.

Radford A. Breastmilk: A world resource. World Alliance for Breastfeeding Action. Penang, Malaysia. Undated. Mimeo.

These papers summarize the ecological impact of bottle feeding and some quantitative data from some countries. The estimates used to calculate cost estimates are not well described and derive from different countries so that overall national and/or global costs cannot be estimated. Breastfeeding is viewed as an ecologically sound activity as it requires no packaging or transport. Breastfeeding does not result in wastage since the mother produces exactly the amount of milk the infant consumes. Breastfeeding is also viewed as a natural, renewable resource.

Bottle-feeding is associated with a large number of products, most of which are not recycled and result in environmental damage to produce. These products/materials are related to those involving waste, the dairy industry, processing and transport, inappropriate use of land and resources, and population. Items related to waste include the following: 1) tin plate for the production of milk tins; 2) plastics, rubber, and silicon for the production of bottles and teats; 3) increased use of feminine hygiene products; and 4) clean water and sterilizing fluids. Examples given in this category of products include 4.5 million plastic bottles sold in Pakistan in 1987, the 3,000 tons of paper that would be saved on feminine hygiene products if every mother in England were to breastfeed her

infant, and the 73 kg of fire wood needed to sterilize water to formula feed an infant for one year.

The environmental costs of the dairy industry are illustrated with respect to the number of cows it would take to replace current breastmilk production. For example, the author cites a study showing that it would take 135 million cows in India to replace current breastmilk output. Cows also need pasture, which requires cutting of trees with the resultant deforestation and erosion. Cattle also produce 100 million tons of methane per year, which is an estimated 20% of total annual methane emissions. Nitrate fertilizers used in dairy feed production also can contaminant ground water.

Processing of infant formula is done under high temperature conditions, which requires fuel and may result in air pollution. Transport of formula in the international market also results in air pollution and fuel use.

Bottle-feeding also contributes to inappropriate use of land and resources. External debt is increased from imported formula and supplies. For example, in Mozambique it was estimated that a 20% increase in bottle-feeding over a two-year period would cost $10 million for the importation of formula. It was also calculated that the fuel required to boil water would use up the entire resources from a major forestry project. Excess health care costs associated with bottle-feeding are also discussed. The contraceptive effects of breastfeeding are discussed briefly.

Melville BF. Letter to the editor: Can low income women in developing countries afford artificial feeding? J Trop Pediatr 1991;37:141–2.

COUNTRY: Jamaica

This letter examines the monthly cost of artificially feeding a 3-month-old infant and expresses the results as a percentage of the net monthly salaries for selected jobs. Data were collected during the first 4 months of 1990. The cost was calculated at $43.30/month (more than 90% of which can be attributed to purchasing infant formula). The cost of bottles, cooking pot for sterilization, and fuel added another $3.40/month. These costs constituted 90%, 78%, 36%, 22%, and 26% of monthly salaries for a household helper or minimum wage worker, community health aide, clerk, registered nurse, and teacher, respectively. The author estimates that the economic cost of lost breastmilk because of the 17-percentage-point drop in the number of women fully breastfeeding at 6 weeks was more than $200,000 per month worth of foreign exchange. The authors also cite a study showing that artificial feeding costs as much as feeding a family of 5 with the basic food basket. This letter also discusses the risks of contaminated and diluted formulas to infant health but does not quantify these risks.

Levine RE, Huffman SL. The economic value of breastfeeding, the national, public sector, hospital, and household levels: A review of the literature. Center to Prevent Childhood Malnutrition. Washington, D.C. 1990.

COUNTRY: Multicountry

This paper develops a framework for analyzing the economic value of breastfeeding and, to the extent that data are available, discusses the actual costs of breastfeeding versus

formula-feeding from 4 perspectives: national, public sector, hospital, and household. It also identifies data gaps in the literature and recommends future research directions. The paper focuses on the economic consequences of infant feeding decisions rather than on the economic considerations that are involved in infant feeding decisions. The authors argue that the relative costs of breastfeeding and bottle-feeding are experienced at distinct levels and differ depending on the perspective being examined. They conclude that data are inadequate to provide quantitative estimates of a number of components of their economic framework.

At the national level, the costs of breastfeeding include the potential loss of women's productivity and economic contribution (the opportunity cost of breastfeeding because of the time involved and the need for the mother to be in close proximity to her infant) and the potential loss of revenues from the sale of locally produced breastmilk substitutes. The costs of bottle-feeding include the aggregate expenditures on breastmilk substitutes and supplies and the infant and child lives lost because of increased morbidity. Although no data were available on the costs of breastfeeding, the costs of bottle-feeding were well documented in terms of the cost of replacing breastmilk. Since these costs were estimated in different ways and used different assumptions, it is difficult to draw straightforward comparisons. (To derive comparable estimates, the cost of breastmilk substitutes would need to be calculated as a function of the number of women breastfeeding and the durations of exclusive and partial breastfeeding; the cost of substitutes, which involves assumptions about what the replacement product actually is; and the nutrient cost of producing the breastmilk.) Estimates for the costs of replacing breastmilk ranged from $1.8 million in Singapore (based on a decline in breastfeeding prevalence over a 9-year period) to $16 million in the Philippines (based on a decline in breastfeeding prevalence over a 10-year period). Other authors have estimated the cost of breastmilk substitutes if all breastmilk were to be eliminated, such as the estimate of $500 million annually for Indonesia. Most of these estimates do not include the savings in reduced nutrient cost to the mother of producing breastmilk.

At the public-sector level, the costs of breastfeeding include the costs of breastfeeding promotion and the potential loss of tax revenues from local breastmilk substitute manufacturers. The costs of bottle-feeding include public expenditures for breastmilk substitutes and supplies, public health care costs, family planning costs, and interest on debt incurred by importation of substitutes. The evaluation of public-sector costs was limited by the paucity of data on public expenditures related to breastfeeding and required assumptions about the health and fertility benefits to derive costs. No data were available on the potential loss of tax revenues from local breastmilk substitute manufacturers or on the debt incurred by the importation of substitutes. Breastfeeding promotion campaigns have been associated with costs of $1–$11 per mother. In Indonesia, $40 million per year would be required for diarrhea treatment if breastfeeding prevalence declined by 25%. The authors estimate that if breastfeeding currently accounts for a 20% reduction in total world wide fertility, this is worth $65 million. In Indonesia, it is estimated that an additional $80 million per year would have to be spent on family planning if breastfeeding were to cease.

At the hospital level, the costs of breastfeeding include staff training, education and support of new mothers, and modifications to permit rooming-in. The costs of bottle-feeding include staff time for preparation and feeding; expenditures on breastmilk substitutes, bottles, and other equipment; pharmaceutical supplies; and increased health care costs. The data available to quantify these costs were not comparable, which made it impossible to arrive at net cost calculations. However, data were available to show that

direct savings realized from such changes offset the costs associated with changes in hospital practices to promote breastfeeding. For example, the following costs were summarized: lobbying/conferences ($51–$600 per participant); staff training ($10–$860 per participant); lactation counseling $.35–$4.00 per participant; and rooming-in (no cost). The savings were summarized as follows: reduced staff time because of rooming-in ($4.20 per delivery in the Philippines, and a 34% reduction in personnel costs in Chile); less infant formula ($0.50–$0.82/delivery); fewer bottles ($0.32–$0.60); and less oxytocin ($0.10–$0.32/delivery).

At the household level, the costs of breastfeeding include maternal time, lost employment opportunities, and increased maternal food consumption to support breastfeeding. The costs of bottle-feeding include expenditures on formula and other supplies, caretaker's time for bottle preparation and feeding, expenditures on health care for ill children, caretaker's time for care of ill child, loss of the child's potential productivity and economic contribution to the household, and expenditures associated with higher fertility or increased use of contraceptives. While data were not available to quantify the opportunity costs of breastfeeding, maternal employment outside the home was related to early supplementation of bottle-feeding in some urban settings. The time costs of breastfeeding also need to be balanced against the time costs of bottle-feeding, which one study has found to be 3 times as time-intensive as breastfeeding. The costs of increased maternal diet to produce a given volume of breastmilk were less than the cost of formula. The costs of breastmilk substitutes were well documented and ranged from 8% of the minimum wage in Yemen to 264% of the minimum wage in Nigeria. These estimates assume that an adequate amount of formula was provided, which may not be a realistic assumption. None of the costs includes the cost of additional supplies needed to bottle-feed. Data are not available to quantify what may be the most important economic aspects of breastfeeding—lower costs associated with caring for a sick child and purchasing medicines—as well as the savings associated with reduced fertility.

Huffman S, et al. Assessment of infant feeding in Peru. Chapter XIV. Economic value of breastfeeding. Wellstart International. Washington, DC . 1992.

