

Effect of early infant feeding practices on infection-specific neonatal mortality: an investigation of the causal links with observational data from rural Ghana^{1–3}

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ABSTRACT

Background: Strong associations between delayed initiation of breastfeeding and increased neonatal mortality (2–28 d) were recently reported in rural Ghana. Investigation into the biological plausibility of this relation and potential causal pathways is needed.

Objective: The objective was to assess the effect of early infant feeding practices (delayed initiation, prelacteal feeding, established neonatal breastfeeding) on infection-specific neonatal mortality in breastfed neonates aged 2–28 d.

Design: This prospective observational cohort study was based on 10 942 breastfed singleton neonates born between 1 July 2003 and 30 June 2004, who survived to day 2, and whose mothers were visited in the neonatal period. Verbal autopsies were used to ascertain the cause of death.

Results: One hundred forty neonates died from day 2 to day 28; 93 died of infection and 47 of noninfectious causes. The risk of death as a result of infection increased with increasing delay in initiation of breastfeeding from 1 h to day 7; overall late initiation (after day 1) was associated with a 2.6-fold risk [adjusted odds ratio (adj OR): 2.61; 95% CI: 1.68, 4.04]. Partial breastfeeding was associated with a 5.7-fold adjusted risk of death as a result of infectious disease (adj OR: 5.73; 95% CI: 2.75, 11.91). No obvious associations were observed between these feeding practices and noninfection-specific mortality. Prelacteal feeding was not associated with infection (adj OR: 1.11; 95% CI: 0.66, 1.86) or noninfection-specific (adj OR: 1.33; 95% CI: 0.55, 3.22) mortality.

Conclusions: This study provides the first epidemiologic evidence of a causal association between early breastfeeding and reduced infection-specific neonatal mortality in young human infants. *Am J Clin Nutr* 2007;86:1126–31.

KEY WORDS Breastfeeding, infectious disease, neonatal mortality

INTRODUCTION

Neonatal mortality remains unacceptably high in developing countries despite significant reductions in postneonatal mortality (1, 2). Most neonatal deaths occur at home in these countries, and effective community level interventions are urgently needed (3).

We recently reported a strong association between delayed initiation of breastfeeding and increased neonatal mortality in a large observational study in rural Ghana (4). Other studies have

also suggested that breast milk may have its greatest effects in the neonatal period (5–7). However, there is little evidence from randomized controlled trials, and inferring causation from observational studies is fraught with difficulties. We reported a marked dose-response relation in our previous analysis; with neonatal mortality increasing significantly as delay in initiation of breastfeeding increased (4). However, evidence about biological plausibility and effect on cause-specific mortality in neonates is sparse.

Early initiation of breastfeeding may reduce neonatal mortality by decreasing the ingestion of infectious pathogens (8). Early breast milk also provides many immunocompetent factors, including immunoglobulins and lymphocytes that may stimulate humoral or cell-mediated immune systems (9–11), and it may also prime the gastrointestinal tract (GIT) and decrease intestinal permeability and translocation of infectious pathogens, including HIV (12, 13). Close skin-to-skin contact between the maternal-infant dyad may also stimulate the mucosa-associated lymphoid tissue system (14, 15). In contrast, prelacteal feeding and predominant and partial breastfeeding may result in the ingestion of infectious pathogens and may also act on the early GIT to increase permeability (12, 16). Metabolic pathways (especially glucose or sodium homeostasis) may also be significantly disrupted (17–19).

This study was thus designed to evaluate the associations between 1) timing of initiation of breastfeeding, 2) prelacteal and nonprelacteal feeding, and 3) established neonatal breastfeeding (exclusive, predominant, and partial) and infection-specific neonatal mortality in breastfed neonates aged 2–28 d. A secondary objective was to explore the effect of these practices separately on noninfection-related deaths.

