**ORIGINAL ARTICLE**

# Oral misoprostol for preventing postpartum haemorrhage in home births in rural Bangladesh: how effective is it?

Hashima-E-Nasreen[1]*, Shamsun Nahar[2], Mahfuz Al Mamun[1], Kaosar Afsana[3] and Peter Byass[4]

[1]Research and Evaluation Division, BRAC Centre, Dhaka, Bangladesh; [2]Department of Family and Community Medicine, King Khalid University Abha, Kingdom of Saudi Arabia; [3]BRAC Health Programme, BRAC Centre, Dhaka, Bangladesh; [4]Umeå Centre for Global Health Research, Umeå University, Umeå, Sweden and IMMPACT, University of Aberdeen, Aberdeen, Scotland

***Aims***: Evidence exists about prevention of postpartum haemorrhage (PPH) by oral administration of misoprostol in low-income countries, but effectiveness of prevention by lay community health workers (CHW) is not sufficient. This study aimed to investigate whether a single dose (400 µg) of oral misoprostol could prevent PPH in a community home-birth setting and to assess its acceptability and feasibility among rural Bangladeshi women.

***Methods***: This quasi-experimental trial was conducted among 2,017 rural women who had home deliveries between November 2009 and February 2010 in two rural districts of northern Bangladesh. In the intervention district 1,009 women received 400 µg of misoprostol immediately after giving birth by the lay CHWs, and in the control district 1,008 women were followed after giving birth with no specific intervention against PPH. Primary PPH (within 24 hours) was measured by women's self-reported subjective measures of the normality of blood loss using the 'cultural consensus model.' Baseline data provided socio-economic, reproductive, obstetric, and bleeding disorder information.

***Findings***: The incidence of primary PPH was found to be lower in the intervention group (1.6%) than the control group (6.2%) ($p < 0.001$). Misoprostol provided 81% protection (RR: 0.19; 95% CI: 0.08–0.48) against developing primary PPH. The proportion of retained and manually removed placentae was found to be higher in the control group compared to the intervention group. Women in the control group were more likely to need an emergency referral to a higher level facility and blood transfusion than the intervention group. Unexpectedly few women experienced transient side effects of misoprostol. Eighty-seven percent of the women were willing to use the drug in future pregnancy and would recommend to other pregnant women.

***Conclusion***: Community-based distribution of oral misoprostol (400 µg) by CHW appeared to be effective, safe, acceptable, and feasible in reducing the incidence of PPH in rural areas of Bangladesh. This strategy should be scaled up across the country where access to skilled attendance is limited.

Keywords: *prevention of postpartum haemorrhage*; *misoprostol*; *BRAC*; *rural Bangladesh*

Postpartum haemorrhage (PPH) is the single most important cause of maternal mortality worldwide, accounting for one-third of maternal deaths (1). Ninety-nine percent of these deaths occur in low-income countries in women who rarely receive prophylaxis because they give birth outside of a hospital setting (1). Failure of the uterus to contract adequately after childbirth – known as uterine atony – is the leading cause of PPH. Postpartum haemorrhage is most preventable and treatable through active management of the third stage of labour (AMTSL) by conventional uterotonics, among which oxytocin is usually preferred (2). However, use of oxytocin is not feasible in many low-income settings where most births take place at home with untrained birth attendants (3). Moreover, oxytocins are injectable uterotonics, unstable at high temperatures, and requiring cold chain storage and skills that birth attendants, who do not practice AMTSL, might not possess (4).

Misoprostol, an $E_1$ prostaglandin analogue, has been suggested as an alternative to oxytocin since it could act as an effective uterotonic agent, is inexpensive, can be taken orally, does not need refrigeration, and has a long shelf-life (5). The International Federation of Gynecology and Obstetrics (FIGO) and the International Confederation of Midwives (ICM) jointly recommended that in home births without a skilled birth attendant, misoprostol may be the only available technology to control PPH (6). The World Health Organisation (WHO) has also recommended that in the absence of AMTSL, misoprostol can be offered by a health worker trained in its use for PPH prevention (7). A number of studies have examined the role of misoprostol in preventing PPH and proven its safety and efficacy (8–11). Efficacy of misoprostol in preventing PPH has also been well demonstrated in trials in India (8), Afghanistan (12), Indonesia (13), Nepal (14), Tanzania (15), and Ethiopia (16). A meta-analysis provided consistent evidence to support a recommendation for use of misoprostol to prevent PPH when oxytocin is unavailable (3).

Bangladesh is a country of over 150 million people; nearly two-thirds of the population live in rural areas and over one-third (35.7%) below the poverty line (17, 18). In Bangladesh, more than 85% of deliveries take place at home and only 18% of births are attended by a skilled provider (18). Approximately 11,000–12,000 women die each year due to maternal causes and PPH accounts for 28% of these deaths (19). There have been encouraging reductions in maternal mortality ratio (MMR) during 1990–2003 (from 574 to 320, respectively, /100,000 live births). In recent years, the rate of decline of MMR has stagnated, making it difficult to achieve the target of Millennium Development Goal 5 (MDG 5) by 2015 (i.e. 143/100,000 live births) (20). Under such circumstances, strategies to reduce the risk of PPH at home births are urgently needed.

