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ORIGINAL ARTICLE

Effect of community-based newborn care on cause-specific neonatal mortality in Sylhet district, Bangladesh: findings of a cluster-randomized controlled trial

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OBJECTIVES: Community-based maternal and newborn intervention packages have been shown to reduce neonatal mortality in resource-constrained settings. This analysis uses data from a large community-based cluster-randomized trial to assess the impact of a community-based package on cause-specific neonatal mortality and draws programmatic and policy implications. In addition, the study shows that cause-specific mortality estimates vary substantially based on the hierarchy used in assigning cause of death, which also has important implications for program planning. Therefore, understanding the methods of assigning causes of deaths is important, as is the development of new methodologies that account for multiple causes of death. The objective of this study was to estimate the effect of two service delivery strategies (home care and community care) for a community-based package of maternal and neonatal health interventions on cause-specific neonatal mortality rates in a rural district of Bangladesh.

STUDY DESIGN: Within the general community of the Sylhet district in rural northeast Bangladesh. Pregnancy histories were collected from a sample of women in the study area during the year preceding the study (2002) and from all women who reported a pregnancy outcome during the intervention in years 2004 to 2005. All families that reported a neonatal death during these time periods were asked to complete a verbal autopsy interview. Expert algorithms with two different hierarchies were used to assign causes of neonatal death, varying in placement of the preterm/low birth weight category within the hierarchy (either third or last). The main outcome measure was cause-specific neonatal mortality.

RESULT: Deaths because of serious infections in the home-care arm declined from 13.6 deaths per 1000 live births during the baseline period to 7.2 during the intervention period according to the first hierarchy (preterm placed third) and from 23.6 to 10.6 according to the second hierarchy (preterm placed last).

CONCLUSION: This study confirms the high burden of neonatal deaths because of infection in low resource rural settings like Bangladesh, where most births occur at home in the absence of skilled birth attendance and care seeking for newborn illnesses is low. The study demonstrates that a package of community-based neonatal health interventions, focusing primarily on infection prevention and management, can substantially reduce infection-related neonatal mortality.

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INTRODUCTION

An estimated 2.9 million neonatal deaths occur globally every year, comprising 44% of under-five child deaths.[1] Globally, the primary causes of neonatal mortality are preterm birth complications (35%), intrapartum-related complications (23%) and sepsis or meningitis (13%), but the cause structure varies by setting. Neonatal deaths in the Southeast Asia region represent 36% of global neonatal deaths.[2] National-level data on causes of neonatal death are lacking from this region as well as from other high burden areas, and cause-of-death estimates are based largely on modeling.[3] Effective interventions to reduce neonatal deaths are known; determining how to deliver these interventions effectively at scale is a critical goal.[4,5] Understanding the cause-specific burden and impact of specific interventions on various causes of neonatal deaths is important for the design and implementation of these interventions at scale.

Neonatal deaths frequently occur at home in communities lacking vital registration systems and with limited access to healthcare; thus, the causes of death in neonates are rarely ascertained.[6] Even in communities with established community-based surveillance systems, like Sylhet district in Bangladesh, causes of neonatal deaths are challenging to determine given that the clinical symptoms of the major contributing causes may overlap and are difficult to attribute to a single identifiable cause.[6,7] Verbal autopsy is a valuable tool for ascertaining cause of death in settings lacking formal vital registration systems, but methods and accuracy vary substantially for major causes of neonatal deaths.[6,7] Neonatal infection-related deaths are particularly difficult to validate and are frequently under-assigned.[6]

We conducted a cluster-randomized controlled trial of two service delivery strategies for a package of maternal and newborn health (MNH) interventions in rural northeastern Sylhet district,

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Bangladesh. One delivery strategy, home-based care by community health workers (CHWs), led to a 34% reduction in neonatal mortality relative to the comparison arm which received standard health services available in the community.[8] Another delivery strategy, MNH promotion through community-level activities, showed improvements in MNH care practices, but did not show any significant reduction in neonatal mortality relative to the comparison area. Investigators designed the MNH package to promote the prevention, early recognition and treatment of neonatal infections because it was thought that this condition was the top cause of neonatal deaths[9] and could be effectively managed at home in this setting. This study uses verbal autopsy data and two varying hierarchies to establish cause-specific mortality rates for each of the three study arms before and during the trial's implementation to assess the impact of the intervention package on cause-specific mortality.

