The effects of a peripartum strategy to prevent and treat primary postpartum haemorrhage at health facilities in Niger: a longitudinal, 72-month study

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Summary

Background Primary postpartum haemorrhage is the principal cause of birth-related maternal mortality in most settings and has remained persistently high in severely resource-constrained countries. We evaluate the impact of an intervention that aims to halve maternal mortality caused by primary postpartum haemorrhage within 2 years, nationwide in Niger.

Methods In this 72-month longitudinal study, we analysed the effects of a primary postpartum haemorrhage intervention in hospitals and health centres in Niger, using data on maternal birth outcomes assessed and recorded by the facilities' health professionals and reported once per month at the national level. Reported data were monitored, compiled, and analysed by a non-governmental organisation collaborating with the Ministry of Health. All births in all health facilities in which births occurred, nationwide, were included, with no exclusion criteria. After a preintervention survey, brief training, and supplies distribution, Niger implemented a nationwide primary postpartum haemorrhage prevention and three-step treatment strategy using misoprostol, followed if needed by an intrauterine condom tamponade, and a non-inflatable anti-shock garment, with a specific set of organisational public health tools, aiming to reduce primary postpartum haemorrhage mortality.

Findings Among 5 382 488 expected births, 2 254 885 (41·9%) occurred in health facilities, of which information was available on 1 380 779 births from Jan 1, 2015, to Dec 31, 2020, with reporting increasing considerably over time. Primary postpartum mortality decreased from 82 (32·16%; 95% CI 25·58–39·92) of 255 health facility maternal deaths in the 2013 preintervention survey to 146 (9·53%; 8·05–11·21) of 1532 deaths among 343 668 births in 2020. Primary postpartum haemorrhage incidence varied between 1900 (2·10%; 2·01–2·20) of 90 453 births and 4758 (1·47%; 1·43–1·52) of 322 859 births during 2015–20, an annual trend of 0·98 (95% CI 0·97–0·99; p<0·0001).

Interpretation Primary postpartum haemorrhage morbidity and mortality declined rapidly nationwide. Because each treatment technology that was used has shown some efficacy when used alone, a strategic combination of these treatments can reasonably attain outcomes of this magnitude. Niger's strategy warrants testing in other low-income and perhaps some middle-income settings.

Funding The Government of Norway, the Government of Niger, the Kavli Trust (Kavlifondet), the InFiL Foundation, and individuals in Norway, the UK, and the USA.

Lancet Glob Health 2023; 11: e287–95

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Introduction

Obstetric haemorrhage occurs mostly postpartum and is estimated to cause 16–53% of maternal deaths around the world, with one estimate for the global average being 27%. CIs for maternal deaths caused by obstetric haemorrhage in some regions are higher than 60% (data from 2003 to 2012).[1–4] In northern Africa which Niger borders and resembles, primary postpartum haemorrhage causes 32·0% (95% CI 18·9–47·3) of maternal deaths.[2] Up to 18% of births entail more than 500 mL blood loss in 24 h, the threshold defining primary postpartum haemorrhage.[5,6] About 10·5% of births cause severe excessive maternal bleeding (≥1000 mL) if nothing is done to prevent it.[7] In women who are anaemic, even 250 mL (normal) blood loss can cause problems.[5] Within minutes, healthy women can become critically ill.[5] Death from primary postpartum haemorrhage often occurs within 2 h of bleeding onset.

Niger is, to our knowledge, the first country that has aimed to rapidly reduce mortality and incidence of a biologically non-eradicable condition nationwide using three well documented, low-cost technologies and organisational public health tools from successful disease-eradication programmes.[1,8]

Several factors contributed to Niger's decision to test its integrated, complex intervention, aimed at reducing the mortality associated with primary postpartum haemorrhage: rapid reduction in primary postpartum haemorrhage mortality when a 400 µg misoprostol prevention dose was introduced into a community-based

Research in context

Evidence before this study

We searched PubMed for papers published between Jan 1, 1990, and May 1, 2021, without language restrictions, using the search terms "postpartum hemorrhage" OR "haemorrhage" AND "prevention". The search produced 484 998 results. Adding AND "Africa" to our search terms produced 21 217 results. We reviewed the title of the first 3000 articles, the vast majority from continents other than Africa, and examined the abstract when available and the full article when the abstract indicated possible relevance. Other peer-reviewed, relevant publications, and UN agency reports that we found during the course of our work on primary postpartum haemorrhage from 2010 onwards also contribute to the evidentiary context. The existing evidence documented the efficacy of each technology that we used in the intervention tested in our study. After our study started, a Cochrane systematic review in 2020 and WHO recommendations were published on uterine balloon tamponades, and a March, 2022 article by the authors of the WHO recommendations summarised that uterine balloon tamponades should not be used alone, but as part of a wider range of quality-improvement measures. Although the literature has many articles about primary postpartum haemorrhage mortality, morbidity, and individual interventions, sometimes in combination, we found no articles that discussed systematically combining a set of low-cost technologies and specific public health tools, as described in this study.