COUNTRY: Peru

The assessment includes a chapter that compares the costs in 1991 to the public sector of breastfeeding promotion to the costs of inadequate breastfeeding practices. A workbook for assessing the economic value of breastfeeding in Peru is provided in an appendix. Overall, the authors estimate that $742,300 was spent in the public sector on breastfeeding promotion, and $463,200 was derived from tax revenues from the domestic production of infant formula. In contrast, current public-sector expenditures on health care costs associated with suboptimal infant feeding were as follows: $946,750 for treatment of diarrhea and acute respiratory infection; $50,400 for institutional bottle-feeding; $541,400 for oxytocin and glucose; and $35,800 for interest on the external debt to import substitutes. Overall, conservative estimates of public expenditures associated with suboptimal infant feeding exceeded $800,000 per year.

The costs of inadequate breastfeeding practices were derived estimates of "excess morbidity and mortality." Using the relative risks associated with breastfeeding versus bottle-feeding for diarrhea and acute respiratory infection, the authors calculated 7,012 excess deaths due to inadequate breastfeeding practices for these two illnesses.

Calculations of excess morbidity from diarrhea and acute respiratory infection were based on national-level data on the prevalence of these illnesses and the relative risks of becoming ill. Treatment costs associated with this excess morbidity were estimated from national-level data showing that treatment is sought for 25% of diarrhea cases and 50% of respiratory cases, and from data on treatment costs for the two illnesses. These calculations show the total cost of treating excess cases of diarrhea and acute respiratory infection was $4,733,750. Assuming that 20% of these costs were borne by the public sector, the authors calculate that this represented a cost of $946,750 or 3.7% of the country's Maternal and Child Health budget.

The cost of bottle-feeding infants in public institutions was estimated to be $58,660, which included $17,700 for formula for newborns and $40,960 for formula for hospitalized infants. Costs for oral glucose tolerance tests and methergine, which may be unnecessary for newborns who are breastfed immediately after birth, were estimated to be $541,420. The interest for the payment of external debt to purchase infant formula, subsidized by the Swiss government, was $35,777. The monetary value of deaths averted through optimal infant feeding practices and births averted because of lactational amenorrhea was not quantified.

Daga SR, Daga AS. Impact of breast milk on the cost-effectiveness of the special care unit for the newborn. J Trop Pediatr 1985;31:121–3.

COUNTRY: India

This article evaluates the cost-effectiveness of a special care unit for low birth weight newborns over 2 1-year periods: one during which newborns were breastfed from 8 a.m. until 8 p.m. and formula-fed during the night, and one during which more than 95% of infants were exclusively breastfed and the remaining 5% were given breastmilk for most of their feeds. Only mortality after 3 days was considered. A reduction in costs associated with the purchase of formula and medicines, from $0.75 to $0.40 per bed per day, was found. The average stay in the hospital declined from 11.4 to 9.06 days. Total mortality declined from 38% to 16%, as did the mortality rate by birth weight category. The authors argue that the improvements seen were due to increased breastfeeding because no new diagnostic or therapeutic equipment was purchased, and the time period was too short for improvements in staff experience to have resulted in reduced mortality.

Rohde JE. Mother milk and the Indonesian economy: A major national resource. J Trop Pediatr 1982;28:166–74.

COUNTRY: Indonesia

This article, and the one that follows, estimate the economic value of breastmilk to the Indonesian economy and conclude that breastfeeding currently contributes $520 million/year to the economy, which amounts to 10% of the value of all exports, 2.5% of the total national budget, and about 1.5% of gross national product. To arrive at these estimates, the author estimates the following: the volume of breastmilk produced by breastfeeding mothers/year; the cost of purchasing the extra nutrients (calories and protein) to produce this breastmilk; the cost of purchasing an equivalent volume of

formula; the cost of reduced medical treatment for diarrhea cases prevented/year; and the cost of more family planning services/year needed to replace the contraceptive effect of lactational amenorrhea provided by current breastfeeding practices.

The volume of breastmilk produced per year is estimated by multiplying the average daily milk volume by the duration of breastfeeding for urban and rural women. This volume of milk is compared with the cost of purchasing infant formula, which would be about $500 million. To arrive at the net value of this breastmilk, the protein and calorie cost of producing this breastmilk is subtracted. Using a figure for the efficiency of conversion of 90% for calories and 55% for protein, and rice and tempe as the food source, the author calculates that it costs about $100 million/year to produce breastmilk. Thus, the net value of breastmilk produced/year was calculated at $400 million. The cost of bottles, teats, fuel, formula spoilage, and refrigeration are not included in these costs, nor are the opportunity costs associated with breastfeeding or formula-feeding, which, the author argues, are similar.

The author estimates the cost of reduced medical treatment for diarrhea by assuming that a 25% reduction in the prevalence of breastfeeding would double the total cases of diarrhea, which currently accounts for one-third of pediatric admissions to the hospital. Applying the cost per diarrhea treatment, the author estimates that $40 million/year is saved by current breastfeeding practices, a figure that is considered to be very conservative.

The cost of increased family planning services per year needed to replace the contraceptive effect of lactational amenorrhea is calculated as a function of current mean durations of lactational amenorrhea for urban and rural women and the number of urban and rural women currently breastfeeding, which provides an estimate of the couple-protection-years provided. This estimate shows that 4.5 million couple-years of contraception are provided annually. Using the cost of providing a year of contraceptive protection, an annual savings of $80 million is estimated.

Rohde JE. Mother milk and the Indonesian economy: A major national resource. Indian J Pediatr 1981;48:125–32.

(The results of this study were the same as the one preceding it; therefore, we chose to summarize only one of them, while making reference to both.)

Fallot ME, Boyd JL, Oski FA. Breast-feeding reduces incidence of hospital admissions for infections in infants. Pediatrics 1980;65;1121–4.

COUNTRY: United States

This article compares the prevalence of exclusive breastfeeding among infants < 3 months of age in the community with the prevalence of exclusive breastfeeding in similarly aged infants hospitalized during the course of 1 year (n = 136). The prevalence of exclusive breastfeeding among 2 groups of infants was examined: those attending a hospital clinic and those attending private practices. The prevalence of exclusive breastfeeding was higher among infants cared for in private practice (38.0%) than among those attending a hospital clinic (13.5%). At the time of admission, the prevalence of

exclusive breastfeeding among clinic and private-practice infants was 8.5% and 13.8%, respectively. Of the 136 infants admitted, only 15 were being exclusively breastfed. Chi-square analysis showed a significant underrepresentation of exclusively breastfed infants among the hospitalized infants. The authors estimate that exclusive breastfeeding could have prevented 75 hospital admissions over 1 year at a savings of $50,000.

This study does not control for other factors that could be related to both infant feeding mode and risk of disease, such as exposure to household smoke, use of day care, and other preventive and caregiving measures. It also has been suggested that physicians may be less likely to hospitalize a breastfed infant.

Almroth S, Greiner T. FAO Food and Nutrition Paper. The economic value of breast-feeding. Food and Agriculture Organization, Rome, Italy. 1979.

COUNTRY: Ivory Coast and Ghana

This report summarizes the costs of breastfeeding and bottle-feeding in 2 African countries. The costs associated with breastfeeding were related to increased maternal nutrient intake and opportunity costs. Those associated with bottle-feeding—related to the costs of breastmilk substitutes, other supplies, and time—were quantified at both the household and national levels. Due to data limitations, the same estimates for household costs were used for both countries. Of interest is the methodology used to estimate the time costs of breastfeeding and formula-feeding, which was based on national-level data on wages and assumptions about the amount of time needed to prepare safe bottles, and observations on the length of time spent breastfeeding. The results show that the cost of increased maternal consumption to produce breastmilk ranged from $51 to $100 over a 2-year period, depending on the foods chosen. The costs of formula-feeding over an equivalent period, based on the costs of substitutes, supplies, and fuel, ranged from $310 to $390, depending on the type of substitute chosen. The estimated opportunity costs for breastfeeding and artificial feeding were $210 and $600 over the 2-year period, respectively. Thus, breastfeeding rather than artificial feeding for 2 years could save the average family between $600 and $730.

At the national level, the authors show that imports of breastmilk substitutes accounted for only 1% of the total volume of breastmilk produced. Estimates were made for the economic impact of a hypothetical change in feeding patterns in terms of increases in cost and foreign exchange used to purchase substitutes. Estimates of the number of children malnourished as a result of suboptimal practices were calculated. The actual costs of rehabilitation were not made.

The authors note that the most important national-level indirect costs of bottle–feeding, because of increased morbidity and fertility, cannot be quantified in monetary terms. Overall, this paper contributes to the theoretical development of a model to estimate economic impacts. In particular, it points out that the costs and benefits of breastfeeding differ at different levels of analysis, and it attempts to quantify the opportunity cost of breastfeeding and bottle-feeding. The data used are outdated and no longer useful.

Lamm E, Delaney J, Dwyer J. Economy in the feeding of infants. Pediatric Clinics of North America 1977;24(1):71–84.

