SCALING UP OF MISOPROSTOL FOR PREVENTION OF POSTPARTUM HEMORRHAGE IN 29 *UPAZILAS* OF BANGLADESH

FINAL REPORT

May 2011

Special Publication No. 133

ISBN 978-984-551-323-4

SCALING UP OF MISOPROSTOL FOR PREVENTION OF POSTPARTUM HEMORRHAGE IN 29 *UPAZILAS* OF BANGLADESH

Md Abdul Quaiyum
Martine Holston
S A Shahed Hossain
Suzanne Bell
Ndola Prata

Additional Contributors:

Salima Rahman, Mohsina Begum, Ashrafi Jahan Azmi, Arshadul Islam, Jennet Arcara and Emma Nesper

The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) is an international health research institution located in Dhaka, the capital of Bangladesh. In collaboration with partners from academic and research institutions throughout the world, the Centre conducts research, training and extension activities as well as program-based activities.

Venture Strategies Innovations (VSI) is a California-based nonprofit organization committed to improving women's health in developing countries by creating access to effective and affordable technologies on a large scale. VSI's innovative approach involves partnerships that build upon existing infrastructure, resources and markets. VSI focuses on reducing barriers to access and enhancing human capacity to bring about sustainable improvements in health.

Bixby Center for Population, Health and Sustainability is a research center within the University of California, Berkeley School of Public Health. The Center is dedicated to developing innovations to improve reproductive health in resource-poor settings, including reliable health information systems, local access to essential technologies, and guidelines for prioritizing interventions to maximize health impact. The Center assists in the implementation of maternal health programs and seeks to improve the health outcomes of the world's poorest and most vulnerable women and their families.

RDRS Bangladesh is a large, long-established development NGO working in 64 *upazilas* of eleven districts among a total population of 14.52 million in northern part of Bangladesh for over 30 years. RDRS began its reproductive health program in 29 *upazilas* in 1985. RDRS provides care from one maternity center providing basic emergency obstetric care and 214 antenatal clinics (at Government satellites and their own Federation Centres) run by 531 trained birth attendants, 90 community health workers, six nurses, one obstetrician and 20 field supervisors.

ICDDR,B
GPD Box 128
Dhaka 1000
Bangladesh
Tel +1 88 02 886 0523 32
Website: www.icddrb.org

Venture Strategies Innovations
2401 East Katella Avenue
Suite 400
Anaheim, California 92806 USA
Tel +1 714 221 2040
Website: www.vsinnovations.org

RDRS Bangladesh
House 43, Road 10, Sector 6
Uttara, Dhaka-1230
Bangladesh
Tel +1 88 02 895 4384 85
Website: www.rdrsbangla.net

Bixby Center for Population, Health and Sustainability
School of Public Health
17 University Hall
University of California
Berkeley, California 94720-7360 USA
Tel +1 510 643 7627
Website: http://bixby.berkeley.edu

Acknowledgements

This operations research project was funded by Venture Strategies Innovations (VSI), grant number 00616 to ICDDR,B. ICDDR,B acknowledges with gratitude the commitment of VSI to its research efforts. This project could not have been completed without the expert staff and colleagues at the ICDDR,B, the Bixby Center for Population, Health and Sustainability**,** School of Public Health, University of California, USA and RDRS Bangladesh whose dedication to this project and invaluable contributions to its development led to its successful implementation. We wish to acknowledge the six district coordinators, field supervisors and community health workers of RDRS, the eight field research assistants of ICDDR,B, and the RDRS birth attendants whose dedication to the women of Bangladesh was the cornerstone of this project. Most importantly, we wish to thank the women and communities in Lalmonirhat, Thakurgaon, Nilphamari, Dinajpur, Kurigram and Panchagarh districts of Bangladesh for welcoming us, participating in the project, and sharing their experiences.

Executive Summary

In Bangladesh, the estimated maternal mortality ratio (MMR) is 194 deaths per 100,000 live births (BMMS preliminary results, 2011). More than 12,000 deaths occur due to pregnancy-related causes every year (WHO, 2010). Postpartum hemorrhage (PPH) contributes to almost a third of maternal deaths in Bangladesh (31%)(BMMS preliminary results, 2011). The majority of births in Bangladesh take place at home (77%), and only 26.5% of births are attended by a skilled birth attendant (BMMS preliminary results, 2011). The lack of an effective method for assessing blood loss and the underestimation that usually follows can result in delayed referral and subsequently fatal consequences. To measure postpartum blood loss for timely referral and management of PPH at the household level, Dr. Md Abdul Quaiyum developed and tested a low-cost, standardized mat. In addition, misoprostol tablets offer a safe, affordable, and effective means of preventing PPH when taken immediately after delivery.

As part of its reproductive health program, RDRS Bangladesh distributes clean delivery kits (CDKs) to pregnant women, which include instructions and supplies to enable the use of clean delivery practices by unskilled providers. Community health workers (CHWs) distribute CDKs during antenatal care (ANC), and trained traditional birth attendants (RDRS birth attendants) provide the CDKs at delivery. While RDRS has demonstrated that it can reach a large proportion of the women delivering at home using these channels, the current items included in a CDK do not equip the user to identify nor prevent one of the leading causes of maternal death, PPH.

The International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) and RDRS Bangladesh collaborated with Venture Strategies Innovations (VSI) and the Bixby Center for Population, Health and Sustainability, at University of California, Berkeley, on an operations research project that scaled up the introduction of two interventions to prevent and recognize PPH – misoprostol and Quaiyum's mat (a blood loss measuring tool) – into the existing RDRS system for distributing CDK. The project was implemented in the six northwestern districts of Bangladesh, comprised of 29 *upazilas*, (sub-districts) where RDRS has a pre-existing reproductive health program: Lalmonirhat, Kurigram, Nilphamari, Thakurgaon, Dinajpur and Panchagarh. The purpose of this operations research was to provide empirical evidence to inform policy decision makers in Bangladesh on the feasibility of scaling up PPH prevention interventions, including the use of misoprostol and Quaiyum's mat at home births, as included in a modified CDK distributed during pregnancy by CHWs at ANC and by trained RDRS birth attendants at delivery.

In this operations research project, CHWs and RDRS birth attendants distributed the new CDKs from May 2009 through September 2010. During the 17 months of data collection, 118,594 women registered with RDRS. The data in this analysis includes information collected during ANC and postnatal care from the 77,337 women who delivered during the period of data collection, as well as from 3,016 postpartum interviews.

Over two-thirds of the women who delivered during the operations research received a CDK (70%). The majority of women enrolled in the project delivered at home (87%). Almost all of the women who received a CDK obtained it during their pregnancy at an ANC visit with a CHW (>99%). A very small number of women obtained the CDK directly from a RDRS birth attendant at delivery. For the purposes of this project, a birth was considered "protected" from PPH if misoprostol was available at a home delivery or if the woman delivered at a health facility or with a skilled birth attendant.

Misoprostol distribution in CDKs protected 60% of births in the project from PPH that would not have otherwise been protected.

Overall, delivery complications were few in proportion to the number of deliveries. Perceived PPH occurred in less than 1% of deliveries, regardless of if the woman used misoprostol, delivered in a health facility or with a skilled provider, or if she delivered at home and did not use misoprostol. Only 17 women who took misoprostol at a home birth required a bleeding-related referral (<1%): ten for excessive bleeding (nine assessed blood loss using Quaiyum's mat and one using other cloths) and seven for retained placenta. All went to the health facility, where they received treatment. Most women who delivered at home and took misoprostol (1,893 out of 2,011) reported that they took the correct dose of three tablets (97%). All but four women reported taking misoprostol immediately after delivery of the baby. The most common symptoms reported by the 12% of misoprostol users experiencing postpartum symptoms included: shivering (6%), rise in body temperature (3%), and nausea (2%). Most of these symptoms resolved within one half (66%) to one hour (16%).

Virtually all women regardless of if they received a CDK stated that bleeding was a life-threatening complication of delivery. Using Quaiyum's mat was mentioned most often as a means of recognizing when a woman who had bled too much (75% overall); almost twice as many women who received a CDK mentioned Quaiyum's mat than women who did not (83% vs. 45%, respectively). Nurses and health care providers providing ANC were mentioned most frequently as the source of information about complications of childbirth (58%). Almost all women who took misoprostol felt that the drug was useful to them (98%) and that they would recommend misoprostol to a friend (99%). Almost all women who used Quaiyum's mat said they benefitted from the mat (98%); would use the mat in a future delivery (87%); and would purchase the mat (89%).

A total of 113 deaths were reported in the project areas coinciding with the operations research time period. Eclampsia accounted for the largest proportion of deaths (35%), followed by PPH and bleeding-related causes (30%) and other direct causes (19%). Of the 34 women who died as a result of PPH and bleeding-related causes, only 16 had taken misoprostol for prevention of PPH. Thirty-seven fewer deaths were observed than expected in this project using the most recent MMR estimate.

With enrollment of over 118,500 women, this is one of the largest operations research projects assessing the use of misoprostol distributed directly to women for the prevention of PPH. This project demonstrated that misoprostol and Quaiyum's mat are two simple interventions that can easily be added to current CDKs and, for the first time, equip women and attendants at home deliveries to protect women from PPH.

Acronyms and Local Terms

ANC	Antenatal care
CDK	Clean delivery kit
CHW	Community health worker
EmOC	Emergency Obstetric Care
FIGO	International Federation of Gynecology and Obstetrics
ICDDR,B	International Centre for Diarrhoeal Disease Research, Bangladesh
ICM	International Confederation of Midwives
MMR	Maternal mortality ratio
MOHFW	Ministry of Health and Family Welfare
NGO	Non-governmental organization
PI	Principle investigator
PPH	Postpartum hemorrhage
RDRS	Rangpur Dinajpur Rural Service
SBA	Skilled birth attendant
TBA	Traditional birth attendant
Upazila	Sub-district
VA	Verbal autopsy
VSI	Venture Strategies Innovations
WHO	World Health Organization

Table of Contents

List of Boxes, Tables and Figures

1. Introduction

1.1 BACKGROUND

1.1.1 Postpartum Hemorrhage in Bangladesh

Maternal mortality is an important public health issue worldwide. In Bangladesh, the estimated maternal mortality ratio (MMR) is 194 deaths per 100,000 live births (BMMS preliminary results, 2011) and more than 12,000 deaths occur every year due to pregnancy-related causes (WHO, 2010). Due to its high population density, Bangladesh is one of eleven countries that comprised 65% of all maternal deaths in 2008 (WHO, 2010). While the country is committed to achieving the fifth Millennium Development Goal of reducing the MMR to 144 deaths per 100,000 live births by the year 2015 (UNDP), targeted efforts aimed at the major causes of maternal mortality are needed to achieve this goal.