METHODS

Study population

Details of the study population, intervention package, trial design, trial profile and data collection methodology have been described in detail elsewhere.[8] Briefly, a total of 24 unions (the smallest governmental administrative unit in Bangladesh with an average population of about 20 000 each) were randomized to one of the two delivery strategies (home care or community care) or to the comparison arm. Before the study was implemented, in 2002, a household survey was conducted and truncated pregnancy histories were collected from a random sample of women who reported a pregnancy during the 15 months before the survey. A separate team later conducted verbal autopsy interviews with all families that reported a stillbirth or neonatal death during the 15-month pre-intervention period. This team of data collectors had at least 12 years of schooling and had received 6 days of training in verbal autopsy methodology.

The intervention was rolled out during the last 6 months of 2003 and was fully implemented during 2004 to 2005. An endline household survey was conducted during January to June 2006. Pregnancy histories that included recall of all pregnancy outcomes were collected from all women who reported a pregnancy outcome during 2003 to 2005. All families that reported a neonatal death or stillbirth during 2003 to 2005 were later visited again and asked to complete the verbal autopsy questionnaire. The completion rate for the verbal autopsy study was 92% at baseline and 89% at endline. In 94% of cases at baseline and 98% at endline, the infant's mother was the principal respondent for the verbal autopsy interview. Neonatal death was defined as the death of a liveborn infant < 29 days old. Stillbirth was defined as a fetus born dead after 7 months or more gestation.[9] The impact of the intervention on all-cause neonatal mortality was reported separately.[8]

Study instrument, data collectors and data quality

The verbal autopsy questionnaire was adapted from the instrument used in a World Health Organization three-country verbal autopsy validation study, with added questions about pregnancy and childbirth and a new module to distinguish between stillbirths and early neonatal deaths.[10] The verbal autopsy interview started with open-ended questions to elicit a narrative about the newborn's death, followed by close-ended questions. The instrument was translated from English to Bangla, and local terms for specific illnesses were used when appropriate.

Analysis

Expert algorithms to assign causes of death were the same as those published previously by our group using data from Uttar Pradesh, India.[9] The cause of death was assigned using a computer algorithm created in Stata Version 10 (StataCorp, College Station, TX, USA) that included responses from both open-ended narrative and close-ended questions. Potential causes of death were: tetanus, congenital abnormality, preterm birth or low birth weight, birth asphyxia (intrapartum-related complications), birth injury, serious infection (which was called sepsis/pneumonia in the Uttar Pradesh analysis[9]) and diarrhea. Birth asphyxia and birth injury were later combined into one category because the birth asphyxia category captured nearly all the deaths that met the criteria for birth injury. Deaths that met none of the criteria were classified as 'not identified'.

Two hierarchies were used to assign a primary cause of death (Figure 1). The first was the same as was used in our Uttar Pradesh analysis and is similar to the classification system by Lawn *et al.* in previous global estimates of neonatal mortality[11,12] and by the Child Health Epidemiology Reference Group (CHERG).[2] The hierarchy used in the study by Lawn *et al.* and CHERG analyses considers 'preterm birth complications' after 'neonatal tetanus' and 'congenital abnormalities.' In our first hierarchy, the category of 'preterm or low birth weight' is at the same tier as used in the Lawn and CHERG analyses. However, these other studies included a more specific definition of preterm complications: '(1) severe immaturity (< 33 weeks), (2) neonatal death with birth weight < 1800 g where gestational age is unknown or (3) specific complications of preterm birth such as surfactant deficiency'.[12] Applying this definition of preterm complications would not be feasible in this setting, where most women have imprecise information about gestational age, birth weight was rarely measured and most neonatal deaths occurred at home without medical care. Thus, no gold standard assessment of cause of death is available. We applied a less specific definition: 'baby very small or smaller than usual at birth,[9] which could capture either preterm or low birth weight births and thus is a combination of direct, underlying and contributory causes. Therefore, we present another hierarchy in which the preterm/low birth category was assigned at the lowest tier to minimize overestimation of the preterm category as the cause of death.