COUNTRY: United States

This article examined the cost of feeding various breastmilk substitutes during infancy versus the cost of feeding a breastfeeding mother. The costs of breastmilk substitutes ranged from $133/year for evaporated milk-corn syrup to $276/year for ready-to-serve Similac. The costs of purchasing food to meet the additional daily recommended dietary intakes for a lactating woman ranged from $156 to $281/year, depending on the diet chosen. Food costs associated with breastfeeding depend on the choice of foods purchased to meet the caloric demands of lactation. The costs associated with breastmilk substitutes depend on type and form of the product and source of supply rather than on brand name. Powdered or concentrated formulas are less expensive than ready-to-serve formulas. Overall, food costs of different infant feeding patterns vary by as much as 100%; however, according to the data presented in this paper, the ranges are similar for formula-fed and breastfed infants. Both this and the previous article look at the costs of breastfeeding based on high estimates of what lactating women need to consume to meet their additional recommended dietary allowances rather than on the additional calories lactating women actually consume. To the extent that breastfeeding women actually consume fewer additional calories/day than recommended, this would reduce the cost of the foods needed to provide those calories.

The calculation for the cost of feeding formula ignores the cost of bottles, sterilizers, fuel, soap, and other items needed to serve formula in a safe and hygienic manner. The cost of mother's time for both breastfeeding and formula-feeding are not addressed, nor are the medical and time costs associated with different morbidity rates between breastfed and bottle-fed infants.

McKigney J. Economic aspects. Amer J Clin Nutr 1971;24:1005–12.

COUNTRY: Jamaica

This article compares the cost of purchasing infant formula with the nutrient costs of producing an equivalent amount of breastmilk. Three different diets are used to estimate the cost of producing breastmilk: a low-, intermediate-, and high-cost diet. Likewise, 3 different artificial infant feeding modes are used for estimating the cost of infant formula. The estimates show that the cost of breastfeeding ranges from $0.54 to $3.78 per week, while the cost of purchasing an equivalent amount of breastmilk ranges from $0.76 to $5.54 per week. The author argues that there is a definite nutrient cost advantage to breastfeeding over artificial feeding, which, although small on a weekly basis, is significant on an annual basis, especially for poor families. These estimates also used an extra 1,000 calories/day calories needed to support lactation rather than the current figure of 600 calories/day, which would reduce the nutrient cost of breastfeeding by another 40%. The author suggests that "economy" in the nutrient cost of breastfeeding can be achieved by purchasing cheaper foods that would not have nutritional costs to the mother. However, "economy" in infant artificial feeding can be achieved only through overdilution of formula, which would have serious adverse effects on the infant.

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TABLES

The following tables are intended to provide a quick guide to the literature reviewed and annotated here, particularly regarding the magnitude of the effects described. Review articles and those not reporting an effect size are not represented in the tables. Although the table formats vary, depending on the outcome, the last two columns in every case are "effect size" and "comments." In "effect size" we provide the authors' quantitative estimate of the effect of breastfeeding on the outcome in question. As the effect size takes many forms (e.g., relative risk, odds ratio, correlation coefficient, absolute measure, etc.) we use the "comments" column to specify the meaning of the numbers provided and to provide other explanatory remarks. Unless otherwise stated, the differences given are statististically significant.

The "BF Practices" column uses the following abbreviations:

BF	Breastfed
EBF	Exclusively breastfed
FBF	Fully breastfed
PBF	Partially breastfed
NBF	Not breastfed
FF	Formula fed

1.1 Effect of Breastfeeding on Diarrheal Morbidity

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size		Comment
Kramer et al., 2001	Belarus Urban/rural	Randomized controlled trial	0–12 mo	intervention control	0.60 1		Adjusted odds ratio for GI tract infection
				intervention control	0.54 1		Adjusted odds ratio for atopic eczema
Clemens et al., 1999	Egypt Rural	Prospective	< 6 mo	EBF PBF FF	0.67 0.72 1		Adjusted rate ratios of diarrhea. Infants who initiated BF early (within the first 3 days after birth) had 26% lower rate of diarrhea than those who initiated BF late (after the third day), $p < 0.05$
Nacify et al., 1999	Egypt Rural	Prospective (population-based)	< 36 mo	BF FF	0.30 1		Adjusted hazard ratios for the association of incidence of rotavirus diarrhea and infant feeding mode for children aged < 1 year
Meremikwu et al., 1997	Nigeria Calabar	Case-control (clinic-based)	< 5 yrs		PD	UW	Percent of children with persistent diarrhea (PD) or underweight (UW)
				BF FF	0.4% 1.9%	35.9% 49.6%	
Scariati et al., 1997	United States Nationwide	Longitudinal	2–7 mo (diarrhea)	EBF PBF FF	1 0.9-1.3 1.8		Adjusted odds ratio of experiencing diarrhea
			2–7 mo (ear infection)	EBF PBF FF	1 1.2-1.6 1.7		Adjusted odds ratio of experiencing ear infections
Mølbak et al., 1997	Guinea-Bissau Peri-urban	Longitudinal		EBF FF	1 1.34		Adjusted rate ratio
Mondal et al., 1996	India Rural	Prospective	< 12 mo	EBF ≥ 4 mo BF ≤ 3 mo	3.02 1		Incidence rate ratio
Bohler et al., 1995	Bhutan Rural	Prospective	12–36 mo	BF Non-BF	0.51 1		Odds ratio for diarrheal disease

1.1 Effect of Breastfeeding on Diarrheal Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Dewey et al., 1995	United States Urban	Prospective	0–12 mo	BF FF	0.14 0.31	Adjusted incidence of number of diarrhea episodes per 100 days at risk FF included infants who breastfed < 3 mo
			12–24 mo	BF FF	No Difference	
Mazrou et al., 1995	Saudi Arabia Urban/rural	Cross-sectional	< 5 yrs	EBF PBF FF Foods	18.5% 23.3% 17.7% 13%	Prevalence of diarrhea
Long et al., 1994	Mexico Urban	Prospective	3–50 wk	EBF PBF FF	1 1.5 3	Incidence ratio of diarrhea
Mølbak et al., 1994	Guinea-Bissau Urban	Longitudinal	12–23 mo	BF Weaned	1 1.41	Relative risk of diarrhea
			24–35 mo	BF Weaned	1 1.67	
VanDerslice et al., 1994	Philippines	Prospective	< 6 mo	EBF Full BF PBF FF	0.1 0.1 0.13 0.25	Predicted probabilities of diarrhea Adjusted for potentially confounding factors
Clemens et al., 1993	Bangladesh Rural	Case-control	0–11 mo	EBF PBF FF	0.06 0.44 1	Relative risk for severe rotavirus diarrhea Overall no protective effect of BF for severe rotavirus infection in first 2 years of life Authors suggest that BF temporarily postponed rather than prevented infection
			12–23 mo	BF FF	Not signif	
Ahmed et al., 1992	Bangladesh Matlab surveillance area	Case-control	0–11 mo	BF FF	0.02 1	Adjusted odds ratio of episodes of shigellosis and culture-negative dysentery The odds ratio for an overall protective association was 0.27 (95% CI = 0.20 – 0.38; p < 0.001). The protective association appeared to be stronger in children who were most stunted (Z score ≤ –3.0).
			12–23 mo	BF FF	0.19 1	
			24–35 mo	BF FF	0.48 1	

1.1 Effect of Breastfeeding on Diarrheal Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Hossain et al., 1992	Egypt Rural	Prospective	0–2.9 mo	Prelacteals No prelacteals	1.4 1	Incidence density ratio of diarrheal disease
			3–5.9 mo	Prelacteals No prelacteals	Not signif	
			6–8.9 mo	Prelacteals No prelacteals	Not signif	
			9–12 mo	Prelacteals No prelacteals	Not signif	
Morrow et al., 1992	Mexico Urban	Prospective	< 18 mo	EBF PBF FF	1 3 5	Adjusted rate ratios for incidence of giardia infection
Ruuska, 1992	Finland Urban	Prospective	0–6 mo	BF < 6 mo BF ≥ 6 mo	2.42 1	Odds ratio of occurrence of acute diarrhea
			7–12 mo	BF < 6 mo BF ≥ 6 mo	Not signif	
			13–24 mo	BF < 6 mo BF ≥ 6 mo	Not signif	
Howie et al., 1990	Scotland (Dundee)	Prospective/ retrospective	0–13 wk 14–26 wk 27–39 wk 40–52 wk	See Comment	6.6–16.8% 4.0–16.2% 2.5–16.1% 5.1–18.5%	Confidence interval for risk difference (% point reduction in risk) among BF vs. FF infants Shows a protective effect after BF ceased
Ketsela et al., 1990	Ethiopia Rural	Cross-sectional	< 6 mo	EBF PBF	1 5–5.42	Age adjusted relative risk of developing diarrhea Effect only significant at age 2–4 and 4–6 mo
Megraud et al., 1990	Algeria Urban/rural	Case-control	< 6 mo	EBF PBF	0.1 1	Odds ratio for presence of campylobacter in stool Few infants > 6 mo breastfed
Popkin et al., 1990	Philippines Urban/rural	Prospective	< 6 mo	EBF FBF PBF FF	1 2.0–3.2 4.7–13.1 4.7–16.8	Range of adjusted relative risks for diarrhea, depending on age Risk greatest for infants < 2 mo
			> 6 mo	PBF FF	Not signif	Relative risk not significant