Added value of this study

To our knowledge, this prevention and three-step treatment strategy to reduce primary postpartum haemorrhage mortality and incidence nationwide in a severely resource-constrained country is the first of its kind. Drawing on information from 1 380 779 births in health facilities during the initial 72 months, this study demonstrates reductions in primary postpartum haemorrhage morbidity and mortality seen parallel to the implementation of low-cost, heat-stable, recent primary postpartum haemorrhage interventions when these were combined in a systematic manner with a set of 11 public health tools, tools that are usually seen in disease eradication efforts, that could help strengthen the health system at the same time, and that could help improve clinical outcomes more rapidly than would otherwise be possible.

Implications of all the available evidence

There are two principal implications from the evidence. First, Niger's strategy should be replicated in other low-income and perhaps middle-income countries. In Niger, primary postpartum haemorrhage mortality more than halved and incidence decreased by 90% within 1 year to 2 years; if similar results were obtained in other low-income and middle-income countries, the prevention and three-step treatment strategy could become standard operating procedure. The second implication is that if the strategy is to become standard procedure, global production of two low-cost inputs (misoprostol of WHO-approved quality, and non-inflatable anti-shock garments) would need to be rapidly scaled up, involving collaboration between the international community, including UN agencies and manufacturers of misoprostol and non-inflatable anti-shock garments, to increase global production to the required levels, including for multination studies.

project designed to prevent obstetric fistula (data unpublished); 29% of Niger's maternal deaths reportedly being caused by haemorrhage; the severe implications of primary postpartum haemorrhage in resource-constrained situations generally; and key elements of primary postpartum haemorrhage management (blood-loss measurement, intrauterine condom tamponade, and non-inflatable anti-shock garments [NASG]) being presented individually at the 20th World Congress of Gynaecology and Obstetrics preconference in Rome, in October, 2012.[2,9,10] This study describes the results from 72 months (2015–20) of nationwide implementation of the intervention in Niger.

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Methods

Study design and participants

In this longitudinal study, we assessed the effects of a primary postpartum haemorrhage intervention in all hospitals and health centres in Niger using data on maternal birth outcomes assessed and recorded by each facility's health professionals, reported monthly in aggregated, deidentified form to the national level. The inclusion criterion was all births occurring in all health facilities, with no exclusion criteria. The intervention was implemented after a preintervention survey, brief training, and supplies distribution. Outcome reports were assessed by Health and Development International, a collaborating non-governmental organisation.

Niger's health system, structured into strategic (national), technical (regional), and operational (district) levels had, in 2020, one national maternity hospital, eight regional public health teams with eight regional maternity hospitals, 72 district teams with 35 district hospitals, and 1217 peripheral health centres (typically with one or two health professionals, often without running water or electricity), serving 23·2 million people across 1·27 million km².

Niger's National Consultative Ethics Committee considered and approved monitoring and evaluation aspects (deliberation 006/2016/CCNE, letter dated March 24, 2016) because a portion of the monitoring and evaluation was structured as a study, whereas the Ministry of Health (MOH) implementing the interventions itself as a typical programme, strengthening its reproductive health services using well documented technologies, does not require Committee approval. As neither randomisation

nor person-related inclusion criteria were used, and no identifying information was sent from any health facility about any person, written informed consent was not indicated.

Procedures

Niger's strategy to prevent women from bleeding to death at childbirth and the science behind it have been described.[1] Preintervention data from Nov 1, 2012, to Oct 31, 2013, were collected in November to December, 2013, from all of the hospitals and a subset of peripheral health centres in Niger. Clinics to be surveyed were divided into three strata according to size, listed by district to ensure a sample was taken from each district, and then selected with probability proportional to population size. At selected clinics, records for the preceding 12 months were examined for frequency and causes of maternal deaths, excluding one of Niger's then 42 districts, the Bilma District in the Agadez region, because of its Saharan, desert characteristics that make it unsafe for travel because of insecurity. Records were examined in 150 of the 847 then-existing health centres. Deaths were recorded using five categories, comprising "obstructed labour", "primary postpartum haemorrhage", "eclampsia", "infection", and "other causes".

The Niger MOH's primary postpartum haemorrhage prevention and three-step treatment strategy is a community-based and health facility-based complex intervention launched after the preintervention survey, and restarted after December, 2014 supervision showed cascade training and provisioning to have been unsuccessful. In 2015, introduced from January onwards, all health personnel in every health facility where births occur received 90-min theoretical and hands-on training, and supplies from national teams.[1,8] Implementation commenced immediately, with reporting to start that same month.

