

A Regional Comparison of Distribution Strategies and Women's Awareness, Receipt, and Use of Misoprostol to Prevent Postpartum Hemorrhage in Rural Amhara and Oromiya Regions of Ethiopia

Lynn M. Sibley, CNM, RN, PhD, Sydney A. Spangler, CNM, MSN, PhD, Danika Barry, MPH, Solomon Tesfaye, MD, MPH, Binyam Fekadu Desta, MPH, Abebe Gebremariam Gobeze, MD

Introduction: In Ethiopia, postpartum hemorrhage is a leading cause of maternal death. The Maternal Health in Ethiopia Partnership (MaNHEP) project developed a community-based model of maternal and newborn health focusing on birth and early postpartum care. Implemented in the Amhara and Oromiya regions, the model included misoprostol to prevent postpartum hemorrhage. This article describes regional trends in women's use of misoprostol; their awareness, receipt, and use of misoprostol at project's endline; and factors associated with its use.

Methods: The authors assessed trends in use of misoprostol using monthly data from MaNHEP's quality improvement database; and awareness, receipt, use, and correct use of misoprostol using data from MaNHEP's endline survey of 1019 randomly sampled women who gave birth during the year prior to the survey.

Results: Misoprostol use increased rapidly and was relatively stable over 20 months, but regional differences were stark. At endline, significantly more women in Oromiya were aware of misoprostol compared with women who resided in Amhara (94% vs 59%); significantly more had received misoprostol (80% vs 35%); significantly more had received it during pregnancy (93% vs 48%); and significantly more had received it through varied sources. Most women who received misoprostol used it (> 95%) irrespective of age, parity, or education. Factors associated with use were Oromiya residence (odds ratio [OR] 9.48; 95% confidence interval [CI], 6.78–13.24), attending 2 or more Community Maternal and Newborn Health (CMNH) family meetings (OR 2.62; 95% CI, 1.89–3.63), receiving antenatal care (OR 1.67; 95% CI, 1.08–2.58) and being attended at birth by a skilled provider or trained health extension worker, community health development agent, or traditional birth attendant versus an untrained caregiver or no one. Correct use was associated with having attended 2 or more CMNH family meetings (OR 2.02; 95% CI, 1.35–3.03).

Discussion: Multiple distribution channels increase women's access to misoprostol. Most women who have access to misoprostol use it. Early distribution to pregnant women who are educated to use misoprostol appears to be safe and unrelated to choice of birthplace.

J Midwifery Womens Health 2014;59:S73–S82 © 2014 by the American College of Nurse-Midwives.

Keywords: community intervention, global health, misoprostol, postpartum hemorrhage

INTRODUCTION

Hemorrhage is the leading cause of maternal mortality globally; approximately two-thirds of these deaths occur postpartum and are primarily because of atonic uterus.¹ Active management of third-stage labor, most importantly, giving an uterotonic drug (preferably oxytocin [Pitocin]) that is administered after birth of the neonate, has been shown to effectively reduce postpartum blood loss.² The relative efficacy and safety of misoprostol (Cytotec) to reduce blood loss because of atonic uterus (compared with oxytocin, ergometrine, or a placebo) has been demonstrated in hospital and community settings.^{3–9} When active management cannot be safely performed, the World Health Organization (WHO) and international professional associations recommend that misoprostol be offered to women for oral administration by community or lay health workers trained in its use to prevent postpartum hemorrhage (PPH).^{2,10,11} A recent systematic qualitative review including 8 published studies and 10 eval-

uation reports from programs distributing misoprostol for PPH prevention at home birth showed that community-based programs were able to achieve high coverage.¹²

In Ethiopia, the large majority of the population resides in rural areas (85%); virtually all births occur at home (90%); skilled providers (physicians, health officers, nurses, or midwives) attend few births (10%); and maternal mortality is high.¹³ PPH is a leading cause of maternal death.¹⁴ In June 2010, the Ethiopian Federal Drug Administration and Control Authority approved registration of misoprostol tablets for oral administration to prevent postpartum hemorrhage, paving the way for the distribution of tablets to community-level health workers who are closest to women in rural communities.¹⁵ The Federal Ministry of Health's *Road Map for Accelerating the Reduction of Maternal and Newborn Morbidity and Mortality 2011–2015* aims to ensure provision of a core package of maternal and newborn health services through the Health Extension Program, including oral misoprostol to prevent PPH.¹⁶

The Health Extension Program is implemented through health extension workers and community health development agents. Health extension workers are government employees, mostly young women, with at least a 10th grade

Address correspondence to Lynn M. Sibley, CNM, RN, PhD, Nell Hodgson Woodruff School of Nursing, Emory University, 1520 Clifton Road, NE, Room 268, Atlanta, Georgia 30322. E-mail: lsibley@emory.edu



Quick Points

- ◆ Distribution of misoprostol to prevent PPH through multiple channels has potential to greatly increase women's access to this life-saving drug.
- ◆ Most women who have access to misoprostol will use it.
- ◆ Distribution of misoprostol during pregnancy to women who are educated to use it correctly appears to be safe and unrelated to choice of birthplace.
- ◆ Early distribution of misoprostol during pregnancy for women's self-administration after birth would further expand access and use.
- ◆ A program of rigorous research comparing the safety and effectiveness of community distribution strategies, including early distribution for women's self-administration, is needed to generate evidence to inform policy recommendations.

education, and one year of mostly didactic training in a package of primary health care focusing on preventive and curative health, including maternal and newborn health. Compared with health extension workers, community health development agents are volunteers—both women and men—with more years of education. Health extension workers operate at a ratio of 1:2500 households; community health development agents operated at a ratio of 1:30-50 households.^{16,17}

The Ethiopian Federal Ministry of Health's Extension Program authorizes health extension workers to give misoprostol to women to prevent PPH immediately after birth of the neonate. However, health extension workers attend less than 1% of births.¹³ Low attendance derives from a variety of factors: limited numbers of health extension workers per health post catchment area, lack of confidence in attending births because of limited clinical training and experience, the distance from the health posts to women's homes, conflicting job responsibilities, and women's preference for relatives—or traditional birth attendants (TBAs). In Ethiopia TBAs are older women who typically learned basic midwifery through apprenticeship with another TBA.

