MAPPING MISOPROSTOL FOR POSTPARTUM HEMORRHAGE:
Organizational Activities, Challenges, and Opportunities
EXECUTIVE SUMMARY

Postpartum hemorrhage (PPH) is the single largest cause of maternal mortality worldwide, accounting for nearly one-quarter of maternal deaths. Preventing and treating PPH is especially difficult in places where most births occur in homes or local clinics and access to emergency services, obstetric care, and surgery is limited. Evidence to date shows that misoprostol can play an important, perhaps life-saving, role in preventing and treating PPH. It remains unclear, however, how misoprostol’s clinical efficacy translates into program effectiveness in different contexts, particularly at the community level and for home births. In addition, there continues to be great variability in clinical practice and lack of clear, evidence-based policies and guidelines to enable policy makers to make sound decisions related to introducing misoprostol at the national level.

To address these issues, Family Care International (FCI), working with Gynuity Health Projects, commissioned this survey to begin to map current activities and approaches of the many organizations working globally on misoprostol for PPH. Over 30 organizations were asked to describe their organizational activities, share their motivations for involvement, discuss the barriers they have encountered in use of misoprostol, and suggest strategies for addressing these barriers. This report details the findings of the survey and makes recommendations on how to move forward.

One of the clearest findings from this exercise is that the use of misoprostol for PPH is rapidly gaining traction with organizations working to improve women’s health. An impressive (and growing) number of organizations are working in this area, and most of the respondents made the case for integrating the use of misoprostol into reproductive health services programming worldwide. There is a belief among respondents that misoprostol offers a real opportunity to make a difference in maternal mortality—one that is not dependent on waiting for health systems to be strengthened—and they want to act on this opportunity as quickly as possible to save women’s lives.

Given the rapid forward momentum around misoprostol, action is needed to address key barriers in several areas:

- **Consensus on evidence-based guidelines:** Respondents noted the absence of a global consensus, and clear and updated evidence-based guidelines for misoprostol use for PPH; they specifically highlighted the lack of strength and clarity of the World Health Organization (WHO) guidelines (specifically related to the role of misoprostol in prevention of PPH and its use at the community level). Respondents called for WHO to review available data and produce clear and updated guidelines as soon as possible.\(^1\)

- **The association of misoprostol with abortion:** Rather than hiding misoprostol’s abortion indication to avoid controversy, this indication should be presented as one of many ways misoprostol can potentially save women’s lives.

- **Misoprostol’s role at the community level:** More operations research is needed to determine the feasibility and desirability of distribution of misoprostol for PPH at the community and home level, including distribution through pharmacies and direct use by women.

- **Products:** While several organizations are working to address the product-related issues associated with misoprostol—including appropriate dosages, labeling, and packaging—more needs to be done to address the fact that the drug is already readily accessible. Information about the proper use of misoprostol needs to be given directly to women and the pharmacists, traditional birth attendants, and others who serve them.

While the true extent to which misoprostol can benefit women’s health remains to be seen, it is clear that it is quickly being integrated into reproductive health programming. Urgent action is needed to ensure that it is made available to women in ways that best benefit them in terms of safety and effectiveness.

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\(^1\) Since the interviews were conducted, WHO began the process of updating its guidelines for the prevention and treatment of PPH.
BACKGROUND

Postpartum hemorrhage (PPH) is a serious medical problem in need of urgent attention. PPH is the single largest cause of maternal mortality, accounting for nearly one-quarter of maternal deaths worldwide. Effectively preventing and treating PPH is especially difficult in areas where most births occur in homes or local clinics and access to emergency services, obstetric care, and surgery is limited.

Efforts to address PPH have focused primarily on active management of the third stage of labor (AMTSL), with oxytocin as the preferred uterotonic drug. More recently, however, the availability, and in some cases promotion, of the drug misoprostol as an alternative when AMTSL and oxytocin are not available has made the discussion about how to best prevent and treat PPH more complex.

Evidence to date shows that misoprostol, an oral tablet initially designed to prevent gastric ulcers, can play an important role in preventing and treating PPH. It remains unclear, however, how misoprostol’s clinical efficacy translates into program effectiveness in different contexts, particularly at the community level and for home births. In addition, there continues to be great variability in clinical practice, with health providers employing differing regimens and routes of administration, and lack of clear, evidence-based policies and guidelines to enable policy makers to make sound decisions related to introducing misoprostol at the national level. An additional issue is that misoprostol can also be used to induce abortion, raising concerns among some policy makers about its introduction for other indications.

To address these issues, FCI is working with Gynuity Health Projects and other partners to develop an evidence-based policy and advocacy agenda for promoting misoprostol for PPH at the global, regional, and country levels. An important step in this process is to map current activities and approaches of the many organizations working globally on misoprostol for PPH. The primary objectives of the mapping exercise were to:

- map key advocacy goals, messages, and strategies used by organizations working on misoprostol for PPH;
- identify advocacy and policy priorities and challenges; and
- assess opportunities for collaboration, and advocacy and policy change at the global, regional, and country levels.

This report details the findings and recommendations of the survey, including the methodology, organizational motivations for involvement in misoprostol work, organizational activities, perceived barriers, and suggested strategies for addressing barriers. The report recommends key areas for moving forward.
The survey was conducted between April and September 2010. As a starting point, a list of 17 individuals at 16 organizations known to be working on the use of misoprostol for PPH was prepared, and each was sent a letter of invitation to participate. Phone interviews were conducted with these individuals, with a 100% response rate.

As the interviews progressed, it became clear that additional organizations needed to be included in the survey. Additional contacts were identified using a “snowball sampling” technique that relied on information from the original interviews as well as knowledge of organizations and contacts working in reproductive health. Input from 14 additional organizations was included in the mapping survey; in total, 41 individuals representing 30 organizations participated. A full list of the participating organizations can be found in Appendix A.

Interviews followed an open-ended questionnaire covering topics such as: current organizational activities related to using misoprostol for PPH (advocacy, policy, research, program implementation, etc.); perceived barriers to using misoprostol for this indication; and possible strategies for addressing the barriers. Respondents were asked to provide information about and links to publications and materials produced on the topic (Appendix B). A copy of the survey questionnaire can be found in Appendix C.

Data were compiled for each survey question, and then analyzed for content to identify both common themes and unique but important perspectives. For the responses to the question, “What are the main barriers to using misoprostol for PPH?” the number of organizations that mentioned different types of barriers were tallied to get a rough sense of the relative perceived importance of the various barriers mentioned. When several interviewees from the same organization mentioned the same barrier, this was counted as one mention. With the exception of Appendix D, which lists activities by organization, all responses have been reported without attribution to protect the confidentiality of interviewees.