Niger's primary postpartum haemorrhage intervention aimed to provide every pregnant woman with information and a primary postpartum haemorrhage prevention dose of 600 µg misoprostol at her late third-trimester prenatal consultation, to keep and bring when she returned to give birth at the health centre. If a woman did not arrive at a health facility in time, she was to take the tablets within 1 min of the birth after palpating her abdomen to ensure no twin remained inside, taking the misoprostol before the umbilical cord was cut or anything else was done. Oxytocin was used in health facilities, if available. To measure blood loss, the wrap-around garment worn by the woman was placed under her immediately after birth.[11] A small experiment previously showed that a fully soaked wrap in Niger contains about 500 mL of blood; if the garment was blood soaked, she was to receive the three-step treatment administered by a health professional.

Treatment step 1 consisted of 800 µg misoprostol. If bleeding continued after 20 min, step 2 was implemented, and consisted of insertion and inflation of an intrauterine condom tamponade,[12–14] with components provided as a kit in a transparent sleeve (appendix p 9). If bleeding persisted for 6–12 min, step 3 was implemented, consisting of an NASG (appendix p 9) and transfer to a predefined hospital for definitive treatment, even if far away.[1] If the woman was in shock or preshock, the NASG (step 3) was placed first, followed immediately by steps 1 and 2. As a key component of its strategy, Niger also uses a set of 11 public health tools most commonly combined in successful disease eradication programmes (appendix pp 2–3).

See Online for appendix

Given the documented efficacy of each component of the intervention, the Niger MOH concluded that there was no ethical way to decide which regions should not benefit from the intervention from the start of the study. The intervention was therefore rolled out nationwide, with no control group.

Maternal birth outcomes in health facilities were assessed and recorded prospectively by the health professionals of each facility and reported monthly in aggregated, deidentified form to the national level, first by text message to a toll-free telephone, after which reports were recorded by the collaborating non-governmental organisation onto spreadsheets. Then, beginning in March, 2017, birth outcomes were recorded as part of routine MOH reporting, which from January, 2019, was done via the internet onto MOH computers, as described in the appendix (p 3). Numbers that appeared aberrant were verified by calling the relevant health facility. Reported numbers were also verified by comparing to original log books and partograms during supervisory visits to health facilities.

Outcomes

Prespecified outcome indicators including the aggregated number of primary postpartum haemorrhage cases, obstructed labour deaths, primary postpartum haemorrhage deaths, eclampsia deaths, infection deaths, and deaths from all other causes were assessed in health facilities. Throughout, the terms "deaths" and "maternal deaths" or "maternal mortality" always referred to birth-related maternal deaths in health facilities, unless otherwise specified.

Statistical analysis

Data are presented as numbers and percentages. The count data of the reported main parameters were aggregated by year and health facility category. The observed crude incidence rates of the main outcomes were calculated on the basis of Poisson distribution (appendix pp 5–6).

Incidence rate ratios (IRRs) were estimated to compare the outcome rates against the preintervention survey data, and then over the intervention period. For comparison of outcome rates against the preintervention survey data, the overall and annual birth-related maternal mortality rates were compared with those of 624 women recorded as having died during health-facility childbirth

	2015	2016	2017	2018	2019	2020
Overall						
Number of health facilities expected to report once per month	873	914	998	1052	1135	1261
Total reports received for a 12-month period	867	1959	7941	10737	10865	11563
Annual reports received as a percentage of expected reports*	8%	18%	66%	85%	80%	76%
Health centres						
Number expected to report once per month	829	870	954	1008	1091	1217
Total reports received for a 12-month period	757	1674	7484	10240	10362	11076
Annual reports received as a percentage of expected reports*	8%	16%	65%	85%	79%	76%
District hospitals						
Number expected to report once per month	35	35	35	35	35	35
Total reports received for a 12-month period	98	211	351	391	398	379
Annual reports received as a percentage of expected reports*	23%	50%	84%	93%	95%	90%
Regional and national referral hospitals						
Number expected to report once per month	9	9	9	9	9	9
Total reports received for a 12-month period	12	74	106	106	105	108
Annual reports received as a percentage of expected reports*	11%	69%	98%	98%	97%	100%

*Total reports received for 12-month period divided by the number of health facilities expected to report once per month times 12.

Table 1: **Reporting performance as a percentage of annual reports received versus annual reports expected**