Under leadership of the Federal Ministry of Health, MaNHEP¹⁸ worked in 6 *woredas* (districts) of the Amhara and Oromiya regions to strengthen implementation of the Health Extension Program's community maternal and newborn health (CMNH) component, specifically focusing on improving care during birth and during the early postnatal period when women and newborns are at greatest risk of death. MaNHEP was funded by the Bill and Melinda Gates Foundation and led by Emory University in collaboration with the JSI Research & Training Institute, Inc., University Research Co., LLC, and Addis Ababa University.¹⁸ MaNHEP's objectives were to: 1) improve the capacity and performance of health extension worker, community health development agent, and TBA teams to provide the focused CMNH care; 2) increase women's demand for focused CMNH care and improve their self-care behaviors; and 3) develop and demonstrate the effectiveness of lead *woredas* to improve CMNH care and services—that is, model districts committed and able to continuously improve care and service delivery to meet the needs of childbearing families.¹⁸ To achieve these objectives, MaNHEP deployed a 3-pronged intervention: 1) facility-based CMNH training of health extension

workers, coupled with community-based training and support of health extension workers, community health development agents, and TBAs—who in turn trained pregnant women and family caregivers through a series of CMNH family meetings; 2) continuous quality improvement training and support for community stakeholder groups to ensure that the CMNH care reached women and newborns in a reliable and timely manner; and 3) behavior change communications (TV spots, mobile van video show, poetry contests) to reinforce the above objectives and to shift community norms around the value of CMNH care.¹⁸ Relevant to this article, the CMNH training and CMNH family meetings included knowledge and skills related to the safe use of misoprostol (take 3 tablets by mouth immediately after birth of the placenta), its side effects and what to do if these occur.

MaNHEP conducted a baseline survey from July through August 2010.¹⁹ The survey targeted 3 groups: community-level health care providers (health extension workers, community health development agents, and TBAs), adult women and men aged 18 years and older, and women who gave birth in the year prior to the survey. The survey included a systematic random sample of 1027 women.¹⁸ The findings of this survey indicated that the women had a low awareness of misoprostol to prevent postpartum hemorrhage, particularly in Amhara (< 1% vs 27% Oromiya). The women's use of misoprostol was also low (0% Amhara vs 20% Oromiya).

In late August 2010, MaNHEP initiated the CMNH training of health extension workers, community health development agents, and TBAs. By March 2011, the MaNHEP-trained community health development agents and TBAs began conducting CMNH family meetings with pregnant women and their family caregivers. MaNHEP also purchased and distributed misoprostol tablets to the project area *woreda* health offices, stipulating that they distribute misoprostol to health extension workers to give to women for PPH prevention. MaNHEP requested approval from the regional health bureaus to allow community health development agents and TBAs to distribute misoprostol to pregnant women during CMNH family meetings for use after birth. Only the Oromiya Regional Health Bureau approved the strategy. Thus, in the Amhara region, only skilled providers and health extension workers were allowed to provide misoprostol to women, whereas in the Oromiya region skilled providers and health extension workers as well as trained community

health development agents and TBAs were allowed to provide it, effectively creating a natural experiment of 2 regionally distinct misoprostol distribution strategies.

By February 2012, MaNHEP's monthly quality improvement monitoring data showed rapid increases in women's use of misoprostol in both regions. However, the baseline difference in use between regions persisted: 31% in Amhara versus 93% in Oromiya.

The purpose of this article is to describe—in the context of these 2 strategies—the regional trends in women's use of misoprostol; differences in their awareness, receipt, and use of misoprostol at the project's endline; and the factors that were associated with the correct use of the drug. We then discuss implications for practice and research. A related article in this issue of the *Journal of Midwifery & Women's Health* focuses on the policy context of misoprostol to prevent PPH in Ethiopia at national, regional, and local levels.²⁰

METHODS

Design

MaNHEP used an uncontrolled before-and-after design and multiple data collection methods to evaluate the achievement of overall project objectives.²¹ The methods relevant to this article are described below.

Sites

MaNHEP was implemented in 3 *woredas* in each of the 2 regions, Amhara and Oromiya. The Federal Ministry of Health selected the regions. The Amhara and Oromiya Regional Health Bureaus and MaNHEP selected the *woredas* according to need, population size, and number of expected births; accessibility of health services; presence of health extension workers, community health development agents, and TBAs; and the absence of other development partners working on maternal and newborn health. In each *woreda*, the project area consisted of a vertical "slice" of the health system comprised of 2 health centers and their associates health posts and all pregnant or newly postpartum women and newborns within the health posts' catchment areas. The total project area encompassed a population of about 350,000 residing in 51 *kebeles* (villages) with about 12,000 births per year.²¹

Sampling, Procedures, and Analyses

To assess regional trends in women's use of misoprostol, we collected data on women's use of misoprostol from MaNHEP's quality improvement monitoring database from March 2011 through October 2012. The data for this database are derived from each health extension worker's routine monthly health post report. We used the statistical process-control U chart to analyze the pattern of women's use of misoprostol over time.²² The U chart provides the upper and lower control limits (3 standard deviations) and a central line (mean) to help detect a trend in plotted values. Each data point represents the average proportion of women who used misoprostol in all 51 *kebeles* in a given month out of all reported births for that

month. When a data point falls within the control limit, the observed variation is considered to be a normal fluctuation (in this case, misoprostol use). When a data point falls outside of the control limit, the variation may be because of some special cause, such as introducing a strategy to improve misoprostol coverage (a positive change) or a decline in the stock of misoprostol at the health post (a negative change). We conducted the U chart analysis using Microsoft Excel.²³