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TABLE 1
Classification system for neonatal deaths in the study population¹

Cause	Definition
Congenital abnormality	Neonatal death as a result of ≥ 1 of the following: major or lethal congenital abnormalities unspecified; specific abnormality, eg, neural tube defect, hydrocephalus
Prematurity	Neonatal death as a result of ≥ 1 of the following: severe immaturity (< 33 wk), birth weight < 1.8 kg when gestation is unknown; specific severe complications of prematurity such as surfactant deficiency and necrotizing enterocolitis
Birth asphyxia	Neonatal death in an infant ≥ 33 wk gestation as a result of ≥ 1 of the following: obstetric complications, maternal hemorrhage, neonatal encephalopathy, clinical diagnosis of birth asphyxia
Infection	Neonatal death in an infant ≥ 33 wk gestation as a result of ≥ 1 of the following: tetanus, meningitis, pneumonia, diarrhea, septicemia, other infection
Other specific cause	Neonatal death in an infant ≥ 33 wk gestation as a result of a cause not included in the first 4 selected causes, including accident or injury, infant hemorrhage, respiratory distress syndrome
Unexplained	Neonatal death as a result of an unknown cause, including sudden infant death syndrome

¹ Adapted from the Child Health Epidemiology Reference Group Classification system (22), using a hierarchical classification approach with each of the conditions sought in the order listed.

SUBJECTS AND METHODS

Setting and participants

Data were collected as part of the ObaapaVitA trial, a large cluster randomized trial based in rural Ghana. The ObaapaVitA trial studied the effect of weekly vitamin A supplementation to women of childbearing age on maternal and infant mortality. The study setting was described in detail elsewhere (4).

Data collection and study definitions

Women were visited at 4-wk intervals by a network of trained village-based fieldworkers to distribute vitamin A capsules and to collect data on morbidity and mortality. When a birth was reported, the fieldworker administered a birth questionnaire that collected information on birth outcome, birth weight (if taken within 48 h of birth at a health facility), gestational age, details of the delivery, antenatal care, health of the mother, socioeconomic and environmental characteristics, and early breastfeeding practices. The mother was asked when she initiated breastfeeding and was prompted for the exact timing (within 1 h, after 1 h but the first day, day 2, day 3, days 4–7, or after day 7). She was then asked what she offered her newborn to eat or drink in the 24 h before the interview. After noting the unprompted response, the mother was asked whether she offered her own breast milk, breast milk from a wet nurse, animal milk, infant formula, milk-based fluids, water-based fluids, or solid foods. The mother was also asked about the newborn's health on the day of birth and in the previous 24 h. At the next 4-wk visit an infant questionnaire was administered to obtain further outcome data (infant morbidity and mortality) and information on infant feeding practices. Infants were followed up at subsequent 4-wk visits until they reached 12 mo of age.

A newborn was considered to be breastfed if breast milk constituted any portion of his or her diet. Newborns were classified according to the timing of breastfeeding initiation (first hour, after first hour but day 1, day 2, day 3, and after day 3). Early initiation of breastfeeding referred to breastfeeding that started on the first day of life. Late initiation indicated breastfeeding that began after the first day of life. Prolacteal feeding was any non-human milk food or fluids provided to the newborn before breastfeeding on the first day of life. Established breastfeeding referred to the reported breastfeeding pattern in the 24 h before the first interview, excluding the first day (median: 14 d postpartum;

interquartile range: 7–21 d). Exclusive breastfeeding was defined as feeding of only breast milk and nothing else, not even water, with the exception of vitamin supplements and prescribed medicines. Predominant breastfeeding was defined as feeding of breast milk along with other nonmilk fluids. Newborns who were offered breast milk and animal milk, infant formula, or solids were considered to be partially breastfed. These definitions were consistent with current definitions for breastfeeding patterns from the World Health Organization (WHO) (20).

Verbal autopsy and classification of cause of death

In the ObaapaVitA trial, all stillbirths and neonatal deaths were followed up within 6 mo by a trained fieldwork supervisor and cause of death was determined with the use of the standard WHO verbal autopsy (VA) questionnaire adapted for use in the study area (21). The classification system used for assigning the cause of the neonatal deaths is presented in **Table 1**. This was adapted from a system developed by the WHO Neonatal Child Health Epidemiology Reference Group in 2003 (22). In developing the classification system, the Child Health Epidemiology Reference Group neonatal group considered the following: the expected public health importance of the individual causes of death, differing implications for intervention, and the ability to distinguish between the individual causes in low-resource settings (22). The ObaapaVitA VA questionnaire was formally evaluated in 2004 (23); diagnostic accuracy was reported to be high for both infectious (sensitivity: 74%; specificity: 87%) and noninfectious causes (sensitivity: 87%; specificity: 74%) (23). In this analysis, an infection-related death was defined as a neonatal death as a result of ≥ 1 of the following: tetanus, meningitis, pneumonia, diarrhea, septicemia, or other neonatal infection. All other deaths (prematurity, birth asphyxia, other specific cause) were considered to be noninfection related, and deaths without a known cause were labeled as unexplained.