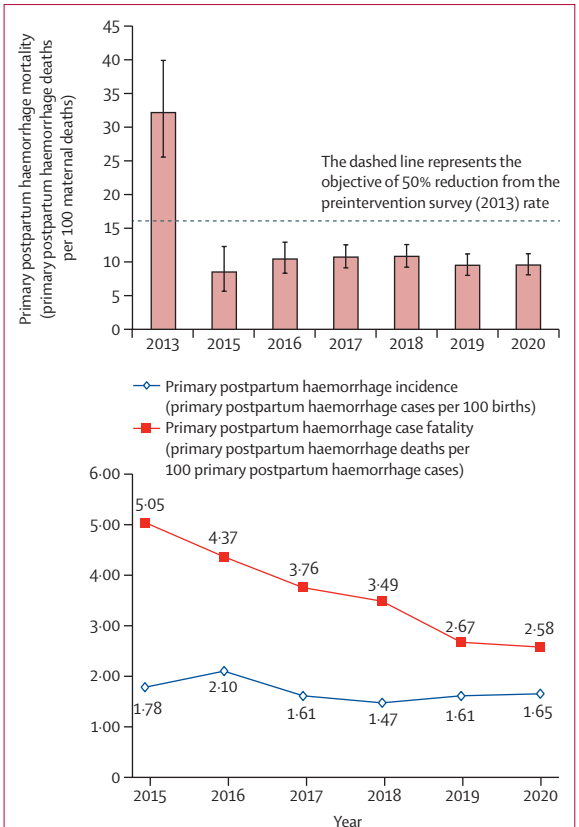

Figure 1: **Mortality associated with primary postpartum haemorrhage (per 100 maternal deaths), and incidence and case fatality of primary postpartum haemorrhage in Niger**

from November, 2012, to October, 2013, the retrospective preimplementation survey period. Cause of death was not available in 369 cases of these 624 deaths, and these deaths were excluded from further analysis, leaving 255 deaths to be used for cause-of-death comparisons between years. Annual rates were also compared to 2015 and 2016, and to 2015 and 2016 combined. Poisson regression models were used for the aggregated count data, and coefficients were exponentiated and reported as unadjusted IRRs together with the corresponding 95% CIs. IRRs were calculated for the overall data and stratified by health-facility category for each year compared to the reference year, using year as a categorical predictor variable in the models. Annual trends were calculated for one-unit change in year using year as a continuous predictor variable in the models. Statistical analyses were done using Stata version 16.1. A p value of 0·05 or less was defined as being statistically significant.

Role of the funding source

The funders had no role in study design, data collection, data analysis, data interpretation, or writing of this report.

Results

Among 5 382 488 expected births, 2 254 885 (41·9%) occurred in health facilities, of which information is available on 1 380 779 births from Jan 1, 2015, to Dec 31, 2020. The proportion of health facilities that reported their results in any given month increased over time (table 1). We also saw an increase over time in the number of births for which information was available, which increased from 90 453 (26·02%) of 347 571 reported health-facility births in the first full year of implementation in 2016, to 257 722 (80·32%) of 320 865 births in 2017, reaching a maximum of 322 859 (94·06%) of 343 237 births in 2018 (appendix pp 12–13).

Crude numbers for national and health-facility-level indicators before and after intervention are presented in the appendix (p 11). Of the 7171 women who died of any cause during 1 380 779 births at health facilities within the entire intervention period (2015–20), 723 (10·08%; 95% CI 9·37–10·84) died of primary postpartum haemorrhage (appendix p 11). Compared with 82 (32·16%; 95% CI 25·58–39·92) of the 255 women for whom cause of death was available in the 2013 preintervention survey, primary postpartum haemorrhage mortality decreased to 146 (9·53%; 8·05–11·21) of 1532 deaths among

	Primary postpartum haemorrhage deaths per 100 maternal deaths		Primary postpartum haemorrhage death rate (primary postpartum haemorrhage deaths per 1000 births)		Primary postpartum haemorrhage case fatality rate (deaths per 100 primary postpartum haemorrhage cases)		Primary postpartum haemorrhage incidence (primary postpartum haemorrhage cases per 100 births)	
	Incidence rate (95% CI)	Incidence rate ratio (95% CI)	Incidence rate (95% CI)	Incidence rate ratio (95% CI)	Incidence rate (95% CI)	Incidence rate ratio (95% CI)	Incidence rate (95% CI)	Incidence rate ratio (95% CI)
2013	32·16 (25·58–39·92)	Reference year	0·90 (0·71–1·11)	Reference year	..	..	..	..
2015	8·48 (5·64–12·26)	0·26 (0·17–0·41)	0·90 (0·60–1·30)	1·01 (0·65–1·54)	5·05 (3·36–7·30)	Reference year	1·78 (1·64–1·94)	Reference year
2016	10·43 (8·31–12·93)	0·32 (0·24–0·44)	0·92 (0·73–1·14)	1·03 (0·76–1·39	4·37 (3·48–5·42)	0·86 (0·56–1·33)	2·10 (2·01–2·20)	1·18 (1·07–1·3)
2017	10·70 (9·09–12·52)	0·33 (0·25–0·43)	0·61 (0·51–0·71)	0·68 (0·52–0·88)	3·76 (3·20–4·40)	0·74 (0·5–1·11)	1·61 (1·56–1·66)	0·9 (0·83–0·99)
2018	10·80 (9·22–12·57)	0·34 (0·26–0·44)	0·51 (0·44–0·60)	0·57 (0·44–0·75)	3·49 (2·98–4·06)	0·69 (0·46–1·03)	1·47 (1·43–1·52)	0·83 (0·76–0·9)
2019	9·49 (8·00–11·19)	0·29 (0·22–0·39)	0·43 (0·36–0·51)	0·48 (0·37–0·63)	2·67 (2·26–3·15)	0·53 (0·35–0·79)	1·61 (1·56–1·65)	0·9 (0·83–0·99)
2020	9·53 (8·05–11·21)	0·30 (0·23–0·39)	0·42 (0·36–0·50)	0·47 (0·36–0·62)	2·58 (2·18–3·03)	0·51 (0·34–0·76)	1·65 (1·61–1·69)	0·93 (0·85–1·01)
Annual trend (2015–20)*	NA	0·89 (0·86–0·92)	NA	0·88 (0·85–0·91)	NA	0·87 (0·83–0·91)	NA	0·98 (0·97–0·99)