To assess regional differences in women's awareness, receipt, and use of misoprostol at the project's endline, we collected data from the women's endline survey database. The women's endline survey was conducted during May 2012 and June 2012 by a team that was trained by Addis Ababa University. The survey involved face-to-face interviews with a systematic random sample of 1019 women who had given birth during the year prior to the survey.²⁴ The details of this survey are described elsewhere.²⁴ *Receipt* was defined as a woman having obtained misoprostol from a provider (distinguished from having actually taken the drug). *Use* was defined as a woman's consumption of misoprostol. *Correct use* was defined as the oral consumption of 3 misoprostol tablets immediately after birth of the placenta. We calculated frequencies for the women's sociodemographic characteristics, misoprostol use, and correct use and conducted Fisher exact tests to examine regional differences in these variables (2-tailed test, $\alpha = .05$). Analyses were performed in SAS version 9.3 (Cary, NC).²⁵

To assess factors that may be associated with use of misoprostol, we conducted univariate logistic regression to calculate the unadjusted odds ratios for the associations between women's characteristics, use, and correct use of misoprostol. We then constructed multivariate logistic regression models for each of these outcomes, controlling for age, parity, education, and region of residence. In the *use* model, the exposures of interest were whether the pregnant woman received any antenatal care with a skilled provider or health extension worker, the number of CMNH family meetings she attended, and the type of provider who attended her most recent birth. In the *correct use* model, additional exposures included the type of provider who gave the woman misoprostol, whether she received it during pregnancy (vs during labor or after birth), her knowledge of the main benefit of misoprostol to prevent PPH, and whether she received counseling on safe use of the drug. Lastly, the authors constructed a model for *place of birth* (home vs health facility). In this model, the exposures of interest were whether the woman received any antenatal care with a skilled provider or health extension worker, the number of CMNH family meetings she attended, and whether she received misoprostol during pregnancy. Collinearity diagnostics were performed using a SAS macro, and variable screening was performed using condition indices and variance decomposition proportions.^{26,27} The authors used the Hosmer-Lemeshow test statistic to assess goodness of fit.

Ethical Considerations

In 2010, Emory University and Addis Ababa University institutional review boards reviewed the MaNHEP

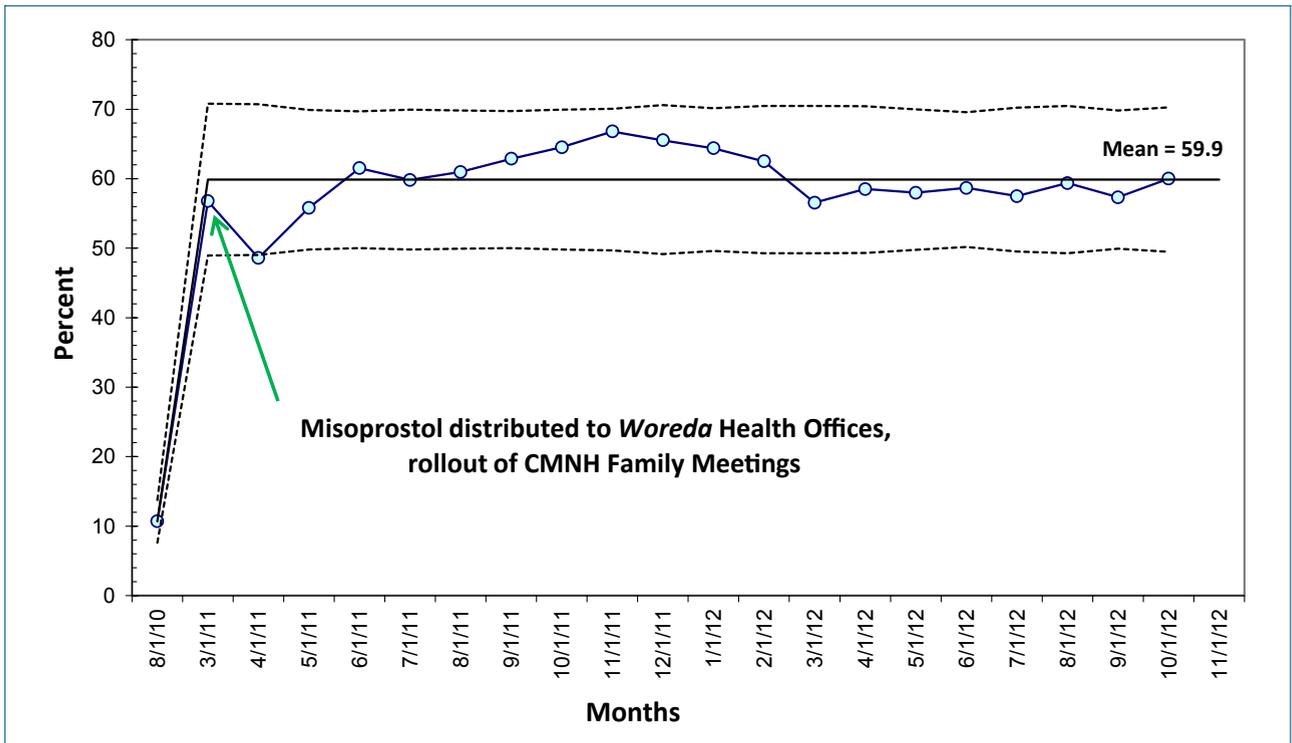


Figure 1. Percent of Women Who Received Misoprostol Immediately After Birth of Placenta, August 2010 (baseline) and March 2011 to October 2012. The dotted lines denote the upper and lower control limits; the solid line denotes the mean.

project proposal and judged the project to be exempt from further oversight. Both considered the project to be public health implementation, monitoring, and evaluation and not research for knowledge generation alone. The Ethiopia Federal Ministry of Health and the Amhara and Oromiya Regional Health Bureaus also reviewed and approved the project proposal. The baseline survey was conducted following informed consent using standard disclosure procedures.

RESULTS

Regional Trends in Women's Use of Misoprostol

Quality improvement data for all 51 *kebeles* in the Amhara and Oromiya regions show that once misoprostol was made available, on average, 60% of postpartum women residing in the project area used misoprostol each month and that the observed variation reflected normal fluctuations in use (Figure 1). Oromiya women's use of misoprostol continued to be much higher than their Amhara counterparts (95% vs 25%) (Figure 2). For Oromiya women, the consecutive data points lie relatively close to centerline or average (95%) over the 20-month period, indicating normal fluctuations in use. For Amhara women, the data points exceed the lower control limit on several occasions, indicating some special cause(s) for decreased use (Figure 2). These occasions coincided with the Easter holiday and with a government-sponsored summer training course for health extensions workers—both of which caused the health extension workers to be absent from their health post.