Postpartum hemorrhage (PPH), defined as bleeding after delivery in excess of 500 mL (WHO, 1990), is among the leading causes of maternal death in Bangladesh. Almost a third of maternal deaths in the country (31%) are attributable to hemorrhage (BMMS preliminary results, 2011). Without any intervention, a woman can die from PPH within two hours of delivery (Gynuity, 2006). Even if she survives, the consequences of PPH, such as severe anemia, may take years to overcome, impacting her overall health, energy levels, productivity, and subsequent birth outcomes (AbouZahr *et al*., 2003).

Most deliveries take place at home in Bangladesh (85%); traditional birth attendants, relatives, or neighbors most often attend these deliveries (BDHS, 2009). This has implications for both recognition of obstetric emergencies, like PPH, and the availability of life-saving technologies to treat and manage these emergencies. Blood loss is generally underestimated even by skilled providers (Maslovitz *et al*., 2008), and since any delay in assessing and treating PPH can be deadly, it is important for women and those attending her at home births to be able to recognize PPH, and facilitate a quick referral for treatment. In most clinical practice early blood loss in childbirth is measured subjectively and this visual estimation is often inaccurate (Patel *et.al*, 2006). Other methods such as direct collection, venous blood sampling, dye dilution techniques for plasma volume measurement, and red blood cell and plasma volume determinations using radioactive tracer elements have not been widely adopted because they are neither practical nor affordable in most clinical or community settings (Patel *et al.*, 2006).

To date, tools to identify PPH at the community level are not commercially available on a large scale worldwide, including in Bangladesh. The lack of an effective method for assessing blood loss and the underestimation that usually follows can result in delayed referral and subsequently fatal consequences. In addition, emergency obstetric care (EmOC) is neither easily available nor accessible to many pregnant women in rural Bangladesh, and few if any interventions exist to manage obstetric emergencies at the household level. Current efforts to improve safe motherhood focus on increased coverage of skilled birth attendants (SBAs) and access to EmOC. Waiting for these interventions to reach women who are delivering at home in rural Bangladesh will result in continued high levels of preventable, PPH-related morbidity and mortality.

1.1.2 Misoprostol for Prevention of PPH

PPH can be prevented with the administration of uterotonic drugs during the management of the third stage of labor. Uterotonic drugs induce contractions in the uterus, which reduce the amount of postpartum bleeding, thus decreasing the risk of PPH and the need for additional interventions. The currently recommended first line uterotonic is oxytocin, which requires injection by a trained provider, and special storage conditions. Due to the fact that most births in Bangladesh occur in the home, unattended by a trained provider, use of oxytocin is generally infeasible.

Misoprostol is an effective uterotonic with an excellent safety profile that has been increasingly used in obstetrical and gynecological practice, including for the prevention and treatment of PPH (Derman *et al.*, 2006; Alfirevic *et al*., 2007). It is a low-cost drug that is thermo-stable in field conditions, easy to store, and easily administered for the prevention of PPH by swallowing 600 mcg (usually three tablets of 200 mcg each) (Alfirevic *et al*., 2007). The International Confederation of Midwives (ICM) and the International Federation of Gynecology and Obstetrics (FIGO) have jointly recommended that in home births without a skilled attendant, misoprostol may be the only available technology to control PPH (ICM/FIGO, 2006). The World Health Organization (WHO) added misoprostol to its Model List of Essential Medicines for the prevention of PPH where oxytocin is not available or cannot be safely used (WHO, 2011).

Derman *et al*. illustrated that oral misoprostol distributed by auxiliary nurse midwives is effective compared to placebo in reducing four key outcomes associated with maternal death: blood loss of 500mL or more, blood loss of 1000mL or more, mean blood loss, and need for transfer (Derman *et al.,* 2006). Several large, randomized controlled trials evaluated the use of 600 micrograms of misoprostol orally or sublingually to prevent PPH at the community level (Mobeen *et al.* 2011, Walraven et al., 2005). All have concluded that misoprostol has significant impact on blood loss after birth in low resource settings.

1.1.3 History of Misoprostol in Bangladesh

Three manufacturers produce misoprostol in Bangladesh. To date, Incepta Pharmaceuticals Limited, Square Pharmaceuticals Limited and Gonoshasthaya Pharmaceuticals Limited have 200 mcg misoprostol tablets registered for a PPH indication. All three manufacturers have also registered misoprostol for induction of labor.

The Ministry of Health and Family Welfare (MOHFW) and other key agencies have committed to integrating misoprostol use into government policies and plans for reducing maternal death. The *Misoprostol Use Policy and Rollout Plan* was drafted by the National Task Force for Prevention of PPH in 2007 and subsequently approved by the Director General of Health Services. The plan aims to reduce the incidence of PPH at community-level deliveries by using misoprostol in the third stage of labor. The plan has been successfully implemented by the MOHFW and EngenderHealth in two districts (The RESPOND Project, 2010). EngenderHealth completed its project and expanded distribution of misoprostol in 2010.

Additionally, misoprostol has been included in the program of activities for community health workers (CHWs) and family welfare agents under the USAID-funded MaMoni project. The MaMoni project – awarded to Jhpiego and implemented by Save the Children, the MOHFW, and several community-based organizations—focuses on promoting evidence-based interventions at both the facility and community levels. In Sylhet and Habiganj districts, CHWs, family welfare agents, and

facilities provide misoprostol to expectant mothers at either household or facility antenatal care (ANC) visits. Misoprostol for postpartum hemorrhage was included in the Government's Operational Plan and the National Maternal Health Strategy for 2011.

1.2 RATIONALE FOR INCLUDING MISOPROSTOL AND THE DELIVERY MAT IN CLEAN DELIVERY KITS FOR PREVENTION OF POSTPARTUM HEMORRHAGE AT HOME BIRTHS

Ideally, all deliveries would take place in a facility with an SBA and access to EmOC. Delivering in such a setting allows for the prevention and management of PPH and other potential complications. Unfortunately, a myriad of barriers prevent Bangladeshi women from receiving such care, including women's preference to deliver at home. The majority of births take place at home (77%), and only a minority of births is attended by an SBA (26.5%)(BMMS preliminary results, 2011). Therefore, it is necessary to identify targeted interventions to address both the recognition and prevention of PPH at home births that are primarily attended by lay providers, and to establish distribution mechanisms for interventions that can reach the most women.

Research by the WHO suggests that pre-assembled clean delivery-kits (CDKs) with instructions for use can be a vital component in improving hygiene at delivery, particularly for deliveries conducted by unskilled care providers (WHO, 1987). The CDK promotes and supports the use of clean delivery practices, specifically the 'cleans' defined by the WHO, i.e. clean hands, perineum, delivery surface, cord-cutting surface, cord-cutting, and tying instruments. In the late 1980s, the Christian Commission for Development in Bangladesh developed and field-tested a simple, affordable birth kit to sell to pregnant women in rural areas. The bright red and blue box with a logo of a breast-feeding mother contained a plastic bag to protect the contents, which included soap, two pieces of gauze, a polythene sheet, three sterilized cord ties and a new razor blade. Pictures on a pretested, folded panel were used to convey directions on how to use the kits (Nessa *et al*., 1992). Subsequently many nongovernmental organizations (NGOs) like BRAC and RDRS introduced it in their programs. RDRS's reproductive health program has demonstrated that CDK distribution during ANC by community health workers and at delivery by trained traditional birth attendants can reach a large proportion of the women delivering at home (see Box 1). However, the current items included in the CDK do not equip the user to identify nor prevent one of the leading causes of maternal death, PPH.

Since there has been no effective method or tool to measure blood loss objectively after childbirth in home settings, Dr. Quaiyum, an Associate Scientist in the Reproductive Health Unit at ICDDR,B, designed a pre-weighted "delivery mat." A study conducted among women delivering vaginally in two tertiary medical institutions and a nearby Dhaka community found that the fully soaked mat retains 448.0±58.2 mL of blood (Quaiyum *et al.*, 2006). This standardized mat (referred to as "Quaiyum's mat" in this report) was also used in a quasi-experimental study in a rural community of Bangladesh to identify women with excessive blood loss after delivery for referral. Subsequently this mat is being adopted and integrated into clean delivery kits by many NGO service providers in Bangladesh. ICDDR,B began local production of these mats, and Dr. Quaiyum has since received a Grand Challenges Explorations grant from the Bill and Melinda Gates Foundation to design and test a similar mat but environment friendly and made of biodegradable materials.

Recently-published research demonstrates that women are able to safely self-administer misoprostol for PPH prevention at home births after distribution of misoprostol by a CHW and being educated on proper use (Rajbhandari *et al*., 2010; Sanghvi *et al.,* 2010). Distribution of misoprostol

for use at home births significantly increases the proportion of deliveries protected from PPH; this is especially true among women of lower economic status who cannot reach a facility to deliver (Rajbhandari *et al*., 2010). Further, Mobeen *et al*. illustrated that traditional birth attendants (TBAs) in Pakistan could effectively reduce the burden of PPH by 24% in community settings (Mobeen *et al*., 2011). Results from studies indicate that safety is not compromised by including CHWs in misoprostol distribution. Moreover, in Afghanistan, births attended by skilled providers were higher in areas where misoprostol was made available directly to women, likely as a result of CHWs reinforcing messages about the importance of delivering in a facility (Sanghvi *et al*., 2010).

Adding misoprostol and Quaiyum's mat to the CDK already distributed by RDRS birth attendants could help reduce the incidence of PPH at home births, and assist birth attendants, women and their family members in identifying PPH to facilitate a timely referral. Since a functioning distribution mechanism already exists for CDKs, this would ensure that the many women delivering at home would be protected from PPH.

In addition, the 2007 Bangladesh Demographic and Health Survey shows that 52% of women with a birth in the five years preceding the survey received ANC from a medically trained provider (BDHS, 2009). ANC providers have a unique opportunity to educate women on the risks of pregnancy, the importance of delivering in a facility, and the use of misoprostol. Distributing a modified CDK that includes Quaiyum's mat and misoprostol during ANC can provide women who cannot reach a facility at the time of delivery with access to this life-saving technology. In addition, with the modified CDK, RDRS birth attendants who make home visits in advance of delivery can reach those women who may not attend facility-based ANC and who deliver at home.

2. Operations Research Description

2.1 OPERATIONS RESEARCH GOALS AND OBJECTIVES

The purpose of this operations research project was to provide empirical evidence to inform policy decision makers in Bangladesh on scaling up the use of misoprostol and Quaiyum's mat at home births, as included in a modified CDK distributed during pregnancy by CHWs at ANC and by trained RDRS birth attendants at delivery. This project assessed the programmatic implications of scaling up misoprostol use in rural areas of Bangladesh through integration into the existing CDK distribution system of RDRS. The results will help inform policy for improving safe delivery programs in Bangladesh and other low-resource settings.