Primary postpartum haemorrhage incidence was not systematically recorded before intervention. NA=not applicable. *Annual trends were calculated for one unit change in year using the year as a continuous predictor variable in the models.

Table 2: **Key primary postpartum haemorrhage preintervention and postintervention outcomes**

343 668 births in 2020 (p<0·0001; figure 1). This finding shows a 70·37% reduction in the proportion of maternal deaths that primary postpartum haemorrhage caused compared to the preintervention survey, and a 67·14% reduction from Niger's officially used 29% of maternal mortality being caused by primary postpartum haemorrhage. The case fatality rate per 100 primary postpartum haemorrhage cases decreased from 28 (5·05%; 95% CI 3·36–7·30) of 554 deaths in 2015, the first year for which incidence of primary postpartum haemorrhage was available, to 146 (2·58%; 2·18–3·03) of 5667 deaths in 2020 (p<0·0001; table 2, figure 1). Incidence of primary postpartum haemorrhage varied between 1900 (2·10%; 2·01–2·20) of 90 453 births and 4758 (1·47%; 1·43–1·52) of 322 859 births during 2015–20; an annual trend of 0·98 (95% CI 0·97–0·99; p<0·0001). All-cause maternal mortality declined from 681 per 100 000 births (624 [0·68%] of 91 668; 95% CI 629–737) in the preintervention survey to 446 per 100 000 births (1532 [0·45%] of 343 668; 424–469) in 2020 (p<0·0001; appendix pp 12–13).

The IRR for mortality associated with primary postpartum haemorrhage (per 100 maternal deaths) for 2015–20 compared with the preintervention period in 2013 was 0·31 (95% CI 0·25–0·39; p<0·0001; table 3). Although IRR for overall maternal mortality was 0·76 (0·70–0·83), there was no significant decline in IRRs for the other causes of death (table 3). Case fatality and incidence of primary postpartum haemorrhage cannot be compared with preintervention data because blood-loss information was not recorded systematically in Niger before implementation. The annual trend for the case fatality for primary postpartum haemorrhage during the intervention period itself was 0·87 (95% CI 0·83–0·91) and the trend for incidence was 0·98 (0·97–0·99; table 2).

To assess whether the retrospective preintervention survey provided a comparator of adequate quality, we also compared subsequent years to 2015, the year throughout which the project was restarted, 2016, the first full year of implementation, and to 2015 and 2016 combined. By 2016, the proportion of deaths caused by primary postpartum haemorrhage had declined by 67·6% from the preintervention period, from 32·16% (95% CI 25·58–39·92) to 10·43% (8·31–12·93) and remained stable up to 2020 (table 2, figure 1).

An estimated 1417 fewer women died (appendix p 16), and 122 577 fewer cases of primary postpartum haemorrhage occurred (appendix p 16).

The contribution of primary postpartum haemorrhage to maternal mortality declined in all categories of health

	Incidence rate (95% CI)	Incidence rate ratio (95% CI)
Overall maternal mortality		
2013	681 (629–737)	Reference year
2015–20	520 (510–530)	0·76 (0·70–0·8)
Primary postpartum haemorrhage deaths per 100 maternal deaths		
2013	32·16 (25·58–39·92)	Reference year
2015–20	10·08 (9·37–10·84)	0·31 (0·25–0·39)
Obstructed labour deaths per 100 maternal deaths		
2013	3·14 (1·35–6·18)	Reference year
2015–20	7·07 (6·48–7·71)	2·25 (1·12–4·53)
Eclampsia deaths per 100 maternal deaths		
2013	15·29 (10·88–20·91)	Reference year
2015–20	13·29 (12·47–14·16)	0·87 (0·63–1·20)
Infection deaths per 100 maternal deaths		
2013	22·35 (16·93–28·96)	Reference year
2015–20	18·60 (17·63–19·63)	0·83 (0·64–1·08)
Other causes deaths per 100 maternal deaths		
2013	27·06 (21·05–34·24)	Reference year
2015–20	50·96 (49·33–52·63)	1·88 (1·48–2·39)

