SPECIAL ARTICLE

Newborn-Care Training and Perinatal Mortality in Developing Countries

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ABSTRACT

BACKGROUND

Of the 3.7 million neonatal deaths and 3.3 million stillbirths each year, 98% occur in developing countries. An evaluation of community-based interventions designed to reduce the number of these deaths is needed.

METHODS

With the use of a train-the-trainer model, local instructors trained birth attendants from rural communities in six countries (Argentina, Democratic Republic of Congo, Guatemala, India, Pakistan, and Zambia) in the World Health Organization Essential Newborn Care course (which focuses on routine neonatal care, resuscitation, thermoregulation, breast-feeding, "kangaroo" [skin-to-skin] care, care of the small baby, and common illnesses) and (except in Argentina) in a modified version of the American Academy of Pediatrics Neonatal Resuscitation Program (which teaches basic resuscitation in depth). The Essential Newborn Care intervention was assessed among 57,643 infants with the use of a before-and-after design. The Neonatal Resuscitation Program intervention was assessed as a cluster-randomized, controlled trial involving 62,366 infants. The primary outcome was neonatal death in the first 7 days after birth.

RESULTS

The 7-day follow-up rate was 99.2%. After birth attendants were trained in the Essential Newborn Care course, there was no significant reduction from baseline in the rate of neonatal death from all causes in the 7 days after birth (relative risk with training, 0.99; 95% confidence interval [CI], 0.81 to 1.22) or in the rate of perinatal death; there was a significant reduction in the rate of stillbirth (relative risk with training, 0.69; 95% CI, 0.54 to 0.88; P=0.003). In clusters of births in which attendants had been randomly assigned to receive training in the Neonatal Resuscitation Program, as compared with control clusters, there was no reduction in the rates of neonatal death in the 7 days after birth, stillbirth, or perinatal death.

CONCLUSIONS

The rate of neonatal death in the 7 days after birth did not decrease after the introduction of Essential Newborn Care training of community-based birth attendants, although the rate of stillbirths was reduced. Subsequent training in the Neonatal Resuscitation Program did not significantly reduce the mortality rates. (ClinicalTrials.gov number, NCT00136708.)

Annually, there are approximately 3.7 million neonatal deaths and 3.3 million stillbirths worldwide.[1] Approximately 38% of deaths among children younger than 5 years of age occur during the first 28 days of life, and 75% of the neonatal deaths occur within the first 7 days.[1-3] Without a major reduction in neonatal deaths in the first 7 days after birth, achievement of the United Nations' Millennium Development Goal 4 — a reduction in mortality by two thirds among children younger than 5 years of age[2] — is unlikely to be realized.

In areas of the world with high rates of home delivery, stillbirths are prevalent, but they are difficult to distinguish from early neonatal deaths.[4,5] Therefore, examining both stillbirths and early neonatal deaths is important in an evaluation of perinatal programs that are designed to reduce mortality.[4]

Major global causes of perinatal mortality are asphyxia at birth, low birth weight, and prematurity. Low-cost interventions, including training in neonatal resuscitation[6] and "kangaroo" (skin-to-skin) care,[7] may effectively reduce deaths from these causes; it has been estimated that introducing these interventions as a package might decrease perinatal deaths by 50% or more.[8,9] A recent study that used a "before-and-after" implementation design showed that training in the World Health Organization (WHO) Essential Newborn Care course[10] improved midwives' skill and knowledge[11] and reduced neonatal deaths in the first 7 days after birth among low-risk women who delivered in first-level clinics in Zambia.[12] A systematic review of the literature suggests that perinatal mortality may be decreased by training birth attendants.[13] Thus, wide-scale implementation and evaluation of evidence-based interventions are needed to improve perinatal outcomes, particularly in rural settings, where more than 50% of neonatal deaths occur. The First Breath study was designed to test the primary hypothesis that training birth attendants in the WHO Essential Newborn Care course and in a modified version of the American Academy of Pediatrics Neonatal Resuscitation Program would reduce the rate of death from all causes in the first 7 days after birth, among infants with birth weights of at least 1500 g who were born in rural communities in developing countries.

METHODS

STUDY SITES AND STUDY POPULATIONS

We conducted the before-and-after study of training in Essential Newborn Care in rural communities in seven sites of the Global Network for Women's and Children's Health Research in six countries (Argentina, Democratic Republic of Congo, Guatemala, India, Pakistan, and Zambia) from March 2005 through February 2007 (Fig. 1) with the use of an active baseline design.[14] This design requires the protocol to be initiated before data collection is started. (In the case of this study, all training except for training in the Essential Newborn Care intervention was conducted before the initiation of data collection.) The cluster-randomized trial of training in the Neonatal Resuscitation Program was conducted in 88 communities in five countries (the same as those in the Essential Newborn Care study, except for Argentina) from July 2006 through August 2008 (Fig. 2). The communities were selected to represent rural areas, to be geographically distinct, and to have at least 300 births per year. Most communities had poor health systems and a high rate of home births assisted by traditional birth attendants.