The results are limited by several factors, including:

- **Sampling:** Because a “snowball sampling” technique was employed, there is no way of knowing which or how many organizations working on this topic might have been missed. However, given the interviewers’ knowledge of the field and the fact that most of the major U.S.-based international nongovernmental organizations (NGOs) are involved in reproductive health, the survey is fairly comprehensive. A more problematic limitation is relying on the report of a single individual to represent an organization’s entire scope of work related to misoprostol; while interviews were sometimes conducted with multiple individuals at a single organization, in most cases only a single individual was interviewed. As a result, important information and perspectives may have been missed.

- **Reporting bias:** The group of organizations working on the use of misoprostol for PPH is a small one, in which everyone knows each other. While confidentiality was ensured, given the politically charged nature of some of the questions, some respondents may have tempered or qualified their responses. Nevertheless, in general, respondents showed a remarkable openness to discuss the topic, and several shared information they identified as confidential.

- **Interviewer bias:** While data were analyzed as objectively as possible, interviewers’ personal knowledge and attitudes may have biased the interpretation of the comments. This was controlled by independently tabulating the data and by checking one interviewer’s interpretation against the other’s.

- **Time:** Limited time prevented a deeper investigation of country-specific activities and approaches. The scope of work also did not include an in-depth review of articles and other print materials that interviewees provided. Many of these contain information about organizational approaches to advocacy and messaging about misoprostol for PPH that could have helped inform the recommendations. FCI will produce a separate report with these findings.

On a positive note, none of the respondents hesitated to participate in the survey. On the contrary, all were very willing to talk, and many expressed appreciation for the exercise, saying they looked forward to seeing the results. The fact that every person contacted took the time to participate in the survey was another indicator of just how compelled everyone is to address the problem of PPH (see discussion of results).
Respondents were asked about their organizational goals and strategies relating to the use of misoprostol for PPH prevention and treatment. Respondents overwhelmingly indicated that their primary goal was to reduce maternal mortality. Almost everyone spoke of the huge toll of PPH on women’s health and lives and the urgent need to take action.

Within this broad goal, organizations reported using multiple strategies and implementing a wide range of activities related to the use of misoprostol for PPH, including operations research, policy guidance, advocacy, product registration and quality assurance, and program implementation (see Appendix D). Some organizations were focused in only one area, while others were working in multiple areas. Examples of strategies employed by organizations are listed in Table 1.

The 30 organizations interviewed are working with misoprostol in more than 35 countries (see Appendix E). An additional four organizations are working with misoprostol but have no current activities related to misoprostol for PPH.

It is worth noting that many of the organizations interviewed do not view themselves as specifically “promoting” misoprostol for PPH or even introducing misoprostol for PPH. Rather, they describe themselves as working to address PPH using whatever means is best suited to the specific setting in which they are working; at times this means addressing the use of misoprostol. A few of the organizations interviewed are working to improve maternal health by increasing access to safe abortion services and/or postabortion care, and have begun to address the use of misoprostol for PPH as well.
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| Research          | ● Continue research on safety and effectiveness – in particular, the safest dose that can be used for prevention and treatment – and translate that work into policy and advocacy at the program level  
|                   | ● Undertake operations research to test the safety of advance distribution of misoprostol for home use  
|                   | ● Conduct studies to document the cost effectiveness of using misoprostol to treat PPH – in particular, the cost effectiveness of widespread prevention versus targeted treatment approaches |
| Policy/Advocacy   | ● Ensure that recommendations for the use of misoprostol for PPH are based on sound scientific evidence  
|                   | ● Make available evidence-based guidelines on using misoprostol to treat PPH  
|                   | ● Disseminate evidence-based information for misoprostol use for various indications, including PPH, by publishing research articles, review articles, and guidelines (such as the International Federation of Gynecology and Obstetrics [FIGO] guidelines) and posting materials on websites such as www.misoprostol.org |
| Drug Regulation/Drug Quality | ● Register and introduce misoprostol in countries where it is not yet registered for PPH treatment and prevention indications  
|                   | ● Assure that a quality misoprostol product is available at an affordable price for PPH indications  
|                   | ● Identify poor-quality products and work toward a supply of better-quality product |
| Program/Service Delivery | ● Scale up PPH prevention activities started under the Prevention of Postpartum Hemorrhage Initiative (POPHI); the primary aim is to promote AMTSL, but supplement with misoprostol where AMTSL is not feasible  
|                   | ● Increase access to misoprostol to reduce maternal mortality, both through PPH indications and medical abortion  
|                   | ● Introduce misoprostol as part of a package of interrelated interventions including family planning and the use of magnesium sulfate during delivery  
|                   | ● Make misoprostol available through facilities, both community and hospital, as a backup or alternative to oxytocin  
|                   | ● Make misoprostol available for prevention and treatment of PPH at the lowest levels possible (“as close to the community as possible”) and where oxytocin is not available by training midwives and traditional birth attendants in its use  
|                   | ● Reduce maternal mortality by educating nonmedical local community leaders (such as village officials and key opinion leaders) and women themselves about using misoprostol at home births for PPH prevention |
COMPELLING NEEDS, PASSIONATE RESPONSES

Organizations were asked why it was worthwhile to invest resources in misoprostol for PPH. Most of the respondents were passionate about the need for their work in this area, reiterating the overall concern about reducing maternal mortality as well as raising other compelling issues. Below are the key reasons identified by respondents for investing in misoprostol, along with direct quotes from interviewees. (Note: these are the respondents’ perceptions and may not always be supported by the available evidence.)

**MISOPROSTOL CAN SAVE WOMEN’S LIVES.**

We believe that anything that can have an impact on PPH, which is a major cause of maternal mortality, should be addressed.

PPH is still a leading cause of maternal mortality. Women don’t have that many options for prevention/treatment. A reduction in risk of even 30–50% is a good enough reason to make it available.

We work on maternal health and mortality, and PPH is the main cause [of mortality] – misoprostol can make a significant difference.

Misoprostol is a life saver, especially at the community level.

**MISOPROSTOL FILLS AN UNMET NEED IN THE CONTINUUM OF PPH CARE: WOMEN DELIVERING AT HOME.**

We see misoprostol as part of the continuum of care for PPH, which includes AMTSL and/or misoprostol, [use of an] anti-shock garment for stabilization, and transport to a higher-level facility.

Misoprostol is currently the only way we have of helping women without access to health services. In the long term, we hope that misoprostol will not be needed because women will have access to attended birth, oxytocin, etc.

Right now, misoprostol is the only tool that exists for unskilled people at the home and community level.

If there is something that safely prevents PPH for women delivering at home, it would be a very important tool to promote.

We saw a big gap in countries where maternal mortality is highest—women deliver at home and there is nothing to help them. Misoprostol can help them.

**WOMEN DESERVE TO BE EMPOWERED TO HELP THEMSELVES HAVE SAFE BIRTHS.**

There is one person who will always be present at birth: the woman herself. Therefore, she should be empowered to help herself, even in the absence of skilled care.