1.1 Effect of Breastfeeding on Diarrheal Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Rubin et al., 1990	Denmark Urban	Prospective	< 12 mo	breast>formula vs. breast formula	Not signif	Misclassification may be a problem Large drop-out rate
Brown et al., 1989	Peru Urban	Prospective	< 6 mo	EBF BF & liquids BF & milk BF & solids FF	1 1.2–1.4 1.3–1.8 1.6–1.8 2.8–3.1	Adjusted relative risk for diarrhea incidence Relative risks are higher for prevalence (reported in text summary)
			> 6 mo	PBF FF	1 1.2–1.5	
Jalil et al., 1989	Pakistan Urban slum	Prospective	< 24 mo	Poorly defined	No association found Poorly defined feeding modes and diarrheal episodes	
Mahmood et al., 1989	Iraq Urban	Case-control	2–3 mo	EBF PBF FF	1 6.2 36.7	Adjusted relative risk of hospitalization for severe diarrhea
			4–5 mo	EBF PBF FF	1 Not signif 23.8	
			6–7 mo	PBF FF	1 3.9	
			8–11 mo	PBF FF	Not signif	
Campbell & Latham, 1988	Rural Mexico	Prospective	< 8 mo	Not reported	Not reported	BF had a significant protective effect, but magnitude cannot be quantified from data presented
Oyejide & Fagbami, 1988	Nigeria Urban	Prospective	< 24 mo	BF FF	No associations found Poor definition of feeding modes and diarrheal episodes Within the first month, 90% of infants were partially breastfed	
Unni & Richard, 1988	India Urban	Prospective	< 6 mo	EBF PBF	6 wk: 2% 24%	14 wk: 0% 7.5% Percent infants with diarrhea
Clemens et al., 1986	Bangladesh Rural	Case-control	< 36 mo	BF FF	0.38 1	Adjusted odds ratio for severe infection

1.1 Effect of Breastfeeding on Diarrheal Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size		Comment
Duffy et al., 1986	United States Urban	Prospective	< 4 mo	EBF Any formula	Not signif		Relative risk of nonspecific gastroenteritis
			≥ 4 mo	EBF Any formula	0.29 1		
Scott-Emuakpor & Okafor, 1986	Nigeria Urban	Cross-sectional	< 24 mo	EBF PBF FF	35% 76% 74%		Percent of infants with diarrheal disease with or without vomiting in the first 24 months of life
Feachem & Koblinsky, 1984	14 developed and developing countries Various settings	Review	< 6 mo	EBF vs. FF EBF vs. PBF PBF vs. FF	3.5 – 4.9 1.4- 2.6 1.7-1.9		Relative risk for morbidity of diarrhea
			6–11 mo	PBF vs. FF	1.3- 1.5		
			12–23 mo	PBF vs. FF	Not signif		
Clavano, 1982	Philippines Urban	Cross-sectional	Neonatal period	EBF PBF FF	4% 6% 90%		Percent infants with diarrhea
Paine & Coble, 1982	United States Rural	Retrospective	< 6 mo	BF FF	1.5 12.1		Office visits/100 infant months of observation
Kumar et al., 1981	India Urban and rural	Prospective	0–4 mo		Urb.	Rural	Relative risk of diarrhea Insufficient number of FF infants in rural areas to compare
				BF BF & formula FF	1 5.3 5.7	1 4.1	
			5–12 mo	BF BF & formula FF	1 1.3 1.4	Not signif	
Fergusson et al., 1978	New Zealand Urban	Prospective	< 4 mo	EBF FF	1 31.6		Relative risk of diarrhea
Cunningham, 1977	United States Rural	Retrospective	< 12 mo	BF FF	2.0 4.9		Episodes of vomiting/diarrhea per 1000 patient – weeks, not corrected for age

1.2 Effect of Breastfeeding on Respiratory Infection Morbidity

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size		Comment
César et al., 1999	Brazil Urban (Pelotas)	Nested case-control	< 3 mo	EBF PBF FF	1 2.9 61.1		Adjusted odds ratio for developing pneumonia
			3–6 mo	EBF PBF FF	1 3.4 10.1		
			6–12 mo	EBF PBF FF	1 3.7 9.2		
Levine et al., 1999	United States and Canada Urban	Case-control	2–11 mo	Current BF	0.27		Adjusted odds ratio for invasive pneumococcal disease (IPD), separated for age groups 2–11, 12–23, and 24–59 months Only significant inverse association between breastfeeding and IPD found was in the 2–11 months age group
Perera et al., 1999	Sri Lanka Urban	Descriptive recall (hospital-based)	< 12 mo	EBF ≥ 4 mo EBF to 3 mo Never BF	0.09 0.39 0.60		Risk of first acute respiratory infection in the period after the period of exclusive breastfeeding Shows that EBF delays respiratory illness
Silfverdal et al., 1999	Sweden Urban/rural	Ecologic	5–10 yrs	BF FF	0.6		Strong negative correlation between BF and *Haemophilus influenzae* infection incidence 5–10 years later
Nafstad et al., 1996	Norway Urban (Oslo)	Prospective	< 12 mo	BF FF	AI 1 2.2	HI 1 4.6	Adjusted odds ratio of all infections (AI) and hospitalized infections (HI) of infants whose mothers smoked by feeding mode
Cushing et al., 1998	United States Urban	Prospective	< 6 mo	Full BF FF	0.81 1		Adjusted odds ratio for incidence of lower respiratory illness
Lopez-Alarcón et al., 1997	Mexico Urban	Prospective	0–6 mo	Full BF duration	Inc -0.17	Prev -0.16	Coefficient of correlation between full BF duration and incidence (Ino) and prevalence (Prev) of acute respiratory infection
Scariati et al., 1997	United States Nationwide	Longitudinal	2-7 mo	EBF PBF FF	1 1.2–1.6 1.7		Adjusted odds ratio of experiencing ear infections

1.2 Effect of Breastfeeding on Respiratory Infection Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Silfverdal, 1997	Sweden (1 county)	Prospective Case-control HI infection		EBF ≤ 12 wks EBF > 13 wks	3.6 1	Odds ratio of *Haemophilus Influenza* (HI) infection by duration of EBF
				PBF ≤ 20 wks PBF > 21 wks	2.9 1	Odds ratio of *Haemophilus Influenza* (HI) infection by duration of PBF
Zaman et al., 1997	Bangladesh Rural	Cohort (community-based)	0–59 mo	EBF ≥ 4mo EBF to 3 mo Never BF	Few More Most	Number of hospital admissions for an acute respiratory infection
Beaudry et al., 1995	Canada New Brunswick	Retrospective	0–6 mo	BF FF	RI: 0.78 1 HA: 0.32 1	Adjusted incidence density ratio for respiratory illnesses (RI) and hospital admissions (HA)
Bohler et al., 1995	Bhutan Rural	Prospective	12–36 mo	BF Non-BF	0.63 1	Odds ratio for respiratory tract infection
Dewey et al., 1995	United States Urban	Prospective	0–12 mo	BF FF	Not signif	Adjusted incidence of number of days with respiratory illnesses per 100 days at risk Formula-fed included infants who breastfed < 3 mo
			12–24 mo	BF FF	Not signif	
Wright et al., 1995	United States Urban	Prospective/ retrospective	6 years	BF < 1 mo FF	1 3.03	Adjusted odds ratio of recurrent wheezing at 6 yrs of age for nonatopic children only No effect for atopic children
Douglas et al., 1994	Austrailia Urban	Prospective	< 24 mo	PBF duration	Mo / OR 0 / 5.6 1-3 / 6.1 4-6 / 6.5 7-12 / 6.5 >12 / 7.0	Adjusted odds ratio of respiratory illness in second year, corresponding with different breastfeeding durations in months (P=0.006)
Pisacane et al., 1994	Italy	Case-control, Hospital-based	< 6 mo	BF FF	0.22 1	Odds ratio for hospitalization with pneumonia or bronchiolitis
Howie et al., 1990	Scotland Community setting	Prospective	< 24 mo	Full BF PBF FF	25.6% 24.2% 37%	Adjusted rates of respiratory infection and full, partial or no breastfeeding during the first 13 weeks of life

1.2 Effect of Breastfeeding on Respiratory Infection Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Launer et al., 1990	Indonesia Rural	Prospective	3–12 mo	Q1* Q2 Q3 Q4	2.4 1.7 1.3 0.9	Mean number of days with respiratory tract illness per 3-week period by quartiles ofntime spent breastfeeding from lowest (Q1) to highest (Q4)
Rubin et al., 1990	Denmark Urban	Prospective	0–12 mo	EBF BF> FF vs. BF < FF & FF	Not signif	Misclassification may be a problem. Large drop-out rate
Brown et al., 1989	Peru Urban	Prospective	< 6 mo	EBF BF & liquids BF & milk BF & solids FF	1 1.8 1.4 2.7 4.1	Adjusted relative risk for incidence of acute respiratory infection
Jalil et al., 1989	Pakistan Urban slum	Prospective	< 24 mo	Age at weaning	Not signif	Poorly defined feeding variable, outcome neasure and analytical methods
Wright et al., 1989	United States Urban	Prospective/ Retrospective	< 12 mo	BF FF	Not signif	Odds ratio for hospitalization with pertussis-like illness
			< 4 mo	BF > 1 mo BF < 4 mo	1 1.7	Adjusted odds ratio of wheezing during infancy Only age interval < 4 mo was significant
Chen, et al. 1988	China Urban	Community-based retrospective	< 18 mo	Ever BF Never BF	1 2.11	Adjusted odds ratio for hospitalization with respiratory infection
Forman et al., 1984	United States Rural (American Indians)	Retrospective	> 6 mo	PBF FF	1 1.2	Calculated relative risk from data presented
			< 4 mo	EBF FF	0.3 1	
Campbell & Latham, 1988	Mexico Rural	Prospective	0–8 mo	BF FF	Not signif	Negative association for frequency of breastfeeding and respiratory infections at 2 of 3 rounds of data collection (p < 0.5)

1.2 Effect of Breastfeeding on Respiratory Infection Morbidity (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Kumar et al., 1981	India Urban/rural	Prospective	5–12 mo	BF BF and bottle	7.6 16.0	Episodes/100 child-mo of observations No effects detected in urban cohort or among rural infants < 4 mo
Fergusson et al., 1978	New Zealand Urban	Prospective	< 4 mo	EBF FF	Not signif	No association was found after controlling for confounding variables
Cunningham, 1977	United States Rural	Retrospective	< 12 mo	EBF Bottle-fed	0.5 1	Episodes of respiratory infections/1,000 weeks of observation
			< 12 mo	BF Bottle-fed	1.1 5.6	

1.3 Effect of Breastfeeding on Otitis Media and Ear Infection

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Daly et al., 1999	United States Rural	Prospective cohort (community-based)	0–59 mo	EBF ≥ 3 mo Yes No	 0.8 1	Relative risk for otitis media No significant differences found between infants EBF for at least 3 months or for greater than 6 months and infants who were not EBF.
				EBF = 6 mo Yes No	 0.7 1	
Duffy et al., 1997	United States Suburban	Prospective cohort	< 3 mo	EBF Mixed feeding FF	1 Not reported 1.22	Overall relative risk of first episode of acute otitis media and otitis media with effusion during the first 12 months of life
			3–6 mo	EBF Mixed feeding FF	1 1.28 1.59	
			> 6 mo	EBF Mixed feeding FF	1 1.30 1.70	
Dewey et al., 1995	United States Urban	Prospective	< 12 mo > 12 mo	BF FF	0.45 0.53	Adjusted episodes/100 days at risk
				BF FF	Not signif	

1.3 Effect of Breastfeeding on Otitis Media and Ear Infection (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size			Comment
Aniansson et al., 1994	Sweden Urban	Prospective	< 12 mo	EBF PBF weaned	1–3 1% 5%* 6%	4–7 4% 7% 14%*	8–12 0% 9% 20%*	Percent of children with acute otitis media by age group (in months) *significantly different (p < 0.05) in comparison with EBF
Duncan et al., 1993	United States Urban	Retrospective review of medical records	< 12 mo	FF & BF<4mo suppl <4 mo suppl 4–6 mo suppl 6 mo	ROM 1 0.73 0.54 0.39	AOM 1 0.85 0.72 0.61		Adjusted odds ratio for recurrent otitis media (ROM) and acute otitis media (AOM)

1.4 Effect of Breastfeeding on Other Aspects of Infant Health

Author & Year	Country & Setting	Design & Outcome	Age Group	BF Practices	Effect Size				Comment
Bertini et al., 2001	Italy Urban	Prospective Jaundice	72 hrs after birth	EBF Mixed feeding FF	2.7 5.9 13.1				Percent of infants with total serum bilirubin (TSB) > 12.9 mg/dL Mixed feeding value not statistically different from EBF
Oddy et al., 1999	Australia	Prospective Asthma and atopy	< 6 yrs	EBF ≥ 4 mo EBF < 4 mo	As 1 1.25	Wh 1 1.41	SP 1 1.30		Adjusted odds ratio for asthma (As), wheezing ≥ 3 times since age 1 year (Wh), and positive skin prick test (SP) by age of introduction of other milks
Raisler et al., 1999	United States Nationwide	Retrospective Illness	< 6 mo	EBF BF > FF BF = FF BF < FF Non-BF	D 0.54 0.83 NS NS 1	C/W 0.83 0.81 0.68 NS 1	V 0.71 NS NS NS 1	TI 0.78 NS NS NS 1	Adjusted odds ratio for diarrhea (D), cough/ wheeze (C/W), vomiting (V) and total illness (TI) NS = not signif

1.4 Effect of Breastfeeding on Other Aspects of Infant Health (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size					Comment
Wilson, et al., 1998	United Kingdom Urban (Scotland)	Follow-up Respiratory illness, growth, body compo-sition and blood pressure	6–9 yrs	EBF ≤ 15 wk Solid feeding before 15 wks	RI 17% 32%	WZ 10% 21%	BF 17% 19%			Estimated probabilities of ever having respiratory illness (RI), wheeze (WZ), and percent body fat (PBF) presented Children who were EBF had higher systolic blood pressure; diastolic blood pressure was not influenced.
Wright et al., 1998	United States (Navajo community)	Prospective Childhood illness	< 12 mo	EBF FF	OM 0.70 1	GE 0.52 1	BL 0.39 1	NP 0.77 1	FV 0.65 1	Relative risk of otitis media (OM), gastroenteritis (GE), bronchiolitis (BL), nasopharyngitis (NP) and fever > 100.4°F (FV)
Chandra RK., 1997	Canada (Newfoundland)	Prospective Atopy	< 5 yrs	EBF ≥ 4 mo FF whey FF soy FF cow's milk	0.422 0.322 0.759 1					Odds ratio of cumulative incidence of allergic disease in high-risk infants by feeding mode
Wang & Wu, 1996	China	Prospective Childhood illness	< 12 mo	EBF ≥ 4 mo BF ≥ 4 mo	2.58 ± 1.38 3.10 ± 1.65					Mean ± standard deviation of cumulative incidence of infection ($p < 0.05$)
Brown et al., 1989	Peru Urban	Prospective Skin infections	< 6 mo	EBF BF & liquids BF & milk BF & solids	1 3.8 1.9 2.8					Relative risk of skin infections
			6-11 mo	BF FF	1 5.7					

2.1 Effect of Breastfeeding on Infant Diarrheal Mortality

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Arifeen et al., 2001	Bangladesh Urban (slums)	Prospective	<12 mo	EBF Predominant PBF + FF	1 Not signif 3.94	Adjusted hazard ratio BF practices measured <4 m
Betran et al., 2001	Latin America and the Caribbean Urban/rural	Ecological	< 3 mo	EBF PBF FF	1 4.1 15.1	Relative risk of death from diarrheal disease
			4–11 mo	PBF FF	1 2.2	
WHO collaborators, 2000	Brazil, Pakistan, Philippines	Meta analysis	0–5 mo	BF FF	1 6.1	Adjusted odds ratio
			6–12 mo	BF FF	1 1.9	
Yoon et al., 1996	Philippines Urban	Prospective	< 5 mo	BF FF	1 9.7	Adjusted rate ratio No associations were found for children 6-11 mo or 12-23 mo
Victora et al., 1992	Brazil Urban	Case-control	< 12 mo	EBF Any BF FF	1 3.7 9.6	Age-adjusted relative risk
Sachdev et al., 1991	India Urban	Prospective Hospital-based	0–6 mo	Any BF FF	1 6.0	Adjusted odds ratio
			7–12 mo	Any BF FF	1 2.6	
			13–18 mo	Any BF FF	1 1.8	

2.1 Effect of Breastfeeding on Infant Diarrheal Mortality (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Victoria et al., 1989	Brazil Urban	Case-control	< 2 mo	EBF FF	1 23.3	Adjusted odds ratio
			< 12 mo	EBF Any BF FF	1 4.2 14.2	
Feachem & Koblinsky, 1984	14 developed and developing countries Various settings	Review	< 6 mo	EBF vs. FF EBF vs. PBF PBF vs. FF	25 8.6 3.5	Relative risk of diarrhea mortality
Robinson M, 1951	England Urban/rural	Review	1–7 mo	BF BF + formula FF	0 2.0 7.0	Diarrhea deaths per 1000 infants Statistical significance not tested

2.2 Effect of Breastfeeding on Infant Respiratory Infection Mortality

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Arifeen et al., 2001	Bangldesh Urban (slums)	Prospective	<12 mo	EBF Predominant PBF & FF	1 Not signif 2.40	Adjusted hazard ratio BF practices measured < 4 mo
Betran et al., 2001	Latin America and the Caribbean Urban/rural	Ecological	< 3 mo	EBF PBF FF	1 2.9 4.0	Relative risk of death from acute respiratory infections
			4 – 11 mo	PBF FF	1.0 2.1	
WHO collaborators, 2000	Brazil, Pakistan, Philippines	Meta-analysis	0 – 5 mo	Any BF FF	1 2.4	Adjusted odds ratio
			6–12 mo	Any BF FF	1 2.5	

2.2 Effect of Breastfeeding on Infant Respiratory Infection Mortality (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size		Comment
Yoon etal., 1996	Philippines Urban	Prospective	< 24 mo	Any BF vs. FF	Not signif		No associations were found for children 0-5, 6–11, or 12–23 mo.
Victora et al., 1989	Brazil Urban	Case-control	< 12 mo	EBF PBF FF	1 Not signif 3.59		Odds ratio of mortality from respiratory infections
Robinson M, 1951	England Urban and rural	Review	1–7 mo		RI	OM	Deaths due to respiratory infection (RI) and otitis media (OM) per 1,000 infants Statistical significance not tested
				BF	8.2	0.0	
				BF + formula	15.9	2.0	
				FF	31.6	8.1	

2.3 Effect of Breastfeeding on All-cause Infant Mortality

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Arifeen et al., 2001	Bangladesh Urban (slums)	Prospective	< 12 mo	EBF Predominant PBF + FF	1 Not Signif 2.23	Adjusted hazard ratio BF practices measured <4 m
Manda, 1999	Malawi Nationwide	Retrospective	0 – 11 mo	BF Weaned	1 10.12	Adjusted relative risk of mortality
			12 – 59 mo	BF Weaned	1 not signif	
Terra de Souza et al., 1999	Brazil Urban and rural	Ecological	< 12 mo	EBF ≥ 4 mo	5.9	Percentage reduction in infant mortality for every 10% increase in rate of EBF (≥ 4 mo)
Augustine & Bhatia, 1994	India Hospital-based	Retrospective	< 7 days	EBF PBF FF Not yet fed	29% 43% 43% 64%	Mortality rate
Mølbak et al., 1994	Guinea-Bissau Urban	Prospective	12–25 mo	BF Weaned	1 3.5	Relative risk of mortality

2.3 Effect of Breastfeeding on All-cause Infant Mortality (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size			Comment
Shahidullah, 1994	Bangladesh	Prospective	< 5 y	EBF BF + suppl	1 2.1			Adjusted relative risk of mortality
Srivastava et al., 1994	India Urban	Prospective Hospital-based	< 6 mo	BF FF	E 7.8 9.37	L 2.14 3.12	P 15.5 23.0	Mortality rates (%) during the early neonatal (E), late neonatal (L) and post neonatal to 6 mo (P) periods by feeding mode in infants with birth weight > 2.5 kg No tests of statistical significance
Singh & Srivastava, 1992	India Urban and rural	Cross-sectional	Neonatal (NN) Postnatal (PN)	Colostrum No colostrum	Urban NN PN 0 1.7 4.3 5.3	Rural NN PN 2.2 3.7 5.7 4.3		Percent infant deaths *Only results for high urban and medium rural socioeconomic levels are shown here.
Awathi et al., 1991	India Urban	Prospective	1–6 mo	Premature BF FF	>2.5kg 0.47 1.1	<2.5kg 6.94 1.96		Percent dying by birth weight and feeding mode
				Postnatal BF FF		<2.5kg 2.7 3.7		
Briend & Bari, 1989	Bangladesh Rural	Prospective	12–17 mo	Any BF FF	1 6.1			Unadjusted relative risk of death Risk for the 30- to 36-mo period were not signif
			18–23 mo	Any BF FF	1 4.5			
			24–29 mo	Any BF FF	1 3.7			
Molteno & Kibel, 1989	South Africa Urban	Case-control	< 12 mo	BF vs. FF	Deaths: 66.7 Controls: 92.8			Breastfeeding rates among infants who died (cases) and lived (controls). Odds ratio not calculated
Retherford et al., 1989	Nepal Urban/rural	Cross-sectional	< 18 mo	Any BF FF	0.19 1			Adjusted relative risks
			18–60 mo	Any BF FF	0.45 1			
Habicht et al., 1988	Malaysia Urban and rural	Retrospective	< 12 mo	Bf FF	NTW 1 5.20	T 1 2.67	T&W 1 2.51	Adjusted relative risk of all cause mortality according to living conditions: neither toilet nor water (NTW), toilet only (T), both toilet and water in the home (T&W)

2.3 Effect of Breastfeeding on All-cause Infant Mortality (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Habicht et al., 1986	Malaysia Urban/rural	Retrospective	8-28 days	Full BF	68.6	Adjusted reduction in deaths per 1,000 infants per added mo of breastfeeding
			29 days - 6 mo	Full BF PBF	24.9 11.2	
			7-12 mo	Full BF PBF	3.4 1.7	
Butz et al., 1984	Malaysia Urban and rural	Retrospective	< 12 mo	EBF>1 wk vs. PBF EBF>4 wk vs. FF EBF=6 mo vs. FF	16 25 20	Reduction in deaths per 1,000 in days 8 – 28, months 2 – 6 and months 7- 12, respectively
Plank & Milanesi, 1973	Chile Rural	Cross-sectional	1—12 mo	EBF Any BF Bottle	29.2 56.0 60.5	Unadjusted mortality rate/1,000 living at beginning of interval
			3—12 mo	EBF Any BF Bottle	13.8 37.5 38.7	
			6—12 mo	EBF Any BF Bottle	10.0 14.0 19.9	

3 Effect of Breastfeeding on Intellectual and Motor Development

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size		Comment
Mortensen et al., 2002	Denmark	Prospective	18–34 yrs	Duration (mo): 1 2-3 4-6 7-9 >9	WAIS 99.4 101.7 102.3 106.4 104.0	BPP 38.0 39.2 39.9 40.1 40.1	Adjusted test scores for the Wechsler Adult Intelligence Scale (WAIS), and the Børge Priens Prøve (BPP)
Dewey et al., 2001	Honduras	Prospective/ observational	0–4 mo	EBF to 6 mo SF at 4 mo	Crwl 6.3 m 7.3 m	Wlk 60% 41%	Mean age (mo) for ability to crawl and percent infants walking by 12 mo according to BF pattern: EBF for 6 mo or EBF for 4 mo + solid foods (SF) from 4–6 mo
Horwood et al. 2001	New Zealand Nationwide	Prospective	7-8 yrs	FF BF < 4 mo BF 4-7 mo BF > 8 mo	VIQ 96.1 98.1 100.1 102.1	PIQ 99.6 100.8 102.1 103.3	Adjusted verbal (VIQ) and performance (PIQ) intelligence quotient scores by BF duration among surviving very low birthweight children Only VIQ differences are statistically significant ($p<0.05$)
Anderson et al., 1999	Multicountry Urban/rural	Meta-analysis	6–23 mo	BF vs FF	3.11		Weighted mean difference in cognitive developmental score between breastfed and formula-fed children by age at measurement
			2–5 yrs	BF vs FF	2.53		
			6–9 yrs	BF vs FF	3.01		
			10–15 yrs	BF vs FF	3.19		
Horwood & Fergusson, 1998	New Zealand Urban	Longitudinal	8–18 yrs	FF BF < 4 mo BF 4-7 mo BF > 8 mo	IQ 98.7 99.7 100.6 101.5	RC 98.9 99.8 100.7 101.6	Adjusted scores of mean cognitive ability, WISC-R total IQ, at 8 years of age by BF practice (IQ) and mean standardized achievement test scores for reading comprehension (RC) at 10 years of age
Wang & Wu, 1996	China	Prospective	< 1 yr	EBF $\geq$4 mo Non-EBF $\geq$ 4 mo	47.37 30.68		% of infants passing all Gross Motor items in the Denver Developmental Screening Test ($p < 0.05$)
Florey et al., 1995	Scotland Urban (Dundee)	Prospective/ Retrospective	< 18 mo	BF FF	110.2 102.5		Mental development scores assessed with Bayleys Indices; mean difference = 7.7 points
Greene et al., 1995	England (South Tees)	Retrospective	11-16 yrs	BF$\leq$ 12 wk vs BF > 12 wk	V-IQ 6.0	R-IQ 5.4	Adjusted point advantage in verbal (V) and reasoning (R) IQ- ($p<0.01$)
Lucas et al., 1994	England Neonatal clinics	Prospective	< 18 mo	BF vs FF	8.8		Increased points scored by BF infants on the Bayley index of psychomotor development

3 Effect of Breastfeeding on Intellectual and Motor Development (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Pollock, 1994	England Nationwide	Prospective/ Retrospective	5 yrs	EBF vs FF	1.5	Adjusted odds ratio for English picture vocabulary scores above the mean
			10 yrs	EBF vs FF	1.64 1.49 1.55 1.64	Adjusted OR for total British Ability Scales (BAS) above the mean Adjusted OR for picture leanguage test above mean Adjusted OR for word definition (BAS) above mean Adjusted OR for similarities (BAS) above mean
Rogan & Gladen, 1993	Untied States North Carolina	Prospective	2 yrs	BF long vs. short	6.7	Adjusted difference in Bayley Mental Score
			5 yr	BF long vs. short	3.9	Adjusted difference in McCarthy Quantitative score
				BF long vs. FF	3.5 4.8 0.24	Adjusted difference in McCarthy Quantitative score Adjusted difference in McCarthy Memory score Adjusted difference in English report card grade
Lucas et al., 1992	England Neonatal clinics	Prospective	< 8 yrs	BM FM	Verb: 102, 92 Perf: 103, 93 IQ: 103, 93	Unadjusted verbal, performance and overall IQ scores in preterm infants receiving breastmilk (BM) or formula milk (FM). IQ advantage after adjustments continued to be significant (7.5 points, p < 0.001).
Morrow-Tlucak et al., 1988	United States Inner city	Prospective	< 2 yrs	BF > 4 mo vs BF < 4 mo	2.5	Increased Bayley Mental Developmental Index scores
Taylor & Wadsworth, 1984	United Kingdom	Prospective/ Retrospective	5 yrs	NBF BF < 1 mo BF 1-2 mo BF > 3 mo	*PVT*: -0.05, -0.05, 0.08, 0.12 *CD*: 4.62, 4.76, 4.93, 4.95 RCB: 0.01, 0.04, 0.03, -0.03	Adjusted English Picture Vocabulary Test (PVT), Copying Design (CD), and Rutter Child Behavior (RCB) scores by BF duration. PVT and CD trends are statistically significant (p<0.001), non-linear RBC trend is also significant (p<0.05)
Fergusson et al., 1982	New Zealand Dunedin	Prospective	3 yrs	BF>4 mo FF	I: 101.4, 99.0 C: 100.9, 98.2 E: 100.6, 98.8 A:	Adjusted mean intelligence (I), comprehension (C), expression (E), and articulation (A) scores- All differences shown are statistically significant.
			5 yrs	BF>4 mo FF	I: 100.9, 98.5 C: 100.7, 98.8 E: 100.2, 98.7 A: 100.6, 99.7	
			7 yrs	BF>4 mo FF	I: 101.1, 98.8 C: 100.1, 98.8 E: 100.1, 99.7 A: 101.0, 99.1	

3 Effect of Breastfeeding on Intellectual and Motor Development (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size			Comment
Rodgers, 1978	England Nationwide	Prospective	8 yrs	EBF vs FF	PI 1.76	WR Not signif		Difference in scores on different tests between breastfed and bottle-fed group, uncorrected for background factors Picture intelligence (PI) and Word Reading (WR) scores at 8 yrs, non-verbal ability (NV), mathematics (Math), and sentence completion (SC) scores at 15 years of age.
			15 yrs	EBF vs FF	NV 1.76	Math 1.55	SC 1.73	

4.1 Effect of Breastfeeding on Obesity

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Gillman et al., 2001	United States Nationwide	Cohort	9–14 yrs	Mostly BF for first 6 mo Only formula for first 6 mo	0.78 1	Adjusted odds ratio for risk of being overweight as an adolescent, according to feeding pattern of first 6 mo of life
				BF ≥ 7 mo BF < 3 mo	0.80 1	Adjusted odds ratio for risk of being overweight as an adolescent, according to BF duration
Hediger et al., 2001	United States Nationwide	Cross-sectional (NHANES III)	3–5 yrs	Ever BF Never BF	0.63 1	Adjusted odds ratio of being "at risk" (85th-94th percentile) of overweight according to feeding pattern. Odds ratio of being overweight (95th percentile) was not statistically significant.
von Kries et al., 1999	Germany Rural	Cross-sectional	5–6 yrs	Ever BF Never BF	0.75 1	Adjusted odds ratio of risk of being obese, according to BF duration
				EBF ≤ 2 mo EBF 3–5 mo BF 6–12 mo BF > 12 mo	0.90* 0.65 0.57 0.28*	*CIs include 1 (not statistically significant)

4.2 Effect of Breastfeeding on Risk of Diabetes

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Jones et al., 1998	United Kingdom Urban	Case-control	< 20 yrs	Ever BF Never BF	1 1.33	Relative risk
Pettitt et al., 1997	United StatesR	Longitudinal	10-40 yrs	EBF PBF FF	0.64 0.41 1	Odds ratio of noninsulin-dependent diabetes before age 40 years by feeding mode during first 2 months
Norris and Scott, 1996	Multicountry Europe & United States	Meta-analysis	Lifetime	Ever BF Never BF	1 1.13	Odds ratio for risk of IDDM associated with ever being breastfed or never being breastfed.
				BF 3 mo BF < 3 mo	1 1.23	Odds ratio for risk of IDDM for being breastfed for less than 3 months
Samuelsson et al., 1993	Sweden	Case-control	< 15 yrs	EBF PBF	Not signif	Slight association with shorter duration of breastfeeding and risk of developing diabetes

4.3 Effect of Breastfeeding on Later Risk of Cancer

Author & Year	Outcome	Country	Design	BF Practices	Effect Size		Comment
Shu et al., 1999	Childhood acute leukemia	Multicountry	Case-control	BF > 6 mo 1–6 mo any BF FF	0.70 not signif 0.79 1		Odds ratio for childhood acute leukemia
Titus-Ernstoff et al., 1998	Breast cancer	United States	Case-control	Any BF FF	Not signif		Examined both pre- and post-menopausal breast cancer but pre-menopausal women not well represented in sample
Potischman et al., 1995	Premenopausal breast cancer	United States	Case-control	Any BF FF	0.76 1		Adjusted odds ratio. Not statistically significant (95% CI: 0.54–1.08)
Fruedenheim et al., 1994	Breast cancer	United States	Case-control	Any BF FF	0.74 1		Odds ratio for pre- and post-menopausal breast cancer combined. Similar odds ratios were observed for each type separately (pre-: 0.76; post-: 0.73) but these were not statistically significant
Davis et al., 1988	Childhood cancer	United States	Case-control	BF > 6 mo BF 6 mo FF	All 1 1.89 1.75	L 1 8.19 5.62	Odds ratios for all cancers (All) and lymphoma (L) from 1.5 to 15 years of age

4.4 Effect of Breastfeeding on Development of Other Chronic Diseases

Author & Year	Country & Setting	Design	Outcome	BF Practices	Effect Size	Comment
Singhal et al., 2001	United Kingdom	Cohort	Blood pressure at 13–16 yrs	Banked breastmilk Preterm formula Term formula	81.9 86.1 85.5	All study children were born preterm. Mean arterial blood pressure (mm Hg) at 13–16 yrs, according to feeding pattern
Ravelli et al., 2000	Netherlands Urban	Cohort	Adult outcomes: glucose tolerance, lipid profile, blood pressure, and obesity	EBF Bottle	Glu: 5.69 5.87 Ins: 46.4 52.7 L:H: 2.86 3.14	Adjusted geometric means of glucose tolerance (Glu), insulin (Ins), LDL:HDL ratio (L:H) No differences on blood pressure or anthropometry were found between infants who were EBF and those who were bottlefed.
Saarinen & Kajosarri, 1995	Finland	Prospective	Atopic disease	BF ≥ 6 mo BF 1–6 mo BF < 1 or FF	42% 36% 65%	Prevalence
Wingard et al., 1994	United States	Prospective (population-based)	Adult longevity	BF 12–36 mo BF 6–11 mo BF 1–5 mo FF		No associations found
Koletzko et al., 1991	Canada	Case-control	Ulcerative colitis	EBF PBF		No associations found
Koletzko et al., 1989	Canada	Case-control	Crohn's disease in childhood	EBF PBF	1 3	Odds ratio

5.1 Effect of Breastfeeding on Maternal Risk of Breast Cancer[1]

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Tryggvadottir et al., 2001	Iceland	Case-control	<40 yrs 40-55 yrs > 55 yrs 25-90 yrs	Ever vs Never BF	0.09 0.51* 0.32 0.33	Adjusted odds ratio (relative to never breastfed) * not signif (CI includes 1)
Gao et al., 2000	China Urban	Case-control	25–64 yrs	BF ≥ 24 mo Ever BF Never BF	0.6 0.9 1	Adjusted odds ratio for breast cancer
Zheng et al., 2000	China (less industrialized community)	Case-control	20–80 yrs	BF 1–36 mo BF 37–72 mo BF 73–108 mo BF ≥ 109 mo FF	1.00 1.01* 0.47 0.24 0.84*	Adjusted odds ratio for risk of breast cancer by duration of lactation * not signif (CI includes 1)
Furberg et al., 1999	United States	Case-control	20–74 yrs	Ever vs Never BF	0.7	Adjusted odds ratio for breast cancer
Marcus et al., 1999	United States North Carolina	Case-control	20–74 yrs	BF ≥ 1 yr Ever BF Never BF	0.1 0.2 1	Adjusted odds ratio for breast cancer for women who breastfed before 20 yrs of age
Newcomb et al., 1999	United States Multicenter	Case-control	50–79 yrs	BF ≥ 24 mo Ever BF Never BF	0.73 0.87 1	Adjusted relative risk of breast cancer
Romieu et al., 1996	Mexico Urban	Case-control	Lifetime duration	Ever BF BF > 60 mo BF 37–60 mo BF 25–36 mo BF 13–24 mo BF 4–12 mo BF 1–3 mo Never BF	0.54 0.23 0.27 0.60 0.47 0.59 0.48 1	Adjusted odds ratio presented BF associated with risk of breast cancer for both pre- and postmenopausal women Most of protective effect was associated with the first live birth

[1] All effects are significant unless otherwise noted.