Statistical analysis

Primary comparisons were made between 1) early and late initiation of breastfeeding, 2) prolacteal and nonprolacteal feeding on day 1, and 3) the types of established neonatal breastfeeding pattern after day 1 (exclusive, predominant, or partial).

To reduce problems with reverse causality (ie, the possibility that the breastfeeding pattern was affected by serious illnesses that lead to death), only newborns who survived to day 2 and who

were successfully breastfed were included in the primary analyses. Multiple births, noninitiators, those interviewed outside the neonatal period, and deaths without a VA were also excluded.

Logistic regression was used to estimate crude and adjusted odds ratios for mortality associated with the breastfeeding exposure variables. Potential confounders (factors associated with both exposure and the outcome that are not on the causal pathway) relating to the mother (health, parity, age, educational level, cash income), household (water supply, place of defecation), health system utilization (number of antenatal visits, place of birth, birth attendant), and the newborn (sex, birth size, gestational age, presence of a congenital anomaly, health on the day of birth, health at the time of interview) were included a priori in the infection and noninfection-specific models. The ObaapaVitA Data Monitoring and Ethics Committee were contacted in October 2004, and they confirmed that maternal vitamin A supplementation was not associated with any early infant feeding practices. Receipt of vitamin A was therefore not considered to be a confounder and was not included in any logistic regression models.

Only 3264 newborns had their weight measured within 48 h of birth, but perceived birth size was available from all mothers. We reported previously that mother's perception of a newborn as "very tiny" or "smaller than average" gave a sensitivity of 80% and specificity of 95% in detecting a birth weight < 2.0 kg (4). Thus, mother's perception of birth size was used in the logistic regression models as a proxy for birth weight.

To further reduce problems with reverse causality, analyses were repeated, excluding other newborns at high risk of death and ill health (unwell on the day of birth, congenital abnormalities, premature). All analyses were conducted in STATA version 8.2 (Stata Corporation, College Station, TX). Adjusted odds ratios (adj ORs) and 95% CIs are presented. Because neonatal mortality is a relatively rare event, these ORs closely approximate risk ratios and are referred to as such in the text.

Sample size and power were calculated with the use of EPI-INFO version 6.04d (Centers for Disease Control and Prevention, Atlanta, GA). The 10 000 infants included in this study during the 12-mo surveillance period provided 80% power to detect a 1.4-fold effect on neonatal mortality at a significance level of 5% and mortality risk of 2.9% in the breastfed group.

Ethical issues

Both the ObaapaVitA trial and this nested study were approved by the ethics committees of the Ghana Health Service and the London School of Hygiene and Tropical Medicine. The procedures followed were in accordance with the ethical standards of these committees.

RESULTS

Birth and death surveillance

There were 14 403 live births in the ObaapaVitA trial area from 1 July 2003 to 30 June 2004 and 433 neonatal deaths, giving a neonatal mortality rate of 30.1 per 1000 live births. Data were captured for 11 316 (82%) of the 13 860 singleton births within 28 d of delivery (median: 14 d postpartum; interquartile range: 7–21 d). This included 268 neonatal deaths, 109 (41%) of which occurred within the first day of birth. We excluded 106 (0.9%) of

TABLE 2

Causes of neonatal deaths in the study population

Cause of neonatal death	Value
	<i>n</i> (%)
Infection	93 (66.4)
Tetanus	2 (1.4)
Meningitis	11 (7.9)
Pneumonia	45 (32.1)
Diarrhea	2 (1.4)
Septicemia	33 (23.6)
Noninfection	47 (33.6)
Congenital abnormality	6 (4.3)
Prematurity	21 (15)
Birth asphyxia	16 (11.8)
Other specific cause	4 (2.9)
Accident or injury	2 (1.5)
Hemorrhage	2 (1.5)
Unexplained	0 (0)
Total	140 (100)

the day 2 singleton survivors who either did not initiate breastfeeding or started then stopped, plus 154 (1.4%) whose mothers moved out of the study area before the second infant interview, and 5 deaths without a VA. This analysis was based on the remaining 10 942 infants, among whom there were 140 neonatal deaths from day 2–28. Overall 93 (66.4%) deaths were due to infectious and 47 (33.5%) to noninfectious causes (**Table 2**). The major causes of death in the noninfection-related group were asphyxia and prematurity. Only 2 infection-related deaths were due to tetanus. Sociodemographic characteristics were similar in newborns included and excluded from this study (data not shown).