Government officials and community leaders facilitated the training of all birth attendants in the two courses and in the collection of data. The studies were approved by the institutional review board at each participating site in the developing countries and in the United States. An independent data and safety monitoring committee reviewed recruitment, outcomes, and adverse events. Additional monitoring included site visits by local and central personnel and monthly recruitment reports.

Maternal and neonatal data were collected for all births with a gestation period that was considered to have been 28 weeks or longer (on the basis of the mother's last menstrual period and other clinical information) and a birth weight of 1500 g or more (including stillbirths). We excluded fetuses and neonates with a birth weight of less than 1500 g because advanced medical care for very-low-birth-weight infants was not available in most of the study communities. In cases in which the birth weight was not measured, infants were included if the birth weight was

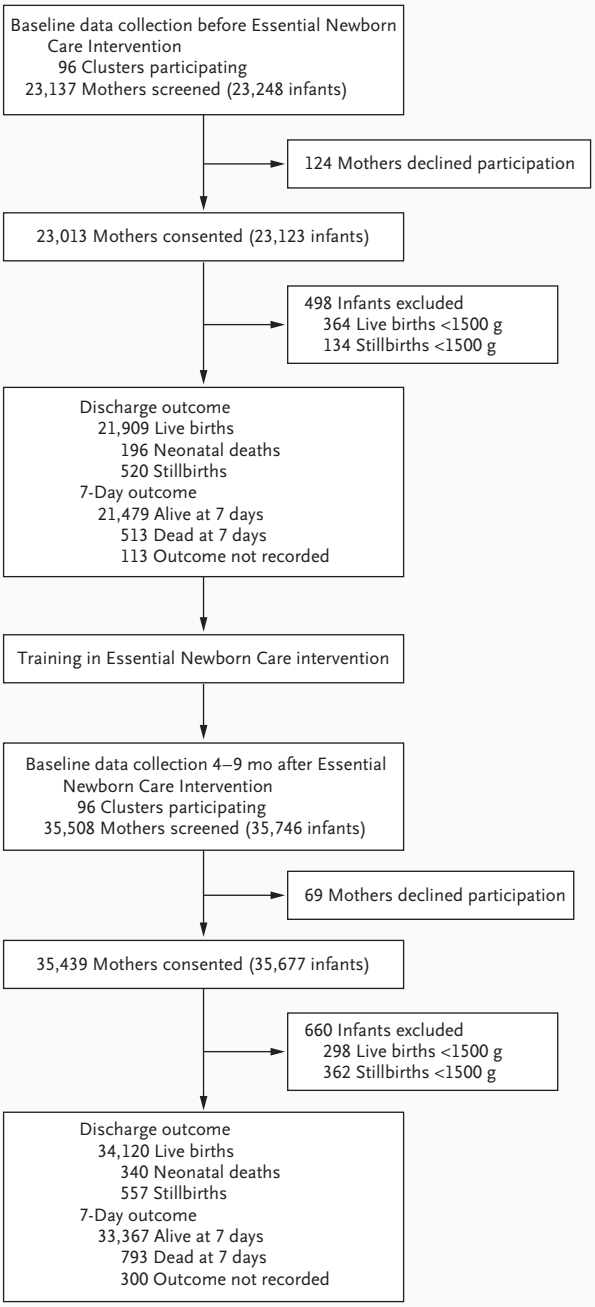

Figure 1. Study Procedures and Outcomes in the Trial of the Essential Newborn Care Program.

estimated by the birth attendant to be 1500 g or more.

PROCEDURES

Various teaching methods were used in the train-the-trainer educational program, including clinical practice sessions and demonstrations to train all birth attendants in the study procedures and in the implementation of the two programs. These courses were first tested in a clinic-based study in Zambia[11,12,15] and were modified for the current study so that they would also be appropriate for use by community-based birth attendants; modifications included the development of materials for illiterate participants. During a 3-day course before the baseline data collection, three experienced trainers trained two master trainers at each site in data collection, the differentiation between stillbirth and early neonatal death, clinical assessments (i.e., monitoring of fetal heart rate, signs of life at delivery, and Apgar scores), and adult education and training techniques. The master trainers then trained one or more community coordinators (either a physician or a nurse) in each community. The community coordinators trained the birth attendants within each community before the baseline period. Birth attendants included traditional birth attendants, nurses, midwives, and physicians. Ventilation bags and masks, spring scales (Salter Brecknell, purchased from the United Nations Children's Fund [UNICEF]), and clean delivery kits were distributed after training.

After the baseline data-collection period, an experienced WHO trainer taught the 3-day Essential Newborn Care course (2004 edition) to master trainers; these trainers then taught the community coordinators, who then taught the birth attendants. The contents of the Essential Newborn Care course included routine neonatal care, initiation of breathing and resuscitation (including bag-and-mask ventilation), thermoregulation, early and exclusive breast-feeding, kangaroo (skin-to-skin) care, care of small babies, recognition of danger signs, and recognition and initial management of complications. The birth attendants taught the mothers to implement the Essential Newborn Care practices.

After completion of the data-collection period that followed the Essential Newborn Care course (March 2005 through February 2007), a 3-day course in the Neonatal Resuscitation Program (2000 edition), led by an experienced trainer, was conducted only for birth attendants in the birth clusters that were randomly assigned to the Neonatal Resuscitation Program; a refresher course was given 6 months later. The contents of the Neonatal Resuscitation Program course included

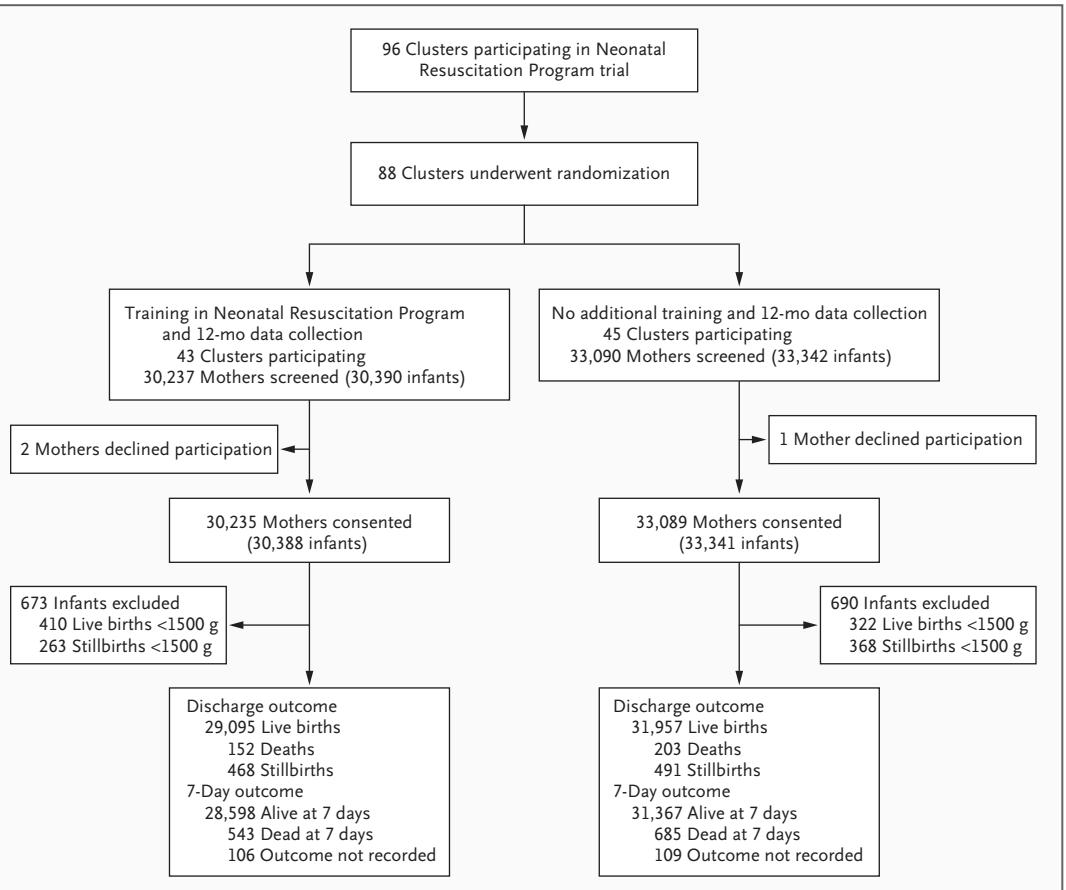

Figure 2. Study Procedures and Outcomes in the Neonatal Resuscitation Program Trial.

in-depth hands-on training in basic knowledge and skills of resuscitation, including initial steps in resuscitation and bag-and-mask ventilation, but did not include training in chest compressions, endotracheal intubation, or administration of medications.

The birth attendants or community coordinators obtained written informed consent from all mothers and collected all data on standardized data forms. Data were reviewed by the community coordinators during weekly visits before local entry of the data and transmission of the data to the data center.

STUDY OUTCOMES

The primary outcome in both studies was the rate of death from all causes in the first 7 days after birth. Prespecified secondary outcomes in both studies included death in the first 7 days specifically attributed to birth asphyxia (defined as failure to initiate or sustain normal breathing at birth,[16] as determined by the birth attendant); the overall rate of stillbirth and fresh stillbirth (which was defined as the absence of maceration); the rate of perinatal death, which included stillbirths plus neonatal deaths in the first 7 days; the rate of death in the first 24 hours after birth; rates of death stratified according to sex, birth weight, location of birth, and type of birth attendant; 1-minute and 5-minute Apgar scores (dichotomized according to prespecified thresholds of <4 and ≥4); use of resuscitation techniques; and neurologic outcome at 7 days as assessed by the community coordinators with the use of an examination developed by Ellis et al.[17]

DATA MANAGEMENT AND MONITORING OF THE STUDY

Consistency checks of the data were performed, and the data were edited as appropriate. The data

and safety monitoring committee reviewed the data for efficacy and safety. There were no formal stopping rules during the Essential Newborn Care study. The O'Brien–Fleming boundary method was used to determine the stopping boundary for efficacy at the planned 3-month and 6-month interim reviews during the cluster trial of the Neonatal Resuscitation Program.

STATISTICAL ANALYSIS

On the basis of data collected during the period after the Essential Newborn Care training and implementation, it was estimated that for the Neonatal Resuscitation Program intervention, randomization of 88 clusters of at least 300 to 500 births each would be required for the study to have at least 80% power to detect a 20% reduction in the relative risk of neonatal death from all causes in the 7 days after birth (and a reduction in the absolute risk of 5 deaths per 1000 live births), with the use of a two-tailed test at a significance level of 5%; an estimated intra-cluster coefficient was determined by simulation and confirmed with baseline data.[18] The variances were adjusted for the primary outcome variable to account for the intra-cluster correlation (design effect).[19]

Chi-square tests and Student's t-tests were used to test for differences in maternal and neonatal characteristics before and after the Essential Newborn Care intervention and for differences between the outcome in the intervention group and that in the control group in the Neonatal Resuscitation Program trial.[19] Multivariate logistic-regression models with generalized estimating equations accounting for the cluster effect were used to test for differences in the rates of neonatal death in the first 7 days after birth, stillbirth, and perinatal death before and after the Essential Newborn Care intervention and to assess interactions of death with category of birth attendant and location of birth. Adjustments were made for significant variables in the models among the following explanatory variables: trial site, maternal age at delivery, maternal education, gestational age, parity, birth weight, sex, birth location, and category of birth attendant. P values have not been adjusted for multiple comparisons. A "difference-in-differences" analysis tested whether there were time-trend effects. We calculated the difference in differences by dividing each intervention period into equal time periods and using the Wilcoxon rank-sum test to evaluate the difference between two differences. The data were analyzed with the use of SAS software, version 9.1.3 (SAS Institute).[20,21]

RESULTS

ESSENTIAL NEWBORN CARE STUDY

At study baseline, the largest proportion of births was attended by traditional birth attendants; and this proportion increased, from 33.2 to 39.2%, after implementation of the Essential Newborn Care intervention (Table 1). The majority of births occurred at the mother's home. After the Essential Newborn Care intervention, the proportion of Apgar scores of less than 4 at 1 and 5 minutes after birth decreased, and the use of bag-and-mask ventilation increased.

Outcome data at 7 days were available for 99.2% of the births. The rate of neonatal death in the 7 days after birth did not decrease significantly after Essential Newborn Care training in the overall cohort (Table 2) or in any prespecified subgroup (Table 1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). The overall rate of stillbirth decreased (Table 2), owing primarily to a reduction in the rate of fresh stillbirth (Table 2 in the Supplementary Appendix). The rate of perinatal death did not decrease significantly after Essential Newborn Care training (Table 2, and Table 3 in the Supplementary Appendix). To eliminate the possibility of bias due to differential exclusion of cases on the basis of an estimated (rather than measured) birth weight of less than 1500 g, we performed another analysis that was limited to births in which birth weight was measured (94.9% of the infants); the results were materially unchanged (data not shown).

When data were analyzed in multivariate logistic-regression models with adjusted generalized estimating equations, there was no significant difference between the rates of neonatal death in the 7 days after birth and of perinatal death before the Essential Newborn Care intervention and the rates after the intervention ($P=0.60$ for neonatal death in the 7 days after birth, and $P=0.10$ for perinatal death), but the rate of stillbirth before the intervention still differed significantly from the rate after the intervention ($P=0.04$). In tests for interaction with the use of generalized estimating equations in

Table 1. Demographic and Clinical Characteristics of Subjects before and after Implementation of the Essential Newborn Care Intervention and of the Intervention and Control Groups in the Neonatal Resuscitation Program.

Variable	Essential Newborn Care Intervention			Neonatal Resuscitation Program		
	Before Intervention (N=22,626)	After Intervention (N=35,017)	P Value	Intervention Group (N=29,715)	Control Group (N=32,651)	P Value
	no./total no. (%)			*no./total no. (%)*		
Birth attendant			<0.001			<0.001
Physician	4,061/22,623 (18.0)	5,311/34,978 (15.2)		1,864/29,707 (6.3)	4,092/32,651 (12.5)	
Nurse or midwife	7,326/22,623 (32.4)	8,531/34,978 (24.4)		10,353/29,707 (34.9)	9,764/32,651 (29.9)	
Traditional birth attendant	7,521/22,623 (33.2)	13,718/34,978 (39.2)		10,770/29,707 (36.3)	13,327/32,651 (40.8)	
Family member, other attendant, or no attendant	3,715/22,623 (16.4)	7,418/34,978 (21.2)		6,720/29,707 (22.6)	5,468/32,651 (16.7)	
Location of birth			<0.001			<0.001
Hospital	5,980/22,625 (26.4)	8,381/35,000 (23.9)		4,304/29,707 (14.5)	5,068/32,651 (15.5)	
Clinic	1,712/22,625 (7.6)	3,704/35,000 (10.6)		5,253/29,707 (17.7)	5,556/32,651 (17.0)	
Birth attendant's home	1,524/22,625 (6.7)	4,224/35,000 (12.1)		2,176/29,707 (7.3)	2,464/32,651 (7.5)	
Mother's home	13,365/22,625 (59.1)	18,640/35,000 (53.3)		17,932/29,707 (60.4)	19,470/32,651 (59.6)	
Other	44/22,625 (0.2)	51/35,000 (0.1)		42/29,707 (0.1)	93/32,651 (0.3)	
Multiple birth	604/22,625 (2.7)	977/35,017 (2.8)	0.39	617/29,715 (2.1)	583/32,651 (1.8)	0.008
Male sex	11,781/22,567 (52.2)	18,262/34,937 (52.3)	0.87	14,995/29,325 (51.1)	17,371/32,569 (53.3)	<0.001
Birth weight*			0.04			<0.001
1500–1999 g	460/19,085 (2.4)	808/33,800 (2.4)		968/28,904 (3.3)	649/32,144 (2.0)	
2000–2499 g	2,216/19,085 (11.6)	3,681/33,800 (10.9)		3,810/28,904 (13.2)	4,106/32,144 (12.8)	
>2500 g	16,409/19,085 (86.0)	29,311/33,800 (86.7)		24,126/28,904 (83.5)	27,389/32,144 (85.2)	
Apgar score <4						
At 1 min	806/20,750 (3.9)	983/33,532 (2.9)	<0.001	891/28,523 (3.1)	847/31,125 (2.7)	0.003
At 5 min	618/20,734 (3.0)	697/33,553 (2.1)	<0.001	540 /28,527 (1.9)	551/31,131 (1.8)	0.26
Apnea at birth	2,071/22,521 (9.2)	2,153/34,860 (6.2)	<0.001	1,470/29,305 (5.0)	1,680/32,551 (5.2)	0.41
Bag-and-mask ventilation	251/22,625 (1.1)	613/35,017 (1.8)	<0.001	1,256/29,715 (4.2)	1,174/32,651 (3.6)	<0.001

* Data on birth weight were available for 94.9% of the infants.

multivariate logistic-regression models, there was no significant interaction between the category of birth attendant and the rate of neonatal death in the 7 days after birth or the rate of perinatal death (P=0.13 for neonatal death in the 7 days after birth, and P=0.08 for perinatal death), but there was a significant interaction between the category of birth attendant and the rate of stillbirth (P=0.04). In subgroup analyses according to the category of birth attendant, the rate of stillbirth decreased significantly when nurses or midwives assisted the birth (relative risk, 0.50; 95% confidence interval [CI], 0.35 to 0.72) and when traditional birth attendants assisted (relative risk, 0.63; 95% CI, 0.45 to 0.88) but not when physicians assisted (Table 2 in the Supplementary Appendix). For the difference-in-differences analysis, the cut-offs shown in Figure 3 were used to divide the data into two consecutive phases; the differences between the two pre-intervention periods and the two post-intervention periods were then compared. There was a significant difference between the pre- and post-Essential Newborn Care differences in the rate of neonatal death in the 7 days after birth but no significant difference in the rates of stillbirth or perinatal death (P=0.03 for neonatal death in the first 7 days, P=0.60 for stillbirth, and P=0.32

Table 2. Mortality Rates before and after Implementation of the Essential Newborn Care Intervention and in the Intervention and Control Groups in the Neonatal Resuscitation Program.

Variable	Essential Newborn Care Intervention			Neonatal Resuscitation Program		
	Before Intervention	After Intervention	Relative Risk (95% CI)	Intervention Group	Control Group	Relative Risk (95% CI)
	no./total no. (rate/1000)			*no./total no. (rate/1000)*		
Neonatal deaths in the 7 days after birth	513/21,992 (23.4)	793/34,160 (23.2)	0.99 (0.81–1.22)	543/29,141 (18.6)	685/32,052 (21.4)	0.87 (0.65–1.16)
Stillbirths	520/22,625 (23.0)	557/35,017 (15.9)	0.69 (0.54–0.88)*	468/29,715 (15.7)	491/32,651 (15.0)	1.05 (0.82–1.33)
Perinatal deaths	1033/22,512 (45.9)	1350/34,717 (38.9)	0.85 (0.70–1.02)	1011/29,609 (34.1)	1176/32,543 (36.1)	0.94 (0.76–1.17)

* P=0.003

for perinatal death). An assessment of temporal changes within each intervention period suggested that the observed effects were not explained simply by changes over time (Fig. 3).

The rate of moderately or severely abnormal[17] neurologic examinations at 7 days decreased from 8.0% before the intervention to 6.4% after (P=0.01). The rates of death within 24 hours after birth before and after Essential Newborn Care training did not differ significantly (Table 4 in the Supplementary Appendix).

NEONATAL RESUSCITATION PROGRAM TRIAL

Despite an increased use of bag-and-mask ventilation in the intervention clusters, the rates of neonatal death from all causes in the 7 days after birth, stillbirth, and perinatal death in the Neonatal Resuscitation Program clusters did not differ significantly from the rates in the control clusters (Table 2). There were no significant differences in mortality between clusters in any of the subgroups (Tables 1, 2, 3, and 4 in the Supplementary Appendix). The difference-in-differences analyses showed no significant changes in mortality between the intervention and control clusters.

DISCUSSION

This large, multicenter study conducted in rural communities in developing countries showed that training in and implementation of the Essential Newborn Care program were not associated with a decrease in the primary outcome of neonatal death. In secondary analyses, implementation of this program was associated with a significant decrease in the rate of stillbirth but not with a decrease in the rate of perinatal death.

Although the before-and-after study design precludes a conclusion of causality, it is plausible that the observed reduction in stillbirths may be due to training in the Essential Newborn Care program.[22-24] Before this training, liveborn infants without obvious signs of life may have been misidentified as stillbirths; such misclassification has been reported previously.[4,5,22-24] After training, resuscitation was more likely to be attempted, with a consequent reduction in births classified as stillbirths. The decrease in fresh stillbirths, but not in macerated stillbirths, after Essential Newborn Care training supports this hypothesis. Furthermore, previous studies showed that training in neonatal resuscitation, which was part of Essential Newborn Care training, decreased the rate of stillbirth.[23,24] The decrease in stillbirths in our study was not associated with an increase in neonatal deaths, suggesting that the decrease in deaths was real and not only the result of classification bias. The reduction in the rate of stillbirths occurred despite a 5% increase in unattended deliveries or deliveries attended by family members in the period after the Essential Newborn Care program was implemented.

The reduction in stillbirths after Essential Newborn Care training appeared to be most pronounced in the case of deliveries that were assisted by nurses or midwives and those that were assisted by traditional birth attendants, who previously might not have known all the information or been trained in the techniques taught in the program. Among births assisted by these birth attendants, rates of perinatal death

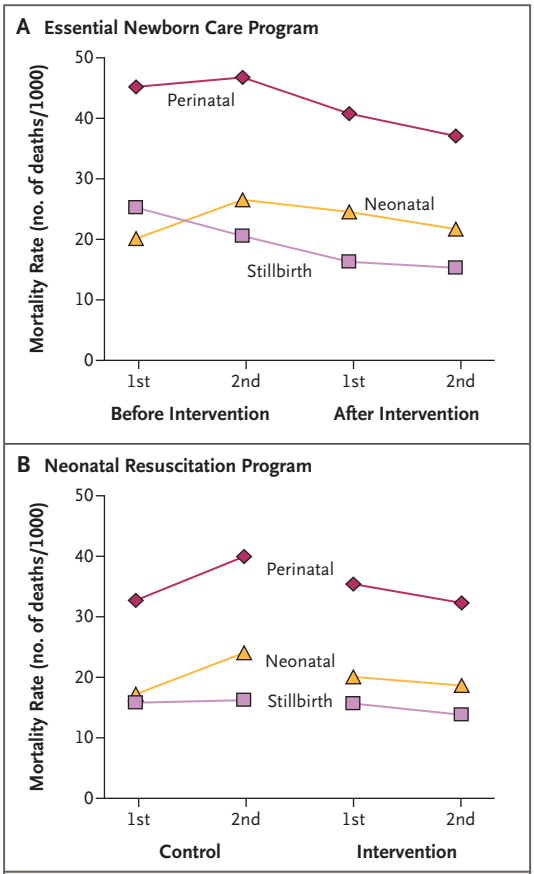

Figure 3. Rates of Stillbirth, Neonatal Death from All Causes in the 7 Days after Birth, and Perinatal Death before and after Training in the Two Programs.

Data are divided into two consecutive phases (1st and 2nd) for each study period. After implementation of the Essential Newborn Care program, the rate of stillbirth decreased significantly (P=0.003). However, the rate of neonatal death from all causes in the 7 days after birth did not change. In the Neonatal Resuscitation Program trial, the rates of stillbirth, perinatal death, and neonatal death from all causes in the 7 days after birth did not differ significantly between the intervention group and the control group.

and stillbirth decreased to levels similar to those associated with deliveries performed by physicians. In addition to the increased survival, there was a decrease in moderately or severely abnormal[17] neurologic findings at the 7-day follow-up assessment. Rates of neonatal death, stillbirth, and perinatal death were not decreased further after training in the Neonatal Resuscitation Program.

The strengths of our studies include the multicountry, population-based design, the large sample sizes, the rigorous training with master instructors, the exclusive use of local trainers to train birth attendants, the use of pregnancy and birth registries to capture data on all births, the inclusion of all birth attendants, and the high rates of consent to participate in the study and of 7-day follow-up assessments. However, a limitation of the study of the Essential Newborn Care course was the before-and-after design. We used an active baseline design, in which all training except the Essential Newborn Care training was conducted before the initiation of data collection. This approach decreased the likelihood that concurrent changes in practice influenced the outcomes,[14] although we cannot rule out this possibility. Because of ethical concerns about withholding a basic WHO course and because of constraints on resources, this intervention was not introduced with a randomization design. Another limitation was that data were collected by the birth attendants who implemented the intervention. However, they were closely supervised by the community coordinators to promote reliable collection of data.

The Essential Newborn Care course has been used previously,[25,26] but the assessment of its effect on outcomes has been limited. A study that involved 1186 newborns in Sri Lanka showed that training doctors, nurses, and midwives in community hospitals in the Essential Newborn Care course improved care practices; however, clinical outcomes were not reported.[27,28] Evaluations of other programs of neonatal care have been reported,[13] but none of the studies were randomized, and most used historical controls. A recently published pilot study of the implementation of community-based perinatal care in four intervention clusters and four control clusters, involving almost 11,000 births, showed that training existing health care workers reduced perinatal mortality.[29] In contrast, implementation of the Integrated Management of Childhood Illness, a package of interventions for the care of children that is designed to be started a week after birth, improved intermediate care indicators but did not decrease mortality.[30]

Previous large, observational studies of resuscitation training in facilities[6,31,32] and communities[33,34] in developing countries have shown that neonatal mortality was reduced among infants whose birth attendants received training, as compared with historical controls. However, one small facility-based trial showed that training in

neonatal resuscitation had no effect on neonatal mortality.[35] The lack of an effect of this training on the rate of perinatal death in our large, randomized trial of neonatal resuscitation could be due to the fact that Essential Newborn Care training, which includes very basic resuscitation training, was already in place before the Neonatal Resuscitation Program was initiated.

In summary, training birth attendants in Essential Newborn Care was not associated with a reduction in neonatal mortality but was associated with reduced rates of stillbirth; further training in neonatal resuscitation did not have a significant effect on outcomes. These data suggest that training in basic neonatal care may have a role in improving perinatal outcomes in the developing world, although more work is needed to further reduce perinatal mortality.

No potential conflict of interest relevant to this article was reported.

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APPENDIX

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REFERENCES

1. Neonatal and perinatal mortality: country, regional and global estimates 2006. Geneva: World Health Organization. (Accessed January 25, 2010, at http://www.who.int/reproductivehealth/docs/neonatal_perinatal_mortality/text.pdf.)
2. Lawn JE, Cousens S, Zupan J. 4 Million neonatal deaths: When? Where? Why? Lancet 2005;365:891-900.
3. Murray CJ, Laakso T, Shibuya K, Hill K, Lopez AD. Can we achieve Millennium Development Goal 4? New analysis of country trends and forecasts of under-5 mortality to 2015. Lancet 2007;370:1040-54.
4. Lawn J, Shibuya K, Stein C. No cry at birth: global estimates of intrapartum stillbirths and intrapartum-related neonatal deaths. Bull World Health Organ 2005;83:409-17.
5. Stanton C, Lawn JE, Rahman HZ, Wilczynska-Ketende K, Hill K. Stillbirth rates: delivering estimates in 190 countries. Lancet 2006;367:1487-94.
6. Deorari AK, Paul VK, Singh M, Vidyasagar D. Impact of education and training on neonatal resuscitation practices in 14 teaching hospitals in India. Ann Trop Paediatr 2001;21:29-33.
7. Conde-Agudelo A, Diaz-Rossello JL, Belizan JM. Kangaroo mother care to reduce morbidity and mortality in low birth weight infants. Cochrane Database Syst Rev 2003;2:CD002771.
8. Darmstadt GL, Bhutta ZA, Cousens S, Adam T, Walker N, de Bernis L. Evidence-based, cost-effective interventions: how many newborn babies can we save? Lancet 2005;365:977-88.
9. Haws RA, Thomas AL, Bhutta ZA, Darmstadt GL. Impact of packaged interventions on neonatal health: a review of the evidence. Health Policy Plan 2007;22:193-215.
10. Essential newborn care. Geneva: World Health Organization, 1996. (Accessed January 25, 2010, at http://www.who.int/reproductive.health/publications/MSM_96_13/MSM_96_13_table_of_contents_en.html.)
11. McClure EM, Carlo WA, Wright LL, Chomba E, Lincetto O, Bann C. Evaluation of the educational impact of the WHO Essential Newborn Care course in Zambia. Acta Paediatr 2007;96:1135-8.
12. Carlo WA, McClure EM, Chomba E, et al. Impact of World Health Organization (WHO) Essential Newborn Care Course (ENC) training: a multicenter study. Presented at the Annual Meeting of the Pediatric Academic Societies, Baltimore, May 2–5, 2009. abstract.
13. Bhutta ZA, Darmstadt GL, Hasan BS, Haws RA. Community-based interventions for improving perinatal and neonatal health outcomes in developing countries: a review of the evidence. Pediatrics 2005;115:519-617.
14. Spilker B. Guide to clinical trials. Philadelphia: Lippincott Williams & Wilkins, 1997.
15. Carlo WA, Wright LL, Chomba E, et al. Educational impact of the neonatal resuscitation program in low-risk delivery centers in a developing country. J Pediatr 2009;154(4):504.e5-508.e5.
16. Basic newborn resuscitation: a practical guide. Geneva: World Health Organization, 1997.
17. Ellis M, Manandhar DS, Manandhar N, Wyatt J, Bolam AJ, Costello AM. Stillbirths and neonatal encephalopathy in Kathmandu, Nepal: an estimate of the contribution of birth asphyxia to perinatal mortality in low-income urban population. Paediatr Perinat Epidemiol 2000;14:39-52.
18. Chakraborty H, Moore J, Carlo WA, Hartwell TD, Wright LL. A simulation based technique to estimate intra-cluster correlation for a binary variable. Contemp Clin Trials 2009;30:71-80.
19. Chakraborty H. The design and analysis aspects of cluster randomized trials. In: Biswas A, Datta S, Fine JP, Segal MR, eds. Statistical advances in the biomedical sciences: clinical trials, epidemiology, survival analysis, and bioinformatics. New York: John Wiley, 2008:67-75.
20. Stokes ME, Davis CS, Koch GG. Categorical data analysis using the SAS system. Cary, NC: SAS Institute, 2000.
21. SAS software, version 9.1.3. Cary, NC: SAS Institute, 2007.
22. Spector JM, Daga S. Preventing those so-called stillbirths. Bull World Health Organ 2008;86:315-6.
23. Daga SR, Daga AS, Dighole RV, Patil RP, Dhinde HL. Rural neonatal care: Dahanu experience. Indian Pediatr 1992;29:189-93.
24. Cowles W. Decreasing perinatal mortality in rural India: a basic neonatal resuscitation program. Acad Emerg Med 2007;14:e109.

25. Uxa F, Bacci A, Mangiaterra V, Chiaffoni GP. Essential newborn care training activities: 8 years of experience in Eastern European, Caucasian and Central Asian countries. Semin Fetal Neonatal Med 2006;11:58-64.
26. Vidal SA, Ronfani L, da Mota Silveira S, et al. Comparison of two training strategies for essential newborn care in Brazil. Bull World Health Organ 2001;79:1024-31.
27. Senarath U, Fernando DN, Rodrigo I. Newborn care practices at home: effect of a hospital-based intervention in Sri Lanka. J Trop Pediatr 2007;53:113-8.
28. *Idem*. Effect of training care providers on practice of essential newborn care in hospitals in Sri Lanka. J Obstet Gynecol Neonatal Nurs 2007;36:531-41.
29. Bhutta ZA, Memon ZA, Soffi S, Salat MS, Cousens S, Martines J. Implementing community-based perinatal care: results from a pilot study in rural Pakistan. Bull World Health Organ 2008;86:452-9.
30. Arifeen SE, Hogue DME, Akter T, et al. Effect of the Integrated Management of Childhood Illness strategy on childhood mortality and nutrition in a rural area in Bangladesh: a cluster randomised trial. Lancet 2009;374:393-403.
31. Zhu XY, Fang HQ, Zeng SP, Li YM, Lin HL, Shi SZ. The impact of the neonatal resuscitation program guidelines (NRPG) on the neonatal mortality in a hospital in Zhuhai, China. Singapore Med J 1997;38:485-7.
32. O'Hare BA, Nakakeeto M, Southall DP. A pilot study to determine if nurses trained in basic neonatal resuscitation would impact the outcome of neonates delivered in Kampala, Uganda. J Trop Pediatr 2006;52:376-9.
33. Bang AT, Bang RA, Baitule SB, Reddy HM, Deshmukh MD. Management of birth asphyxia in home deliveries in rural Gadchiroli: the effect of two types of birth attendants and of resuscitation with mouth-to-mouth, tube-mask or bag-mask. J Perinatol 2005;25:Suppl 1:S82-S91.
34. Kumar R. Training traditional birth attendants for resuscitation of newborns. Trop Doct 1995;25:29-30.
35. Opiyo N, Were F, Govedi F, Fegan G, Wasunna A, English M. Effect of newborn resuscitation training on health worker practices in Pumwani Hospital, Kenya. PLoS One 2008;3(2):e1599.