Distributions of age-at-death in days were comparable between deaths with and without verbal autopsy data. About one-third of neonatal deaths occurred within the first day of life, at both baseline and endline; of these deaths, 7% (8/121) and 12% (57/473), respectively, did not receive a verbal autopsy. Assuming that the cause structure would be comparable if the distribution of age-at-death was similar, deaths with missing verbal autopsy data were proportionally distributed among all primary causes of death. Cause-specific mortality rates were originally calculated by year. Rates during 2003 were comparable to rates at baseline, which was expected since the intervention was implemented beginning July 2003 but it was not fully in place until the end of 2003. Rates during years 2004 and 2005 were similar to each other. As a result, in this analysis we compare cause-specific mortality rates at baseline with combined rates for years 2004 and 2005 in all study arms.

Analysis was by intention to treat at the cluster level. We estimated cause-specific mortality rates for each intervention arm relative to the comparison arm and constructed 95% confidence intervals (CIs) with Taylor series approximated variance,[13] adjusting for mother's age and years of education, sex and birth order of the index child, and wealth index. To address the cluster-randomized study design, we used a *t*-test to compare differences in cause-specific neonatal mortality rates between intervention and comparison clusters.[14,15] The study received ethical approval from the Johns Hopkins Bloomberg School of Public Health's Institutional Review Board and the Ethical Review Committee of the International Centre for Diarrheal Disease Research, Bangladesh.

RESULTS

The baseline sample survey recorded 8141 live births and 379 neonatal deaths, and the endline pregnancy histories from the entire study population recorded 30 041 live births and 1245 neonatal deaths during the years 2004 to 2005 (Table 1).

Mortality rates because of tetanus were reduced in all three study arms during the intervention period compared with baseline, but this change was significant only in the comparison arm, from 3.7 (95% CI = 1.4 to 6.0) at baseline to 0.7 (95% CI = 0.2 to 1.2) at endline (Tables 2 and 3). Rates of congenital abnormality were similar across the three study arms and showed no evidence of change from baseline to intervention.

Using hierarchy 1, in which the definition for preterm or low birth weight was applied after tetanus and congenital abnormality, preterm or low birth weight was the main cause of death, and was comparable across all study arms at both baseline, ranging from 14.2 to 17.3, and endline, ranging from 10.7 to 13.2 (Table 2). Serious infection was the second most common cause of death in this hierarchy, and infection death rates declined significantly in the home-care arm from baseline (13.6 per 1000

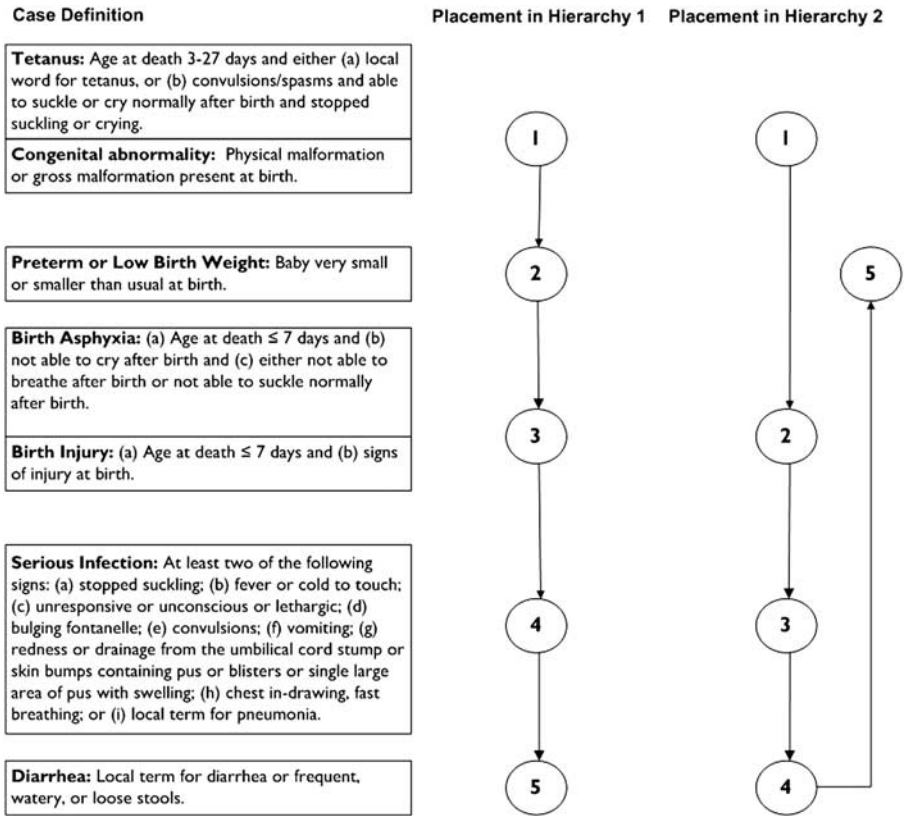

Figure 1. Hierarchical application of cause-of-death definitions.

Table 1. Live births, neonatal deaths and completed verbal autopsy interviews by study arm

Survey timing	*Home care*	*Community care*	*Comparison*
Baseline (2002)			
Live births	2846	2657	2638
Neonatal deaths	129	122	128
Verbal autopsy completed	118 (91.5%)	114 (93.4%)	118 (92.2%)
Endline (2004–2005)			
Live births	9630	10 586	9852
Neonatal deaths	325	489	435
Verbal autopsy completed	317 (97.5%)	413 (84.5%)	376 (86.4%)

live births, 95% CI = 9.4 to 17.9) to endline (7.2 per 1000 live births, 95% CI = 5.5 to 8.9). Birth asphyxia mortality rates were comparable across study arms and time periods, from 7.7 to 8.6 at baseline and 6.1 to 8.8 at endline.

In hierarchy 2, in which preterm or low birth weight was placed lowest, serious infection was the most common cause of death across all study arms, and a 55% reduction in infection-specific mortality rates was measured in the home-care arm, from 23.6 per 1000 live births (95% CI = 18.0 to 29.2) at baseline to 10.6 (95% CI 8.5 to 12.6) at endline (Table 3). The infection-specific mortality also declined in the comparison arm by about 26% between baseline and endline. Taking into account the reduction in the comparison arm, the net reduction of infection-specific mortality, using the two different hierarchies, in the intervention arm was about 30 to 35%. Rates of birth asphyxia were similar at baseline (ranging from 8.1 to 12.5) and endline (from 9.0 to 12.1). Mortality rates because of preterm or low birth weight were also comparable across the three study arms at baseline (ranging from 2.8 to 5.6) and endline (from 4.0 to 6.5).

DISCUSSION

We have presented cause-specific mortality rates from a cluster-randomized trial of a package of neonatal health interventions delivered through two service delivery strategies. We have previously shown that overall neonatal mortality was reduced only in one of the three study arms, the home-care arm.[16] Cause-specific mortality data suggest that the interventions implemented in the home-care arm were effective primarily at reducing deaths because of serious infections such as sepsis, meningitis and pneumonia. In prior studies, we have shown that the study's CHWs were able to identify sick newborns requiring antibiotic treatment using a simple algorithm,[17] that the validity of their assessments compared well with medical doctors,[17] and that their management of neonates with signs and symptoms of illness classified as very severe disease was as good as qualified medical providers.[17] We have also shown that home visits by CHWs improved breastfeeding practices[18] and that other preventive care practices aimed to reduce risk for infections (for example, clean cord care) were improved in the home-care arm during the intervention.[8] This study suggests that this intervention reduced all-cause neonatal mortality primarily by preventing and treating neonatal infections.

Tetanus mortality rates were low at baseline and were halved in all three study arms during the intervention, although the difference was statistically significant only in the comparison

Table 2. Cause-specific mortality rates and 95% CIs by study arm, using hierarchy 1

Cause of death	*Home care*				*Community care*				*Comparison*			
	Baseline		*Endline*		*Baseline*		*Endline*		*Baseline*		*Endline*	
	Rate	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*
Tetanus	2.0	(0.4–3.6)	0.2	(0.0–0.6)	1.5	(0.0–3.0)	0.8	(0.3–1.3)	3.7	(1.4–6.0)	0.7	(0.2–1.2)
Congenital abnormality	2.4	(0.6–4.2)	0.9	(0.3–1.5)	2.4	(0.5–4.3)	2.6	(1.6–3.5)	1.9	(0.3–3.6)	2.7	(1.7–3.7)
Preterm or low birth weight	14.2	(9.9–18.6)	10.7	(8.6–12.7)	17.3	(12.4–22.3)	13.2	(11.0–15.3)	16.7	(11.8–21.6)	11.7	(9.6–13.8)
Birth asphyxia or injury	7.7	(4.5–10.9)	6.0	(4.4–7.5)	8.6	(5.1–12.1)	8.6	(6.8–10.3)	7.7	(4.4–11.0)	7.0	(5.3–8.6)
Serious infection	13.6	(9.4–17.9)	7.2	(5.5–8.9)	9.9	(6.1–13.6)	8.3	(6.6–10.1)	13.3	(8.9–17.7)	11.6	(9.5–13.7)
Diarrhea	0.0	(0.0–0.0)	0.1	(0.0–0.3)	0.0	(0.0–0.0)	0.1	(0.0–0.3)	0.0	(0.0–0.0)	0.3	(0.0–0.7)
Not identified	6.3	(3.4–9.3)	6.8	(5.2–8.4)	6.5	(3.4–9.5)	9.9	(8.1–11.8)	4.4	(1.9–6.9)	8.6	(6.7–10.4)