Regardless of WHO’s lofty goals for skilled attendants at birth, many women deliver at home. This is because facilities are too crowded or women can’t get there (for a variety of reasons). It may take us 25 to 30 years to get to the point that most births are attended, if we can even reach that point. In the meantime, women are dying from preventable causes, and misoprostol needs to get into women’s hands.

**MISOPROSTOL IS OUT THERE BEING USED—WE NEED TO PROMOTE SAFE USE.**

Because misoprostol is available and being used, it is important to understand and promote evidence-based practices for its safe use in reproductive health applications. For instance, we have heard anecdotal reports of ruptured uteri and high fevers associated with misoprostol use (though not clear if this is associated with PPH use or for induction). We need to know more in order to promote safe guidelines.

Though there is lots of talk about limiting circulation [in Nigeria], it is widely available to women through other means.

In Asia, we see lots of products on the market, primarily marketed for abortion.

**MISOPROSTOL WILL HELP EXPAND UTEROTONIC COVERAGE.**

The only way to get universal uterotonic coverage is with an oral uterotonic.

Oxytocin is the first choice for effectiveness, but since it is still not available in many areas or its quality is compromised, it is important to make an effective alternative available.

We know that women give birth in low-resource settings where no oxytocin is available.
MISOPROSTOL IS AFFORDABLE AND ACCESSIBLE.
Visiting a provider is expensive; misoprostol provides a low-cost, easy-access medicine with huge implications for health.

Misoprostol has an easy supply chain because it requires no refrigeration.

WE NEED MORE INFORMATION ABOUT SAFE AND EFFECTIVE DOSES.
To date, there is not sufficient evidence on effectiveness and safety of doses—we want to find the lowest effective dose.

We want to explore misoprostol for its full potential and all uses but also want to evaluate it for the benefits and harms—this is important because it is a systemic drug and a powerful one.

INTRODUCING MISOPROSTOL FOR PPH OPENS THE DOOR TO USING IT FOR ABORTION, WHICH WILL SAVE WOMEN’S LIVES.
Access to misoprostol for PPH and its availability will also mean access to safe abortion (and greatly reduced mortality).

Because misoprostol for PPH is less controversial than misoprostol for safe abortion, it is a “door-opener.”

We really like that misoprostol is used for other purposes as well (abortion). We’d like to see it as freely available as possible.
Interviewees provided rich details about the numerous barriers to and complexities of introducing misoprostol for PPH prevention and/or treatment. Barriers ranged from practical issues, such as the lack of a global consensus, clear guidelines, and availability of a misoprostol product labeled for PPH use, to broader societal concerns, such as a lack of willingness to empower women to participate in their health care and the controversy surrounding the use of misoprostol for abortion.

Reported barriers are listed here in order of perceived importance (as roughly indicated by the number of organizations that mentioned each barrier), with the most frequently mentioned barriers listed first:

- Lack of global consensus and clear, updated evidence-based protocols and guidelines
- Association with abortion
- Concerns about safety and side effects
- Product issues
- Controversy over who can provide misoprostol at the community level
- Fear of women’s empowerment

More detailed descriptions of each barrier are below, followed by strategies suggested by respondents for addressing them.

**Lack of Global Consensus and Clear Evidence-Based Protocols**

The lack of global consensus and evidence-based protocols was the most frequently mentioned barrier. Specifically, respondents spoke of the lack of strength and clarity of the WHO guidelines for misoprostol use for PPH (particularly related to its role in prevention of PPH and use at the community level). Many interviewees acknowledged the difficulties of sorting through available research to determine the best protocol recommendations (i.e., studies have used different approaches/doses/routes of administration, some are less rigorous than others, etc.). Some respondents noted that WHO can play an important role in formulating a clear set of guidelines for informing programming and policy; many

**Respondents’ Suggestions for Addressing Lack of Clear and Updated Global Guidelines**

Update WHO guidelines related to misoprostol for PPH and add to Model Essential Medicines List (EML). Over and over, respondents called for clear, evidence-based guidelines on misoprostol use for PPH and to add misoprostol to the EML for this indication. Suggestions for accomplishing this included: organizations joining together to exert more pressure on WHO to use existing data to develop a recommendation in line with the FIGO/ICM statement; holding another meeting with WHO and NGO leaders to secure the WHO’s commitment to develop clearer guidelines.2

Use evidence-based advocacy. Many respondents mentioned the success of and need for further evidence-based advocacy to help governments and programmers understand the benefits and risks of using misoprostol in their programs. Some recommended urging countries to think independently of WHO to make their own evidence-based decisions. Several mentioned the strategy of gaining stakeholder support using evidence-based advocacy, and then piloting programs to demonstrate effectiveness in a real-life setting.

A number of respondents urged that advocacy focus not on misoprostol but rather on appropriate strategies for prevention and treatment of PPH in different settings, which may include misoprostol and/or other uterotonics.

Encourage NGO coordination and cooperation. One respondent suggested that international NGOs working in a given country synchronize their agendas so that messages about misoprostol are consistent and a broad range of audiences (doctors, midwives, pharmacists, governments, women’s groups, etc.) are reached without duplication of effort.

Another respondent suggested that programs having success with misoprostol for PPH could have an influence in convincing programs in neighboring countries of their region to adopt a similar approach. Regional bodies could also play a role. If, for example, the African Union were to endorse misoprostol for PPH, one could use this to encourage supportive policies at the country level.

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2 Since the interviews were conducted, applications for the addition of misoprostol for prevention and treatment of PPH to the WHO’s Essential Medicines List were submitted for consideration with the WHO Expert Committee during their meeting from March 21–25 2011.
cited the joint International Federation of Gynecology and Obstetrics (FIGO)/International Confederation of Midwives (ICM) recommendations\(^3\) as an important model and a step toward developing a set of consensus guidelines.

Given the weight that WHO carries with country governments and decision makers, interviewees expressed disappointment that the WHO statements were not more definitive (particularly regarding misoprostol use at the community level), and also that misoprostol is not included on the WHO Model Essential Medicines List (EML) for PPH indications.\(^4\) As two interviewees put it:

\textit{WHO has been a huge barrier—their statement on misoprostol is “lukewarm.”}

\textit{WHO has not been as aggressive as it could have been in using available data to make a clear recommendation and putting misoprostol on the EML—this is really sad.}

Several interviewees provided examples of WHO country representatives blocking or attempting to block efforts that promote misoprostol for PPH. For example, one organization was ready to move forward with misoprostol introduction in Nepal when the local WHO representative advised the government against it. One respondent reported that planned work in Cambodia was successfully blocked by the WHO representative in that country. The perception is that WHO country representatives do not understand the WHO statement on misoprostol:

\textit{Country-level personnel believe that WHO/Geneva is against use of misoprostol.}

While countries are not bound by WHO recommendations and guidelines, these do hold enormous sway for many country decision makers. As one interviewee said:

\textit{It is hard to tell countries, “Ignore that normative body.”}

One result of not having clear and updated global guidelines is that some organizations are moving ahead with misoprostol introduction strategies that are not evidence based. Several respondents expressed concern about this practice, both because it may place women at risk and also because it may encourage the further spread and acceptance of non-evidence-based practice:

\textit{All of us are aware of individual clinical providers who use regimens that are not evidence based but that they believe work well. This can be especially detrimental if those individuals are in positions of leadership, which can in turn lead to policies and clinical practices that are not based on current science. We also see this with other advocates and agencies working in the field that develop policies and programs that are not supported by the latest evidence.}

**THE ASSOCIATION OF MISOPROSTOL WITH ABORTION**

While some groups believe that using misoprostol for PPH might be a “door opener” to its life-saving use for abortion (see above), others see the fact that misoprostol can also be used for abortion as “muddying the waters” and significantly hindering the introduction of misoprostol for postpartum indications. This was the next most frequently mentioned barrier after the lack of updated and clear evidence-based guidelines. A key perception is that government officials will fear that there will be “leakage” of misoprostol for abortion use if it is made available for PPH indications. This fear has played out in several countries (e.g., Brazil, Philippines, Thailand, and Nicaragua) where governments have restricted private sector misoprostol sales due to self-induced abortion. Related fears include: women might harm themselves if they use it for abortion too late in their gestations; midwives may be pressured into supplying misoprostol for abortion where it is illegal. As one respondent put it:

\textit{Hypersensitivity of misoprostol as an abortifacient is a barrier. We see this in clinical providers, government officials, even donors—a disproportionate concern that if misoprostol were to be made available for PPH prevention and treatment, it would be used for abortion. This is a major obstacle in accepting misoprostol for other OB/GYN indications—the abortion stigma.}

Several groups mentioned the need for transparency about misoprostol’s indications. For example, when groups want to introduce misoprostol for PPH, they should be disclosing all of its uses and indications. Many of the decision makers are not OB/GYNs and are not aware of misoprostol’s multiple uses. These respondents


\(^4\) WHO is in the process of updating its guidelines for the prevention and treatment of PPH in 2011. As noted previously, there are applications in process to add misoprostol to the WHO EML.
One respondent pointed out that because misoprostol is widely available in many countries (through official or unofficial channels), talk about limiting circulation due to concerns that it might be used for abortion is not productive:

*Given the widespread availability of misoprostol, this concern shouldn’t be used as an excuse not to make it available for PPH.*

**CONCERNS ABOUT SAFETY AND SIDE EFFECTS**

More than half of the organizations mentioned concerns about safety and side effects as barriers:

*We need more evidence that it doesn’t do more harm than good.*

Comments about safety focused mainly on the concern that misoprostol can cause uterine rupture if used improperly for induction or augmentation of labor, or if given too early for PPH prevention (as in the case of an undelivered twin). About a third of the respondents raised this issue:

*People have big safety concerns—such as taking it at the wrong time during labor and possible ruptured uterus. Misoprostol is a powerful drug.*

Several people qualified their responses, saying that while this was something that is important to be aware of, it should not be overstated:

*I am not saying that misoprostol is unsafe, but there are early signs that are worrisome and we need to tread very carefully.*

Others suggested that the risks of misoprostol use need to be considered in conjunction with the benefits, stating that the benefits “far outweigh” concerns of overdosing or incorrect use:

*Many people are more concerned about what might happen with an intervention (i.e., side effects) than what might happen without an intervention (i.e., maternal death). In this case, women are more likely to be harmed by omission of the intervention than from any danger posed by the intervention itself.*

Only a few people mentioned concerns about side effects, stating that we need better information about optimal dosing to reduce shivering and fever.
RESPONDENTS’ SUGGESTIONS FOR ADDRESSING CONCERNS ABOUT SAFETY AND SIDE EFFECTS

Conduct additional, targeted research. Although about half of respondents felt that research was sufficient to move forward with using misoprostol for PPH, numerous respondents identified specific research needs to strengthen the evidence base for decision making by policy makers and practitioners.

We need to do research and do it well. I have great respect for my colleagues, but much of the research that has been done is not quite good enough. We need to have more concrete outcome measures.

We need to position misoprostol carefully and introduce it well.

Based on frequency of mention, the rough order of importance of research needs is:

Distribute within the community for home use. The biggest call was for operations research on the feasibility of distribution of misoprostol at the community and home level, including the benefits and risks of distribution by nonskilled workers, distribution through pharmacies, and direct use by women. An important question for the research to determine is whether providing misoprostol discourages women from accessing health facilities.

Determine the best dosage. A number of respondents also felt a need for more research on the lowest effective dose for prevention of PPH, with the emphasis on ensuring effectiveness while decreasing side effects.

Scale up from pilot to wider introduction. Several people suggested the need for careful design of studies of scale up from pilot projects to larger-scale introduction with emphasis on good training and monitoring. This would include careful monitoring and evaluation of the adequacy of information given to women about how to use misoprostol, its safety, and its effectiveness.

Examine the costs and benefits of use. A couple of respondents called for costing studies of community interventions in preventing PPH to make the case for governments to invest in large-scale national PPH prevention programs. An important cost consideration is whether to focus on prevention at the community level or just promote treatment when PPH occurs. Both approaches are possible with misoprostol and have cost implications for governments. Related to this is the question:

Are we overtreating by asking all women to take misoprostol for prevention? We are asking all women to take three pills upon delivery, yet not all will need them. We need to test the alternative of “liberal treatment”—women would be told to use misoprostol only if she bleeds a certain amount—for both effectiveness and cost.

Determine the best route of administration. A couple of respondents also mentioned that differing practices related to the route of administration—sublingual, oral, vaginal, and rectal—need to be sorted out.

Other research needs mentioned by single individuals included:

• More research on the uses of misoprostol for inducing and augmenting labor should be done so that there can be clear guidelines on its use for this indication, thus avoiding confusion with dosages used for PPH.

• If product quality becomes an issue, research should be conducted on the stability and shelf life of misoprostol at 25 or 30 degrees Celsius and high humidity.

• In some cases, country-specific operations research may be needed to identify appropriate service delivery mechanisms in a specific setting and/or to satisfy government concerns.

• Research on better mechanisms to monitor maternal mortality is needed.
PRODUCT ISSUES
About half of the interviewees mentioned various product issues as barriers. These include:

- **Dosing and packaging for reproductive health indications**: Two doses of tablet are needed—a 25 mcg dose labeled for induction of labor as well as a 200 mcg tablet for all other indications. The number of pills per package should be appropriate to the indication, and the packaging should include instructions for reproductive health indications.

- **Registration for reproductive health indications**: Registration can be difficult—it can take up to four years, can be expensive, and can be difficult to negotiate. Registration for PPH indications is challenging because it is not registered for that indication in the United States or the United Kingdom, which many countries look to as a basis for registration decisions. In addition, drug companies are unwilling to register their products for a drug with a potentially controversial indication.