Initiation of breastfeeding

Strong evidence showed that risk of death as a result of infection increased as the delay in initiating breastfeeding increased (**Table 3**). This trend was still apparent after adjusting for pre-lacteal feeding and established breastfeeding and after excluding newborns at high risk of death (unwell on the day of birth, congenital abnormalities, premature) (adj OR: 2.78; 95% CI: 1.65, 4.67; $P < 0.0001$). No interactions were observed with other infant feeding practices (prelacteal feeding, established neonatal breastfeeding), gestational age, or mother's perception of size. Overall, late initiation of breastfeeding (after day 1) was associated with a 2.6-fold increased risk of infection-specific neonatal mortality.

In contrast, there was only weak evidence of increasing mortality risk from noninfectious causes with increasing delay in initiation of breastfeeding (Table 3). No interactions were observed with other infant feeding practices (prelacteal feeding, established neonatal breastfeeding), gestational age, or mother's perception of size. The high OR for the association between initiation of breastfeeding after day 3 and noninfection-specific mortality was considered to be due to the small sample size and was much lower (adj OR: 1.30; 95% CI: 0.40, 4.28) when newborns who initiated breastfeeding on day 3 and after day 3 were combined. No striking differences were observed between the effects of late initiation on individual causes of death (congenital abnormalities, prematurity, birth asphyxia,

TABLE 3
Neonatal mortality risk by early infant feeding practices¹

	Infection-specific mortality				Noninfection-specific mortality		
	Infants <i>n</i> (%)	Deaths <i>n</i> (% risk)	Unadjusted OR (95% CI)	Adjusted OR ² (95% CI)	Deaths <i>n</i> (% risk)	Unadjusted OR (95% CI)	Adjusted OR ² (95% CI)
Timing of initiation of breastfeeding							
Within 1 h	4763 (43)	22 (0.5)	1	1	12 (0.3)	1	1
From 1 h to end of day 1	3105 (28)	19 (0.6)	1.33 (0.72, 2.46)	1.16 (0.62, 2.17)	15 (0.5)	1.92 (0.90, 4.11)	1.47 (0.65, 3.30)
Day 2	2138 (20)	32 (1.5)	3.28 (1.90, 5.65)	2.55 (1.44, 4.53)	15 (0.7)	2.80 (1.31, 6.00)	2.34 (1.00, 5.33)
Day 3	797 (7.3)	17 (2.1)	4.71 (2.49, 8.91)	3.57 (1.82, 6.99)	2 (0.3)	1.00 (0.22, 4.47)	0.47 (0.08, 2.68)
After day 3	144 (1.3)	3 (2.1)	4.59 (1.36, 15.50)	2.44 (0.69, 8.60)	3 (2.1)	8.42 (2.35, 30.2)	6.71 (1.61, 27.9)
<i>P</i> for trend				<0.0001			0.11
Late (after day 1) compared with early (day 1) initiation of breastfeeding							
Early initiation	7866 (71.9)	41 (0.5)	1	1	27 (0.3)	1	1
Late initiation	3076 (28.1)	52 (1.7)	3.28 (2.17, 4.95)	2.61 (1.68, 4.04)	20 (0.7)	1.90 (1.06, 3.39)	1.63 (0.85, 3.11)
<i>P</i> ³				<0.0001			0.15
Prelacteal feeding compared with no prelacteal feeding on day 1							
No prelacteal feeding	9143 (83.6)	67 (0.7)	1	1	39 (0.4)	1	1
Prelacteal feeding	1799 (16.4)	26 (1.5)	1.99 (1.26, 3.13)	1.11 (0.66, 1.86)	8 (0.4)	1.04 (0.49, 2.23)	1.33 (0.55, 3.22)
<i>P</i> ³				0.71			0.53
Established neonatal breastfeeding days 2–28							
Exclusive	7676 (70)	49 (0.6)	1	1	31 (0.4)	1	1
Predominant	3033 (27)	33 (1.1)	1.71 (1.10, 2.67)	1.45 (0.90, 2.34)	14 (0.5)	1.14 (0.61, 2.15)	0.97 (0.45, 2.04)
Partial	233 (2.1)	11 (4.7)	7.71 (3.96, 15.0)	5.73 (2.75, 11.91)	2 (0.9)	2.14 (0.51, 8.97)	0.80 (0.14, 4.61)
<i>P</i> for trend				<0.0001			0.83
Total	10942 (100)	93 (0.85)			47 (0.4)		

¹ OR, odds ratio.² Adjusted for maternal educational level, maternal cash income, water supply, sanitation, overcrowding, antenatal care, delivery attendant, site of delivery, maternal ethnicity, maternal age, parity, maternal perinatal health, neonate sex, congenital abnormalities, gestational age, neonate size at birth, neonate perinatal health, and other breastfeeding practices.³ Determined with likelihood ratio test.

other); the numbers of deaths in these groups were too small to assess effects more fully.