Regional Differences in Women's Awareness, Receipt, and Use of Misoprostol at Endline

Survey data show that the women in the 2 regions were similar in age and parity (Table 1). However, significantly more women in Oromiya completed any primary or secondary education, received any antenatal care from a skilled provider or health extension worker, attended any CMNH family meetings, and were attended at birth by a community health development agent or a TBA (for the 2 provider groups combined, 57% Oromiya vs 37% Amhara). More women in Amhara were attended by a skilled provider or health extension worker (for the 2 provider groups combined, 96% Amhara vs 52% Oromiya).

There were substantial increases in women's awareness of misoprostol to prevent PPH in both regions. However, at endline, significantly more Oromiya women were aware of misoprostol (94.1% in Oromiya vs 58.7% in Amhara; $P < .001$). Similarly, there were substantial increases in women's receipt of misoprostol in both regions. However, significantly more Oromiya women received misoprostol (80% in Oromiya vs 35.1% in Amhara; $P < .001$). In addition, there was significant diversity in from whom the women received the drug in these 2 regions, as shown in Table 2. Among women who received misoprostol, those who resided in Oromiya were also more likely to have received the tablets during pregnancy (92.8% in Oromiya vs 47.6% in Amhara; $P < .001$), to know its benefit to prevent postpartum hemorrhage (97.5% in Oromiya vs 93.5% in Amhara; $P = .03$), and to have been counseled in its correct use (98.4% in Oromiya vs 92.1% in Amhara; $P < .001$). Almost all women in both regions who received misoprostol

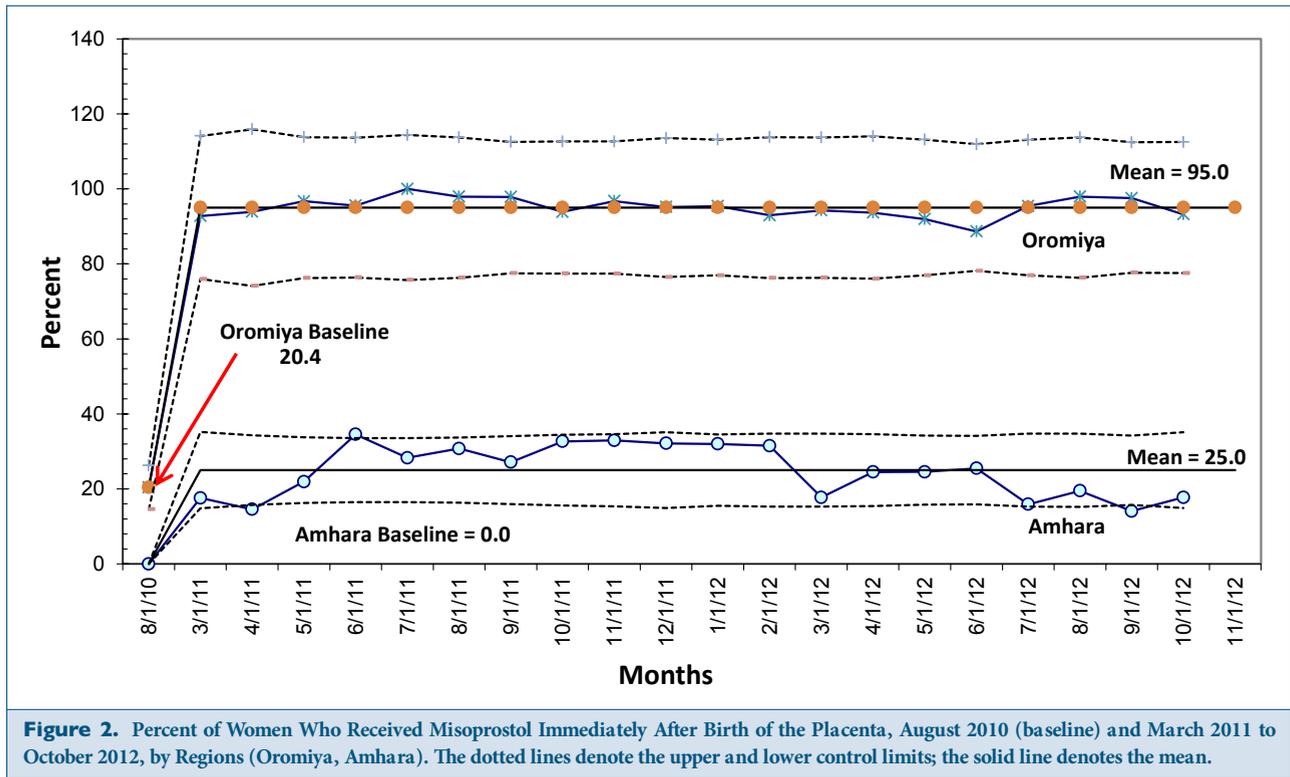


Figure 2. Percent of Women Who Received Misoprostol Immediately After Birth of the Placenta, August 2010 (baseline) and March 2011 to October 2012, by Regions (Oromiya, Amhara). The dotted lines denote the upper and lower control limits; the solid line denotes the mean.

used it (> 95%) and the majority of those who received it used it correctly (71%). Incorrect use involved taking fewer than 3 tablets after birth (10%) or taking the tablets before birth (< 2%).

Stillbirths were infrequent among both users and nonusers of misoprostol (0.7% vs 0.5%, respectively; $P = 1.0$), as were newborn deaths (0.4% vs 0.2%, respectively; $P = 1.0$). At the time of the endline survey, there were no newborn deaths among the women who reported having taken misoprostol tablets before birth.