Abbreviation: CI, confidence interval.

Table 3. Cause-specific mortality rates per 1000 live births and 95% CIs by study arm, using hierarchy 2

Cause of death	*Home care*				*Community care*				*Comparison*			
	Baseline		*Endline*		*Baseline*		*Endline*		*Baseline*		*Endline*	
	Rate	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*	*Rate*	*95% CI*
Tetanus	2.0	(0.4–3.6)	0.2	(0.0–0.6)	1.5	(0.0–3.0)	0.8	(0.3–1.3)	3.7	(1.4–6.0)	0.7	(0.2–1.2)
Congenital abnormality	2.4	(0.6–4.2)	0.9	(0.3–1.5)	2.4	(0.5–4.3)	2.6	(1.6–3.5)	1.9	(0.3–3.6)	2.7	(1.7–3.7)
Birth asphyxia or injury	8.1	(4.8–11.3)	9.3	(7.4–11.3)	10.9	(7.0–14.9)	11.9	(9.9–14.0)	12.5	(8.2–16.7)	9.0	(7.1–10.9)
Serious infection	23.6	(18.0–29.2)	10.6	(8.5–12.6)	18.4	(13.3–23.5)	11.8	(9.7–13.8)	22.4	(16.7–28.0)	16.5	(14.0–19.1)
Diarrhea	0.0	(0.0–0.0)	0.1	(0.0–0.3)	0.8	(0.0–1.9)	0.1	(0.0–0.3)	0.0	(0.0–0.0)	0.6	(0.1–1.1)
Preterm or low birth weight	3.8	(1.6–6.1)	4.0	(2.7–5.2)	5.6	(2.8–8.4)	6.3	(4.8–7.9)	2.8	(0.8–4.8)	4.4	(3.1–5.8)
Not identified	6.3	(3.4–9.3)	6.8	(5.2–8.4)	6.5	(3.4–9.5)	9.9	(8.1–11.8)	4.4	(1.9–6.9)	8.6	(6.7–10.4)

Abbreviation: CI, confidence interval.

arm. In the two intervention arms, women were encouraged to receive tetanus immunization, but the project did not provide immunization. The decline perhaps reflects a nation-wide declining trend that Bangladesh has been experiencing since the 1990s,[19] likely the result of continuous efforts by the Bangladeshi government and nongovernmental organizations to improve coverage of tetanus toxoid immunization.[20]

This study benefits from a large sample size and high response rates. We used the same case definitions and hierarchy that we applied to a verbal autopsy study in Uttar Pradesh, India, to improve comparability with other settings.[9] The case definitions were validated in a previous multi-country study that included Bangladesh.[10] However, applying the verbal autopsy methodology to neonatal deaths presents some challenges, as has been reviewed in-depth.[21] Many signs and symptoms of the common causes of neonatal deaths are common to more than one cause of death, and thus the cause-of-death distribution becomes highly dependent on the hierarchy. We have addressed this issue by utilizing more than one hierarchy. It is also known that many neonatal deaths cannot be classified using verbal autopsy, particularly those that occur very soon after birth and those for which the symptoms are difficult to observe, particularly by those without formal health care training. In this study, no cause was identified for 19% of deaths, a figure which is comparable to that of many other studies.[21]

Because the verbal autopsy included no information on gestational age and birth weight, it is difficult to draw conclusions about the impact of the intervention on preterm babies as opposed to term babies with low birth weight; future analysis using other data sources is planned to address this question. This intervention package sought to achieve universal coverage, and this may have been at the expense of identifying preterm or low birth weight babies to receive extra interventions, although CHWs instructed families about the importance of avoiding hypothermia and seeking care for small babies from qualified providers. It is also possible that deaths because of preterm were among infants who were too severely preterm or low birth weight to be managed in the community.[22] In these cases, it is likely that deaths occurred too quickly to seek effective care, that their families rarely complied with referral or that available health facilities had insufficient resources to treat these infants. It is also likely that a package of interventions to improve maternal nutrition and to diagnose and treat a host of maternal infections would be needed to reduce the incidence of preterm and low birth weight, but no consensus exists on how to implement these interventions at the community level.[23] Some evidence suggests that community-based workers can manage issues related to thermal care, for example, through promotion of skin-to-skin care, and feeding in preterm and low birth weight babies and improve outcomes.[22,24,25]

This study also measured no change in deaths because of birth asphyxia and injury. Birth asphyxia deaths have ranged from 10 to 33% in other studies from regions with a similar burden of neonatal mortality,[9,26–32] likely reflecting differences in case definition and methodology for assigning cause of death. Our estimates fell in the middle of this range. The CHWs in this setting were trained in neonatal resuscitation but attended less than 5% of births. During antenatal home visits, they also used a doll to

demonstrate how to clear a neonate's airway and how to dry and wrap a newborn in a manner that could stimulate a mildly asphyxiated newborn. Traditional birth attendants in the study area were oriented in essential newborn care, which included resuscitation. However, access to skilled birth attendance and emergency obstetric care was severely limited in this setting at baseline and during the intervention, and this may have prevented the intervention from having an impact on birth asphyxia and injury.

Our findings are consistent with other estimates suggesting that infections cause one-third to one-half of neonatal deaths in settings similar to the study area.[33–36] Using the first hierarchy, the proportional distribution of cause of death for the three study arms combined at baseline is roughly 34% for preterm, 17% for birth asphyxia and 26% for serious infection. This distribution is similar to the one presented from our study in Uttar Pradesh, India, which used hierarchy 1,[9] and other studies in Nepal[29] and India.[9,28,29] However, given that preterm or low birth weight (< 2500 g, LBW) should be considered as the primary cause of death only if the baby is severely preterm (< 33 weeks) or has a complication particular to preterm babies, the first hierarchy may overstate the true burden of death because of prematurity, and under-estimate the burden because of serious infections in the community.

Specificity is especially important for those algorithms placed at the top of hierarchies.[7,10] In a previous validation study, the definition for preterm birth used here was found to have a sensitivity of 93%, but a low specificity of 68%.[10] The low specification for the preterm birth definition used ('baby very small or smaller than usual at birth') and the placement of 'preterm birth or low birth weight' above 'serious infection' may have also contributed to an overestimation of the proportion of deaths because of preterm and an underestimation of deaths because of infections.[10] Using the second hierarchy, where 'preterm or low birth weight' is placed last, ~9% of deaths were attributed to preterm complications, 22% to birth asphyxia and 46% to serious infections. Preterm and low birth weight estimates from the second hierarchy are comparable to those published from Gadchiroli, India,[26] Uttar Pradesh, India,[9] Ghana[31] and Pakistan.[32] The second hierarchy may reflect more clearly the burden of infection-related deaths in this setting, where antenatal and delivery care remains sub-optimum and postpartum care is rarely sought.

The study demonstrates that a package of community-based neonatal health interventions can reduce infection-related neonatal mortality. In addition, this study has shown that cause-specific mortality rates may vary substantially by hierarchy for the leading causes of neonatal deaths, despite a large sample size. Additional community-based research to measure verbal autopsy validation and standardization of hierarchies to assess cause-specific mortality is needed. Finally, the design of community-based MNH intervention packages should take into account the local epidemiology including cause structure of neonatal mortality. Moreover, the package of interventions may need to be adjusted as the mortality rate comes down and the cause structure of deaths changes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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DISCLAIMER

All authors external and internal had full access to the data in the study and can take responsibility for the integrity of the data and accuracy of the analysis.

AUTHOR CONTRIBUTIONS

AHB, GLD, SEA and REB designed the original study. AHB, SEA, IM and SMR supervised and supported the study implementation. AHB, EW, NB and SA conceptualized this analysis. EW, NB, SA and AHB conducted the analysis and interpreted the data. EW and AHB drafted the manuscript. JAA provided inputs in the manuscript finalization. All authors reviewed and approved the paper.

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