The specific aims of this operations research were:

- To assess feasibility and acceptability of scaling up the use of misoprostol and a delivery mat (Quaiyum's mat) to prevent PPH in selected rural areas of Bangladesh (RDRS working areas).
- To understand the barriers, logistics, facilitators, and other management implications in scaling up the use of misoprostol and Quaiyum's mat for prevention of PPH in the selected rural areas.
- To assess the effectiveness of misoprostol and Quaiyum's mat in reduction of maternal morbidity and mortality from PPH in the RDRS areas.

2.2. LOCATION

The project was implemented in 29 *upazilas* (sub-districts) in the six northwestern districts of Bangladesh, where RDRS has a pre-existing reproductive health program (see Box 1). The six districts included: Lalmonirhat, Kurigram, Nilphamari, Thakurgaon, Dinajpur and Panchagarh.

All RDRS ANC clinics in these six districts that provide ANC participated in the project. RDRS ANC clinics are located in government family welfare centers and RDRS Federation offices, staffed by CHWs. No hospitals or dispensaries participated in the project. Table 1 specifies the population, ANC coverage, and resources in each of the operations research areas.

Table 1: District fertility, ANC and delivery characteristics

District	Population[1]	Estimated Births/Year[1]	# ANC Sites[2]	# RDRS birth attendants[2]
Lalmonirhat	1,088,918	22,540	32	51
Panchagarh	829,374	17,168	33	99
Thakurgoan	1,196,429	24,767	36	108
Nilphamari	1,550,686	32,099	30	90
Kurigram	1,782,277	36,893	65	129
Dinajpur	2,617,942	54,191	18	54
Total	**90,65,626**	**1,87,658**	**214**	**531**

Source: [1]Government of Bangladesh data, 2010
[2]RDRS data, December 2010

Box 1: RDRS Reproductive Health Program

RDRS Bangladesh has been working in the northwest region of Bangladesh for three decades. Currently RDRS operates 214 high-quality, weekly antenatal clinics in 29 *upazilas* in all six districts of the working area, and a small maternity center in Aditmari, Lalmonirhat. Of the 214 clinics, 73% (156) are held in the Government's Union Family Welfare Centers, 18% (39) in the RDRS Federation centers and the remaining nine percent (19) in community houses. Approximately 100,000 pregnant women register every year, paying a one-time registration fee of Bangladesh Taka 15 (USD 0.21). In 2010, about 84,000 (45%) pregnant women of the working area were registered at these clinics. Pregnant women, who normally give birth at home, are encouraged to use the services of RDRS birth attendants. Complicated cases are referred to Government Upazila Health Complexes. The women and RDRS birth attendants are encouraged to make use of RDRS-produced clean delivery kits (sold at production price of Taka 15) during deliveries.

2.3 OPERATIONS RESEARCH TIMELINE

The operations research project took place over the course of three years (Figure 1). In 2008, the partners began preparing project protocol for submission to the relevant institutional review boards, developing project materials, and drafting the manual of operations and data collection tools. CDKs including misoprostol and Quaiyum's delivery mat were assembled from January to March 2009 and initially distributed to the sites. Training of CHWs, RDRS birth attendants and field research supervisors occurred in April and May of 2009. Implementation, as well as ongoing monitoring and evaluation, began in May 2009 for a planned duration of 12 months.

2.2. LOCATION

The project was implemented in 29 *upazilas* (sub-districts) in the six northwestern districts of Bangladesh, where RDRS has a pre-existing reproductive health program (see Box 1). The six districts included: Lalmonirhat, Kurigram, Nilphamari, Thakurgaon, Dinajpur and Panchagarh.

All RDRS ANC clinics in these six districts that provide ANC participated in the project. RDRS ANC clinics are located in government family welfare centers and RDRS Federation offices, staffed by CHWs. No hospitals or dispensaries participated in the project. Table 1 specifies the population, ANC coverage, and resources in each of the operations research areas.

Table 1: District fertility, ANC and delivery characteristics

District	Population[1]	Estimated Births/Year[1]	# ANC Sites[2]	# RDRS birth attendants[2]
Lalmonirhat	1,088,918	3,149	32	51
Panchagarh	829,374	4,433	33	99
Thakurgoan	1,196,429	7,654	36	108
Nilphamari	1,550,686	4,699	30	90
Kirugram	1,782,277	4,054	5	129
Dinajpur	2,617,942	9,994	18	54
Total	**90,65,626**	**187,658**	**214**	**471**

Source: [1]Government of Bangladesh data, 2010
[2]RDRS data, December 2010

Box 1: RDRS Reproductive Health Program

RDRS Bangladesh has been working in the northwest region of Bangladesh for three decades. Currently RDRS operates 214 high-quality, weekly antenatal clinics in 29 *upazilas* in all six districts of the working area, and a small maternity center in Aditmari, Lalmonirhat. Of the 214 clinics, 73% (156) are held in the Government's Union Family Welfare Centers, 18% (39) in the RDRS Federation centers and the remaining nine percent (19) in community houses. Approximately 100,000 pregnant women register every year, paying a one-time registration fee of Bangladesh Taka 15 (USD 0.21). In 2010, about 84,000 (45%) pregnant women of the working area were registered at these clinics. Pregnant women, who normally give birth at home, are encouraged to use the services of RDRS birth attendants. Complicated cases are referred to Government Upazila Health Complexes. The women and RDRS birth attendants are encouraged to make use of RDRS-produced clean delivery kits (sold at production price of Taka 15) during deliveries.

2.3 OPERATIONS RESEARCH TIMELINE

The operations research project took place over the course of three years (Figure 1). In 2008, the partners began preparing project protocol for submission to the relevant institutional review boards, developing project materials, and drafting the manual of operations and data collection tools. CDKs including misoprostol and Quaiyum's delivery mat were assembled from January to March 2009 and initially distributed to the sites. Training of CHWs, RDRS birth attendants and field research supervisors occurred in April and May of 2009. Implementation, as well as ongoing monitoring and evaluation, began in May 2009 for a planned duration of 12 months.

ICDDR,B data management assistants entered the data between October 2010 and February 2011. Analysis was conducted jointly by ICDDR,B and VSI in March and April 2011, with the presentation of results to stakeholders in June 2011.

Figure 1: Operations research timeline

Sep-Oct 2008	Apr – May 2009	May 2009 – Sep 2010	Oct 2010 – Feb 2011	Mar – Apr 2011
Development	Training	Implementation	Data Entry	Analysis

2.4 ETHICAL REVIEW

Institutional Review Board approval for this operations research was obtained from the University of California, Berkeley (protocol #2008-8-24) and ICDDR,B's Research Administration in Bangladesh. Providers asked women for their informed consent prior to enrollment, and again before participating in the postpartum interview.

3. Methods

3.1 STRATEGY AND DESIGN

3.1.1 Distribution of Modified CDK for Prevention of PPH

RDRS's existing health program distributes clean delivery kits (CDKs) to pregnant women during ANC with a CHW or at delivery with one of its trained birth attendants. This project built upon this existing infrastructure by adding misoprostol and Quaiyum's mat to the CDK, and distributing this modified CDK through RDRS's existing channels. By capitalizing upon a system that already reaches the majority of women in the RDRS catchment areas, the aim of this project was to reach women living in the project areas with these life-saving technologies.

Women could be enrolled at any point during their pregnancy by a CHW providing ANC. Additionally, a woman could be enrolled at delivery with a RDRS birth attendant if not previously enrolled. CDK distribution occurred either during the last ANC visit with a CHW (gestational age of at least 32 weeks) or at the time of home delivery by a RDRS birth attendant, as described below:

1. **ANC distribution:** ANC providers conducted the ANC visit, with specific emphasis on safe delivery and PPH prevention, including information on misoprostol and identification of PPH using Quaiyum's mat. With this information, providers asked women if they would like to participate in the operations research project and to sign an informed consent form if they agreed to enroll. Enrolled women were then provided more in-depth information on the use of misoprostol, screened for medical eligibility, and offered the CDK to take with them for use at home births if they were 32 weeks or greater gestation. Women were not eligible to receive misoprostol if they had bronchial asthma or other chronic disease or if the providers anticipated a complicated delivery. Women could also enroll in the project and decide if they wanted to receive the CDK at a later ANC visit.
2. **RDRS birth attendant distribution:** If a woman was previously enrolled by a CHW during an ANC visit but not given a CDK (i.e. did not return after 32 weeks), the RDRS birth attendant could provide the woman with the CDK during delivery at home and assist her in using its contents.

The original design of the operations research project included RDRS birth attendants distributing CDKs to pregnant women at the time of delivery to those who did not receive them at ANC with a CHW, as is the current program at RDRS. However, this was changed prior to implementation because there was concern that RDRS birth attendants would not be able to accurately and fully explain the study to pregnant women, thus compromising informed consent. TBAs have been included in similar projects in other countries (Prata *et al,.* 2009a, Prata *et al.*, 2005, Prata *et al.*, 2009b, Mobeen *et al.*, 2011), and they have demonstrated their ability to obtain informed consent by memorizing the content of the form and reciting it aloud to the participant. In February 2010, project management decided to return to the original design of CDK distribution by RDRS birth attendants for the remainder of the project and extend implementation of the project until the end of September 2010 (for a total of 17 months). Therefore, from March 2010 until the end of the project, RDRS birth attendants distributed CDKs to women who had not received one from a CHW during ANC.

Among women who chose to participate in the operations research, every twentieth who delivered was selected to participate in a postpartum interview. The interview took place within two months of delivery through active follow-up in the home by an ICDDR,B research assistant. Participants had to be age 18 years or older and able to give informed consent (written or oral depending on her literacy level). Additionally, ICDDR,B research staff identified and performed verbal autopsy (VA) of all reported deaths of reproductive age women during the period of the intervention.

3.1.2 Community Awareness Campaign

RDRS's reproductive health care program includes community awareness activities, called '*health education sessions.'* In this session, the CHWs raise awareness among family members of the pregnant women on providing support for the mother during pregnancy and delivery. CHWs instruct pregnant women to bring family members (specifically, they recommend in-laws and husbands) to their ANC visits to convey the correct messages on pregnancy care and to eliminate common misconceptions about pregnancy and delivery.

CHWs provide information related to ANC, use of the CDK, dietary advice, planning for delivery with a skilled attendant, and following referral instructions. For this project, they also provided information on misoprostol, its benefits, when and how to administer it, when not to use misoprostol, and how to use Quaiyum's mat. A leaflet of messages on misoprostol and Quaiyum's mat was provided to all CHWs for use during the health education session.

3.2 OPERATIONS RESEARCH PERSONNEL AND TRAINING

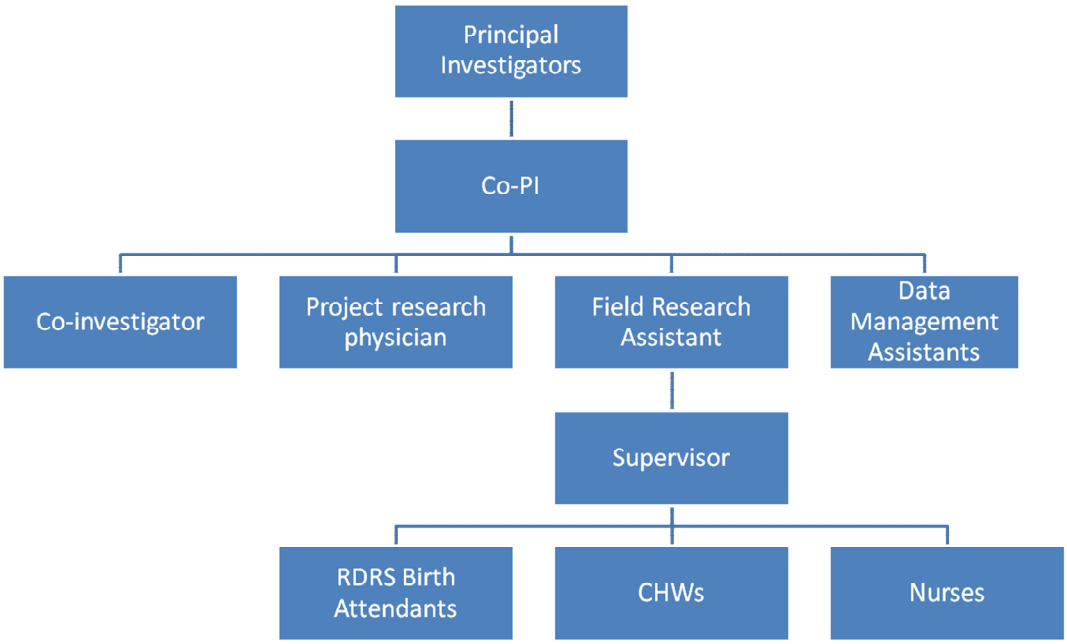
3.2.1 Organizational Structure

Dr. Md Abdul Quaiyum, Associate Scientist in the Reproductive Health Unit at ICDDR,B, and Dr. Ndola Prata, Associate Professor in Residence at University of California, Berkeley School of Public Health, Scientific Director of the Bixby Center for Population, Health and Sustainability at UC Berkeley, and Director, Medical and Programs of VSI, were the Principal Investigators (PIs) of this operations research. Project management also included a co-PI, Dr. SA Shahed Hossain at ICDDR,B, a co-investigator; Dr. Salima Rahman at RDRS; and Drs. Mohsina Begum and Ashrafi Jahan Azmi, Medical Officers at ICDDR,B. Martine Holston, VSI Director of Research and Implementation, provided technical support in the monitoring and evaluation of the project. Suzanne Bell from the Bixby Center at UC Berkeley assisted in the analysis and final report preparation.

ICDDR,B and VSI staff, in collaboration with the Bixby Center, designed the operations research protocol. RDRS Bangladesh with technical assistance from ICDDR,B manufactured the mat and assembled the modified CDKs for the project, which also included misoprostol. ICDDR,B staff organized the training of CHWs, RDRS birth attendants, and RDRS supervisors, and trained staff to do data entry, postpartum interviews, and ongoing monitoring and evaluation for the project, which included field research assistants. RDRS provided the infrastructure for the implementation of the project, and ongoing supervision of logistics and personnel, overseen by Dr. Salima Rahman, Medical Director of RDRS. Each district had a field research assistant who oversaw RDRS supervisors, who in turn managed the CHWs, RDRS birth attendants, and nurses working in each district (Figure 2).

In total, the project included six district managers (RDRS staff), 24 supervisors (RDRS staff), eight health officers (RDRS staff), 65 RDRS CHWs, 588 RDRS birth attendants, and eight field research assistants (ICDDR,B staff).

Figure 2: Organizational structure for operations research on misoprostol distribution in CDKs, showing one of six districts



3.2.2 Training Structure

Between April 1 and May 16, 2009, the project medical officer, PI, and co-PI conducted 19 two-day training sessions of 35 to 45 participants, for a total of 696 field staff. Of these, 588 were RDRS birth attendants.

Training was provided on different aspects of misoprostol (function, dose and time of administration, side effects and their management, etc.) and use of Quaiyum's mat. The training also included orientation on identifying high-risk pregnancies, pregnancy danger signs, referral procedures, stages of labor, newborn resuscitation, maternal infection, and general use of clean delivery kits. Special attention was given to PPH identification and its management, including PPH occurrence after misoprostol administration. A variety of training techniques were used, such as oral presentations, drama sessions, practical demonstrations on models, and video presentations. Special sessions for CHWs, health officers and their respective supervisors included ethical issues related to misoprostol tablet distribution, informed consent procedures before distributing misoprostol, timing

of distribution, ANC card completion, logistics management, and monitoring and supervision. A pre- and post-training evaluation on knowledge, attitude and practices on pregnancy and delivery issues using a structured questionnaire was conducted among 465 RDRS birth attendants.

3.3 DATA MANAGEMENT AND ANALYSIS

3.3.1 Data Collection Tools

Pregnancy Card

Using the **Pregnancy Card**, CHWs collected information on every project participant during her first visit and at subsequent visits. Information collected included including obstetric history, ANC information, enrollment status, and whether or not she had received a CDK. The **Pregnancy Card** was also completed during a post-delivery checkup, where information on place, attendant and outcome of delivery were recorded, including use of misoprostol and Quaiyum's mat.

Postpartum Interview

During enrollment, ANC providers asked enrolled women for their consent to participate in a follow-up postpartum interview. The **Postpartum Interview Questionnaire** collected participants' views of and experience with misoprostol, knowledge about PPH and misoprostol, and delivery experience. The postpartum interview was conducted on every twentieth woman who delivered in the operations research through active follow-up by an ICDDR,B research assistant. Therefore, women participating in the postpartum interview could have delivered at home or at a health facility, and could have received and used a CDK or not.

Verbal Autopsy Guide

At least two weeks after the reporting of a death of a women of reproductive age (generally one to two months), the ICDDR,B Field Research Assistant conducted the VA using a standardized questionnaire from the nearest kin of the deceased who could describe the death. Two physicians independently reviewed the VA questionnaires to determine an immediate and underlying cause of the death using the tenth revision of the World Health Organization's International Statistical Classification of Diseases and Related Health Problems (2007). If two physicians came to different conclusions on the cause of death, the case was reviewed by a third physician. The third physician's diagnosis was accepted if it matched one of the primary physicians' diagnoses; if it differed, cause of death was declared undecided. For analysis, the underlying cause is presented as the 'cause of death'; if there was no underlying cause, then immediate cause was taken as 'cause of death' (e.g. suicide, accident, etc.).

3.3.2 Data Entry and Management

Field supervisors routinely visited the project sites, addressing any challenges arising in the data collection and proper documentation, including recording of adverse events. ICDDR,B data management assistants conducted data entry of project data collection forms at the end of the project. Dr. Quaiyum and the VSI Director of Research and Implementation jointly conducted review and management of the data.

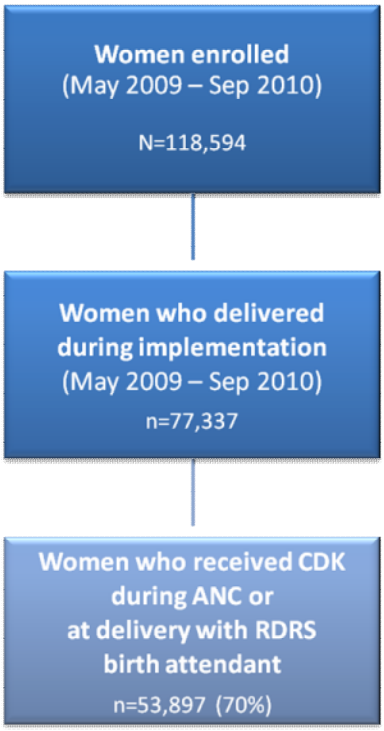
3.3.3 Data Analysis

Data analysis was conducted in *Stata/SE 10* (StataCorp 2007) and in *SPSS* (SPSS 2001). Results were summarized using frequency tables and cross-tabulations, and differences between groups were assessed using a criterion of $p<0.05$ to establish statistical significance.

5. Results

Community Health Workers (CHWs) and RDRS birth attendants began enrolling women in the operations research project in May 2009 and continued through September 2010. During that time period, 118,594 women registered with RDRS (i.e. enrolled in the project). Of these women, 77,337 delivered within the time period of implementation of the project and 53,897 received a CDK during ANC or at delivery with a RDRS birth attendant (Figure 3). ICDDR,B research staff conducted postpartum interviews with 3,016 women, or 4% of those who delivered during implementation of the operations research, in line with its protocol.

Figure 3: Participation in the operations research



Therefore, the results presented in this report include the **Pregnancy Card** data of women who enrolled and delivered during the project implementation period (n=77,337) and the **Postpartum Interview Questionnaires** of the 3,016 who participated in the interview (Table 2). Additionally, the results of the **Verbal Autopsy Guide** are presented for the 113 maternal deaths during the course of the project.

Table 2: Data for analysis

Pregnancy Card	**77,337**
Postpartum Interview Questionnaire	**3,016 (3.9%)**

5.1 CHARACTERISTICS OF THE PARTICIPANTS

The profile of women participating in the operations research is presented in Table 3. Women were generally young (mean age of 23 years) and were of a young age at marriage (17 years). Despite this, over half the women had secondary education or above (53%). Most women were pregnant with their first child during the project (42%). Few had experienced PPH in a previous pregnancy. Women attended an average number of three ANC visits during their pregnancy.

Table 3: Characteristics of participants

	Received CDK[1] (n=53,897)	Did not receive CDK (n=23,466)	Total (n=77,363)
Average age (min; max) ˆ	**22.6 (13; 51)**	**22.8 (13; 51)**	**22.6 (13; 51)**
Average age at marriage (min; max) ˆ	**16.8 (10; 36)**	**16.9 (10; 40)**	**16.8 (10; 40)**
Educationˆˆ			
No education	9,102 (17.0%)	4,924 (21.1%)	14,026 (18.2%)
Primary	14,529 (27.1%)	7,277 (31.2%)	21,806 (28.4%)
Secondary	26,539 (49.6%)	9,815 (42.1%)	36,354 (47.3%)
College	3,370 (6.3%)	1,328 (5.7%)	4,698 (6.1%)
Gravidaˆ			
1	22,665 (42.1%)	9,511 (40.6%)	32,176 (41.6%)
2	17,244 (32.0%)	7,559 (32.2%)	24,803 (32.1%)
3	8,672 (16.1%)	3,881 (16.6%)	12,553 (16.2%)
4 - 11	5,255 (9.8%)	2,499 (10.7%)	7,754 (10.0%)
Experienced PPH in a previous pregnancy	**14 (0.03%)**	**0 (0)**	**14 (0.02%)**
Average number of ANC visits (min; max) ˆ	**3.5 (1; 4)**	**2.5 (1; 4)**	**3.2 (1; 4)**

Source: Pregnancy Card
[1] During ANC or at delivery
ˆ No information for 0.1% of women
ˆˆNo data for 0.6% of women

Location and attendance at delivery are presented in Table 4, and were similar for both women who did and did not receive a CDK during pregnancy or at delivery with a RDRS birth attendant. The majority of women enrolled in the project delivered at home (87%), reflecting national statistics on location of delivery (BMMS preliminary results, 2011). Consequently, few women delivered with a skilled provider such as a doctor (9%) or nurse (4%). Most women delivered with an RDRS birth attendant (72%), and a small proportion delivered with a TBA not trained as part of RDRS's program (15%). The outcome of most of the deliveries was a live birth (97%), although a small number of stillbirths were reported (3%).