- **Challenges of new drug introduction**: The introduction process at the country level has a lot of steps—drug registration for PPH indication, worker training, drug monitoring system, etc.

- **Supply chain problems**: There are concerns about both inadequacies in drug supply chains leading to stock-out problems and leakage of unregistered product from other countries (product coming in across borders, not labeled, taken out of packaging/blisters, no information on use and/or expiration, etc.).

- **Quality concerns**: The quality of misoprostol is often unknown, and this may be a barrier if there is a lot of substandard product on the market. Misoprostol stored at 25 or 30 degrees Celsius and high humidity might degrade. Is the emphasis on generic manufacturers and products at the expense of product quality?

CONTROVERSY OVER WHO CAN PROVIDE MISOPROSTOL AT THE COMMUNITY LEVEL
Slightly less than half of the interviewees mentioned that concerns about who can provide misoprostol at the community level were a barrier. The concerns fell into two categories. A few of these respondents felt that misoprostol should be provided only by trained health workers, citing concerns that use by less-skilled workers or in home settings would reduce the use of facilities for delivery. A greater number felt that appropriate use of misoprostol (i.e., in situations where women do not have access to facilities/oxytocin) was being unnecessarily stymied by this concern. As one respondent put it:

*We get pushback from people who want to increase access to skilled providers and who see our [community-based] approach as undermining this.*

Several people specifically mentioned that the WHO statement on misoprostol does not endorse its use in community-level distribution:

*WHO/MPS [Making Pregnancy Safer] has chosen not to engage itself with community interventions. While it is important to push skilled care at birth, it is still compatible to push for interventions at the home level. Overall, there is a lack of global interest in community-based interventions. WHO spent a lot of energy trying to promote TBAs, then abandoned that along with focus on community-based work. We don’t have evidence to show that bringing all births to facilities is the best way to go (skilled providers at facilities have little time, facilities are overcrowded, women may be better served at [the] community level with good education/prevention information, etc.).*

Others mentioned that ministries of health and drug boards sometimes place restrictions on the level of provider; denying prescriptive authority to midwives is one example:

*Midwives are the front-line workers in most countries with high maternal mortality, so they absolutely need access to supplies and authority to use them.*

Because we anticipated that the issue of qualified providers might be a concern, we specifically asked a direct question about provision of misoprostol by

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**RESPONDENTS’ SUGGESTIONS FOR ADDRESSING PRODUCT ISSUES**

**Register misoprostol products for PPH.** There is a need to have different packages/doses labeled for specific indications, specifically 600 mcg, 200 mcg, and 25 mcg packets, to reduce confusion about its use.

**Make misoprostol available through the private sector.** The availability of misoprostol in the private sector (i.e., pharmacies) may help encourage its use in public sector programs. Private sector distributors can help advocate for product registration. The availability of generic drugs may help get around the reluctance of the main misoprostol manufacturer to label it for uterotonin indications.
traditional birth attendants: “Do you think misoprostol can be safely provided by traditional birth attendants in home-birth settings?” No respondents answered “no” to this question, about two-thirds answered “yes,” and one-third declined to comment, stating either that there was not yet evidence to support an answer one way or the other, or that they were not qualified to make that determination.

FEAR OF WOMEN’S EMPOWERMENT

A handful of respondents identified gender and the continued low status of women as a significant barrier to the use of misoprostol for PPH. They highlighted the desire to control women and the fear of giving women control over their reproduction. One respondent summarized it like this:

*This is a gender issue. Misoprostol faces this unbelievable barrier because it is a drug for women. On the issue of HIV and circumcision, all of the WHO recommendations, guidelines, and materials were planned out completely in advance of the study data by a working group convened to address this issue. WHO has had data on misoprostol for 10 years yet has failed to adopt life-saving policies/guidelines in this area.*

Respondents also reported a perception that local medical professionals are unwilling to give women knowledge about and direct access to use of misoprostol because it will mean losing out on income. These professionals sit on boards and influence decision making about women’s access to services. This medical bias also pertains to the lack of political will to involve traditional birth attendants in service delivery, even though traditional birth attendants are the reality for many women and are “here to stay.”

OTHER BARRIERS

Barriers that were stated by only a few people included:

- **Concerns about efficacy compared with oxytocin:** The results of clinical trials showing that misoprostol is less effective than oxytocin suggest that it should have a more limited role than some had hoped.

- **Lack of resources:** The lack of resources for PPH interventions in general and for misoprostol, specifically, raise questions about how the promotion of AMTSL will continue as well as whether country governments will have resources to pay for prevention strategies, such as universal advance provision of misoprostol at the community level.

- **Challenges of training:** Training doctors and other health workers at multiple levels about misoprostol may be challenging because doctors are not familiar with its PPH indications and using it may be contrary to what is taught in medical schools (i.e., use of oxytocin).

RESPONDENTS’ SUGGESTIONS FOR ADDRESSING CONCERN OVER WHO CAN PROVIDE MISOPROSTOL

- **Conduct research to answer concerns about safety and effectiveness of this approach.** See strategies to address concerns related to safety, above.

- **Focus on prevalence of home births.** Advocacy should emphasize the prevalence of home births. One organization convinced a minister of health to allow traditional birth attendants to provide misoprostol for PPH by pointing out that 80% of deliveries occur at home.

- **Engage professional organizations as advocates.** Professional organizations need to be involved in advocating for task shifting to ensure that lower-level cadres of staff are authorized to use uterotonics. Professional groups, such as country-level FIGO societies, can also help disseminate evidence-based guidelines to providers working at the community level in their countries.

RESPONDENTS’ SUGGESTIONS FOR ADDRESSING FEAR OF WOMEN’S EMPOWERMENT

- **Target women as providers of their own care.** Since women often do not have access to providers, we need to target women as the providers of their own care, including educating their family members, since they are likely to be present at the birth.

- **Utilize women’s organizations’ networks.** Women’s organizations are key players for widely disseminating the information that misoprostol exists, is available, and can be used for PPH (and safe abortion).

*Otherwise local women will not get this knowledge. It has to get out of the medical circuit and reach women directly. The work of non-medical activists is crucial, there is no conflicting agenda (as sometimes it may be for medical professionals) and no legal danger for the groups. Provision of scientific information is a human right and protected by most national constitutions.*
This mapping exercise makes it clear that the use of misoprostol for PPH is an issue that is rapidly gaining traction with organizations working to improve women’s health. The willingness of respondents to participate in the exercise and the passion with which they made the case for why they are working on misoprostol is an indication that misoprostol is here to stay and will increasingly be integrated into reproductive health programming worldwide. People sense a real opportunity to make a difference in maternal mortality—one that is not dependent on waiting for health systems to be strengthened—and want to act on it as quickly as possible to save women’s lives.

**Growing organizational involvement.** In the process of conducting this mapping, it became clear that the original scope of work was too limited: the number of people working on misoprostol for PPH had been significantly underestimated. By expanding our net, nearly twice as many organizations with active involvement in misoprostol were identified. There are likely even more. It is possible that in a few years every organization working on reproductive health will want to be involved at some level, similar to the rapid uptake of programming for postabortion care.

