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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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.

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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

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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.

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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.

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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.

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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).

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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.

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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.

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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.

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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.

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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.

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Duncan B, Ey J, Holberg CJ, Wright AL, Martinez F, Taussig LM. Exclusive breast-feeding 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 breast-feeding 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.

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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.

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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.

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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.

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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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