Prelacteal feeding

Prelacteal feeding was not associated with an increased risk of infection-specific neonatal mortality (adj OR:1.11; 95% CI: 0.66, 1.86; *P* = 0.71) after adjusting for timing of initiation of breastfeeding and established neonatal breastfeeding (Table 3). No association was observed between prelacteal feeding and infection-specific neonatal mortality when the model was refitted to exclude newborns at high risk of death (unwell on the day of birth, congenital abnormalities, premature) (adj OR: 0.90; 95% CI: 0.48, 1.66; *P* = 0.71).

Prelacteal feeding was also not associated with an increased risk of noninfection-specific neonatal mortality (adj OR: 1.33; 95% CI: 0.55, 3.22; *P* = 0.53) even after adjusting for timing of

initiation of breastfeeding and established neonatal breastfeeding (Table 3). No striking differences were observed in the effect of prelacteal feeding on individual causes of death (congenital abnormalities, prematurity, birth asphyxia, other), but sample sizes were too small to assess effects more fully.

Established neonatal breastfeeding

Partially breastfed newborns had an almost 6-fold higher risk of dying of infectious causes than did newborns who were exclusively breastfed even after adjusting for late initiation and prelacteal feeding (Table 3). The size of this effect was even higher (adj OR: 8.78; 95% CI: 3.70, 20.85; *P* < 0.0001) when the model was refitted to exclude newborns at high risk of death (unwell on the day of birth, congenital abnormalities, premature). Risks of infection-specific neonatal mortality were also high in predominantly breastfed newborns (adj OR: 1.45; 95%

CI: 0.90, 2.34). There was a significant trend ($P < 0.0001$) of increasing risk of infection-specific mortality from exclusive to predominant to partially breastfed newborns.

No apparent increased risk of noninfection-specific neonatal mortality was observed in either predominant or partially breastfed newborns compared with those exclusively breastfed (Table 3). There were also no striking effects of predominant and partial breastfeeding on individual causes of death (congenital abnormalities, prematurity, birth asphyxia, other), but the numbers of deaths were too small to assess effects more fully. No significant differences were observed when analyses were repeated to exclude newborns who died on days 1–7 or tetanus-related deaths.

DISCUSSION

These analyses indicate that timing of initiation of and established neonatal breastfeeding exert important and independent influences on deaths as a result of infectious diseases within the neonatal period. The risk of death as a result of infectious causes increased with increasing delay in initiation of breastfeeding. In contrast, little apparent effect of early infant feeding practices was observed on deaths as a result of other causes. Partial breastfeeding was associated with a 5.7-fold increased adjusted risk of death as a result of infectious disease but had no obvious effect on deaths as a result of other causes. Prolactal feeding on the first day of life appeared to exert little significant influence on mortality risks as a result of infection or on noninfection-specific deaths.

This appears to be the first study that has examined the effects of timing of initiation of breastfeeding on cause-specific neonatal mortality. A large study from Brazil reported 5-fold and 2-fold increased risks of death from diarrhea and respiratory infections, respectively, in infants aged birth to 2 mo who were given breast milk plus milk supplements compared with infants who were exclusively breastfed, after controlling for reverse causality (7). A large study from Bangladesh was designed to detect associations between type of neonatal breastfeeding (exclusive, predominant, partial) and cause-specific neonatal mortality, but effects on all-cause neonatal mortality were only reported (24). A study from Pakistan reported a 3-fold reduction in risk of early neonatal sepsis in exclusively breastfed compared with partially breastfed hospitalized neonates (25). However, no other studies have reported on the cause-specific effects of early infant feeding practices specifically in the neonatal period. Case reports were also published that describe hypernatremia, acidosis, and hypoglycemia in neonates provided with prolactal feeds (26–28), but no studies have examined associations between prolactal feeding and cause-specific neonatal mortality.