**Urgent need for updated evidence-based guidelines.** Given this rapid diffusion of misoprostol for PPH, it is absolutely critical that there be global consensus around evidence-based guidelines for this indication. The fact that misoprostol is already available in many countries and being used and promoted for PPH indications makes it all the more urgent that key members of the international reproductive health community show leadership in identifying and promoting evidence-based approaches. This goal is not out of reach, particularly given that FIGO/ICM has already come up with clear evidence-based guidelines that are being well received in the Latin American and Caribbean region.

The survey found that the biggest perceived barrier to moving ahead is WHO’s current position on the use of misoprostol for PPH (specifically related to misoprostol’s use for PPH prevention and use at the community level). As an alternative, the international reproductive health community could put its collective weight behind a jointly developed policy statement. The International Consortium for Emergency Contraception is one example of a successful application of this approach. Alternatively, reproductive health groups could find ways to bring more attention to an updated version of the FIGO/ICM statement and disseminate it more broadly through regional and country-level agencies. There seems to be a sufficient consensus among a critical mass of influential organizations to accomplish this.

**If the gold standard is not achievable, groups will try other options to save lives.** The current stalemate surrounding guidelines for the use of misoprostol for PPH appears to stem primarily from concerns that there are insufficient data to make a recommendation about its distribution and use at the community/home level and that promoting misoprostol use at this level will deter women from seeking care at facilities and/or from trained providers. While these may be valid concerns from an intellectual perspective, they ignore the reality that women face in giving birth in low-resource settings. The reality is that care in facilities (including access to oxytocin) is still not available to a large number of women despite being a long-standing goal.

The mapping results show that organizations are not willing to wait until the gold standard goal of having all births assisted by skilled providers is achieved. Nor are they willing to wait until every angle of research is exhausted and the way forward is crystal clear. They see an opportunity to save lives that is “good enough,” and they are moving forward with programs based on their best estimate of what works.

Groups will adjust their strategies for using misoprostol for PPH as research findings document the best and safest approaches. Therefore, the faster the evidence and information about best practices can be made available, the faster the reproductive health community will move toward consistency in use of evidence-based practices.

**Addressing misoprostol’s association with abortion: embracing misoprostol’s multiple indications.** The second biggest barrier to using misoprostol for PPH was that some of its multiple indications are viewed as being “problematic” and, in some cases, even too controversial to mention. Given the passion that respondents expressed for addressing maternal mortality, it is ironic that many of those working on this issue find themselves trying to either ignore or hide the fact that this drug has multiple promises for saving women’s lives, including its...
use for abortion. While we acknowledge that local solutions to addressing the political implications of misoprostol's abortion indication will have to be sought, there needs to be an international appreciation for the fact that this is a multi-use drug and that part of the challenge is having very good information about how it is best used for each indication — labor induction, PPH prevention, PPH treatment, postabortion care, and abortion.

At the country level, a number of respondents mentioned success with being more open about the multiple indications for misoprostol and that they serve the same goal: to help save women's lives. In these examples, frank and open discussions with ministers of health and others led to acceptance of misoprostol for PPH, despite concerns about its potential use for abortion. This was even true in examples from Latin American countries, where opposition to abortion is strong. This acceptance of and transparency about misoprostol's multiple indications is what will help make it available for women's health indications in the long run. From the perspective of health care workers who deal with women on a comprehensive level, having an easily available drug that can help a woman throughout the continuum of her reproductive needs should be seen as a boon rather than a hindrance.

The recognition of and acceptance of multiple uses of misoprostol also needs to extend to collaborations between agencies working with misoprostol for any indication. Building a firewall between these different applications or the organizations that work on them is detrimental to progress. In conducting this mapping exercise, the organizations most experienced in working with misoprostol are the ones using it for abortion. But, because of the controversy surrounding this use, the linkages between these groups and those working on misoprostol for PPH are lacking. If there is going to be a consortium or formal group of organizations working on misoprostol for PPH, it should include organizations that are using misoprostol for abortion. The knowledge these organizations have about the intricacies of drug registration and supply, as well as service delivery issues, related to misoprostol for abortion is directly relevant to its use for other indications, and these strategies and lessons learned should be shared.

**Product is already available; information on use is key.** In contrast to other reproductive health products, such as microbicides, HIV vaccines, and emergency contraception, which have required significant investment in and coddling of manufacturers to produce a product, we find ourselves in the welcome position of having a product that is already making its way to women through existing supply routes. As respondents indicated, there clearly are some product-related issues associated with misoprostol—including quality, appropriate formulations, labeling, and packaging — and some groups are working to address these by repackaging and registering misoprostol for PPH and other reproductive health indications. These efforts will lend legitimacy to the product and help to ensure proper use over the long term, but they will also take time and money.

While some investment in these efforts seems reasonable, it also makes sense to take advantage of misoprostol's current widespread availability, low cost, and relative stability (compared with other uterotonic) and invest equal or even greater amounts in informing women and service providers, including pharmacists, about how to use it. Because the biggest potential for misoprostol to save lives is at the community/home level, it makes sense to invest in getting information directly to women and the pharmacists, traditional birth attendants, and others who serve them. Investment is also needed to add this information in all reproductive health organization training materials and medical, nursing, and pharmacy school curricula. This “off-label” approach is consistent with current medical practice in the United States and other countries where pharmaceutical products are routinely prescribed and/or used for off-label indications.

**Common themes and messaging.** The mapping exercise revealed a number of common themes and messages that can be used to position misoprostol with policy makers and providers. While these were not universally stated, they may serve as a starting point for developing an advocacy strategy:

- **Our goal is to help women survive.** Misoprostol has the potential to save lives.
- **Women do not have access to health services (and oxytocin) in many areas and likely will not have access for many years to come.** That is why misoprostol is so critical.
- **Misoprostol should be viewed as part of the larger continuum of efforts to reduce maternal mortality and has multiple roles within that continuum.**
- **There is a continuum of care for PPH prevention and treatment.** Misoprostol fills a specific niche within that continuum that supports and expands AMTSL.
- **Women are capable of using misoprostol safely with access to appropriate information.**
Given the growing diffusion of misoprostol into multiple facets of the reproductive health arena, this mapping exercise was extremely timely. The organizations that participated in this survey are clearly the trailblazers on this issue, but they are soon to be joined by others as misoprostol becomes part of mainstream reproductive health programming. Most were quick to acknowledge the need for consensus building around misoprostol, and all expressed interest in receiving the results of this mapping exercise.

The mapping revealed that there are areas of convergence, as well as disagreement, within the global policy and scientific communities. In addition, it is clear that there are misinformation and misconceptions that may have influenced respondents’ opinions and the strategies proposed for addressing the key challenges. Building on the findings of this mapping exercise, and in response to the challenges outlined in this report, FCI will work with the global scientific and policy communities to identify policy approaches on which consensus can be achieved, to harmonize messages regarding the use of misoprostol for PPH, and to influence policy change in support of misoprostol at the national and global levels.