Table 4: Delivery characteristics

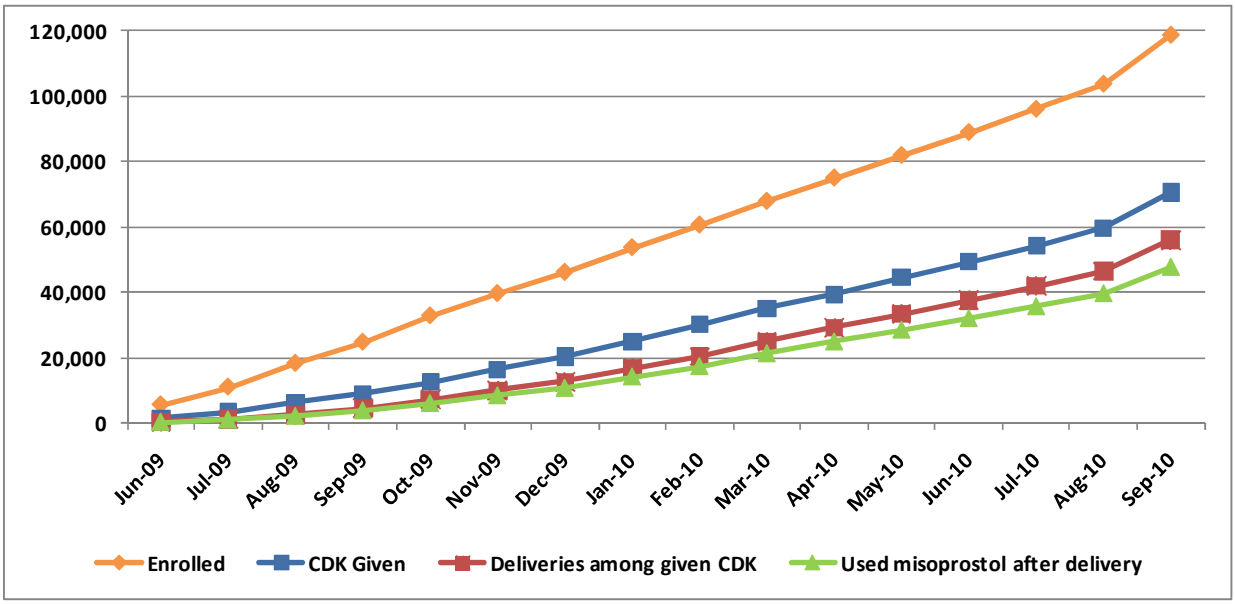
	Received CDK[1] (n=53,897)	Did not receive CDK (n=23,446)	Total (n=77,363)
Location of deliveryˆ			
Home[2]	46,768 (86.8%)	20,843 (88.9%)	67,611 (87.4%)
Health facility	7,112 (13.2%)	2,609 (11.1%)	9,721 (12.6%)
Attendant at deliveryˆ			
Doctor	4,796 (8.9%)	1,813 (7.7%)	6,609 (8.6%)
Nurse	2,038 (3.8%)	678 (2.9%)	2,716 (3.5%)
RDRS birth attendant	40,228 (74.7%)	15,159 (64.7%)	55,387 (71.7%)
Family Welfare Visitor	671 (1.3%)	334 (1.4%)	1,005 (1.3%)
Birth attendant[3]	6,114 (11.4%)	5,450 (23.3%)	11,564 (15.0%)
Outcomeˆ			
Live	52,230 (97.0%)	22,365 (95.4%)	74,595 (96.5%)
Stillbirth	1,320 (2.5%)	949 (4.0%)	2,269 (2.9%)
Died within 24 hours	182 (0.3%)	80 (0.3%)	262 (0.3%)
Died within 2 to 7 days	128 (0.2%)	55 (0.2%)	183 (0.2%)
Caesarean sectionˆˆ	**3,129 (5.8%)**	**1,183 (5.1%)**	**4,312 (5.6%)**

Source: Pregnancy Card
[1]During ANC or at delivery
[2]Includes births *en route* to the health facility
[3]An untrained lay provider, either a family member or TBA not trained by RDRS
ˆNo information for 0.1% of women
ˆˆNo data for 0.2% of women

5.2 FEASIBILITY: COVERAGE OF CDK DISTRIBUTION

Figure 4 shows enrollment, CDK distribution and misoprostol use at delivery. This figure shows a gap between enrollment and CDK distribution, most likely caused by the gestational age requirement: Women were registered early in pregnancy but could not receive a CDK until they reached 32 weeks gestation. This affected CDK distribution in two ways. First, CDK distribution always lags behind enrollment due to gestation age because of the time between enrollment and distribution. Second, women may not return to ANC to receive a CDK once they reach 32 weeks gestation. If a back-up mechanism to reach these women is not in place (e.g. trained TBAs distributing the CDKs at deliveries they attend), then these women will be missed. This was exactly the course the project took in March 2010, when monitoring data showed even larger differences between enrollment and CDK distribution.

Figure 4: Enrollment, CDK distribution and misoprostol use



Over two-thirds of the women who delivered during the operations research received a CDK (70%)(Table 5). Slightly more women who delivered at a facility received a CDK (73%) than women who delivered at home (69%). However, while significant the difference was not large, and most women received a CDK regardless of where they delivered, demonstrating that the CDK distribution mechanism is a feasible way of reaching women.

Almost all of the women who received a CDK obtained it during their pregnancy at an ANC visit with a CHW (>99%). The average gestational age when women received a CDK was 33 weeks (data not shown). A very small number of women obtained the CDK directly from a RDRS birth attendant at delivery, most likely due to the fact that the RDRS birth attendants did not begin distributing the kits until March 2010, 10 months into the project implementation. Of note, 15,007 women (or 72% of the 20,843 women who did not receive a CDK and delivered at home), delivered with a RDRS birth attendant (data not shown); if the RDRS birth attendants had been distributing the modified CDK for the entire duration of the project, these women would have most likely received a CDK with misoprostol and been protected from PPH.

Table 5: Coverage of CDK distribution to enrolled women by home and facility birth

	Home birth[1] (n=67,611)	Facility birth (n=9,721)	Total (n=77,363)
Received a CDK	**46,768 (69.2%)**	**7,112 (73.2%)**	**53,897 (69.7%)**
Received CDK during pregnancy at ANC (% of received CDK)	46,589 (99.6%)	7,096 (99.8%)	53,702 (99.6%)
Received CDK at delivery with trained TBA (% of received CDK)	179 (0.4%)	16 (0.2%)	195 (0.4%)
Did not receive CDK	**20,843 (30.8%)**	**2,609 (26.8%)**	**23,466 (30.3%)**

Source: Pregnancy Card
[1]Includes births *en route* to the health facility

5.3 PROGRAM EFFECTIVENESS

5.3.1 Uterotonic Coverage at Delivery

For the purposes of this operations research, a birth was considered "protected" from PPH if misoprostol was available at a home delivery or if the woman delivered at a health facility or with a SBA such as a doctor or a nurse. Receiving a CDK, either during ANC or at delivery with an RDRS birth attendant, dramatically increased the likelihood that a woman would be protected from PPH compared to women who did not receive a CDK (96% vs. 12%)(Table 6). Women who did not receive a CDK could only be protected from PPH if they delivered in a health facility or with a skilled provider such as a doctor or nurse. Since the majority of women in this project delivered at home without a skilled provider, those that did not receive a CDK were unprotected from PPH.

Conversely, because most women delivered at home, a large proportion of those that received a CDK at some point during pregnancy or delivery were protected from PPH with misoprostol at delivery. Misoprostol distribution in CDKs protected 60% of births from PPH that would have otherwise been unprotected.

Table 6: Births protected from PPH by receipt of CDK^

	Received CDK (n=53,897)	Did not receive CDK (n=23,466)	Total (n=77,363)
Protection from PPH	**51,486 (95.5%)**	**2,865 (12.2%)**	**54,351 (70.3%)**
Misoprostol from CDK at home birth	46,561 (86.4%)	0	46,561 (60.2%)
Delivered in a health facility[1]	4,656 (8.6%)	2,609 (11.1%)	7,265 (9.9%)
Delivered with a doctor or nurse[1]	269 (0.5%)	256 (1.1%)	525 (0.7%)
No protection from PPH[2]	**2,394 (4.4%)**	**20,578 (87.7%)**	**22,972 (29.7%)**

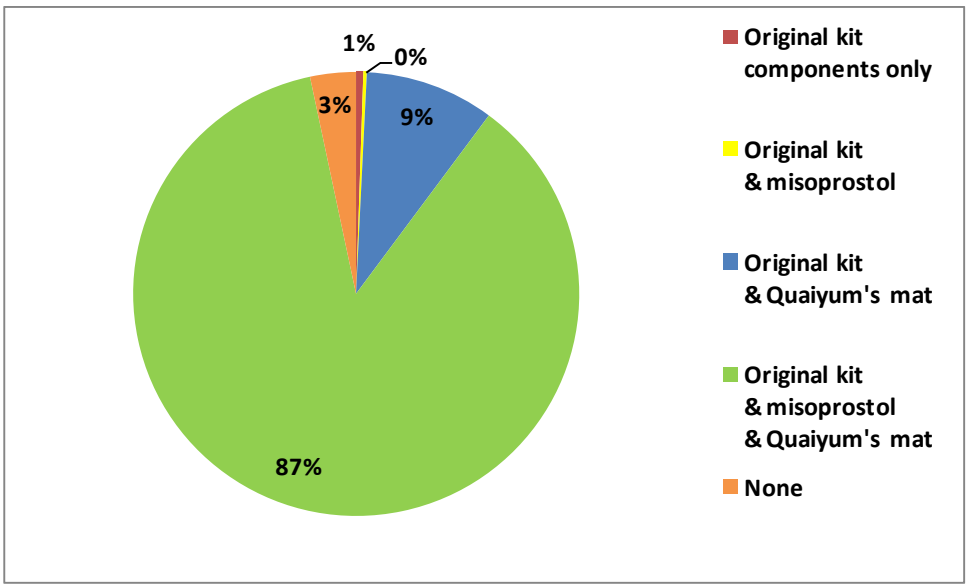
Source: Pregnancy Card
[1]Assumes received a uterotonic for PPH prevention
[2]Delivered at home and did not take misoprostol
^Excludes 40 women with missing information on one or more variables (0.1%)

Misoprostol users participating in the postpartum interview said that RDRS birth attendants (67%) and friends and family members (25%) helped them take the misoprostol tablets after delivery (data not shown). This demonstrates that, while RDRS birth attendants did not always supply the CDK to women at delivery, they play an important role in helping women at delivery use the contents of the CDK, especially misoprostol.

Most women who received the modified CDK used misoprostol and Quaiyum's mat in addition to the original components of the kit (87%)(Figure 5). Few women used some of the components and not others (e.g. only nine percent used the original kit and Quaiyum's mat but not misoprostol).

There were few women who received a CDK and did not use it (n= 1,790; 3%)); however most of these women delivered either at a facility or with a skilled attendant (85%)(data not shown), rendering the kit unnecessary in the presence of other supplies.

Figure 5: Use of modified CDK components (n= 53,897)ˆ



ˆExcludes 315 women who did not have information on the use of CDK components

5.3.2 Bleeding-related Referrals, and the need for Additional Interventions

Delivery complications, referral and mortality were captured on the **Pregnancy Card** when the woman returned for postnatal follow-up, and are presented in Table 7 for the women who delivered during the course of the project. Overall, delivery complications were few in proportion to the number of deliveries. Less than 1% of women experienced retained placenta, eclampsia or tears. Prolonged labor and obstructed labor were experienced by 2% and 3% of women, respectively. Only 2% of women needed referral during labor, delivery or postpartum.

Perceived PPH occurred in less than 1% of deliveries, regardless of whether the woman used misoprostol, delivered in a health facility or with a skilled provider, or if she delivered at home and did not use misoprostol. This rate is much lower than expected based on other studies on maternal health in Bangladesh (BMMS preliminary results, 2011).

Table 7: Delivery complications and referralˆ

	Total (n=77,363)
Postpartum hemorrhageˆˆ	165 (0.2%)
Retained placentaˆˆˆ	98 (0.1%)
Eclampsiaˆˆˆ	80 (0.1%)
Prolonged labor (>24 hours) ˆˆˆ	1,554 (2.0%)
Obstructed laborˆˆˆ	1,934 (2.5%)
Tearˆˆˆ	26 (<0.1%)
Referred during labor, delivery, or postpartum	1,680 (2.2%)

Source: Pregnancy Card

ˆExcludes 40 women missing information on location of delivery and/or misoprostol use

ˆˆNo information for 0.5% of women

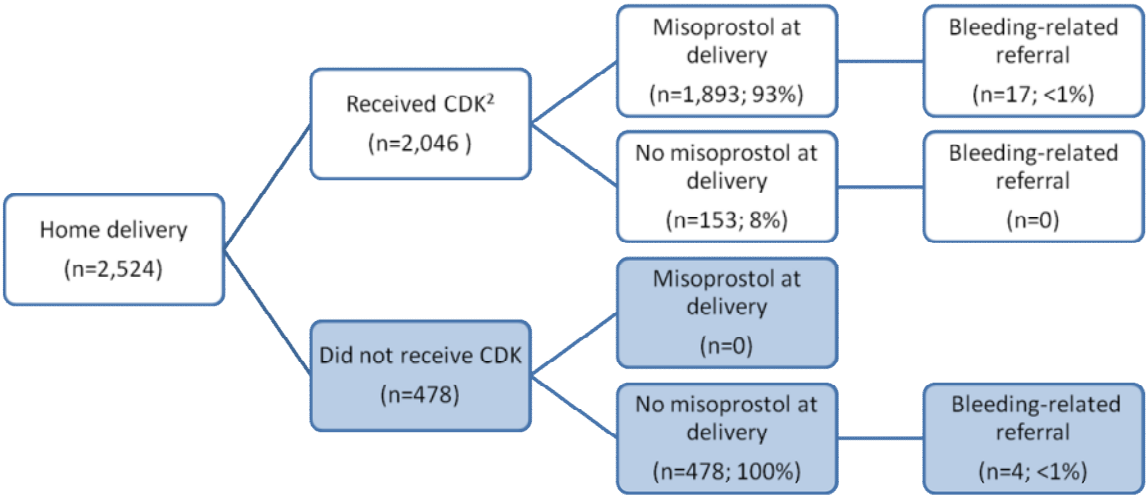
ˆˆNo information for 0.6% of women

[1] Reported soaking blood collection mat completely

Figure 6 presents CDK distribution, misoprostol use, and the need for bleeding-related referral (excessive bleeding or retained placenta) among women who delivered at home and participated in the postpartum interview. Of those women who received a CDK, either during pregnancy or at delivery, and delivered at home, most used misoprostol (93%). Only 17 women who took misoprostol at a home birth required a bleeding-related referral (<1%): Ten for excessive bleeding (nine assessed blood loss using Quaiyum's mat and one using other cloths) and seven for retained placenta. All went to the health facility, where they received treatment, including blood transfusion (n=3), IV saline (n=14), injection (n=14), manual removal of placenta (n=6), and other unspecified treatments (n=6) (women could receive more than one intervention). Of the 153 women who did not take the misoprostol tablets in the CDK they received, none required a bleeding-related referral.

None of the women who did not receive a CDK and delivered at home used misoprostol at delivery. Four women experienced bleeding necessitating a referral, assessed using cloths. All went to a health facility, where interventions received included blood transfusion (n=1), IV saline (n=3), injection (n=3), and other unspecified treatment (n=4).

Figure 6: Use of misoprostol and the bleeding-related referrals[1]



Source: Postpartum Interview
[1]Excessive bleeding or retained placenta
[2] During pregnancy at ANC with a CHW or at delivery with a RDRS birth attendant

5.4 SAFETY: CORRECT USE OF MISOPROSTOL AT HOME DELIVERIES

Of women participating in the postpartum interview, 1,893 out of the 2,011 women who took misoprostol delivered at home. Most women who delivered at home and took misoprostol reported that they took the correct dose of three tablets (97%); a few women took one (<1%) or two (3%) tablets (Table 8). All but four women reported taking misoprostol immediately after delivery of the baby. Therefore, correct use of misoprostol was 96% among women in the postpartum interview sample.

Table 8: Correct use of misoprostol at home births

	Total n= 1,893
Number of tablets^	
1	9 (0.5%)
2	50 (2.6%)
3 (Correct dose)	1,831 (96.7%)
Timing	
Immediately after delivery of the baby	1,889 (99.8%)
Before delivery of the baby	4 (0.2%)
Correct use of misoprostol (correct dose and route)	**1,939 (96.4%)**

Source: Postpartum Interview
^Missing information on the number of tablets for 0.2% of women who took misoprostol at home

In addition, over 46,500 women used misoprostol in this operations research, and there were no adverse events reported in relation to using this drug at home births.

Project participant and RDRS birth attendant after home birth in Nilphamari district

5.5 EXPERIENCE OF POSTPARTUM SYMPTOMS AMONGST MISOPROSTOL USERS

Women's self-reports of symptoms experienced after using misoprostol after delivery are presented in Table 9. Most women did not report experiencing postpartum symptoms after using misoprostol, even after being prompted. The most common symptoms reported by the 12% of misoprostol users experiencing postpartum symptoms included: shivering (6%), rise in body temperature (3%), and nausea (2%). Most of these symptoms resolved with one half (66%) to one hour (16%).

Table 9: Women's reported experience of postpartum symptoms after using misoprostol

	Took misoprostol[1] (n=2,011)
Reported experiencing any symptoms	**238 (11.8%)**
Shivering	125 (6.2%)
Nausea	45 (2.2%)
Vomiting	24 (1.2%)
Rise in body temperature	63 (3.1%)
Diarrhea	16 (0.8%)

Source: Postpartum Interview
[1] At home or facility birth

5.6 WOMEN'S KNOWLEDGE OF PPH AND ACCEPTABILITY OF MISOPROSTOL AND QUAIYUM'S MAT

The postpartum interview assessed women's knowledge of PPH and the information they received about misoprostol, and their acceptability of these two interventions. In general, awareness of delivery complications was relatively low, with one in three women offering that they knew about obstructed labor, prolonged labor, and eclampsia when asked (Table 10). Mentioning excessive

bleeding as a danger sign of delivery was more common among women who received a CDK during pregnancy or delivery than those who did not (45% vs. 28%).

Virtually all women, regardless of if they received a CDK, thought that bleeding was a life-threatening complication of delivery (Table 10). Using Quaiyum's mat was mentioned most often as a means of recognizing when a woman who had bled too much (75% overall); almost twice as many women who received a CDK mentioned Quaiyum's mat than women who did not (83% vs. 45% respectively). Other women mentioned flow of blood (3%), bleeding for more than three days (5%), and when other cloths are soaked with blood (3%). Women who did not receive a CDK were more likely to mention these methods, indicating that women comprehend and use the education accompanying the CDK. Additionally, women who did not receive a CDK were three times more likely not to know how to tell when a woman is bleeding excessively compared to women who received a CDK (27% vs. 9%).

Table 10: Women's knowledge of danger signs and excessive bleeding

	Received CDK (n=609)	Did not receive CDK (n=2,407)	Total (n=3,016)
What danger signs of pregnancy do you know?[1]			
Obstructed labor	825 (34.3%)	194 (31.9%)	1,019 (33.8%)
Prolonged labor	865 (35.9%)	187 (30.7%)	1,052 (34.9%)
Excessive bleeding	1,087 (45.2%)	173 (28.4%)	1,260 (41.8%)
Pre-eclampsia/Eclampsia	814 (33.8%)	200 (62.8%)	1,014 (33.6%)
Abnormal presentation	135 (5.6%)	36 (5.9%)	171 (5.7%)
Retained placenta	54 (2.2%)	15 (2.5%)	69 (2.3%)
Other[2]	80 (3.3%)	11 (1.8%)	91 (3.0%)
Do you think that excessive bleeding is a life-threatening complication of pregnancy/delivery?			
Yes**	2,390 (99.3%)	584 (95.9%)	2,974 (98.6%)
How do you know when a woman is bleeding too much after childbirth?**			
Mat is fully soaked with blood	1,986 (82.5%)	272 (44.7%)	2,258 (74.9%)
Blood coming out continuously	45 (1.9%)	45 (7.4%)	90 (3.0%)
Bleeding continues for more than 3 days after delivery	88 (3.7%)	76 (12.5%)	164 (5.4%)
Cloths, bed sheet, saris are soaked with blood	53 (2.2%)	27 (4.4%)	80 (2.7%)
Don't know	218 (9.1%)	164 (26.9%)	382 (12.7%)
No response	17 (0.7%)	25 (4.1%)	42 (1.4%)
What ways are there to prevent bleeding after delivery?**			
Take 3 misoprostol tablets	1,787 (74.2%)	145 (23.8%)	1,932 (64.1%)
Call a doctor	182 (7.6%)	143 (23.5%)	325 (10.8%)
Don't know	11 (0.5%)	9 (1.5%)	20 (0.7%)
No response	427 (17.7%)	312 (51.2%)	739 (24.5%)

Source: Postpartum Interview

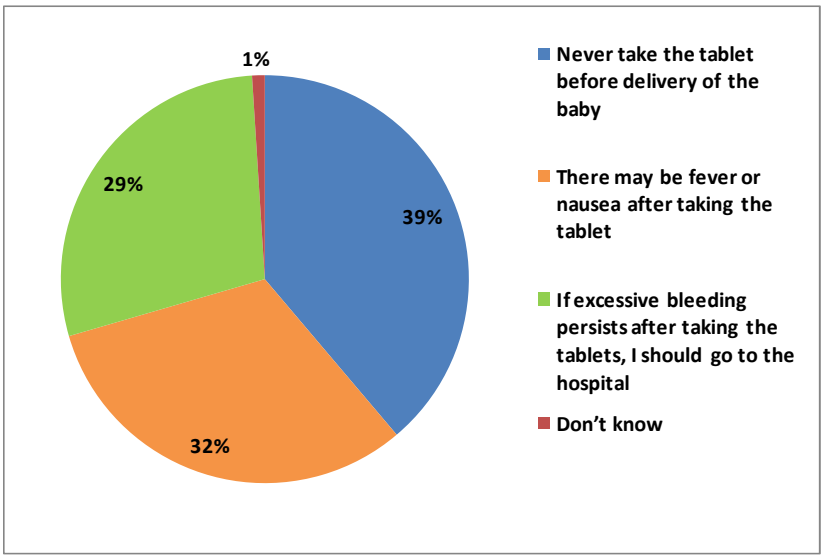
[1] Women could chose more than one response, therefore percentages do not add up to 100%

[2] Includes oral ulcer, excessive vomiting, tetanus, severe fever, anemia and weakness

** p<0.01

When given the CDK, women were educated on how to use its contents, including misoprostol and Quaiyum's mat. Figure 7 presents the information received by women who were given a CDK; women were only coded as giving one response. When asked what information they were given when they were offered misoprostol, respondents mentioned that they should not take the tablets before delivery of the baby (39%), potential symptoms associated with misoprostol use (32%), and the need to seek care should excessive bleeding occur after taking the tablets (29%). Less than 1% of women in the postpartum sample who received a CDK did not know anything about misoprostol.

Figure 7: Women's knowledge on misoprostol (n=2,407)



Source: Postpartum Interview

Nurses and health care providers providing ANC were mentioned most frequently as the source of information about complications of childbirth (58%)(Table 11). Women who received a CDK were significantly more likely to mention RDRS birth attendants as a source of information than those who did not (19% vs. 8%). Friends/relatives were mentioned twice as frequently as a source of information among women who did not receive a CDK (13% vs. 6%).

Table 11: Reported sources of information on complications of childbirth[1]

	Received CDK (n=609)	Did not receive CDK (n=2,407)	Total (n=3,016)
Friend/Relative**	139 (5.8%)	76 (12.5%)	215 (7.1%)
Nurse/health care provider	1,418 (58.9%)	342 (56.2%)	1,760 (58.4%)
RDRS birth attendants**	452 (18.8%)	50 (8.2%)	502 (16.6%)
Don't know**	88 (3.6%)	36 (5.9%)	124 (4.1%)
Did not receive information	310 (12.9%)	105 (17.2%)	415 (13.8%)

Source: Postpartum Interview
[1] Women could chose more than one source of information
** p<0.01

Almost all women who took misoprostol felt that the drug was useful to them (98%) and that they would recommend misoprostol to a friend (99%)(Table 12). The majority of the women said they were willing to purchase misoprostol (87%). Women who used misoprostol at delivery were much more likely to express acceptability of the drug compared to women who did not.

Table 12: Acceptability of misoprostol

	Took misoprostol[1] (n=2,011)	Did not take misoprostol[2] (n=1,005)	Total (n=3,016)
Felt misoprostol was useful to them**	**1,976 (98.3%)**	**276 (27.5%)**	**2,252 (74.7%)**
Would recommend misoprostol to a friend**	**1,996 (99.3%)**	**378 (37.6%)**	**2,374 (78.7%)**
Would purchase misoprostol**	**1,747 (86.9%)**	**289 (28.8%)**	**2,036 (67.5%)**
Average amount willing to pay for misoprostol in Taka (min;max)**	26.5 (1;1,030)	33.6 (1;500)	27.5 (1;1,030)

Source: Postpartum Interview
[1] At home or facility birth
[2] Includes women who received injection (n=491)
** p<0.01

Almost all women who used Quaiyum's mat said they benefitted from the mat (98%); would use the mat in a future delivery (87%); and would purchase the mat (89%)(Table 13). Those that did not use the mat were less likely to state they would use the mat or pay for it (28% and 29% respectively). Of those willing to pay, the average amount was 23.7 Taka (or USD 0.32).

Table 13: Acceptability of mat

	Used mat (n=1,950)	Did not use mat (n=1,066)	Total (n=3,016)
Benefitted from using mat	**1,909 (97.9%)**	--	--
Would use mat in a future delivery	**1,688 (86.6%)**	**299 (28.1%)**	**1,987 (65.9%)**
Would purchase the mat	**1,732 (88.8%)**	**309 (29.0%)**	**2,041 (67.7%)**
Average amount willing to pay for mat in Taka (min;max)	23.6 (2;300)	24.1 (5;150)	23.7 (2;300)

Source: Postpartum Interview

5.7 MATERNAL MORTALITY

A total of 113 deaths were reported in the study areas coinciding with the operations research time period. Results of the verbal autopsy conducted on the 113 deaths of women of reproductive age are presented in Table 14. Of these, 108 deaths were due to direct obstetric causes, including PPH and bleeding-related causes (n=34), antepartum hemorrhage (n=8), eclampsia alone (n=30) and with other causes (n=9), obstructed labor (n=2), ruptured uterus (n=2), complications due to cesarean delivery (n=1), and other direct causes (n=22). Of the 34 women that died as a result of PPH and bleeding-related causes, only 16 had taken misoprostol for prevention of PPH. The two women who died due to ruptured uterus did not take misoprostol.

Table 14: Attributed cause of death, timing of death, and use of misoprostol

Cause of death	Number of deaths	Timing of death^		Number took misoprostol
		Before delivery	Postpartum	
Direct Obstetric causes	**108**	**30**	**76**	**27**
PPH and bleeding-related[1]	34	0	34	16
Antepartum Hemorrhage (APH)	8	4	4	0
Eclampsia	30	11	18	2
Obstructed labor	2	2	n/a	n/a
Eclampsia & PPH and bleeding-related	7	0	7	4
Eclampsia & APH	1	0	1	0
Eclampsia & ruptured uterus	1	1	0	0
Ruptured uterus	2	1	1	0
Complications due to cesarean delivery	1	0	1	0
Other direct causes[2]	22	11	10	5
Indirect causes[3]	**5**	**3**	**2**	**0**

Source: Verbal Autopsy

^ Two women are missing information on timing of death, one who died of eclampsia and one who died of other direct causes

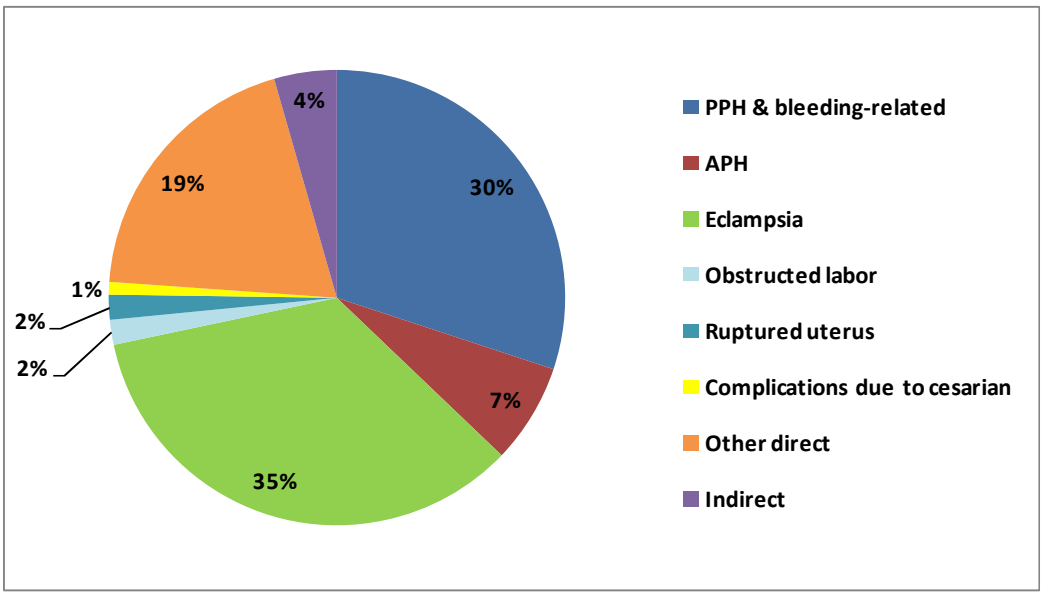
[1] Bleeding-related includes hypovolemic shock and anemia, and retained placenta

[2] Other direct causes include heart disease, respiratory/asthma, etc

[3] Indirect causes include infections, suicide, etc.

Distribution of the attributed cause of death from the verbal autopsy is presented in Figure 8. Eclampsia accounted for the largest proportion of deaths (35%), followed by PPH and bleeding-related causes (30%) and other direct causes (19%).

Figure 8: Causes of maternal mortality (n=113)



Using the most recent MMR estimate of 194 deaths per 100,000 live births (BMMS preliminary results, 2011), we would expect 150 maternal deaths among the 77,363 deliveries conducted by RDRS between June 2009 and October 2010. Therefore, 37 fewer deaths were observed than expected in this project.

6. Conclusions

With enrollment of over 118,500 women, this is one of the largest operations research projects assessing the use of misoprostol distributed directly to women for the prevention of PPH in the world. Given the robust sample size, the following conclusions can be derived from the results of this operations research.