Bangladesh Rural Advancement Committee (BRAC), a non-governmental development organisation, has initiated a 5-year (2008–2012) long intervention on maternal, neonatal, and child health programme (MNCH) in the rural areas of northern Bangladesh. Initially, BRAC undertook a pilot intervention in 2006 in Nilphamari district (in the northern part of the country, also a severely poverty-stricken area) to test the effectiveness of intervention towards improving the demand side of MNCH services. Based on successes of the pilot intervention, BRAC decided to scale it in three northern districts of Bangladesh in 2008 and six more districts in 2010. The design utilises BRAC's comparative advantage at the community level to build up MNCH services, working with UNICEF and Ministry of Health and Family Welfare to improve supply at the facility level – both at the district and sub-district level. The major components included capacity development of grassroot MNCH workers, empowerment of women and support groups, provision of MNCH services, and development of referral linkages with nearby health facilities. Different cadres of community health workers selected from localities such as *Shasthya Kormi* (SK), *Shasthya Sebika* (SS), *Newborn Health Workers* (NHW) deliver relevant services in the community. Recognising a need for strategies to prevent PPH among women who give birth at home without a skilled provider, the programme provides two tablets of misoprostol (200 µg/tablet) to women immediately after delivery of the baby under the direct supervision of a community health volunteer, SS, or NHW. Women were counselled on the use of misoprostol during antenatal visits. This study aimed to investigate whether a reduction in PPH (defined as blood loss of 500 ml or greater) occurred with the use of misoprostol. It also assessed the community acceptability and feasibility of oral misoprostol tablets among women in rural Bangladesh.

## Methods and materials

### Study design and setting
A quasi-experimental study design was used, conducted in Nilphamari district (intervention) and Naogaon district (control) – two rural districts in northern Bangladesh where most deliveries occurred at home (Fig. 1). As is typical of rural Bangladesh, the economy in the study areas is agrarian, and approximately 50% of the population lives below the poverty level. The majority of women are involved in household work and childcare. BRAC is active in both districts implementing its core programmes of micro-finance, health, and education. Typical activities include providing beneficiaries with education and skill development training together with social awareness campaigns and a microfinance programme supporting income generating activities. Regular government activities are in intervention and control districts.

The intervention group received intensive maternity services including misoprostol tablets from the MNCH programme. The other maternity services in the intervention area comprised domiciliary education and services on antenatal, delivery, and postnatal care; identification and management of high-risk cases; and referral to tertiary facilities if any complication arose. The control group received only the essential health care including health and nutrition education, water and sanitation, family planning, immunisation, pregnancy-related care, vitamin-A supplementation, and basic curative services, but neither the intensive maternity care nor the misoprostol tablets after childbirth.

In the intervention area, CHWs routinely identify pregnant women and register them. *Shasthya Kormi* received a 12-day and SS an 18-day basic training, followed by monthly and quarterly 1-day refresher train-
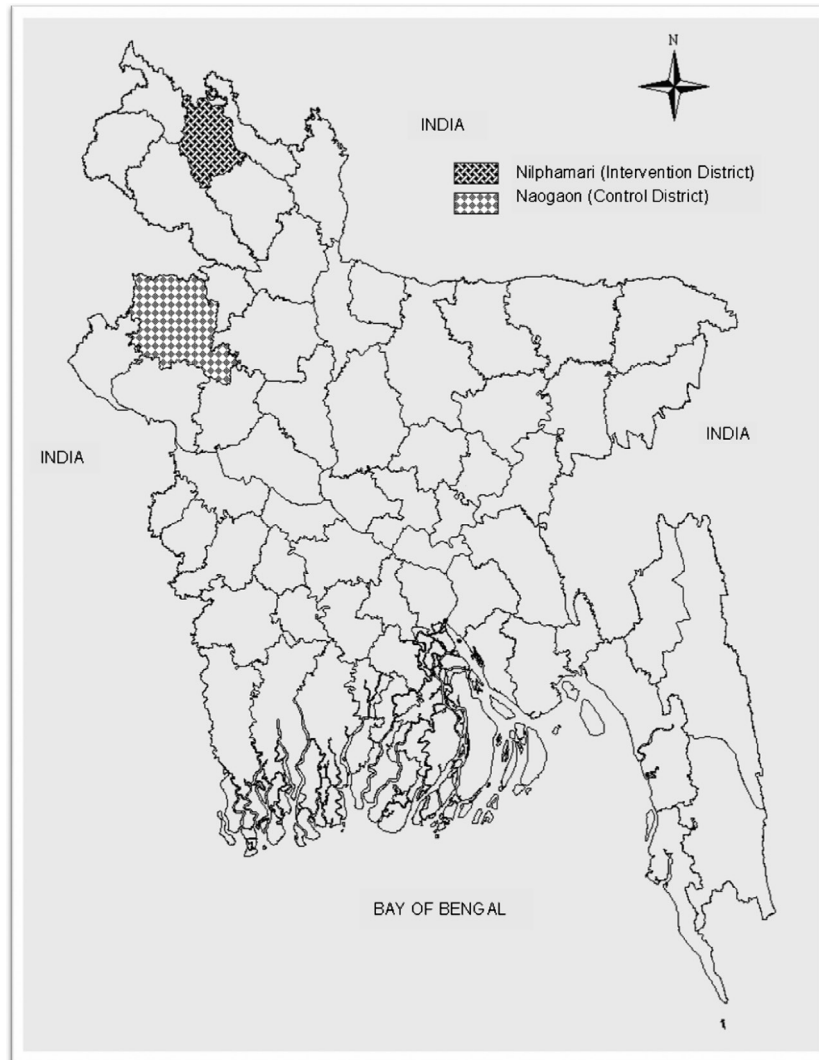
*Fig. 1.* Map of study area.

ings on maternal, neonatal, and child health management and technical issues of field operation. The NHW received 6 days training on birthing care, clean delivery, basic management, and referral of complication. Both SS and NHW received special training on the purpose, correct timing when using misoprostol to prevent PPH, the risks of taking misoprostol before the childbirth, and common adverse effects and their measures.