While more research is needed to monitor and evaluate the various approaches and strategies being explored and there are still issues to be worked out—most notably achieving consensus about what constitutes evidence-based practice—misoprostol clearly shows promise for meeting several reproductive health needs of women, including the prevention and treatment of postpartum hemorrhage. It is time to capitalize on the ready availability, low cost, and convenience of misoprostol and get it to women in ways that will best benefit them. Many organizations are ready, willing, and already moving ahead.
APPENDIXES

APPENDIX A: LIST OF ORGANIZATIONS CONTACTED
APPENDIX B: LIST OF AVAILABLE MATERIALS
APPENDIX C: INTERVIEW GUIDE
APPENDIX D: TYPES OF ACTIVITIES BY ORGANIZATION
APPENDIX E: MAP OF ORGANIZATIONAL INVOLVEMENT
APPENDIX A: LIST OF ORGANIZATIONS CONTACTED

1. Aga Khan Health Services
2. BPAS
3. Christiana Care Health Service
4. Concept Foundation
5. DKT International
6. Effective Care Research Unit, South Africa
7. EngenderHealth
8. Family Care International
9. Family Health International
10. FIGO/SOGC
11. Gynuity Health Projects
12. Ibis Reproductive Health
13. International Confederation of Midwives
14. Ipas
15. Jhpiego
16. John Snow International
17. Latin American Federation of Obstetrics and Gynecology Societies (FLASOG)
18. MacArthur Foundation
19. Management Sciences for Health
20. Marie Stopes International
21. Pathfinder
22. PATH/POPHI
23. Population Council
24. Population Services International
25. University of California, San Francisco
26. University of Illinois, Chicago
27. University of Liverpool
28. USAID
29. Venture Strategies Innovations
30. Women on Waves/Women on Web
31. World Health Organization
APPENDIX B: LIST OF AVAILABLE MATERIALS

EFFECTIVE CARE RESEARCH UNIT, SOUTH AFRICA


ENGENDERHEALTH


FAMILY CARE INTERNATIONAL


PPH Manual for Mid-Level Providers (in press).

FIGO/SOGC
Poster and a card outlining the various uses, dosages, and timing of misoprostol use; http://www.figo.org/news/misoprostol-safe-dosage-guidelines.

GYNUITY HEALTH PROJECTS


Peer-reviewed publications


JHPIEGO


PATHFINDER


Training video includes information about misoprostol for PPH, and examples from Bangladesh, Nigeria, India, and Peru.

POPULATION SERVICES INTERNATIONAL

“Misoprostol Prevents Excessive Bleeding After Childbirth.” Poster (Zambia).

“Como usar o MISO apos o parto para proteger a vida da ma e.” Poster (Mozambique).

“Use o MISO apos o parto para proteger a vida da ma e.” Poster (Mozambique).

“Use of Misoprostol for Prevention of Postpartum Haemorrhage.” Poster (Uganda Ministry of Health).

“Decision Chart for Administration of Misoprostol for the Prevention of PPH.”

“Decision Chart for Administration of Misoprostol for the Treatment of PPH.”

“Take Action Safe Delivery Card.”

PREVENTION OF POST-PARTUM HEMORRHAGE INITIATIVE (POPPHI)

All information and materials are available on the POPPHI website, www.pphprevention.org.


UNIVERSITY OF LIVERPOOL

[www.misoprostol.org](http://www.misoprostol.org)


USAID

USAID materials are produced through collaborating agencies (see POPPHI and other cooperating agency websites).

VSI—VENTURE STRATEGIES INNOVATIONS


All misoprostol publications are accessible at [http://www.vsinnovations.org/resources.html](http://www.vsinnovations.org/resources.html). Search by “misoprostol” to download the following titles:

“Community-Based Availability of Misoprostol: Is It Safe?”

“Community-Level Prevention of Postpartum Hemorrhage: The Role of Misoprostol Evaluation in Brief”


“Misoprostol Distribution at Antenatal Care: Preliminary Report in Brief”

“Misoprostol for Postpartum Hemorrhage in Zanzibar: Evaluation and Policy Brief”

Misoprostol Registration Map

Global registration status of misoprostol for obstetric uses

“Misoprostol: Strategies, Successes, and Challenges”

“Prevention of Postpartum Hemorrhage at Home Births in Afghanistan: Averting Maternal Death and Disability”

“Prevention of Postpartum Hemorrhage: Options for Home Births in Rural Ethiopia”

“Saving Maternal Lives in Resource-Poor Settings: Facing Reality”

WOMEN ON WAVES/ WOMEN ON WEB


WORLD HEALTH ORGANIZATION


OTHER SOURCES


APPENDIX C: INTERVIEW GUIDE

Background
As you know, Family Care International (FCI) is working with Gynuity Health Projects and other partners to develop an evidence-based policy and advocacy agenda for promoting misoprostol for PPH at the global, regional, and country levels. An important step in this process is to map the current policy and advocacy strategies among the many organizations working globally on misoprostol for PPH.

During this interview we will be asking you about:

- your organization’s goals and activities related to promoting misoprostol for PPH (both prevention and treatment), and
- what you perceive as policy and advocacy priorities and challenges.

We will keep all responses confidential. FCI will send you a copy of the mapping report when it is done.

Section A: Organizational Goals and Strategies

1. What is your organization’s main goal(s) in promoting misoprostol for PPH related to research, policy & advocacy, and/or project/program implementation over the next 1–2 years?
2. Why does your organization think it important to invest in or focus on promoting misoprostol for its PPH indications?
3. What are the main activities your institution is pursuing to promote misoprostol for PPH over the next 1–2 years?
4. Who are your main target audiences for promoting misoprostol for PPH?
   a. At the global level?
   b. At the regional level?
   c. At the country level?
5. What materials (i.e., policy/advocacy, educational materials) related to misoprostol and PPH have your organization produced/published in the past 2 years? Please share copies with FCI.

Section B: Overcoming Barriers, Promoting Effective Strategies

6. In your opinion, what are the main barriers to promoting misoprostol for PPH:
   a. At the global level related to research (clinical and operations), policy/advocacy, and project/program implementation?
   b. At the country level related to research (clinical and operations), policy/advocacy, and project/program implementation?
7. What specific actions do you think can be undertaken to overcome these barriers?
   d. By policy makers?
   e. By health providers?
   f. By international/UN agencies and partnerships? Probe for specifics.
   g. Are there other key actors or players (such as community/women’s groups) who can play a role in expanding access to misoprostol for PPH?
8. Do you think that the data currently available are sufficient to convince policy makers to invest in misoprostol for PPH? If not, what additional research is needed?
9. In your view, what are the key areas of controversy/debate related to promoting greater use of misoprostol for PPH?
10. Do you think misoprostol can be safely provided by traditional birth attendants in home-birth settings?
   Probe: How do you see the promotion of misoprostol for PPH in remote settings fitting in with international recommendations related to skilled attendance at birth?
11. Are there upcoming global events or other forums that would provide opportunities for influencing policy change in support of misoprostol for PPH?