Factors Associated With Misoprostol Use and Correct use

Controlling for age, parity, and education, the women who were most likely to have used misoprostol resided in the Oromiya region (OR 9.48; 95% CI, 6.78-13.24), had attended 2 or more CMNH family meetings (OR 2.62; 95% CI, 1.89-3.63), and had received some antenatal care (OR 1.67; 95% CI, 1.08-2.58) (Table 3). Having been attended at birth by a health extension worker was more strongly associated with women's use of misoprostol (OR 6.84; 95% CI, 3.84-12.19) than having been attended by a skilled provider (OR 1.85; 95% CI, 1.12-3.07) or TBA/community health development agent (OR 1.60; 95% CI, 1.10-2.35). The small number of women who used a skilled provider precluded judgment on whether the skilled provider effect was significant. The women who were most likely to have used misoprostol correctly attended 2 or more CMNH family meetings (OR 2.02; 95% CI, 1.35-3.03). Controlling for age, parity, and education, region, any antenatal care, and any CMNH family meeting attendance, a woman's receipt of misoprostol during pregnancy was not

significantly associated with place of birth (OR 0.64; 95% CI, 0.35-1.19).

DISCUSSION

Summary of Findings

This article documents significant increases in women's use of misoprostol to prevent PPH in both the Amhara and Oromiya regions of Ethiopia. Once MaNHEP personnel distributed misoprostol to the *woreda* health offices in the project area, average use increased rapidly and was relatively stable over 20 months of observation. The observed decreases in use among Amhara women were likely because of the absence of health extension workers during the Easter holiday and their attendance at the government-sponsored training course during the summer.

At endline, compared with their Amhara counterparts, significantly more Oromiya women were aware of misoprostol, received misoprostol, received it during pregnancy, and received it through more varied sources. Yet, almost all women in both regions who received misoprostol used it, irrespective of age, parity, and education. These findings together seem to demonstrate that policy and program strategies that support multiple distribution channels are effective in increasing women's access to misoprostol and women's use of misoprostol. Having multiple distribution channels is especially important in offsetting distribution bottlenecks, for example, when health extension workers are absent from their posts during holidays, training events, or maternity leave.

Some policy makers, programmers, and providers²⁰ have voiced the concern that the provision of misoprostol to women during pregnancy for subsequent administration (by a caregiver or the woman herself) will reduce the women's

Table 1. Selected Characteristics of the Sampled Women Who Gave Birth During the Year Prior to the Endline Survey, by Region				
Characteristic	Total Sample (N = 1019)	Amhara Region (n = 479)	Oromiya Region (n = 540)	Regional Comparison P value^a
Age, n (%) y^{b,c}				.90
15-19	55 (5.5)	24 (5.2)	31 (5.7)	
20-34	766 (76.5)	356 (77.1)	410 (75.9)	
≥ 35	181 (18.1)	82 (17.8)	99 (18.3)	
Parity, n (%)				.34
1	145 (14.2)	70 (14.6)	75 (13.9)	
2-4	520 (51.0)	233 (48.6)	287 (53.2)	
>4	354 (34.7)	176 (36.7)	178 (33.0)	
Educational level, highest completed, n (%)^{b,d}				<.001
None	730 (71.9)	377 (79.0)	353 (65.5)	
Any primary	262 (25.8)	89 (18.7)	173 (32.1)	
Any secondary or higher	24 (2.4)	11 (2.3)	13 (2.4)	
Any ANC from a skilled provider or HEW, n (%)^{d,e}	847 (84.5)	368 (79.5)	479 (88.9)	<.001
Birth attendant, n(%)^f				<.001
Skilled provider ^a	151 (14.8)	79 (16.5)	72 (13.3)	
HEW	129 (12.7)	83 (17.3)	46 (8.5)	
TBA	434 (42.6)	169 (35.3)	265 (49.1)	
CHDA	46 (4.5)	6 (1.3)	40 (7.4)	
Other (family, friend, other nontrained)	203 (19.9)	98 (20.5)	105 (19.4)	
None (gave birth alone)	56 (5.5)	44 (9.2)	12 (2.2)	
Any CMNH family meeting attendance, n (%)	597 (58.8)	225 (47.1)	372 (69.1)	<.001
Among women who attended CMNH family meetings, n (%)^{b,g}	n = 597	n = 225	n = 372	
Number of meetings attended				.003
1	68 (11.4)	20 (8.9)	48 (13.0)	
2	111 (18.7)	28 (12.4)	83 (22.4)	
3	170 (28.6)	69 (30.7)	101 (27.3)	
4	246 (41.3)	108 (48.0)	138 (37.3)	
Attended meetings with family team (vs alone), n(%)	364 (62.5)	181 (80.4)	183 (51.3)	<.001

Abbreviations: ANC, antenatal care; CHDA, community health development agent; CMNH, community maternal and newborn health; HEW, health extension worker; TBA, traditional birth attendant.

^aFisher's exact test 2-sided P values.

^bMissing: Amhara (n = 1).

^cDon't Know Amhara (n = 16).

^dMissing Oromiya (n = 1).

^ePhysician, officer, nurse, or midwife.

^fMost skilled person present at birth.

^gMissing, Amhara (n = 1), Oromiya (n = 2). Rounded to nearest 10th percent.

Oromiya (n = 1).

Endline survey conducted May-June 2012.

interest in giving birth in a health facility. MaNHEP's findings show that women's receipt of misoprostol during pregnancy was not significantly associated with place of birth, controlling for age, parity, education, region, any antenatal care, and CMNH family meeting attendance. Moreover, very few women consumed the tablets before birth (< 2%). All of these women and their infants were alive at the time of the endline survey.

Controlling for age, parity, and education, the factors that were significantly associated with women's use of misoprostol were Oromiya residence; having attended 2 or more CMNH family meetings; having received any antenatal care; and having been attended at birth by a skilled provider, health ex-

tension worker, or TBA and community health development agent as opposed to being attended by an untrained family member, neighbor, or no one. Of interest, misoprostol use was more strongly associated with being attended by a health extension worker than being attended by a skilled provider or TBA and community health development agent. This observation may be a reflection of the Ministry of Health's policy that health extension workers who attend birth at their health post or a woman's home administer misoprostol to women after birth.