Table 3: **Causes of death, baseline versus intervention period**

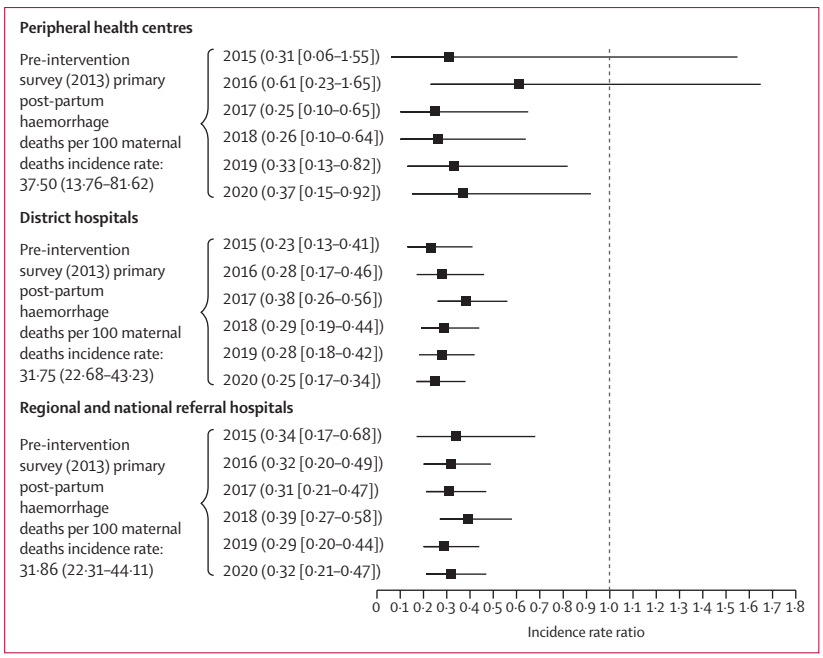

Figure 2: **Annual incidence rate ratios of primary postpartum haemorrhage compared with preintervention rates by health facility level in Niger**

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facilities, and most significantly in district-level and regional referral hospitals, in which 6407 (89·35%) of 7171 deaths occurred (appendix pp 14–15; figure 2). For the 72-month intervention period, the proportion of deaths caused by primary postpartum haemorrhage in peripheral health centres declined from six (37·50%; 95% CI 13·76–81·62) of 16 deaths to 22 (13·92%; 8·73–21·08) of 158 deaths in 2020 (p=0·031). District-hospital primary postpartum haemorrhage deaths declined from 40 (31·75%; 22·68–43·23) of 121 deaths in the preintervention survey to 53 (7·93%; 5·94–10·38) of 668 deaths in 2020, (p<0·0001; appendix pp 14–15). The deaths in regional-level and national referral hospitals caused by postpartum haemorrhage declined from 36 (31·86%; 22·31–44·11) of 113 deaths to 71 (10·06%; 7·85–12·69) of 706 deaths (p<0·0001). The case fatality of primary postpartum haemorrhage decreased significantly during the intervention period compared with 2015 for district hospitals (p=0·036), but not for health centres (p=0·13) and regional-level and national referral hospitals (p=0·90; appendix pp 14–15).

The annual decrease in the proportion of deaths caused by primary postpartum haemorrhage during 2016–20 was not statistically significant for health centres (1·00, 95% CI 0·84–1·19), district hospitals (0·93, 0·85–1·02), or regional referral hospitals (0·99, 0·91–1·07; appendix pp 14–15), indicating that the initial reduction was sustained and stable over time. Reductions in primary postpartum haemorrhage case fatality, incidence, and overall maternal mortality compared with 2016, and with 2015 and 2016 combined, varied in significance across health facility types (appendix pp 14–15).

Discussion

The principal findings from 1 380 779 health-facility births in Niger were that deaths from primary postpartum haemorrhage as a percentage of birth-related maternal deaths, and incidence of primary postpartum haemorrhage compared with typically published incidences, declined by more than half as soon as the prevention and three-step treatment strategy was implemented, a significant improvement compared with preintervention in 2013. There was also significant improvement in the case-fatality rate, incidence, and birth-related maternal mortality associated with primary postpartum haemorrhage, compared with 2015, 2016, and 2015 and 2016 combined. Stability for other causes of death over 72 months indicated that the observed change was not part of any general trend.

From a low level the first year in 2015, reporting increased considerably. The proportion of health facilities reporting monthly increased in marked shifts, attaining 66% in 2017 and remaining high, around 80% thereafter. This result could be attributed to firm engagement from Niger MOH officials, prompting, and changes to the reporting system, but no extra incentives, training, or other programmatic changes were introduced. Low reporting in 2015 and an external evaluation by Gynuity Health Projects, which reported initial non-compliance by some health workers, caused concern that results might reflect reporting from some health-facility employees who might be especially enthusiastic, perhaps implementing the intervention better than others (appendix pp 6–7).[15] To the contrary, outcomes were sustained as reporting increased, including when many additional facilities began reporting from 2017. Facilities that began reporting results later than facilities that adopted the intervention earlier achieved similar results.