### Method of implementation of misoprostol in intervention area

The programme sensitised women, their husbands, and support members in the family about PPH and use of misoprostol tablets during antenatal visits and monthly expected date of delivery (EDD) meetings. The CHWs provided education on misoprostol, its purpose, correct timing of use, the risks of taking misoprostol before birth of the baby, and included common side effects and how to cope with these. Soon after the delivery of the baby,

two tablets of misoprostol (400 µg) were given to parturient free of cost under direct supervision of SS and/or NHW. They then monitored the parturient for 2 hours for assessing further referral to a higher level facility following a written guideline. They also provided referral slips containing reasons for referral and referred by whom.

### Sample size and study population

The delivery registration maintained by BRAC Health Programme provided the sample frame for the study. The estimated sample of 2,017 women (half from each area) delivering at home during November 2009–February 2010 were chosen randomly from the delivery registration. Considering an estimated prevalence of primary PPH of 4.7% in rural Bangladesh (21), the study was designed with a significance of 0.05, power 0.80, non-response rate 0.02, and an effect size of 0.47, presuming that community-based misoprostol administration would

result in 47% reduction in PPH (8). Ten respondents declined to participate and a replacement household was selected at random ensuring that the full sample size was achieved.

### Data collection and quality control

The data were collected during March to April 2010. Female interviewers carried out structured interviews at the respondents' home on socio-economic condition, reproductive health, maternity care, PPH, and use of misoprostol. A well-designed, structured, and pre-tested questionnaire was use for carrying out the study.

A 5-day training course was provided to 28 interviewers and four field monitors on the objectives of the study, different terms used in the questionnaire, techniques of gathering information, communication skills for rapport building, and maintenance of confidentiality and privacy while collecting information. The training course also included 2 days of field practice followed by review and evaluation. A three-layered monitoring system was developed to monitor the field activities of interviewers and supervisors.

### Dependent variable
#### Assessment of PPH

The outcome measure for the study was postpartum blood loss estimated at 500 ml or more within 24 hours of delivery (primary PPH). The PPH was assessed through women's self-reported subjective measures of the normalcy of blood loss using cultural consensus model (22) that was also used by Sibley et al. (23) in Matlab, Bangladesh. The model used six structured questions focusing on three bleeding conditions – normal, abnormal excessive, and scanty. In this model, excessive bleeding was characterised as bleeding that is continuous, forceful, and associated with poor appetite, pallor, weakness, and fainting (23). Secondary outcomes of misoprostol included delivery of placenta within 30 min versus delayed delivery, and whether manual removal of placenta was needed or not.

### Independent variables
#### Assessment of dose, acceptability, and feasibility of misoprostol tablet

The required dose for the study comprised two tablets (200 µg/tablet) of misoprostol taken as a single dose soon after delivery of the baby under direct supervision of SS or NHW. Two measures were used to assess community acceptability of misoprostol tablets: recommendation made to other pregnant women and respondents' willingness to use and buy misoprostol tablets in future pregnancy. Feasibility was measured using two indicators: coverage of women with misoprostol by CHWs and the time at which the tablets were taken (within 5 min of birth) (8).

### Assessment of socio-economic, reproductive, obstetric, and bleeding disorder

Age of the women was calculated in years. Socio-economic status was assessed by respondents' years of schooling and household economic status. Economic status of the household was measured by wealth index to explore inequalities in household income and its association with problems of access to health services and health-related outcomes (21). We used data on household assets and characteristics of the house to calculate the wealth index and ranked the households from one to five. Scores of one and five identified the poorest and richest households, respectively. The reproductive indicators comprised age at first conception, number of pregnancies, number of antenatal consultations (ANC) received in the latest pregnancies, and history of previous uterine operations. Obstetric indicators included prolonged labour measured by the duration of labour pain for more than 12 hours, pregnancy induced hypertension, trained attendants at birth, retained placenta, mal-presentation of the index baby, and oral administration of two misoprostol tablets soon after delivery of the baby. Bleeding disorders were indicated by PPH in previous pregnancies, prolonged clotting time, and severe anaemia necessitating blood transfusion.

For analysis, the explanatory variables were dichotomised or categorised. Maternal age was expressed as <20 years, 20–35 years, and >35 years; women's years of schooling as no schooling, primary (1–5 years of schooling), and secondary (≥6 years of schooling); household economic status as poor (wealth index scored 1–2) versus non-poor (wealth index scored 3–5); number of pregnancies 1–2 versus ≥3; previous uterine operation as yes versus no; prolonged labour as yes versus no; pregnancy induced hypertension as yes versus no; trained attendant at birth as yes versus no; retained placenta as yes versus no; mal-presentation of index baby as yes versus no; PPH in previous pregnancy as yes versus no; and prolonged clotting time and blood transfusion needed for severe anaemia as yes versus no.

### Data analysis

Incidence of primary PPH was calculated for the intervention and control groups. Descriptive analyses were performed to compare the intervention and control group by the background characteristics of respondents, incidence of PPH, and outcome of misoprostol administration. An independent $t$-test was performed to compare means between groups, Mann–Whitney $U$-test the median, and $\chi^2$ test and Fisher's exact two-sided $p$-test the proportion. Univariate logistic regression analyses with a 95% confidence interval ($p < 0.05$) identified the possible risk factors of PPH. Mautinomial logistic regression (Stepwise-Forward method) analysis calculated the adjusted relative risk (RR) after controlling the simultaneous

confounding effects of possible predictors to estimate the independent preventive effect of misoprostol on PPH.