Observational studies of breastfeeding and infant health may be affected by a number of methodologic problems, including self-selection, reverse causality, confounding, and misclassification (5, 29, 30). However, we analyzed data for the entire study population of singleton births. We also addressed reverse causality by excluding all deaths before day 2 and newborns who either did not start or who started and stopped breastfeeding, controlling for high-risk newborns, and repeating all analyses after all deaths before day 8 and high-risk newborns were excluded (which did not alter effect estimates). We also adjusted for

many potential confounding variables, although residual confounding from other unmeasured variables, imperfect measurement of confounding variables, and imperfect assessment of the relation between the confounding variables and the exposure and outcome cannot be discounted. Finally, any nondifferential misclassification of type of breastfeeding would have tended to underestimate rather than overestimate effect sizes.

Cause-specific mortality fractions estimated from VAs can be subject to marked misclassification bias (31). If specificity is low and particular causes of death are rare, the power of individual studies may be reduced and the possibility of type II error (ie, a test result is reported as nonsignificant when in fact there truly is an effect of the exposure) may be increased (32). However, the assessment of the diagnostic accuracy of the ObaapaVitA VA indicated that the specificity was high for all important causes of death, and the VA fulfilled the criteria suggested by Maude and Ross (31) and Anker (32) in 1997. Overall, the VA was considered sufficiently accurate to be used to estimate neonatal cause-specific mortality fractions at the population level and for observational and intervention research targeting the major causes of neonatal deaths in our study area.

Unfortunately, there were insufficient deaths to determine effects on specific causes of death such as prematurity and birth asphyxia. Effects of early infant feeding practices on low-birth-weight infants (premature and small for gestational age) will be published separately. However, larger studies adequately powered to assess effects on other causes of neonatal deaths are needed. Studies of the effects of early infant feeding on neonatal mortality should also be conducted in other developing country regions, because policy decisions should not be based on the results of only one study, and effects may differ according to socioeconomic status and cultural practices.

In contrast to other large mammalian species the human neonate receives transplacental passage of antibodies and other immune components (33, 34). These bloodborne factors are thought to be responsible for many early neonatal humoral and cell-mediated immune responses. These findings have led some investigators to question the active immunologic role of colostrum in young human infants (35, 36). Our findings indicate, however, that early breast milk may have a direct antiinfective action and may stimulate neonatal immune function as well as decreasing the ingestion of infectious pathogens. Close contact between the infant-mother dyad and stimulation of the enteromammary mucosa-associated lymphoid tissue system may also contribute (9). Total protein and immunoglobulin concentrations also decrease markedly in human colostrum during the first days of life (concentrations are highest on day 1, half by day 2, and slowly decrease thereafter) (34, 37). This process could explain the dose-response relation seen in our study.

The lack of an association between early initiation of breastfeeding and noninfection-specific mortality indicates that the direct effects of breast milk on the neonatal GIT (reducing intestinal permeability) and metabolic dysfunction (including sodium and glucose metabolism) may be less important because these mechanisms would be expected to affect noninfection-related deaths (especially prematurity and birth asphyxia-related mortality). Established breastfeeding practices had the strongest associations with infectious disease-specific mortality, highlighting the importance of sustaining optimal breastfeeding practices throughout neonatal and infant life.

Overall, these results indicate that early breast milk is significantly associated with reduced infection-specific neonatal mortality in young infants. This finding provides the first epidemiologic evidence of a causal association between early breastfeeding and reduced risk of infection in young human infants. These findings have important implications for neonatal health programs and policy. They suggest that breastfeeding promotion programs that focus on early initiation of breastfeeding and exclusive breastfeeding in the neonatal period can significantly reduce the burden of infectious disease-related mortality in the rural African neonate. Other low technology community-based approaches are also likely to benefit these neonates. These measures include improving hygiene before, during, and after delivery and maternal vaccination, as well as effective promotion of appropriate nutrition and breastfeeding practices.

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The author's responsibilities were as follows—KME: conceived the idea for this study, took the lead role in its design, oversaw its conduct, carried out the statistical analysis, and wrote the first draft of the paper and was responsible for the final version; BRJ: provided technical input to, and was substantially involved in, all aspects of the study and was responsible for the final version of the paper; SA-E was responsible for the design and execution of the data management system; SO-A provided technical input to the design and conduct; and LSH provided technical input to the design, conduct, and field work components and contributed to the statistical analysis. All authors provided feedback on drafts of the paper and approved the final version. None of the authors had a conflict of interest.

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