To our knowledge, no other country has aimed to halve the mortality associated with primary postpartum haemorrhage nationwide within 2 years through a similar strategy of documented, low-cost interventions combined with a specific set of public health tools from successful disease-eradication efforts. However, so-called bundle approaches are increasingly advocated for various medical conditions, including primary postpartum haemorrhage.[16] The financial benefits to the population have been roughly estimated to be 5·7–7·8 times the annual running cost of the intervention, costing about US$37·94–27·73 per disability-adjusted life-year prevented (appendix pp 7, 17–24), more than Expanded Program on Immunization vaccination, but less than treating diarrhoea or acute respiratory illness in children younger than 5 years.[17]

An interpretation of these findings is that immediate success in reducing primary postpartum haemorrhage mortality and morbidity may occur; each technology having shown some efficacy individually,[8,12–14,18–22] even severely under-resourced health facilities can achieve a 50% reduction in primary postpartum haemorrhage

mortality almost immediately upon introducing this set of technologies in a systematic manner, as Niger is doing.[23] A 400 µg sublingual misoprostol prevention dose alone for primary postpartum haemorrhage reduces incidence by 72·3%.[18] Intrauterine condom tamponade and NASGs have also demonstrated usefulness, and often cost effectiveness.[8,19–22] It is therefore reasonable that a systematically applied combination of these interventions can quickly reduce mortality associated with primary postpartum haemorrhage by 50% or more on a public health scale.

The incidence of primary postpartum haemorrhage was not previously recorded in health facilities, making comparisons with other studies reported in the literature the primary option for assessing any changes in incidence. Among the 1380779 health-facility births, 22407 (1·62%; 95% CI 1·60–1·64) included reports of primary postpartum haemorrhage with blood loss of 500 mL or higher, compared with previous reports that 18% of women can experience primary postpartum haemorrhage, defined as blood loss greater than 500 mL, and WHO's report that globally on average 10·5% experience blood loss greater than 1000 mL if no intervention is implemented to prevent primary post-partum haemorrhage.[5,7]

Mortality associated with primary postpartum haemorrhage in Niger decreased to less than half of the average for eastern, western, southern, and southeastern Asia, and northern African regions.[2] The proportion of birth-related maternal deaths caused by primary postpartum haemorrhage in Niger health facilities (9·53%) is now on par with that of the USA (11%).[2,24]

Overall, the rapid decline of primary postpartum haemorrhage mortality and incidence underscores the ethical assessment that led Niger's MOH to implement the intervention nationwide from the outset, although some researchers might have preferred use of a control group. The present study should be replicated, but randomised controlled trials should not be necessary before deciding whether the new approach should become a standard operating procedure.[23]

Some issues arose from the decision in March, 2014, to change the misoprostol prevention dose from 400 µg (two tablets), the planned dose, to 600 µg (three tablets), the dose used in our study. Packaging misoprostol into separate prevention and treatment doses complicated stock management, and resulted in stockouts.[15] Using 600 µg rather than 400 µg also increased the annual misoprostol procurement cost by 50%, and increased side-effects without any additional therapeutic benefit, as pointed out by WHO.[8,25] We did not use tranexamic acid, which WHO had not yet recommended at the time. Because previous studies have suggested using 1 g (10 mL) tranexamic acid intravenously,[26–28] which Niger's MOH considers realistic in even its most peripheral health centres, intravenous tranexamic could be added to step 2 of the intervention, and might further reduce the mortality associated with primary postpartum haemorrhage.

Reporting over 72 months is a strength of our study, as is nationwide data collection in a large, low-income country with substantial health-system challenges and resource constraints (2020 gross domestic product estimate of US$1200 per capita; rank 225 of 229 countries).[29] Further, each conclusion was based not on one, but on several indicators and analyses leading to similar findings. Our results reflected routine operation outcomes in the face of programmatic challenges that necessarily occur at national scale during a 72-month timespan. Objective blood-loss measurement, although only semiquantitative and approximate, is an important component of the intervention. Resulting earlier recognition of primary postpartum haemorrhage by health workers thus probably strengthened the intervention, as did the fact that 96% of the women giving birth in the community who received a prophylactic dose used it, although relatively few women went for a third-trimester prenatal consultation and received a prophylactic dose.[15]

Our study had several limitations, one of which was the fact that no cause of death was available for 369 of the 624 maternal deaths in the preintervention survey. Moreover, because preintervention surveyors were aware that the main interest behind the survey was primary postpartum haemorrhage, rather than it being a general cause-of-death survey, caution was required with comparisons to the preintervention survey in 2013 for causes other than primary postpartum haemorrhage. However, interestingly, even if we assumed that the proportion of maternal deaths with no diagnosis in the preintervention study that was caused by primary postpartum haemorrhage was similar to the sub-Saharan estimate (15·2%), rather than the estimate for adjoining, more similar countries in northern Africa (32·0%), the resulting (22·1%) preintervention rate of primary postpartum haemorrhage deaths per 100 maternal deaths would be more than twice as high as what was observed in each intervention year. Similarly to other large-scale, nationwide, non-randomised longitudinal studies in comparable settings, another limitation of our study was the uncertainty surrounding the quality of the data, which we endeavoured to address by triangulating the data from different perspectives before reaching each conclusion. Nonetheless, the use of actual registered events without simulations or imputations should appropriately reflect the true effect of the intervention.

Our analysis did not include potential confounders for the observed improvements. The comparison might have been affected by the fact that the preintervention survey covered 150 (18%) of 847 health centres, whereas reporting from 2018 onwards covered more than 75% of health centres even as new ones were established, with hospitals being equally represented (all were included) in both the preintervention and intervention periods. Part of the improvement could be due to increased awareness

in the community, possibly through increased adoption of recommendations. From the preintervention survey to 2020, Niger has not seen changes in its population's socioeconomic status or infrastructure that could affect the results. In addition, primary postpartum haemorrhage mortality in neighbouring countries, which were not unlike the mortality in Niger at the start of the intervention, has to our knowledge not changed markedly. Monthly MOH birth-outcome reports do not contain information about ethnicity or other sociodemographic characteristics of participants; however, such characteristics seem unlikely to explain the observed changes (appendix p 8). Numbers pertaining to usage of misoprostol and tamponade kits, collected solely for stockout prevention purposes, indicate that misoprostol and tamponade kits were generally available and used at all levels of Niger's health-care system (appendix pp 4, 25). Although there might have been other unknown confounders, we believe the conclusions we drew from the data are accurate. Comparisons between regions (eight regions in Niger) can be useful for national monitoring and local programme strengthening, but our analysis did not include these comparisons because we did not think them to be useful for international readers. Supervision was less frequent than intended because of funding constraints; our results might have been further strengthened if nationwide supervision had been implemented as planned.[1]

Nationwide implementation of a low-cost prevention and three-step treatment strategy for primary postpartum haemorrhage achieved the aim of reducing mortality associated with primary postpartum haemorrhage in health facilities by at least 50% nationwide in a large, severely resource-constrained country within 2 years. Results were apparent as soon as the intervention was introduced, and outcomes have been sustained for 6 years so far. Replicating the approach with local adaptations in other low-income and some middle-income countries would seem an appropriate next step.

Contributors

ARS conceived the strategy for primary postpartum haemorrhage mortality and incidence reduction. RB designed the preintervention survey. ZA and IS implemented the preintervention survey and all aspects of the primary postpartum haemorrhage reduction strategy together with Niger's health-system professionals at all levels, including the training, roll-out, supervision, data collection, and initial analysis. AM contributed to developing the primary postpartum haemorrhage module within Niger's DHIS2 information data-collection system (District Health Information System 2; Department of Mathematics, University of Oslo, Oslo, Norway), procured health-statistics data, and reviewed the manuscript. LAA designed and carried out the analysis with input from ZA and ARS. ZA and LAA have directly accessed and verified the underlying data. All authors have had full access to all data. ARS, ZA, RB, and LAA contributed to writing, and IS and AM to reviewing the manuscript. All authors have reviewed and approved the final version for submission and publication. The corresponding author had final responsibility for the decision to submit for publication.

Declaration of interests

ARS is founder and Executive Director of Health and Development International (HDI) and HDI Norway. ZA has been employed by HDI in Niger since Nov 1, 2008. IS was Niger's Director General of Reproductive Health during the period discussed. RB was employed by HDI when she designed the preintervention survey. AM and LAA declare no competing interests.

Data sharing

Upon reasonable request, deidentified data can be made available to researchers after approval from the research ethics committee, and the aggregated crude data have been provided to all readers in the appendix (p 11). Requests should be directed to the corresponding author.

Acknowledgments

Funding from the governments of Norway (grant QZA-0325 NER 13/0003) and Niger, together with the Kavli Trust (Kavlifondet), the InFiL Foundation, and individuals in Norway, the UK, and the USA has made this work possible. Sincere thanks to André Lalonde for help during initial discussions with the Government of Niger and training, to Suellen Miller, Elizabeth Butrick, and the Bixby Center for Global Reproductive Health at the University of California, San Francisco, USA, for help in starting the initiative and initial training, to Suellen Miller for permission to use the non-inflatable anti-shock garment illustrations, to Ramatou Also Alio for her years of dedicated help with data and field activities in the Health and Development International office, to Oumoulkair Hamidou for excellently taking over those activities, to Moni Blazej Neradilek for statistical support in designing and analysing the preintervention survey, to Yaroh Asma Gali for inspiring discussions, her personal commitment, and her leadership, and to Tore Godal, then in the Norway Ministry of Foreign Affairs, for his decision to provide initial funding for this ambitious effort. Most importantly, we extend our sincere appreciation and deep admiration to the thousands of health professionals across Niger, and to the women of Niger and their family members; it is in fact their achievements we have the honour to be reporting here.

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