## Ethical consideration

The study was approved by the Bangladesh Medical Research Council (Ref. no. BMRC/ERC/2007-2010/ 1172). Detailed information about the study was provided verbally to the potential participants. The interviews were conducted after verbal informed consent was obtained. Strict confidentiality was maintained around the identity of the respondents. Data were entered anonymously linking with identification number (ID). Identification of the respondent was concealed and only the principal investigator had the authority to know if any verification of information was needed from the participants.

## Results

Analysis revealed that women in the intervention group were less educated and less likely to be poor than women in the control group. They also had lower mean age of conception and higher average number of pregnancies. In the intervention group, 9/10 of the women received antenatal consultation from a trained health providers compared to 1/4 in the control area. However, delivery by skilled birth attendants and use of oxytocin sometimes before and after delivery were found to be higher in the control area than in the intervention area. The median risk count of primary PPH was found to be lower in the intervention group than in the control group (Table 1). Maternal risk factors for developing primary PPH are summarised in Table 2. The distribution of identified risk factors was found to be significantly higher in the control group compared to the intervention group (data not shown).

Of the 2,017 women who participated in the study, 884 (87.6%) in the intervention group received two tablets of misoprostol under the direct supervision of the CHWs and 125 did not and were excluded from further outcome analysis. The background characteristics of 125 women did not differ from that of the participating women. The reasons for not using misoprostol included lack of knowledge about misoprostol (66%), belief that it is not necessary (14.4%), CHWs were not present or drug was not available (17.6%), and husbands' objection (1.6%) (data not shown). Meanwhile, no women took the allocated treatment in the control group (Fig. 2).

Primary PPH occurred in 84 women (4.2%) in the study (Fig. 2). The incidence of primary PPH was found to be lower in the intervention group than in the control

*Table 1.* Sample profile

|  | Intervention n = 1,009 | Control n = 1,008 | p-value |
|---|---|---|---|
| Socio-economic |  |  |  |
| Mean age in years (±SD) | 23.0±4.8 | 22.9±5.0 | 0.814 |
| Mean years of schooling (±SD) | 3.6±3.4 | 5.0±3.3 | <0.001 |
| Educational status |  |  |  |
| No schooling | 36.1 | 214 (21.2) | 0.000 |
| Primary | 35.3 | 321 (31.8) |  |
| Secondary or higher | 28.6 | 473 (46.9) |  |
| Wealth index (%) |  |  |  |
| Poorest | 14.4 | 25.6 | <0.001 |
| 2 | 21.4 | 18.7 |  |
| 3 | 23.6 | 16.4 |  |
| 4 | 20.2 | 19.8 |  |
| Richest | 20.4 | 19.5 |  |
| Reproductive |  |  |  |
| Mean age at first conception (±SD) | 16.8 (2.1) | 17.5 (2.4) | <0.001 |
| Mean number of pregnancy (±SD) | 2.6 (1.4) | 2.1 (1.2) | <0.001 |
| Obstetric |  |  |  |
| Received 4+ ANC from trained providers | 87.8 | 26.4 | <0.001 |
| Delivery by skilled birth attendants | 9.7 | 20.7 | <0.001 |
| Oxytocin used before/after delivery | 13.8 | 23.5 | <0.001 |
| Median risk count for PPH | 1 (0–6) | 2 (0–8) | <0.001 |

*Table 2.* Risk factors for PPH

|  | OR | CI |
|---|---|---|
| ANC ($<$4) | 2.60 | 1.61–4.19 |
| Antepartum complication | 2.89 | 1.79–4.69 |
| Pre-eclampsia | 5.11 | 1.09–24.05 |
| Complication during delivery | 3.23 | 2.02–5.10 |
| Retained placenta | 15.98 | 9.35–27.29 |
| Prolonged labor | 2.69 | 1.23–5.88 |
| Intrapartum haemorrhage | 24.29 | 7.65–77.13 |
| Manual removal of placenta | 12.34 | 7.28–20.93 |
| Bleeding disorder | 3.75 | 0.45–31.51 |
| Prior PPH | 1.85 | 0.71–4.80 |

group (Table 3). In women receiving misoprostol, the odds ratio of primary PPH was 0.21 (95% CI: 0.11–0.39) compared to women who did not (data not shown). With respect to the secondary outcomes of misoprostol, the intervention group was significantly better than the control group (Table 3). Also, the PPH cases in the intervention group were less likely to need any additional treatment, such as saline and oxytocin injection, emergency transfer to a higher level facility, or need a blood transfusion (Table 4). Among women receiving misoprostol, only 11 (1.2%) had a transient increase in shivering, abdominal pain, fever, and oedema (data not shown).

Multinomial logistic regression analyses showed that after simultaneous adjustment for the biological and socio-economic factors women who received a supervised dose of misoprostol soon after delivery of baby were 81% protected (RR = 0.19; 95% CI: 0.08–0.48) from developing primary PPH compared with women who did not receive misoprostol. The risk factors associated with PPH included manual removal of placenta (RR = 5.21; 95% CI: 2.01–13.49) and intrapartum haemorrhage (RR = 12.79; 95% CI: 3.23–50.50) (Table 5).

The total coverage of oral misoprostol administration to the parturient was around 88% indicating a high feasibility of community-based distribution of misoprostol by the CHWs. In addition, women were asked about the time elapsed from child birth to consumption of the drug. The elapsed time reported by the women was grouped into 5, 10, 15, 20, and 30 min, considering 5 min after birth to be the earliest possible time. The results showed that CHWs were able to cover 46% of the parturient within 5 min, 27% (73%) within 10 min, 9% (82%) within 15 min, 4% (87%) within 20 min, and 5% (92%) within 30 min (Fig. 3).

## Discussion

This non-randomised community trial showed that the community-based distribution of a supervised dose of 400 μg misoprostol reduced primary PPH in women in rural Bangladesh by 81%. Our result is consistent with several other trials in different low-income countries such as India (8), Guinea Bissau (11), Indonesia (13), Nepal (14), and Nigeria (24). In these studies, they have shown that misoprostol is effective in preventing postpartum haemorrhage in community and hospital settings, albeit with a response often less robust than that of oxytocin (3, 11, 25–29). In this study, CHWs provided the two tablets of misoprostol to the parturient under their direct supervision indicated that the correct timing of administration is ensured and is the main difference with other studies. On the contrary, delivery with unskilled birth attendants, poverty, illiteracy, and number of pregnancies were actually higher in our intervention areas than in comparison areas, and misoprostol should be recommended if women could not access skilled birth attendants. Under this circumstance, our study confirms that adequate training to the lay CHWs and ensuring correct timing of administration of misoprostol to the parturient can prevent PPH substantially.
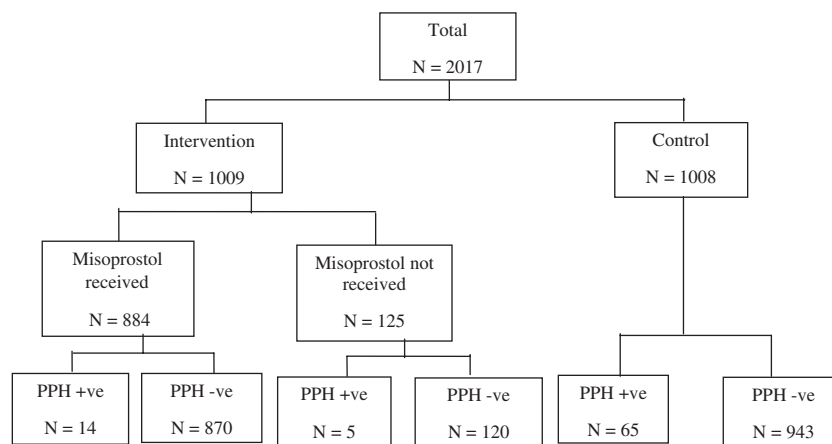


*Fig. 2.* Trial profile.

*Table 3.* Outcome of misoprostol administration according to treatment group

|  | Intervention $n = 884$ (%) | Control $n = 1,008$ (%) | *P*-value |
|---|---|---|---|
| Primary outcome |  |  |  |
| Incidence of PPH | 14 (1.6) | 65 (6.4) | <0.001 |
| Secondary outcome |  |  |  |
| Interval between delivery of baby and placenta (>30 min) | 31 (3.5) | 52 (5.2) | 0.035 |
| Manual removal of placenta | 26 (2.9) | 68 (6.7) | <0.001 |

Multiple studies reaffirm that unskilled birth attendants are able to successfully use misoprostol for the prevention and treatment of PPH. In this study, we chose to provide misoprostol to the women under direct supervision of CHWs just after delivery of baby rather than to distribute misoprostol to the pregnant women for self-administration. The reason for this decision was that women may forget to take two tablets together immediately after delivery. In many resource poor countries like India (8), Afghanistan (12), Tanzania (15), Ethiopia (16), and Indonesia (13) it has been demonstrated that the traditional birth attendants (TBA) can distribute misoprostol to the pregnant women with detailed information, education, and counselling and use the drug safely for the treatment of PPH. Local community agents, CHWs, and unskilled birth attendants thus can be empowered to use this lifesaving medication responsibly and safely.

Consistent with prior studies (30, 31), we found similar risk factors responsible for the primary PPH. However, counts of risk were lower among women in the intervention group indicating that women were more aware about PPH and its risk factors and took necessary precautions accordingly. It may be due to the fact that about 9 in 10 women in the intervention area received more than four antenatal consultation visits. The CHWs educate women, husbands, and family members about PPH and its risk factors, prevention, and management during antenatal care and monthly EDD meetings. Women in the intervention group also received information, education, and services on ANC, high-risk pregnancies and management,

*Table 4.* Additional interventions among PPH cases

|  | Intervention $n = 14$ (%) | Control $n = 65$ (%) |
|---|---|---|
| Need saline and oxytocin injection after delivery at home for treatment of PPH | 3 (21.4) | 26 (40.0) |
| Referred to hospital | 2 (14.3) | 11 (16.9) |
| Need blood transfusion | 0 | 2 (3.1) |
| Need other surgical intervention | 1 (7.1) | 0 |

tetanus toxoid immunisation, iron supplementation, safe delivery care, and management of maternity complications.

The results of univariate analysis revealed a number of potential risk factors for PPH but after adjustment two factors remained significant including manual removal of placenta and intrapartum haemorrhage. In this study, retained and manually removed placentae were found to be more common in women in the control than the intervention group. This is not in agreement with the results of previous studies (2, 32, 33) on misoprostol. This may be due to the fact that the other studies were carried out at tertiary care hospitals and the majority of the patients treated with misoprostol may have also received other measures to quickly deliver the placenta and thus contribute to an insignificant difference in duration with the oxytocin group. In our study, prophylactic use of misoprostol in the intervention areas reduced the rate of bleeding-related referrals and decreased the need for additional interventions. Similar findings were observed in other studies (2, 8, 15). Reducing referrals and other additional measures did not only cut down the burden of maternal deaths and morbidity due to PPH, but also relieved families from high costs of treatment.