The only factor associated with women's correct use of misoprostol was having attended 2 or more CMNH family meetings. These meetings—taught by community health

Table 2. Selected Characteristics of Misoprostol Receipt and Use Among the Sampled Women Who Gave Birth During the Year Prior to the Endline Survey, by Region

Characteristic	Total Sample (N = 1019)	Amhara Region (n = 479)	Oromiya Region (n = 540)	Regional Comparison P value ^a
Aware of misoprostol, n (%)	789 (77.4)	281 (58.7)	508 (94.1)	<.001
Received misoprostol, n (%)	600 (58.9)	168 (35.1)	432 (80.0)	<.001
Among women who received misoprostol^b	n = 600	n = 168	n = 432	
Provided by, n (%)				
Skilled provider ^c	61 (10.2)	42 (25.0)	19 (4.4)	<.001
HEW	323 (53.8)	119 (70.8)	204 (47.2)	
TBA	55 (9.2)	5 (3.0)	50 (11.6)	
CHDA	160 (26.7)	2 (1.2)	158 (36.6)	
Other (family, friend, other nontrained or alone)	1 (0.2)	0 (0.0)	1 (0.2)	
Received during pregnancy, n (%)	481 (80.2)	80 (47.6)	401 (92.8)	<.001
Knows PPH prevention is main benefit, n (%) ^d	577 (96.3)	157 (93.5)	420 (97.5)	.03
Counseled on correct use, n (%) ^e	581 (97.3)	152 (92.1)	429 (99.3)	<.001
Used (consumed) misoprostol, n (%)	585 (97.5)	160 (95.2)	425 (98.4)	.04
Among women who used misoprostol	n = 585	n = 160	n = 425	
Used correctly, n (%) ^{b,d,f}	412 (70.7)	100 (62.9)	312 (73.6)	.01
Used 3 tablets, n (%) ^{d,g}	483 (83.4)	129 (83.2)	354 (83.5)	.11
Used immediately after delivery of placenta, n (%) ^b	491 (84.1)	122 (76.7)	369 (86.8)	<.001

Abbreviations: ANC, antenatal care; CHDA, community health development agent; HEW, health extension worker; PPH, postpartum hemorrhage; TBA, traditional birth attendant.

^aFisher's exact test 2-sided P values.

^bMissing, Amhara (n = 1).

^cPhysician, health officer, nurse, or midwife.

^dMissing, Oromiya (n = 1).

^eDon't Know, Amhara (n = 3).

^fCorrect use is calculated based on route (oral), number of tablets consumed (3), and time that tablets were consumed (eg, immediately after delivery of the placenta).

^gDon't know, Amhara (n = 5). Rounded to nearest 10th.

Endline survey conducted May-June 2012.

pment agents and TBAs and attended by pregnant women and family caregivers—were an independent and important vehicle for health education regarding maternal and newborn health, including safe use of misoprostol to prevent PPH.

The limitations of an uncontrolled before and after evaluation design are well known and include possible loss of internal validity.²⁸ In addition, the survey data are subject to recall bias because the women were asked to report on care received at a birth occurring up to one year before the survey. These data are also subject to response bias since the women in the Amhara region who were not attended by a skilled provider or health extension worker may have withheld information about receipt of misoprostol from community health development agents or TBAs who were not authorized to dispense it in that region. Last, the quality improvement monitoring data included only the number of reported births, which was about 50% of the expected number of births according to Ministry of Health estimates. The monitoring data possibly underestimate the use of misoprostol. The 2 data sources (survey and quality improvement monitoring) produced congruent results, however, and this increases confidence in the findings.

Implications for Policy, Programming, and Research

The government of Ethiopia supports a core package of maternal and newborn health services through the Health Extension Program, including misoprostol to prevent PPH.¹⁶ In-

ternational professional associations,¹⁰ the 2012 WHO recommendations for optimizing health worker roles to improve access to key maternal and newborn health interventions through task shifting,¹¹ and the 2012 WHO guidelines for the prevention and management of PPH² strongly endorse the oral administration of misoprostol by community health workers and lay health workers. The latter guidelines, however, caution that there is insufficient evidence to date to support a recommendation for advance distribution of misoprostol for self-administration.

The systematic qualitative review of programs that distribute misoprostol by Smith et al¹² found that the rate range of distribution was higher when misoprostol was distributed by community health workers (55%-97%) or TBAs (26%-87%) than when misoprostol was distributed only through skilled providers (21%-49%); programs distributing misoprostol during late pregnancy (56%-94%) or at birth (17%-74%) achieved higher coverage than those that distributed it during antenatal care (any 17%-66%, late 16%-36%). Programs educating women and families about self-administration (16%-94%) achieved higher coverage than those in which TBAs (36%-74%) or skilled/semiskilled providers administered the medication (17%). The study authors concluded that misoprostol for PPH prevention appeared to be safe, with a very low rate of incorrect early administration (0.06%). In 3 programs reporting facility birth,

Covariate	Outcome 1		Outcome 2	
	Use Among All Women		Correct Use Among Women Who Received Misoprostol	
	(N = 1019)		(n = 600)	
	OR	95% CI	OR	95% CI
Age, y				
15-19 (ref)	–	–	–	–
20-34	0.66	0.30, 1.44	0.95	0.39, 2.34
≥ 35	0.58	0.24, 1.41	0.77	0.27, 2.16
Parity				
1 (ref)	–	–	–	–
2-4	1.07	0.63, 1.81	0.99	0.52, 1.88
> 4	1.08	0.60, 1.94	1.56	0.76, 3.24
Education (any vs none)	0.98	0.67, 1.44	1.43	0.91, 2.23
Region (Oromiya vs Amhara)	9.48	6.78, 13.24	1.33	0.79, 2.25
ANC with skilled provider or HEW	1.67	1.08, 2.58	0.77	0.41, 1.48
CMNH family meetings attendance				
0 (ref)	–	–	–	–
1 meeting	0.56	0.31, 1.01	1.92	0.79, 4.65
≥ 2 meetings	2.62	1.89, 3.63	2.02	1.35, 3.03
Birth attendant type				
Skilled provider ^a	1.85	1.12, 3.07	0.66	0.33, 1.35
HEW	6.84	3.84, 12.19	0.97	0.50, 1.87
TBA or CHDA	1.60	1.10, 2.35	1.10	0.66, 1.82
Other nontrained or alone (ref)	–	–	–	–
Misoprostol provider type^b				
Skilled provider			1.05	0.44, 2.47
HEW			0.81	0.52, 1.26
TBA or CHDA (ref)			–	–
Received during pregnancy			1.06	0.61, 1.86
Knows main benefit			1.42	0.55, 3.68
Counseled on correct use			2.92	0.87, 9.72
Hosmer-Lemeshow Test	10.35, $\sim\chi^2_{8df}$, $P = .24$		7.10, $\sim\chi^2_{8df}$, $P = .53$	

Abbreviations: ANC, antenatal care; CHDA, community health development agent; CMNH, community maternal and newborn health; HEW, health extension worker; OR, odds ratio; TBA, traditional birth attendant.

^aSkilled provider defined as physician, health officer, nurse, or midwife. Rounded to nearest 10th.

^bOnly one woman in Amhara reported a misoprostol provider in the “other, nontrained” category.

use of misoprostol did not decrease the rate of facility birth. Our findings are similar to the findings of this review.

Programs like MaNHEP, and those reviewed and described by Smith et al, were designed on the assumption that advance distribution with self-administration by trained women is as safe and effective as administration by trained community health workers and lay health workers. However, they were not designed to test this assumption. Although this strategy has potential to save lives through increased coverage, it also has potential for incorrect use, misuse, and adverse outcomes. A 2012 Cochrane review of benefits and risks of advance distribution was unable to identify sufficiently rigorous trials for inclusion.²⁹ In a separate review,³⁰

Oladapo notes that an individually randomized placebo-controlled community trial is underway (site not reported) to determine if advance distribution with self-administration is better than usual care, a prerequisite to more rigorous community trials that generate evidence to guide policy recommendations.

We suggest that until sufficient evidence is available, community programs promoting misoprostol to prevent PPH at home birth—including advance distribution and self-administration—should ensure that women, family caregivers, community health workers, and lay caregivers are trained to safely use misoprostol and to recognize adverse side effects. Such programs should report training inputs, patterns

of distribution (timing, cadre, distribution rate), administration (timing, route, number of tablets, coverage rate), referral, adverse maternal outcomes, and program costs. Standard measures would permit comparisons across programs.

CONCLUSION

As observed in this natural experiment, a strategy that allows for the distribution of misoprostol through multiple channels has the potential to significantly increase women's use of this life-saving drug in rural areas. Early distribution of misoprostol during pregnancy to women who are trained to use it correctly appears to be safe and unrelated to the choice of birthplace. Advance distribution of misoprostol for women's self-administration would further expand use. A program of rigorous research comparing the safety and efficacy of community distribution strategies, and particularly the advance distribution for self-administration, is needed to generate evidence to inform policy recommendations.

AUTHORS

Lynn M. Sibley, CNM, RN, PhD, is Professor at the Nell Hodgson Woodruff School of Nursing and Rollins School of Public Health at Emory University in Atlanta, Georgia, USA. She is Principal Investigator for the Maternal and Newborn Health in Ethiopia Partnership.

Sydney A. Spangler, CNM, MSN, PhD, is Assistant Professor at the Nell Hodgson Woodruff School of Nursing at Emory University in Atlanta, Georgia, USA.

Danika Barry, MPH, is Maternal and Newborn Health in Ethiopia Partnership Research Coordinator at the Nell Hodgson Woodruff School of Nursing at Emory University in Atlanta, Georgia, USA.

Solomon Tesfaye, MD, MPH, is University Research Co., LLC, Quality Improvement Advisor for the Maternal and Newborn Health in Ethiopia Partnership, based in Addis Ababa, Ethiopia.

Binyam Fekadu Desta, MPH, is the JSI Research & Training Institute, Inc. Senior Project Manager for the Maternal and Newborn Health in Ethiopia Partnership, based in Addis Ababa, Ethiopia.

Abebe Gebremariam Gobeze, MD, is Emory University Co-Principal Investigator and Project Director for the Maternal and Newborn Health in Ethiopia Partnership, based in Addis Ababa, Ethiopia.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to disclose.

ACKNOWLEDGMENTS

We would like to thank Dr. Keseteberhan Admassu, Minister of Health, Federal Democratic Republic of Ethiopia; Mr. Ayelegn Mulualem and Mr. Shallo Daba, Amhara and Oromiya Regional Health Bureaus Heads; and the Bill and Melinda Gates Foundation for their support of this MaNHEP supplemental evaluation on misoprostol to prevent postpartum hemorrhage in the community. We are very grateful to Dr. Kenneth Hepburn for his thoughtful editing of the article. Finally, we would like to thank the MaNHEP partners Emory University, JSI Research & Training Institute, Inc., University Research Co., LLC, and Addis Ababa University for their significant contributions to the quality improvement and surveys that generated quantitative data included in the article.