HIGH COVERAGE OF CDK DISTRIBUTION TO WOMEN

Most women in Bangladesh deliver at home, without a skilled attendant. This was true in this project (87% home deliveries, 88% without a skilled provider). In a context like this, reaching women with interventions that can prevent one of the leading causes of maternal mortality can save lives. Of the women who delivered during the implementation of the operations research, 70% received a CDK at some point during pregnancy or delivery, demonstrating that distributing CDKs through these channels is a feasible way to reach a large number of women. Most of the women who did not receive a CDK during pregnancy delivered with a RDRS birth attendant (73%), highlighting the importance of equipping them with CDKs to ensure misoprostol is on-hand to prevent PPH and Quaiyum's mat is available to identify the need for referral.

DISTRIBUTION OF CDKS PROTECTS BIRTHS AT HOME

Of those that delivered at home in the postpartum sample, the majority received a CDK at some point (81%). In addition, protected births were promisingly high: Of all the women that received a CDK, 96% were protected from PPH either by using misoprostol at home or delivering at a health

facility or with a skilled provider. Misoprostol use at home deliveries, distributed through CDKs, increased protected births in the project by 60%.

NEAR UNIVERSAL CORRECT USE OF MISOPROSTOL AT HOME

The safety of using misoprostol at home births as part of a modified CDK for PPH prevention was well demonstrated. Almost all of the 1,893 women who used misoprostol at home and participated in the postpartum interview reported using the drug correctly (96%), taking the correct dose at the right time. The high use rate and data on correct use of misoprostol demonstrate the effectiveness of the education women were given by CHWs and RDRS birth attendants when they received the CDK.

Furthermore, the experience of postpartum symptoms was very low amongst misoprostol users, and self-resolving within an hour.

WOMEN USE QUAIYUM'S MAT TO ESTIMATE BLOOD LOSS

Almost all women who received a CDK used Quaiyum's mat to estimate blood loss at delivery (96%). In addition, women who had received a CDK spontaneously mentioned using the mat when asked how they know if a woman is bleeding too much after delivery. Furthermore, most women who used the mat said they found it useful and would use it again in their next delivery. This is evidence that Quaiyum's mat is a feasible and acceptable means of assessing postpartum blood loss in Bangladesh, improving recognition of PPH and facilitating a timely referral to prevent unnecessary delays in seeking care.

MATERNAL MORTALITY LOWER THAN EXPECTED

A total of 113 deaths were reported in the study areas coinciding with the operations research time period. Eclampsia accounted for the largest proportion of deaths followed by PPH and bleeding-related causes and other direct causes. Thirty-seven fewer deaths were observed than expected in this project using the most recent MMR estimate.

WOMEN FIND MISOPROSTOL AND QUAIYUM'S MAT TO BE HIGHLY ACCEPTABLE

Misoprostol is very acceptable to women who have used the drug. Over 98% of women who took misoprostol consider it useful and would recommend it to a friend. As expected, acceptability measures were lower for women who had not used misoprostol. In addition, most women who used the mat found it helpful and would recommend its use to a friend. Therefore, it can be assumed that integrating these two technologies into a modified CDK is an acceptable intervention to women to prevent and identify PPH at home births.

7. Recommendations

Findings from this operations research demonstrate that including misoprostol and Quaiyum's mat in a modified CDK and distributing it to women during ANC and at delivery with a trained TBA increases the likelihood that women will be protected from PPH at home deliveries. We recommend that scale-up of distribution of such a CDK nationwide in Bangladesh be a priority.

CDK DISTRIBUTION PROGRAMS SHOULD INCLUDE MISOPROSTOL AND QUAIYUM'S MAT

The current contents of CDKs do not directly target the leading causes of maternal mortality. This project demonstrated that misoprostol and Quaiyum's mat are two simple interventions that can easily be added to current CDKs and, for the first time, equip women and attendants at home deliveries to protect women from PPH. All programs in Bangladesh currently distributing CDKs should begin to include misoprostol and Quaiyum's mat to prevent PPH at home births. All providers who distribute CDKs, including CHWs, TBAs, ANC providers and others, should be trained to educate women about PPH, misoprostol and assessing blood loss using Quaiyum's mat. Women's retention of information about and correct use of misoprostol shows the importance of arming community-level providers with specific, concrete messages.

MAXIMIZE ALL POTENTIAL DISTRIBUTION CHANNELS TO REACH WOMEN

While ANC distribution of the CDKs reached a large proportion of women, relying wholly on this strategy misses an important group of women. While these women may attend ANC, they do so early in pregnancy before they reach the gestational age threshold of 32 weeks to receive the CDK. While we recommend greater effort to encourage women to return to ANC after they have reached the gestational age requirement in order to receive the drug, logistical factors may impede women from being able to return.

Therefore, we recommend lowering the gestational age restriction to at least the second trimester or removing it completely to increase coverage of misoprostol distribution to pregnant women at ANC. Other countries, such as Zambia and Kenya, have distributed misoprostol to women at their first ANC visit (no gestational age requirement), resulting in higher coverage of misoprostol distribution without compromising safety. If this were adopted in Bangladesh, marked increases in the number of women taking a CDK home from ANC would be possible.

In addition, other existing networks should be utilized to reach women. While RDRS trained TBAs distributed the minority of CDKs in this project, it is because they only distributed CDKs for seven months, from March to September 2010 (see section 3.1.1). However, even though they were not distributing the CDK, the majority of women who used misoprostol reported that the RDRS trained TBA helped them take the drug. Furthermore, most of the women who did not receive a CDK delivered with a RDRS birth attendant, and if they had been distributing the kits, they would have been covered by these life-saving interventions. We therefore recommend that any program with a network of trained TBAs include them in their distribution network for CDKs. Additional means of reaching women with a modified CDK that includes these life-saving technologies should be considered.

8. References

AbouZahr C. Global burden of maternal death and disability. *British Medical Bulletin* 2003;**67**:1–11.

Alfirevic Z, Blum J, Walraven G, *et al.* Prevention of postpartum hemorrhage with misoprostol. *International Journal of Gynecology and Obstetrics* 2007;**99** (Suppl 2):S198-201.

Derman RJ, Kodkany BS, Goudar SS, *et al.* Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomised controlled trial. *Lancet* 2006;**368** (9543):1248-53.

Gynuity. Postpartum Hemorrhage: Responding to the Challenge. 2006 [cited 2011 28 April]; Accessed online 2 May 2011 at: http://www.gynuity.org/documents/MisoPPH_ProjectDescription_Eng.pdf

ICM/FIGO Prevention and Treatment of Post-partum Haemorrhage: New Advances for Low Resource Settings. ICM-FIGO Joint Statement, November 2006. Accessed online 31 March 2008 at: http:/www.figo.org/news item3.asp.

Maslovitz S, Barkai G, Lessing JB, *et al*. Improved accuracy of postpartum blood loss estimation as assessed by simulation. *Acta obstetricia et gynecologica Scandinavica* 2008;**87** (9):929-34.

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 randomized placebo-controlled trial. *British Journal of Obstetrics & Gynaecology* 2011;**118** (3):353-61.

National Institute of Population Research and Training (NIPORT), MEASURE Evaluation, University of North Carolina – Chapel Hill, ICDDR,B. Bangladesh Maternal Mortality and Health Care Survey 2010: Summary of Key findings and implications, February 2011.

National Institute of Population Research and Training (NIPORT), Mitra and Associates, and Macro International. Bangladesh Demographic and Health Survey 2007. Dhaka, Bangladesh and Calverton, Maryland, USA: National Institute of Population Research and Training, Mitra and Associates, and Macro International, 2009.

Nessa S, Arco E, Kabir I. Birth kits for safe motherhood in Bangladesh. *World Health Forum* 1992;**13**:66-69.

Patel A, Goudar S S, Geller S E, *et al*. Drape estimation vs. visual assessment for estimating postpartum hemorrhage. *International Journal of Gynecology and Obstetrics* 2006;**93:**220–224.

Prata N, Gessessew A, Abraha AK, *et al*. Prevention of postpartum hemorrhage: options for home births in rural Ethiopia. *African Journal of Reproductive Health* 2009a;**13** (2):87-95.

Prata N, Mbaruku G, Campbell M, *et al.* Controlling postpartum hemorrhage after home births in Tanzania. *International Journal of Gynecology and Obstetrics* 2005;**90**:51-55.

Prata N, Mbaruku G, Grossman A, *et al*. Community-Based Availability of Misoprostol: Is It Safe? *African Journal of Reproductive Health* 2009b;**13** (2):117-128.

Quaiyum MA, Hossain SAS, Streatfield PK, *et al*. A simple method of measuring postpartum blood loss in Bangladesh. (Abstract): Proceedings of International Congress on Evidence based interventions to prevent postpartum hemorrhage: Translating research into practice. Goa, India, July 12-15, 2006.

Rajbhandari S, Hodgins S, Sanghvi H, *et al*. Expanding uterotonic protection following childbirth through community-based distribution of misoprostol: operations research study in Nepal. *International Journal of Gynecology and Obstetrics* 2010;**108** (3):282-8.

The RESPOND Project. Mayer Hashi Project. Preventing Postpartum Hemorrhage: Community-based Distribution of Misoprostol in Tangail District, Bangladesh. Project Brief. New York: Engender Health, May 2010/No. 2.

Sanghvi H, Ansari N, Prata NJ, *et al*. Prevention of postpartum hemorrhage at home birth in Afghanistan. *International Journal of Gynecology and Obstetrics* 2010;**108** (3):276-81.

SPSS for Windows, Rel. 11.0.1. 2001. Chicago: SPSS Inc.

StataCorp. *Stata Statistical Software: Release 10*. College Station, TX: StataCorp LP, 2007.

United Nations Development Program (UNDP), Bangladesh. Millennium Development Goals, Goal 5: Improve Maternal Health. Accessed online 18 May 2011 at: http://www.undp.org.bd/mdgs/goals/MDG%205.pdf

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. *British Journal of Obstetrics and Gynaecology* 2005;**112** (9):1277-83.

World Health Organization (WHO). The prevention and management of postpartum hemorrhage. WHO report of technical working group 1990. Report No. WHO/MCH/90.7.

World Health Organization (WHO). Trends in maternal mortality: 1990 to 2008. Estimates developed by WHO, UNICEF, UNFPA and The World Bank. Geneva: WHO, 2010. Accessed 10 May 2011 at: http://www.who.int/reproductivehealth/publications/monitoring/9789241500265/en/index.html

World Health Organization. Guidelines for introducing simple delivery kits at the community level. Geneva: Maternal and Child Health Unit, Division of Family Health, WHO, 1987.

World Health Organization. Unedited report of the 19th expert committee on the selection and use of essential medicines. Geneva: WHO, 2011. Unedited report 5 May 2011. Accessed online 9 May 2011 at: http://www.who.int/medicines/publications/unedited_trs/en/index.html