Previous research indicated that doses of 600 μg of misoprostol resulted in transient chills, nausea, and elevation of temperature. In resource-poor settings, these adverse effects are acceptable and clearly preferable to excessive haemorrhage (2, 8, 34, 35). As stated by Lumbiganon et al. (35), the adverse effects of misoprostol are dose-dependent, determining that the optimal dose of misoprostol for prophylactic postpartum use is 600 μg. However, in a recent review (36), a 400 μg dose of misoprostol was found to be as effective as 600 μg in reducing PPH risk but with fewer side effects. We used a 400 μg dose for our programme and observed that only 1.2% of women who used misoprostol experienced the above side effects. There is currently insufficient evidence for the efficacy of a 400 μg dose in preventing PPH and the current study adds evidence in this respect.

Our findings show that providing community-based education and distribution of misoprostol by CHWs is a safe, acceptable, and effective strategy for prevention of

*Table 5.* Adjusted relative risk of blood loss 500 ml or more with misoprostol

| Factors | Full model | | | Final model | | |
|---|---|---|---|---|---|---|
| | SE | P | RR (95% CI) | SE | P | RR (95% CI) |
| Misoprostol received | | | | | | |
| No | | | 1 | | | 1 |
| Yes | .588 | .001 | 0.13 (0.04–0.43) | .460 | .000 | 0.19 (0.08–0.48) |
| Biological factors | | | | | | |
| Number of conception | | | | | | |
| <3 | | | 1 | | | |
| ≥3 | .479 | .593 | 1.29 (0.51–3.30) | – | | |
| Number of ANC received | | | | | | |
| 4 or more | | | 1 | | | |
| <4 | .498 | .396 | 0.66 (0.25–1.74) | – | | |
| Birth attendant at delivery | | | | | | |
| Trained | | | 1 | | | |
| Untrained | .535 | .739 | 1.19 (0.42–3.41) | – | | |
| Retained placenta | | | | | | |
| No | | | 1 | | | |
| Yes | .833 | .792 | 1.25 (0.24–6.37) | – | | |
| Removal of placenta | | | | | | |
| Spontaneous | | | 1 | | | 1 |
| Manual | .750 | .042 | 4.60 (1.05–20.03) | 0.486 | 0.001 | 5.21 (2.01–13.49) |
| Antepartum complications | | | | | | |
| No | | | 1 | | | |
| Yes | .590 | .207 | 2.11 (0.66–6.69) | – | | |
| Pre-eclampsia | | | | | | |
| No | | | 1 | | | |
| Yes | 1.287 | .614 | 1.91 (0.15–23.87) | – | | |
| Prolong labour | | | | | | |
| No | | | 1 | | | |
| Yes | .507 | .111 | 2.25 (0.83–6.07) | – | | |
| Intrapartum haemorrhage | | | | | | |
| No | | | 1 | | | 1 |
| Yes | .787 | .006 | 8.71 (1.87–40.71) | .702 | .000 | 12.79 (3.23–50.58) |
| Socio-economic factors | | | | | | |
| Educational status | | | | | | |
| No schooling | | | 1 | | | |
| Primary | .539 | .290 | 0.57 (0.20–1.63) | – | | |
| Secondary or higher | .535 | .751 | 0.84 (0.30–2.40) | – | | |
| Wealth index | | | | | | |
| Non-poor | | | 1 | | | |
| Poor | .447 | .196 | 0.56 (0.23–1.35) | – | | |

PPH in a rural area of Bangladesh where women do not have access to skilled birth attendants. In our study, irrespective of the use of misoprostol, 9 in 10 women showed a positive attitude towards the use of the drug, demonstrating high acceptability of misoprostol in the community. It may be speculated that the MNCH
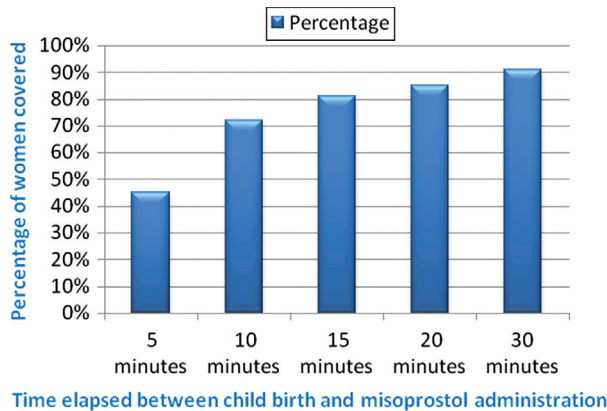
*Fig. 3.* Time elapsed between childbirth and misoprostol administration by the community health workers (CHWs).

programme involving family members and husbands in the health education session in the monthly EDD meetings reinforced the use of misoprostol. It ensured that at least one support person in the household knew about PPH and thus misoprostol was given at most of the births in the intervention area. This is consistent with previous research from other Asian countries documenting that involving husbands, mothers-in-law, and mothers in the educational process enhanced high coverage and acceptability of misoprostol in the community (12, 14).

This study provides evidence on the feasibility of parturients consuming misoprostol at home under direct supervision of CHWs. However, considering feasibility in terms of how effectively the CHWs reached the parturients, the findings suggest that CHWs are not able to cover majority of the parturient immediately after child birth; that is, within 5 min as has been taken as the cut-off in an Indian study (8). This is because the CHWs are not always present at the time of birth or reach there late after child birth. Multiple factors, such as CHWs living far from the parturient, delivery occurring at night, bad road communication, lack of transport, etc. may contribute to the absence or delay. However, even short delays, such as an extra 5 min, in initiating treatment can result in worsening PPH requiring uterotonics, blood, intravenous fluids, and potentially major surgery (12). The programme may use an alternative approach that has already been tested in Afghanistan (12), where the drug was distributed directly to the pregnant women, who were counselled on correct timing of administration, and prepared them to consume the tablets by themselves.

This is the first study in rural Bangladesh to show that distribution of misoprostol by the lay CHWs can effectively prevent PPH where pregnant women do not have access to skilled attendants. This study gives clear evidence from a community-based trial of misoprostol within a defined geographical area in Bangladesh. The study was conducted in two rural districts of Bangladesh and does not represent the urban scenario. Although

there is no evidence for generalising these findings to other rural areas of the country, they are highly likely to be indicative of the situation among rural women. The deficiency in randomisation in the quasi-experimental design limits ruling out confounding variables and introduces new threats to internal validity. Because randomisation is absent even if these threats to internal validity are assessed, causation still cannot be fully established. Measurement of blood loss was based on subjective assessment based solely on recall rather that clinical estimation because the data was collected 4 months after the childbirth. The estimation of blood loss at the time of deliver is difficult even for experienced clinicians and, thus, the blood loss may be over- or under-estimated. Data collection focused on recall of critical information and so the recall bias could not be avoided. However, the same method was used in both districts on a comparable basis, and administration of supervised dose has ensured the correct timing of use of misoprostol.

## Policy implications

The study was done in a comprehensive maternal, neonatal, and child health programme in rural areas of Bangladesh. Although the World Health Organisation does not endorse misoprostol administration for prevention of PPH in community setting, providing this by community health workers as practiced in this programme at least ensures a well-supervised method for PPH prevention. In Bangladesh, 75%–85% of births still take place at home. At this moment, there is no alternative available in community setting apart from giving misoprostol to women during delivery at home for the prevention of PPH. Hence, it is really crucial to consider, at the national level, starting a supervised administration of misoprostol by community health workers. In order to execute this, the government should use community skilled birth attendants and work with NGOs to use their birth attendants/community health workers. In addition, using various avenues to raise community awareness and enhance mother's knowledge about misoprostol use for prevention of PPH is important. The knowledge produced and lessons learned from the use of misoprostol should be taken to global levels especially to use it in the community setting of other developing countries in order to save lives of many mothers who are dying from PPH.

Misoprostol is recommended for medical abortion. However, this is not widely practiced in Bangladesh. Research in this area may inform policy-makers and practitioners about its implications in future.

## Conclusion

This population-based study in rural Bangladesh suggests that community-based education and administration of

supervised 400 µg misoprostol reduces the incidence of PPH and is safe, acceptable, and feasible. This largely accords with findings reported from other low-income countries. Reducing maternal mortality from PPH is a major current priority and a developmental imperative in Bangladesh. In order to achieve the MDG 5 by 2015, we recommend that misoprostol is an essential intervention that can be scaled up in rural communities in Bangladesh with a high rate of unskilled birth attendance for the prevention and treatment of PPH.

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## References

1. Ronsmans C, Graham WJ. Maternal mortality: who, when, where and why. Lancet 2006; 368: 1189–200.
2. Gülmezoglu AM, Villar J, Ngoc NTN, Piaggio G, Carroli G, Adetoro L, et al. WHO multicentre randomised trial of misoprostol in the management of the third stage of labour. Lancet 2001; 358: 689–95.
3. Langenbach C. Misoprostol in preventing postpartum hemorrhage: a meta-analysis. Int J Gynaecol Obstet 2006; 92: 10–8.
4. Miller S, Lester F, Hensleigh P. Prevention and treatment of postpartum haemorrhage: new advances for low-resource settings. J Midwifery Women Health 2004; 49: 283–92.
5. Goldberg AB, Greenberg MB, Darney PD. Misoprostol and pregnancy. N Engl J Med 2001; 344: 38–47.
6. International Confederation of Midwives and International Federation of Gynaecology and Obstetrics. Prevention and treatment of post-partum haemorrhage: new advances for low resource settings. Int J Gynecol Obstet 2007; 97: 160–3.
7. World Health Organisation. WHO recommendations for the prevention of postpartum haemorrhage. Geneva: Author; 2007, pp. 14–15.
8. Derman RJ, Kodkany BS, Goudar SS, Geller SE, Naik VA, Bellad MB, et al. Oral misoprostol in preventing postpartum haemorrhage in resource poor communities: a randomized control trial. Lancet 2006; 368: 1248–53.
9. Bamigboye AA, Hofmeyr GJ, Merrell DA. Rectal misoprostol in the prevention of postpartum hemorrhage: a placebo-controlled trial. Am J Obstet Gynecol 1998; 179: 1043–6.
10. Hofmeyr GJ, Nikodem VC, de Jager M, Gelbart BR. A randomised placebo controlled trial of oral misoprostol in the third stage of labour. Br J Obstet Gynaecol 1998; 105: 971–5.
11. 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. BMJ 2005; 331: 723.
12. Sanghvi H, Ansari N, Prata NJV, Gibson H, Ehsan AT, Smith JM. Prevention of postpartum hemorrhage at home birth in Afghanistan. Int J Gynaecol Obstet 2010; 108: 276–81.
13. Sanghvi H, Wiknjosastro G, Chanpong G, Fishel J, Ahmed S, Zulkarnain M. Prevention of postpartum haemorrhage study, West Java, Indonesia. Baltimore, MD: JHPIEGO, Maternal and Neonatal Health Programme; 2004.
14. Rajbhandri S, Pun A, Hodgins S, Rajendra PK. Prevention of postpartum haemorrhage at home birth with use of misoprostol in Banke District, Nepal. Int J Gynaecol Obstet 2006; 94: S143–4.
15. Prata N, Mbaruku G, Campbell M, Potts M, Vahidinia F. Controlling postpartum haemorrage after home births in Tanzania. Int J Gynecol Obstet 2005; 90: 51–5.
16. Prata N, Gessessew A, Abraha AK, Holston M, Potts M. Prevention of postpartum haemorrhage: options for home birth in rural Ethiopia. Afr J Reprod Health 2009; 13: 87–95.
17. Bangladesh Bureau of Statistics (BBS). Planning commission, Ministry of Planning. Dhaka, Bangladesh: Author; 2004.
18. Bangladesh Demographic and Health Survey. Dhaka, Bangladesh and Calverton, Maryland, USA: National Institute of Population Research and Training (NIPORT), Mitra and Associates, and Macro International Inc; 2007.
19. Bangladesh Maternal Mortality Survey. Final report. Bangladesh maternal health services and maternal mortality survey 2001. Dhaka: National Institute of Population Research and Training (NIPORT) and Measure DHS+ORC Macro; 2003.
20. Government of People's Republic of Bangladesh and UNDP. Millennium development goals: Bangladesh progress report 2008. General Economics Division, Planning Commission, Government of People's Republic of Bangladesh, Dhaka: Author; 2008.
21. Gwatkin D, Rutstein S, Johnson S, Pande R, Wagstaff A. Differences in health, nutrition, and population in Bangladesh 1996/1997, 1999/2000, 2004. Washington, DC: World Bank, Human Development Network; 2007.
22. Romnet AK, Weller SC, Batchelder WH. Cultural as consensus: a theory of culture, informant accuracy. Am Anthropol 1986; 88: 313–38.
23. Sibley LM, Hruschka DJ, Kalim N, Khan J, Paul M, Edmonds JK, et al. Cultural theories of postpartum bleeding Matlab, Bangladesh: implications for community health intervention. J Health Popul Nutr 2009; 27: 379–90.
24. Jadesimi A, Okonofua FE. Tackling the unacceptable: Nigeria approves misoprostol for PPH. J Fam Plann Reprod Health Care 2006; 32: 213–41.
25. Walley RL, Wilson JB, Crane JM, Matthews K, Sawyer E, Hutchens D. A double-blind placebo controlled randomised trial of misoprostol and oxytocin in the management of the third stage of labour. BJOG 2000; 107: 1111–5.
26. Zachariah ES, Naidu M, Seshadri L. Oral misoprostol in the third stage of labor. Int J Gynaecol Obstet 2006; 92: 23–6.
27. El-Refaey H, Nooh R, O'Brien P, Abdalla M, Geary M, Walder J, et al. The misoprostol third stage of labour study: a randomised controlled comparison between orally administered misoprostol and standard management. BJOG 2000; 107: 1104–10.

28. Caliskan E, Dilbaz B, Meydanli MM, Ozturk N, Narin MA, Haberal A. Oral misoprostol for the third stage of labor: a randomized controlled trial. Obstet Gynecol 2003; 101: 921–8.

29. Oboro VO, Tabowei TO. A randomised controlled trial of misoprostol versus oxytocin in the active management of the third stage of labour. J Obstet Gynaecol 2003; 23: 13–6.

30. Maughan KL, Heim SW, Galazka SS. Preventing postpartum haemorrhage: managing third stage of labor. Am Fam Physician 2006; 74: 1015–28.

31. Selo-Ojeme DO, Okonofua FE. Risk factors for primary postpartum haemorrhage. A case control study. Arch Gynecol Obstet 1997; 259: 179–87.

32. Afolabi EO, Kuti O, Orji EO, Ogunniyi SO. Oral misoprostol versus intramuscular oxytocin in the active management of the third stage of labour. Singapore Med J 2010; 51: 207–11.

33. Nisa MU, Zahida, Sadia, Misbah, Nawaz R, Shazia, et al. Prophylaxis of atonic postpartum hemorrhage with misoprostol in underdeveloped countries. Annals of KEMU 2009; 15: 185–9.

34. Hofmeyr GJ, Nikodem VC, de Jager M, Drakely A. Side-effects of oral misoprostol in the third stage of labour – a randomized placebo-controlled trial. S Afr Med J 2001; 91: 432–5.

35. Lumbiganon P, Villar J, Piaggio G, Gulmezoglu AM, Adetoro L, Carroli G. Side effects of oral misoprostol during the first 24 hours after administration in the third stage of labour. BJOG 2002; 109: 1222–6.

36. Hofmeyr GJ, Gulmezoglu AM, Novikova N, Linder V, Ferreira A, Piaggio G. Misoprostol to prevent and treat postpartum haemorrhage: a systematic review and meta-analysis of maternal deaths and dose-related effects. Bull World Health Organ 2009; 87: 666–77.

**\*Hashima-E-Nasreen**
Research and Evaluation Division
BRAC Centre
75 Mohakhali
Dhaka 1212, Bangladesh
Tel: +88 02 8824180 ext. 2708
Fax: +88 02 8823542
Email: nasreen.h@brac.net