REFERENCES

1. Khan KS, Wojdyla D, Say L, Gülmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: A systematic review. *Lancet*. 2006;367:1066-1074.
2. World Health Organization. *WHO Recommendations for the Prevention and Treatment of Postpartum Haemorrhage*. Geneva, Switzerland: WHO; 2012.
3. Begley CM, Gyte G, Murphy DJ, Devane D, McDonald SJ, McGuire W. Active versus expectant management for women in the third stage of labour. *Cochrane Database of Systematic Reviews*. 2010 Jul 7; (7): CD007412. doi 10.1002/14651858.CD007412.pub2.
4. Alfirevic Z, Blum J, Walraven G, Weeks A, Winikoff B. Prevention of postpartum hemorrhage with misoprostol. *International Journal of Gynecology and Obstetrics*. 2007;99(1):S198-S201.
5. Derman RJ, Kodkany BS, Goudar SS, et al. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: A randomised controlled trial. *The Lancet*. 2006;368(9543):1248-1253.
6. Hoj L, Cardoso P, Nielsen BB, Hvidman L, Nielsen J, Aaby P. Effect of sublingual misoprostol on severe postpartum haemorrhage in a primary health centre in Guinea-Bissau: randomised double blind clinical trial. *British Medical Journal*. 2005;331(7519):723-727.
7. Mobeen N, Durocher J, Zuberi N, et al. Administration of misoprostol by trained traditional birth attendants to prevent postpartum haemorrhage in homebirths in Pakistan: a randomised placebo-controlled trial. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2011;118(3):353-361.
8. Walraven G, Blum J, Dampha Y, et al. Misoprostol in the management of the third stage of labour in the home delivery setting in rural Gambia: a randomised controlled trial. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2005;112(9):1277-1283.
9. Prata N, Gessesew A, Abraha A, Holston M, Potts M. Prevention of postpartum hemorrhage: Options for home births in rural Ethiopia. *African Journal of Reproductive Health*. 2009;13(2):88-95.
10. FIGO Safe Motherhood and Newborn Health Committee. Prevention and treatment of postpartum hemorrhage in low resource settings. *International Journal of Gynecology and Obstetrics*. 2012;117(2):108-118.
11. World Health Organization. *WHO Recommendations for Optimizing Health Workers' Roles to Improve Access to Key Maternal and Newborn Health Interventions Through Task Shifting*. Geneva: WHO; 2012.
12. Smith JM, Gubin R, Holston MM, Fullerton J, Prata N. Misoprostol for postpartum hemorrhage prevention at home birth: an integrative review of global implementation experience to date. *BMC pregnancy and childbirth*. 2013, 13:44.
13. Central Statistical Agency [Ethiopia] and ORC Macro. *Ethiopia Demographic and Health Survey 2011*. Addis Ababa, Ethiopia and Calverton, Maryland, USA: Central Statistical Agency and ORC Macro; 2012.
14. Ethiopian Federal Ministry of Health, UNFPA, WHO, AMDD. *National Baseline Assessment for Emergency Obstetric and Newborn Care*. Addis Ababa: The Ethiopian Federal Ministry of Health; 2008.
15. Venture Strategies Innovations. Ethiopia takes important policy step of registering misoprostol for postpartum bleeding. June 11, 2010. Available at: <http://vsinnovations.org/ethiopia-registration.html> Accessed March 26 2013.
16. Ethiopia Federal Ministry of Health. *Road Map for Accelerating the Reduction of Maternal and Newborn Morbidity and Mortality 2011-2015*. Addis Ababa, Ethiopia: Federal Ministry of Health; 2011.

17. Ethiopia Federal Ministry of Health. *Ethiopia Health Sector Development Programme HSDP III Mid-Term Review, Volume I Component Report*. Addis Ababa, Ethiopia: Federal Ministry of Health; 2008.
18. Sibley L. Demonstrate and leverage uptake of scaleable models of delivery and immediate newborn care in rural Ethiopia. Bill and Melinda Gates Foundation Global Health Grant Number OPPGH5309.
19. Stephenson RBA, Finneran C, Dynes M, Apuzzo S, Sibley L. *MaNHEP Baseline Report: Indicators of Knowledge, Attitudes and Practices Regarding Maternal and Newborn Health Care in Amhara and Oromiya Regions of Ethiopia*. Atlanta, Georgia, USA and Addis Ababa, Ethiopia: Maternal and Newborn Health in Ethiopia Partnership (MaNHEP); 2011.
20. Spangler S, Gobezaeyehu A, Hailemariam T, Sibley L. Interpretation of national policy regarding community-based misoprostol for postpartum hemorrhage prevention in Ethiopia: a tale of two regions.
21. Sibley L, Tesfaye S, Desta B, Frew A, Kebede A, Mohammed H, Ethier-Stover K, Dynes M, Barry D, Hepburn K, Gobezaeyehu A. Improving maternal and newborn health care delivery in rural Amhara and Oromiya regions of Ethiopia through the Maternal and Newborn Health in Ethiopia Partnership.
22. Bennayan J, Lloyd R, Plsek P. Statistical process control as a tool for research and healthcare improvement. *Quality and Safety in Health Care*. 2003;12(6):458-464.
23. Zimmerman SM, Icenogle ML. *Statistical Quality Control Using Excel*. Milwaukee, WI: ASQ Quality Press; 2003.
24. Mitike G BA, Barry D, Hill L, Schicker R, Baker H, Sibley L. *MaNHEP End line Survey Report: Indicators of Knowledge, Attitudes and Practices Regarding Maternal and Newborn Health care in Amhara and Oromiya Regions, Ethiopia*. Atlanta, GA and Addis Ababa, Ethiopia: Maternal and Newborn Health in Ethiopia Partnership (MaNHEP); 2013.
25. SAS software Version 9.3 of the SAS System for Microsoft Windows. Cary, NC: SAS Institute Inc.; 2012.
26. Zack M, Singleton J, Satterwhite C. *Collinearity Diagnostics Using the Information Matrix*. SAS Macro. Atlanta, GA: Emory University and Centers for Disease Control; 2005.
27. Wall K, Delaney K. Collinearity diagnostics using the information matrix: updated for GENMOD, MIXED and GLIMMIX. SAS macro. Atlanta, GA: Emory University; 2010.
28. Cook TD, Campbell DT. *Quasi-Experimentation: Design & Analysis Issues for Field Settings*. Boston, MA: Houghton Mifflin; 1979.
29. Oladapo OT, Fawole B, Blum J, Abalos E. Advance misoprostol distribution for preventing and treating postpartum haemorrhage. *Cochrane Database Syst Rev*. 2012;(2). Art. No: CD009336. doi: 10.1002/14651858.CD009336.Pub2.
30. Oladapo OT. Misoprostol for preventing and treating postpartum hemorrhage in the community: A closer look at the evidence. *International Journal of Gynecology & Obstetrics*. 2012;119:105-110.