Thank you for your participation. Would you be willing to participate in a follow-up interview or answer additional questions?
## Appendix D: Activities by Organization

<table>
<thead>
<tr>
<th>Organization</th>
<th>Activity</th>
<th>Countries</th>
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<tbody>
<tr>
<td>Aga Khan Health Services</td>
<td>Has health-related activities. Additional information forthcoming. Conducts introductory trials and treats postpartum hemorrhage through Aga Khan facilities. Additional information forthcoming.</td>
<td>Afghanistan, Turkistan, Kyrgyzstan, Kazakhstan, Pakistan, India, Syria, Kenya, Egypt, Tanzania, Uganda, Mali, Mozambique, and Madagascar</td>
</tr>
<tr>
<td>Christiana Care Health Service</td>
<td>Conducts research at Jawaharlal Nehru Medical College as part of an Emergency Obstetric and Neonatal Care (EmONC) National Institute of Child Health &amp; Human Development (NICHD) project that is using misoprostol for prevention and treatment as standard of care in all sites where misoprostol is available. The goal is to empower village leaders to help improve maternal and child outcomes. In many locations, only auxiliary nurse midwives and higher-level providers are allowed to use misoprostol.</td>
<td>India</td>
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<tr>
<td>Concept Foundation</td>
<td>Conducted an on-the-ground review of misoprostol products, collecting samples in various countries to determine what is available, who is manufacturing, what is the quality of product. Results expected in late 2010. Is working to produce a misoprostol-only formulation (200 mcg tablets) of assured quality with price control for the public sector to use in PPH indications.</td>
<td>Global</td>
</tr>
<tr>
<td>DKT International</td>
<td>Markets and sells DKT-branded misoprostol products, providing education and training to providers, and educates consumers about the product, for both PPH and abortion indications.</td>
<td>Ethiopia, Egypt, Vietnam, Indonesia, India, and Sudan</td>
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<tr>
<td>Effective Care Research Unit, South Africa</td>
<td>Publishes a systematic review of the literature, as well as data from several randomized controlled trials.</td>
<td>South Africa</td>
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<tr>
<td>Organization</td>
<td>Activity</td>
<td>Countries</td>
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<tr>
<td>EngenderHealth</td>
<td>Works in the community to train traditional birth attendants on the use of misoprostol for PPH.</td>
<td>Nepal</td>
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<td></td>
<td>Conduct a pilot program for community-based distribution of misoprostol for PPH prevention. Field workers distribute misoprostol (three-tablet packet with user instructions) to pregnant women.</td>
<td>Bangladesh</td>
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<tr>
<td></td>
<td>Provides AMTSIL training for service providers in maternity wards.</td>
<td>Bangladesh and Nepal</td>
</tr>
<tr>
<td>Family Care International</td>
<td>In collaboration with Gynuity Health Projects, published <em>Postpartum Hemorrhage: A Challenge for Safe Motherhood</em>, providing a fact sheet and specific actions that policy makers and other stakeholders can undertake to address the problem.</td>
<td>Global</td>
</tr>
<tr>
<td></td>
<td>Produced <em>PPH Manual for Mid-Level Providers</em> in collaboration with Aga Khan Health Services, Pakistan in Urdu (in press).</td>
<td>Pakistan</td>
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<tr>
<td></td>
<td>With Gynuity Health Projects, published pocket cards outlining PPH prevention and treatment that highlight the main findings from the Gates-funded research trials.</td>
<td>Global</td>
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<tr>
<td></td>
<td>Conducts ongoing advocacy and policy work at the global, regional, and national levels to harmonize messages, build consensus, and promote supportive policy change.</td>
<td>Global</td>
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<tr>
<td>Family Health International</td>
<td>Works with misoprostol, but detailed information was not available in time for this report.</td>
<td>Global</td>
</tr>
<tr>
<td>FIGO/SOGC</td>
<td>Plans advocacy work on misoprostol for member associations (with Gynuity Health Projects).</td>
<td>Global</td>
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<tr>
<td></td>
<td>Publish guidelines for misoprostol use.</td>
<td>Global</td>
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<tr>
<td></td>
<td>Publish misoprostol study results in journals, special issues, and commissioned articles.</td>
<td>Global</td>
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<tr>
<td>Organization</td>
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<td>Countries</td>
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| Gynuity Health Projects| **Current activities:** Develops approaches to promote evidence-based policy and service delivery models for the prevention and treatment of PPH using misoprostol with a focus on low-resource environments and community-based services. Clinical and operations research objectives and activities include:  
  - Evaluation of the safety and efficacy of administering misoprostol both prophylactically and therapeutically.  
  - Comparison of the administration of oxytocin in Uniject® to oral misoprostol for PPH prevention at the community level.  
  - Comparison of the effect of oxytocin administered intravenously and intramuscularly when given as a primary component of AMTSL.  
  - Identification of pathways for the safe and effective use of misoprostol for PPH outside of tertiary-level facilities, including at the community level.  
  Conducts additional advocacy and policy activities in collaboration with partner agencies (see descriptions for Concept Foundation, Family Care International, FIGO, PATH, Populations Services International [PSI], University of California, San Francisco [UCSF], University of Illinois, Chicago [UIC], University of Liverpool, WHO). | Global; research to be conducted in Afghanistan, Bolivia, Burkina Faso, Ecuador, Egypt, Ethiopia, India, Kenya, Mali, Nepal, Nigeria, Pakistan, Senegal, Tanzania, Tunisia, Turkey, Uganda, and Vietnam |
<p>|                       | <strong>Previous activities:</strong> With Aga Khan University and Aga Khan Health Services, conducted community-based study to test whether 600 mcg oral misoprostol reduces the incidence of PPH when administered by traditional birth attendants during the third stage of labor following home births. | Pakistan |
|                       | With the Effective Care Research Unit, East London, South Africa, conducted research to determine the value added by using misoprostol in conjunction with oxytocin for PPH prevention. | South Africa, Nigeria, and Uganda |
|                       | With country partners, conducted large-scale, multi-site, randomized controlled clinical trials on the effectiveness of misoprostol for the treatment of primary PPH (800 mcg sublingual misoprostol compared with 40 IU oxytocin [IV] for stopping hemorrhage in tertiary care facilities). | Burkina Faso, Ecuador, Egypt, Turkey, and Vietnam |
|                       | With WHO, conducted clinical trial to evaluate whether 600 mcg sublingual misoprostol plus standard injectable uterotonic treatment of PPH has an additional benefit in reducing postpartum blood loss. | Argentina, Egypt, South Africa, