ORIGINAL ARTICLE

Outcomes of a Program to Reduce Birth-Related Mortality in Tanzania

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ABSTRACT

BACKGROUND

Birth-related mortality is a major contributor to the burden of deaths worldwide, especially in low-income countries. The Safer Births Bundle of Care program is a combination of interventions developed to improve the quality of care for mother and baby with the goal of reducing birth-related mortality.

METHODS

We performed a 3-year stepped-wedge cluster-randomized study of the Safer Births program at 30 high-burden facilities in five regions in Tanzania. The bundle of interventions in the program was aimed at continuous quality improvement through regular onsite simulation-based training, the collection and use of local clinical data, the assistance of trained local facilitators, and the use of innovative tools for perinatal care. The primary outcome was perinatal death, which included intrapartum stillbirth (suspected death during labor) and neonatal death within the first 24 hours after birth.

RESULTS

A total of 281,165 mothers and 277,734 babies were included in the final analysis. The estimated incidence of perinatal death decreased from 15.3 deaths per 1000 births in the baseline period of the program to 12.5 deaths per 1000 births after implementation (adjusted relative risk, 0.82; 95% confidence interval [CI], 0.73 to 0.92; P=0.001), with substantial heterogeneity among regions. The incidence of intrapartum stillbirths was 8.6 deaths per 1000 births in the baseline period and 8.7 deaths per 1000 births after implementation (adjusted relative risk, 1.01; 95% CI, 0.87 to 1.17), and the incidence of neonatal deaths within the first 24 hours after birth was 6.4 and 3.9 deaths per 1000 births, respectively (adjusted relative risk, 0.61; 95% CI, 0.49 to 0.77). No serious adverse events were reported.

CONCLUSIONS

Implementation of the Safer Births Bundle of Care program showed the feasibility of integrating quality-improvement efforts targeting birth-related emergencies in resource-limited settings and was associated with a significant reduction in perinatal mortality. (Funded by the Global Financing Facility; ISRCTN Registry number, ISRCTN30541755.)

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*A list of the members of the Safer Births Bundle of Care Study Group is provided in the Supplementary Appendix, available at NEJM.org.

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Birth-related mortality is a major contributor to the burden of deaths worldwide, ranking eighth globally and third in low-income countries.[1] Most stillbirths and neonatal and maternal deaths are preventable if basic quality care is provided, especially during birth, when the mother and baby share common risk factors and complications and jointly benefit from various interventions.[2] In 2020, an estimated 4.5 million combined deaths occurred globally: 0.3 million maternal deaths, 2.3 million neonatal deaths, and 1.9 million stillbirths.[3-5] Ten countries, including Tanzania, account for 60% of this burden.[2]

The World Health Organization (WHO) and the Sustainable Development Goals have specified targets regarding birth-related deaths to reach by 2030.[6,7] These targets include reducing the incidence of stillbirths to at least as low as 12 deaths per 1000 births,[6] the incidence of neonatal deaths to at least as low as 12 deaths per 1000 live births, and maternal deaths to lower than 70 deaths per 100,000 live births.[7] In 2020, global maternal mortality was estimated to be 223 deaths per 100,000 live births.[3] In 2022, the estimated global incidences of neonatal deaths and stillbirths were 17 deaths per 1000 live births and 14 deaths per 1000 births, respectively.[4,5] Approximately 45% of stillbirths are related to complications that occur during the intrapartum period. Annual incidences of reduction in stillbirths and neonatal and maternal deaths are currently too slow to meet the global goals for 2030.[2-5]

The Safer Births Bundle of Care was created to combat birth-related mortality, with an approach that targets intrapartum stillbirths and neonatal and maternal deaths simultaneously.[8,9] The bundle was developed in Tanzania, iteratively over a 10-year period, to improve the quality of care around the time of birth and consists of four main components: innovative simulation training methods and equipment, strategies for data-guided continuous quality-improvement efforts, innovative clinical devices for fetal and neonatal heart-rate monitoring, and processes to support sustainability and scalability. The Helping Babies Breathe[10] (American Academy of Pediatrics) and Helping Mothers Survive Bleeding After Birth Complete, version 2.0,[11] scenarios were integrated into the training component. All the innovative training and quality-improvement strategies and devices were tested separately in multiple studies before being merged into the bundle.[8]

In 2020, the Safer Births Bundle of Care received an Innovation-to-Scale award from the Global Financing Facility to undertake the first phase of implementation at 30 facilities in five regions with a high burden of birth-related deaths in Tanzania, involving approximately 300,000 births over a 3-year period. The primary aim of this study was to document the effect of the interventions on in-hospital perinatal mortality.

METHODS

STUDY OVERSIGHT

Staff at the Haydom Lutheran Hospital, in collaboration with the Ministry of Health, President's Office-Local Government and Regional Authority, professional bodies, and UNICEF in Tanzania, and at the SAFER Simulation Center, Stavanger University Hospital, and Laerdal Global Health in Norway were responsible for implementation. The study was approved by ethics committees in Tanzania and Norway and by the management staff at each participating facility. Women who were in labor were informed about the bundle. Consent from participants was not deemed necessary for this quality-improvement study, given that there were no anticipated risks. The first authors and two authors from the Section of Biostatistics at Stavanger University Hospital vouch for the accuracy and completeness of the data and for the fidelity of the study to the protocol, available with the full text of this article at NEJM.org.

STUDY DESIGN AND SITES

We designed a stepped-wedge cluster-randomized implementation study, including five wedges (regions) with six health facilities each.[8] This design allowed for learning and adjustments, with all the sites eventually receiving the bundle of interventions. The five regions and 30 facilities were selected on the basis of the following inclusion criteria: a consistently high burden of stillbirths and neonatal and maternal deaths, a high volume of deliveries, and categorization as a Comprehensive Emergency Obstetric and Newborn Care (CEmONC) facility. Manyara was intentionally selected as the first region to receive the intervention owing to logistic reasons, whereas subsequent regions were selected at random with the use of simple randomization.

An overview of the project, including details about the regions, health facilities, and project phases from January 2021 through December 2023, is shown in Figure S1 in the Supplementary Appendix, available at NEJM.org. Baseline data collection, with weekly feedback to improve routine clinical data documentation, started at all sites on March 1, 2021. After a transition period, full implementation of the bundle began in Manyara on July 3, 2021, in Tabora on September 25, 2021, in Geita on December 6, 2021, in Shinyanga on March 2, 2022, and in Mwanza on March 6, 2022.

PATIENT POPULATION

The average annual number of births that occurred during the study ranged from 400 to 8000 across the 30 facilities. We enrolled all women in labor and their babies (>28 weeks' gestational age, weighing >800 g, or both).

COMPONENTS AND INTERVENTIONS

The bundle of interventions (Fig. S2) was composed of four main components: training innovations, continuous quality improvement, clinical innovations for fetal and neonatal assessment and ventilation, and efforts to ensure sustainability and scalability of interventions. Training innovations included new training strategies and tools for frequent onsite skills training and team simulation training. From January through February 2021, a total of 15 selected national facilitators representing all the regions were trained by experts in simulation and debriefing techniques with the use of the SimBegin course (Fig. S3).[12] The national facilitators then trained 90 local facilitators and facility champions (2 to 3 per site). Local facilitators received formal training in the SimBegin course. Facility champions received informal training to motivate health care workers in their wards and provide support in onsite training sessions. During the transition period, national and local facilitators trained relevant health care providers at each site. The training was based on the Helping Babies Breathe and Helping Mothers Survive Bleeding After Birth scenarios, with a focus on in situ team simulations and reflective debriefing. Innovative simulators (Laerdal Global Health), which were delivered to every site, included NeoNatalie Live for newborn resuscitation training[13,14] and MamaNatalie for training on identification, prevention, and management of postpartum bleeding.[15,16]

Continuous quality-improvement interventions were driven by the local champions and facilitators, in accordance with strategies developed at Haydom Lutheran Hospital[17-19] and as shown in the Circle of Learning model (Fig. S4). After the start of the implementation period, local facilitators received weekly statistics on clinical performance and patient indicators (i.e., patient outcomes, referrals, fetal heart-rate abnormalities, newborn Apgar scores, and maternal postpartum bleeding) plus training data, so they could adjust the focus of the training program on the basis of identified gaps or needs. Local facilitators were expected to motivate providers to complete frequent individual skills training sessions, help new providers start training, and lead regular team simulations with reflective debriefing, with a focus on newborn resuscitation and postpartum bleeding. The integration of training and clinical care, innovative tools, data collection, and feedback systems facilitated continuous quality-improvement efforts (Fig. S5).

Clinical innovations in this study (all from Laerdal Global Health) included the Moyo Fetal Heart Rate Monitor for fetal heart-rate monitoring,[20-22] the NeoBeat Newborn Heart Rate Meter for immediate assessment at birth (e.g., to distinguish stillbirth from newborns with asphyxia or hypoxia) and for guiding resuscitation attempts,[23] and the Upright Bag Mask for easier bag-mask ventilation of newborns who were not breathing.[24]

Sustainability and scalability were supported through close collaboration with national, regional, and local health authorities and through alignment with national guidelines for obstetrical and newborn care. A "training corner" was created at each labor ward. A mentorship program was established to support the national facilitators, who conducted regular visits to each facility for supportive supervision and mentored the local champions and facilitators.

DATA COLLECTION AND MANAGEMENT

Two data collectors at each site prospectively gathered selected data (e.g., characteristics of mothers and newborns and outcomes up to 7 days after birth) recorded by providers in labor monitoring charts and patient files, which were then entered into an electronic data-collection system. All data were deidentified. Any adverse events related to the medical devices or to training (e.g., suspected worse clinical performance) were reported by providers during the supervision visits.

OUTCOMES

The primary outcome was perinatal death, defined as intrapartum stillbirth (suspected death during labor) or neonatal death within the first 24 hours after birth. A complete list of the prespecified secondary outcomes, many of which were process measures, and additional clinical outcomes, are listed in (Table S1).

STATISTICAL ANALYSIS

The sample size was calculated according to the planned stepped-wedge design on the basis of an assumption of an intracluster correlation of 0.0013.[25] We estimated that 240,000 mother–baby pairs would provide the study with a power of 99% to detect a 25% reduction in perinatal deaths from 20 deaths per 1000 births to 15 deaths per 1000 births.[8,26]

The effects of the bundle of interventions were assessed with the use of logistic-regression models, which allowed for differing effects among regions, and were adjusted for a range of prespecified prognostic covariates. Adjusted marginal relative risks were standardized to the total population by means of G-computation[27] and reported with 95% confidence intervals on the basis of cluster-robust standard errors and the delta method. Similarly, adjusted marginal predictions[27] were estimated for each study period. The heterogeneity of the intervention effects among regions was tested.[28] The numbers of lives saved were calculated from estimated risk differences in perinatal mortality[29] and illustrated by means of variable life-adjusted displays.[30] To handle missing covariate data, we performed multiple imputation. Overall time trends in mortality were estimated with the use of Poisson regression. Sensitivity analyses assessed the affect of modeling choices and assumptions regarding missing outcome data. Detailed descriptions of statistical considerations, including sensitivity analyses, are included in the Supplementary Appendix. The formal statistical analysis plan was finalized after data were available.

RESULTS

INTERVENTIONS

After the start of implementation, a total of 125,758 individual NeoNatalie Live skills training sessions and 1294 facilitator-led team simulations were recorded. The uptake of the Moyo and NeoBeat heart-rate monitors is shown in Figure S6.

PARTICIPANTS

At the start of the study, 464 health care providers were on staff in the 30 labor wards, a number that remained similar for the duration of the study. A total of 281,165 mothers and 277,734 babies were included in the final analysis. The average annual numbers of births and providers for the 30 facilities are available in the Supplementary Appendix, as are the numbers of mothers and babies who were included in the final analysis (Fig. S7).

Table 1 describes the overall characteristics of the mothers, newborns, and facilities in the baseline, transition, and implementation periods; data are shown according to region in Tables S2 and S3. In Shinyanga, the mean percentage of babies with an abnormal fetal heart rate at the time of admission at a study facility was 1.9% in the baseline period and 4.3% after implementation; no material changes over time were noted for this measure in the other regions.

PRIMARY OUTCOME

The observed incidence of perinatal death in the baseline period was 15.9 deaths per 1000 births overall and varied among the sites, from 7.9 deaths per 1000 births in Mwanza to 27.3 deaths per 1000 births in Tabora (Table 2). After implementation of the Safer Births program, the estimated adjusted incidence of perinatal death decreased significantly, from 15.3 deaths per 1000 births in the baseline period to 12.5 deaths per 1000 births after implementation (adjusted relative risk, 0.82; 95% confidence interval [CI], 0.73 to 0.92; P=0.001), which corresponded to an estimated 18% relative risk reduction overall, with substantial variation among the regions.

Table 1. Characteristics of Mothers, Newborns, and Health Facilities in the Baseline, Transition, and Implementation Periods in All Regions Combined.*

Variable	Baseline N=63,868	Transition N=7,227	Implementation N=210,070
Maternal age			
Age — yr	25.6±6.5	25.7±6.5	25.8±6.5
Missing data — no. (%)	224 (0.4)	12 (0.2)	326 (0.2)
Parity			
No. of previous births	2.1±2.2	2.1±2.2	2.1±2.2
Missing data — no. (%)	807 (1.3)	7 (0.1)	118 (0.1)
Any previous intrapartum stillbirth			
No./total no. with data (%)	6,078/60,839 (10.0)	712/7,095 (10.0)	19,688/206,631 (9.5)
Missing data — no. (%)	3,029 (4.7)	132 (1.8)	3,439 (1.6)
Multiple gestation — no. (%)†	886 (1.4)	92 (1.3)	4,068 (1.9)
Referral from other facility			
No./total no. with data (%)	2,324/62,103 (3.7)	382/6,905 (5.5)	8,859/201,066 (4.4)
Missing data — no. (%)	1,765 (2.8)	322 (4.5)	9,004 (4.3)
Fetal heart rate on admission — no. (%)			
>160 beats/min	107 (0.2)	21 (0.3)	990 (0.5)
120–160 beats/min	53,297 (97.5)	6,061 (97.4)	179,069 (96.8)
80–119 beats/min	194 (0.4)	35 (0.6)	1,000 (0.5)
<80 beats/min	1,078 (2.0)	109 (1.8)	4,005 (2.2)
Missing data	9,192 (14.4)	1,001 (13.9)	25,006 (11.9)
Noncephalic fetal presentation			
No./total no. with data (%)	1,045/57,174 (1.8)	148/6,350 (2.3)	4,505/187,450 (2.4)
Missing data — no. (%)	6,694 (10.5)	877 (12.1)	22,620 (10.8)
Birth weight			
Weight — g	3,118±501	3,128±494	3,127±502
Missing data — no. (%)	545 (0.9)	39 (0.5)	980 (0.5)
Female sex			
No./total no. with data (%)	30,784/63,650 (48.4)	3,413/7,209 (47.3)	100,455/209,687 (47.9)
Missing data — no. (%)	218 (0.3)	18 (0.3)	383 (0.2)
Antepartum stillbirth — no. (%)‡	671 (1.1)	92 (1.3)	2668 (1.3)
Level of health facility — no. (%)			
Health center	19,420 (30.4)	1,901 (26.3)	63,345 (30.2)
District hospital	32,889 (51.5)	4,134 (57.2)	116,288 (55.4)
Regional referral hospital	11,559 (18.1)	1,192 (16.5)	30,437 (14.5)
Staff density§	5.0±2.7	5.5±3.1	5.3±3.0

* Plus–minus values are means ±SD. The percentage of missing observations was calculated from total data. Other percentages were calculated from nonmissing data.
† In cases of multiple gestation, only the first baby was included in the analyses. No data were missing for this variable.
‡ Antepartum stillbirths were excluded from the analysis of perinatal and newborn outcomes and were used as an adjustment variable in the analysis of maternal outcome. No data were missing for this variable.
§ Staff density, which was assumed to be constant throughout the observation period, was calculated with the following formula: number of health care workers at the facility in the first year of the study period, divided by the average number of births per month at the facility during the study period, multiplied by 100.

Table 2. Observed and Estimated Incidences of Perinatal Death (Primary Outcome) and Its Components.*

Outcome	Baseline		Implementation		Baseline	Implementation	Implementation vs. Baseline
	Missing Data	Observed Incidence†	Missing Data	Observed Incidence†	Estimated Incidence‡§	Estimated Incidence‡§	Adjusted Relative Risk (95% CI)‡¶
	no. (%)	*no. per thousand (no./total no.)*	*no. (%)*	*no. per thousand (no./total no.)*	*no. per thousand (95% CI)*	*no. per thousand (95% CI)*	
Primary outcome							
Perinatal death							
Overall	1,432 (2.27)	15.9	925 (0.45)	12.5	15.3 (13.3 to 17.3)	12.5 (11.0 to 14.0)	0.82 (0.73 to 0.92)‖
Manyara	586 (15.0)	19.9 (66/3,315)	103 (0.29)	7.9 (277/35,051)	16.9 (8.9 to 24.8)	10.2 (6.8 to 13.6)	0.61 (0.47 to 0.79)
Tabora	203 (3.20)	27.3 (168/6,149)	298 (0.75)	23.7 (932/39,248)	19.1 (16.1 to 22.1)	18.0 (14.8 to 21.2)	0.94 (0.79 to 1.12)
Geita	60 (0.34)	16.7 (296/17,743)	39 (0.06)	9.9 (602/60,881)	20.8 (14.3 to 27.4)	15.3 (11.2 to 19.5)	0.73 (0.61 to 0.90)
Shinyanga	261 (1.72)	10.2 (152/14,950)	136 (0.41)	11.9 (393/33,076)	12.6 (11.2 to 14.0)	7.2 (4.7 to 9.8)	0.58 (0.39 to 0.84)
Mwanza	322 (1.62)	7.9 (154/19,608)	349 (0.90)	11.0 (421/38,221)	7.8 (4.6 to 11.1)	11.6 (7.8 to 15.5)	1.49 (1.15 to 1.92)
Components of the primary outcome							
Intrapartum stillbirth	281 (0.44)	8.8	0	8.6	8.6 (7.4 to 9.9)	8.7 (7.6 to 9.7)	1.01 (0.87 to 1.17)
Neonatal death within 24 hours after birth	1,432 (2.28)	6.8	925 (0.45)	3.9	6.4 (5.0 to 7.8)	3.9 (3.3 to 4.6)	0.61 (0.49 to 0.77)

* The populations for the primary outcome and its components, including the transition period, were as follows: perinatal death, N=275,313; intrapartum stillbirth, N=277,453; and neonatal death within 24 hours after birth, N=272,936. Details regarding additional secondary newborn characteristics and treatment outcomes are available in the Supplementary Appendix. CI denotes confidence interval.

† The overall observed incidences are averages of the incidences for each region weighted by the total number of observations in the baseline and implementation periods, combined, in each region.

‡ Estimates were assessed with the use of logistic-regression models with standard errors robust to clustering on health facilities. The first baby of multiple births was included in the analysis. No secular trend was assumed. Adjustments have been made for the variables of the mothers, newborns, and health facilities. Missing values in adjustment variables were handled with multiple imputation (generating five imputed data sets) and results pooled by means of Rubin's rule. Maternal age, parity, and birth weight were also included as quadratic terms.

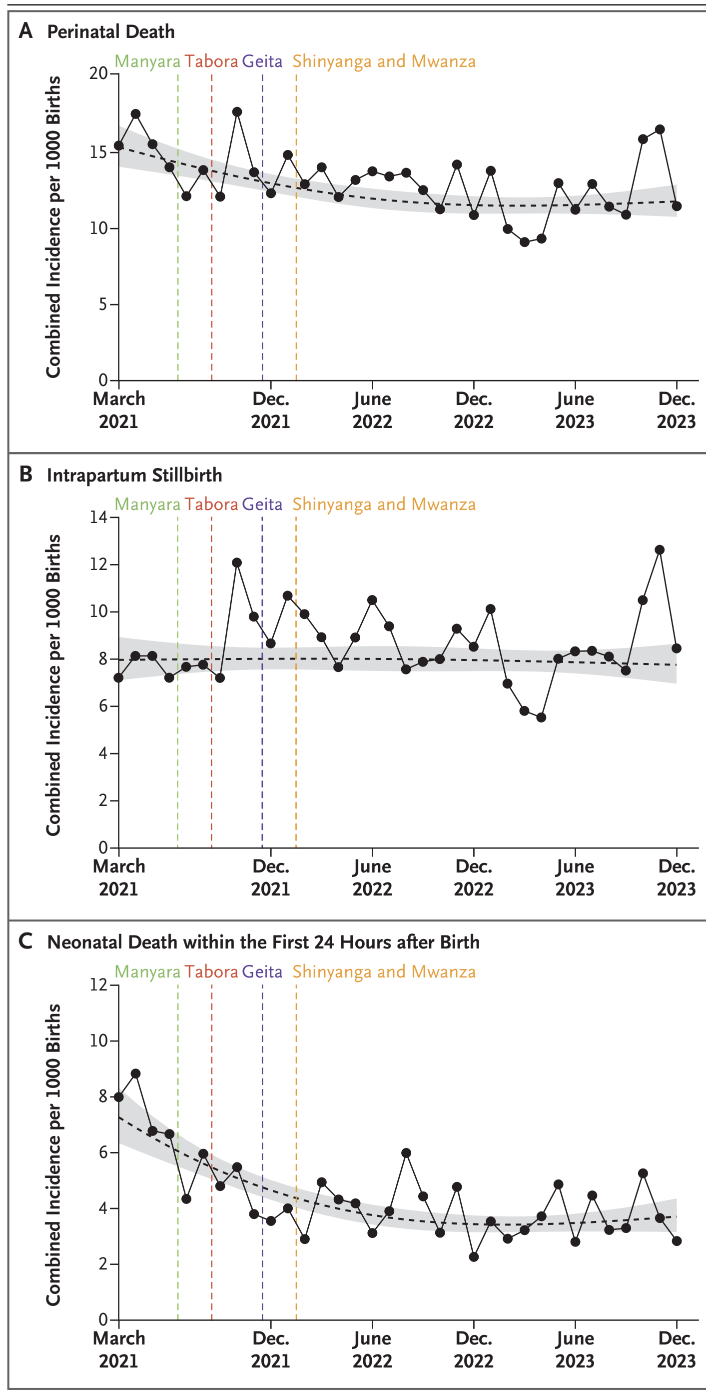
§ Estimated incidences are given as adjusted marginal predictions; predicted rates were calculated with the assumption that all participants were observed with their covariate values (sometimes imputed) in the baseline and implementation periods.

¶ The adjusted marginal relative risk was calculated for the results of the implementation period as compared with those of the baseline period.

‖ P=0.001. Confidence intervals for the estimates in each region and for the components of the primary outcome were not corrected for multiplicity and should not be used in place of hypothesis testing.

Figure 1. Monthly Incidence of Death per 1000 Births in All Regions Combined.

Shown are the combined monthly incidence (black dots) of perinatal death (Panel A), intrapartum stillbirth (Panel B), and neonatal death within the first 24 hours after birth (Panel C). Dashed vertical lines show the start of the implementation period in each region. Nonlinear dashed lines show the estimated overall expected incidence of death as a function of time. These estimates were based on Poisson regression models for the regional counts, with marginalization over the regions and modeling of the time trend by means of a natural cubic spline. The shaded gray areas represent pointwise 95% confidence intervals. Confidence intervals for intrapartum stillbirth and neonatal death within the first 24 hours after birth were not adjusted for multiplicity and should not be used in place of hypothesis testing.

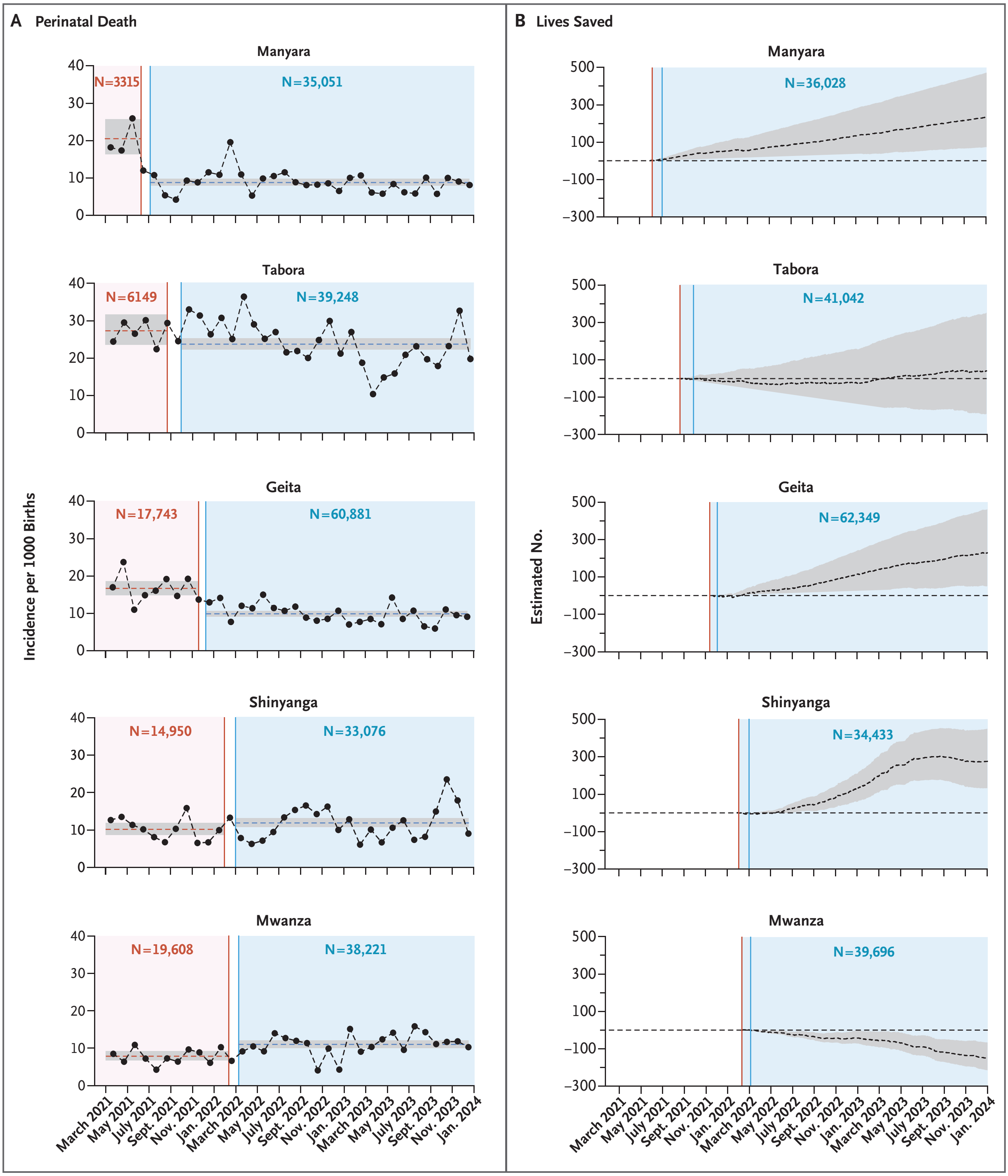


For example, relative risk reductions of 27 to 42% were observed in Geita, Manyara, and Shinyanga; no change was observed in Tabora; and a 49% higher risk was observed in Mwanza. Overall, an estimated 580 perinatal lives (95% CI, 225 to 935), or 2.8 perinatal lives per 1000 births (95% CI, 1.1 to 4.5), were saved by the end of the implementation period. With respect to the individual components of the primary outcome, the overall incidence of intrapartum stillbirths was 8.6 deaths per 1000 births in the baseline period and 8.7 deaths per 1000 births after implementation (adjusted relative risk, 1.01; 95% CI, 0.87 to 1.17), and the overall incidence of neonatal deaths within the first 24 hours after birth was 6.4 and 3.9 deaths per 1000 births, respectively (adjusted relative risk, 0.61; 95% CI, 0.49 to 0.77) (Table 2 and Fig. 1). The results for each region are available in Table S4. The perinatal mortality trends and the estimated number of lives saved according to region are provided in Figure 2. Mortality trends for intrapartum stillbirth and neonatal death within the first 24 hours after birth (components of the primary outcome) are shown in Figures S8 and S9, respectively.

Analysis with imputed data showed no substantial differences from the primary analysis in the characteristics of the mothers and babies (Table S6). The reduction in the risk of perinatal death was maintained across sensitivity analyses that explored additional adjustments and hypothetical missing data mechanisms for the patient outcomes (Tables S7 through S12).

ADDITIONAL ANALYSES

The estimated adjusted incidence of perinatal death within the first 7 days after birth was 16.6 deaths per 1000 births in the baseline period and 13.9 deaths per 1000 births after implementation (adjusted relative risk, 0.84; 95% CI, 0.75 to 0.94) (Table S4). Overall and regional trends



in perinatal mortality within the first 7 days after birth are shown in Figures S10 and S11, respectively. Observed incidences of neonatal death from 2 to 7 days after birth and antepartum stillbirth are shown in Figures S12 and S13, respectively.

The estimated adjusted incidence of in-hospital maternal death within the first 7 days after birth

Figure 2 (facing page). Monthly Incidence of Perinatal Death over Time and Estimated Number of Lives Saved after Start of Implementation Period in Each Region.

Shown for each region is the observed monthly incidence (black dots) of perinatal death per 1000 births (Panel A) during the study period. The N values are the numbers of babies included in the baseline (left, shaded red area) and implementation (right, shaded blue area) periods. The red dashed line represents the mean incidence in the baseline period, the red solid line indicates the start of the transition period, the blue solid line indicates the start of the implementation period, and the blue dashed line represents the mean incidence in the implementation period. The estimated number of lives saved (Panel B) was calculated from both the transition and implementation periods (shaded blue area) for each region by aggregating the differences between the estimated probability for fatal outcome under baseline conditions and the observed outcomes, taking into account prognostic covariates. Shaded gray areas represent 95% confidence intervals. Confidence intervals have not been adjusted for multiplicity and should not be used in place of hypothesis testing.

was 240 deaths per 100,000 births in the baseline period and 60 deaths per 100,000 births after implementation (adjusted relative risk, 0.25; 95% CI, 0.14 to 0.46). Overall and regional trends in maternal mortality are available in Figures S14 and S15, respectively. Descriptive data on newborn variables with respect to the process measures included in the prespecified secondary outcomes are shown in Tables S13 and S14.

No serious adverse events were reported. Two instances of incorrect use of the Moyo monitor occurred early in the implementation period and resulted in retraining of correct use.

DISCUSSION

We documented an estimated risk of perinatal death that was 18% lower overall after implementation of the Safer Births program than before. The reduction was driven by a decrease in the risk of neonatal death within the first 24 hours after birth, which appeared to be almost 40% lower after implementation of the study intervention; no material change in the risk of intrapartum stillbirth was noted. Steady reductions in perinatal mortality occurred during the stepped-wedge implementation process, and a sustained lower mortality was observed after full implementation.

The primary outcome, perinatal death, was a combination of intrapartum stillbirth and neonatal death within the first 24 hours after birth, which reflects the time period when babies are most likely to die due to the pathophysiological end process of birth asphyxia.[31] We chose this composite outcome because of the potential for misclassification of asphyxiated newborns who had been born alive as intrapartum stillbirths.[31] Although the study showed a significant reduction overall in perinatal mortality after implementation of the intervention, the estimated intervention effects in the five study regions varied from a 42% lower to a 49% higher risk of death. This variation can probably be explained in part by underreporting of perinatal deaths in the baseline period,[32,33] especially in Shinyanga and Mwanza, where an unexpected inconsistency was observed in the baseline period between the incidence of maternal death (which was high) and the incidence of perinatal death (which was relatively low). After adjustment for the higher perinatal risk profile observed after implementation in Shinyanga, the risk of perinatal death declined after implementation in this region. The higher incidence of perinatal death in Tabora than in other regions may be explained in part by the higher percentage of women admitted late in labor at the health facilities in this region; we previously reported that intrapartum stillbirths are overrepresented among women referred late in labor.[9]

The substantial decline in neonatal death within the first 24 hours after birth that was observed after implementation of the Safer Births program may be attributable to frequent training on newborn resuscitation that continuously included new providers and the use of innovative clinical tools, including the NeoBeat heart-rate monitor and the Upright resuscitator for newborns. Severely asphyxiated newborns who are successfully resuscitated at birth and who survive the first day after birth may die due to hypoxic–ischemic organ failure within the next few days, particularly in low-resource settings that do not have advanced medical care available for newborns. However, findings from additional analyses of the incidences of perinatal death within the first 7 days after birth and of neonatal deaths from 2 to 7 days after birth do not suggest that an increase in mortality occurs over time.

Factors contributing to the absence of an apparent change in recorded intrapartum stillbirths may include the lack of systematic team simulations to address the management of the labor process and the possibility that delays between the decision to deliver and the actual delivery of babies who had asphyxia or hypoxia may have resulted from infrastructure challenges beyond the scope of this project (e.g., no available theater, vacuum, or doctors, or a combination of these). Moreover, the adoption of the Moyo fetal heart-rate monitor was gradual; it was not until approximately 1 year after the intervention was introduced that this monitor was used in 60 to 80% of deliveries.

Overall, the estimated in-hospital maternal death incidence decreased from approximately 240 deaths per 100,000 births in the baseline period to approximately 60 deaths per 100,000 births after full implementation. The study design precludes a conclusion regarding cause and effect, but we postulate that postpartum bleeding team simulations with reflective debriefings that were led by trained facilitators may have played a role in the apparent reduction. None of the sites had access to calibrated blood-loss drapes or tranexamic acid, both of which have been shown to reduce severe postpartum bleeding and associated complications.[34]

A recent qualitative study involving interviews with providers and managers at 22 of the 30 facilities in this study[32] indicated that after implementation of the bundle of interventions, midwives reported greater confidence in recognizing emergencies (e.g., babies who were not breathing and excessive postpartum bleeding) and starting effective actions while waiting for a doctor. Providers also reported that the "blame and shame" culture was lessened, which led to improved self-confidence and safety.[32]

The study was conducted in regions in which the intervention was most needed; however, it is also challenging to conduct meticulous research in such regions, and some of the limitations of this study should be noted. All baseline periods were shorter than initially planned because anticipation of reduced mortality led to pressure to accelerate implementation; these shortened baseline periods may have increased uncertainty in the baseline risk estimates. There were substantial missing data with respect to some of the secondary process outcomes and, to a lesser extent, the mortality outcomes. After implementation of the program, which included a focus on improved reporting, there were fewer missing data on perinatal mortality and additional patient outcomes, and the incidence of perinatal death was similar in four of the five regions. Results were robust in analyses addressing missing data. We also suspect differential underreporting of perinatal deaths among the regions, especially in the baseline period. In addition, the stepped-wedge design poses a risk of contamination among regions, which may dilute observed effects of the intervention.

In this study, a significant reduction in perinatal mortality was observed after implementation of the Safer Births Bundle of Care program. The study population was representative of populations in similar resource-limited regions (Table S15). Our findings indicate that it is possible to quickly achieve major improvements in birth outcomes in these settings with a combined intervention strategy for the mother–baby dyad[35] that involves frequent on-the-job simulation training and the use of innovative tools. Further data are needed to inform the effects of the bundle more broadly; the Safer Births program is currently scaled to all 152 CEmONC facilities in the five regions.

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