5.1 Effect of Breastfeeding on Maternal Risk of Breast Cancer (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Brinton et al., 1995	United States	Case-control	Lifetime duration	BF > 72 wk BF > 2 wk FF	0.67 (0.4–1.1) 0.87 (0.7–1.0) 1	Adjusted relative risks and CIs. Although CIs include 1, the trend to greater protection with increasing duration was significant (p=0.04). Women who first BF < 22 y had the greatest reduction in risk.
Mayberry, 1994	United States	Case-control	< 40 yrs 40–54 yrs	BF > 8 mo BF 4–7 mo BF < 4 mo	No association	Adjusted odds ratio Small sample size
Newcomb et al., 1994	United States	Case-control	Lifetime duration	FF BF BF > 24 mo BF 13–24 mo BF 4–12 mo BF < 3 mo < 20 y at first lactation and BF > 6 mo	1 0.78 0.72 0.66 0.78 0.85 0.54	Adjusted relative risk presented for premenopausal women only Associations not significant for postmenopausal women Younger age at first lactation was associated with reduced risk
Kelsey et al., 1993	Multicountry	Review (case-control and cohort studies)	Pre- and postmeno-pausal	BF	0.21–0.77	Odds ratios for the protective effect of BF on late breast cancer development in case-control but not in cohort studies
Thomas et al., 1993	Multinational	Case-control	Pre-and postmeno-pausal	BF < 3 mo vs 3 mo	No effect	Women who breastfed < 3 mo were used as reference, possibly minimizing ability to find effect
Yoo et al., 1992	Japan	Case-control	Lifetime duration	FF Any BF BF > 13 mo BF 10–12 mo BF 7–9 mo BF 4–6 mo BF 1–3 mo	1 0.62 0.53 0.59 0.47 0.75 0.71	Adjusted odds ratios Most odds ratios have confidence intervals that include 1; however, trends are significant. Similar associations found for both pre- and postmenopausal women
London et al., 1990	United States	Prospective (cancer incidence)/ Retrospective (BF history)	Associations are examined by BF duration stratified by both age and parity		No effect	No independent association between lactation and risk of breast cancer. Associations did not differ by age or menopausal status.

5.1 Effect of Breastfeeding on Maternal Risk of Breast Cancer (continued)

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size		Comment
Layde et al., 1989	United States	Case-control	Not reported	BF > 24 mo FF	0.67 1		Odds ratio for breast cancer
Siskind et al., 1989	Australia	Case-control	Not reported	Any BF FF	No effect		No effect for either pre- or postmenopausal women
Rosero-Bixby et al., 1987	Costa Rica	Case-control	Not reported	Lifetime duration of BF	No effect		Adjusted relative risk
Byers et al., 1985	United States Urban	Case-control	Lifetime duration	BF > 12 mo BF 7–11 mo BF 1–6 mo BF < 1 mo FF	0.21 0.63 0.57 0.98 1		Adjusted relative risk presented for premenopausal women only Associations not significant for postmenopausal women Cases more likely than controls to report lactation failure due to insufficient milk
Raksasook, 1985	Thailand	Case-control	Not reported	% BF BF duration (mean)	NBD 86.2 9.33	CA 90.1 15.3	Percent ever breastfed and mean BF duration for women with no breast disease (NBD) or with breast cancer (CA). Association not tested for significance. Includes many non-parous women.
Brinton et al., 1983	United States Urban	Case-control	Not reported	Ever BF Never BF	0.94 (0.8–1.1) 1		Adjusted relative risks (and CI)
MacMahon et al., 1982	Estonian Republic Urban	Case-control	Lifetime duration	Not reported	No effect		Adjusted odds ratio
Kalache et al., 1980	England	Case-control	16–50 yrs	Ever BF BF > 16 wk	No effect		Analyses adjusted only for parity
Ing et al., 1977	Hong Kong	Retrospective	> 55 yrs postmeno-pausal	BF duration	No effect		No test of significance provided. Only chose women who breastfed from 1 side.
MacMahon et al., 1970	Multicountry	Case-control	Not reported	BF duration	No effect		Hospital-based controls
Valaoras et al., 1969	Greece Urban	Case-control	Lifetime duration	BF > 24 mo	No effect		Relative risk adjusted for age and parity
MacMahon & Feinleib, 1960	United States	Case-control	Not reported	BF duration	No effect		Hospital-based controls

5.2 Effect of Breastfeeding on Maternal Risk of Ovarian Cancer

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size	Comment
Ness et al., 2000.	United States	Case-control	20–69 yrs	BF ≥ 24 mo FF	0.6 1	Adjusted odds ratio for ovarian cancer (CI includes 1)
Siskind et al., 1997	Australia	Case-control	Pre- and postmenopause	Total duration of unsuppl. BF	0.98	Adjusted odds ratio per month of total unsupplemented BF among premenopausal women only
Rosenblatt et al., 1993	Multicountry	Case-control	Duration of BF/ pregnancy	BF > 13 mo BF 8–12 mo BF 3–7 mo BF < 3 mo	0.68 0.80 0.75 1	Adjusted odds ratios Most of the reduction in risk occurred with short-term lactation, with no further reduction with long-term lactation.
Whittemore et al., 1992	United States	Case-control	Not reported	Ever BF Never BF	0.73 hospital 0.81 comm.	Adjusted odds ratio for hospital and community-based studies Trend to decreasing risk with increasing duration of breastfeeding
Gwinn et al., 1990	United States	Case-control	Lifetime duration	Never BF Ever BF BF > 24 mo BF 12–23 mo BF 6–11 mo BF 3–5 mo BF 1–2 mo	1 0.6 0.3 0.7 0.8 0.8 0.6	Adjusted relative risk Most protection occurred with first lactation
Booth et al., 1989	England	Case-control	Not reported	BF> 2 yr Ever BF	3 1	Risk of ovarian cancer ($p < 0.05$), but no overall significant trend for longer duration of breastfeeding
Risch et al., 1983	United States	Case-control	Lifetime duration	BF > 3 mo BF < 2 mo	0.69 1	Adjusted relative risk

5.3 Effect of Breastfeeding on Other Maternal Outcomes

Author & Year	Country & Setting	Design	Age Group	BF Practices	Effect Size			Outcome & Comment
Dewey et al., 2001	Honduras	Randomized Controlled Trial	0–4 mo		Kg	BMI		Statistically significant reduced body weight (Kg) and body mass index (BMI) after 2 months of intervention among mothers randomized to EBF for 6 months, compared with those who gave solid foods with or without breastmilk from 4 months
				EBF to 6 mo	52.7	22.0		
				EBF to 4 mo	53.2	22.6		
Gigante et al., 2001	Brazil Urban	Longitudinal	20–40 + yrs		BMI	WH	FM	Crude mean values according to breastfeeding duration for body mass index (BMI), waist:hip ratio (WH) and percent fat mass (FM) Mean values were higher for women who BF <1 mo and tended to decrease with increased BF duration, but increased again in women who BF for > 12 mo BMI and % FM tended to be lower for mothers who BF for 6–11.9 mo
				EBF	24.4	0.80	34.4	
				PBF	26.4	0.82	40.1	
				Weaned	26.2	0.81	39.8	
Michaëlsson et al., 2001	Sweden Nationwide	Case-control	50–81 yrs					Adjusted odds ratio for hip fracture, according to breastfeeding duration in postmenopausal women All CIs included 1 No association found for duration of BF with hip fracture risk
				Never BF	1			
				BF 1–5 mo	0.86			
				BF 6–10 mo	0.94			
				BF 11–6 mo	0.92			
				BF > 16 mo	0.98			
Motil et al., 1998	United States	Longitudinal	2-38 yrs					Lean body mass percentage; no significant difference observed at end of study period; however, body fat % decreased throughout the study period in lactating women (35% at first visit and 32% at fifth visit)
				Lactating	68			
				Nonlactating	72			
				Nulliparous	76			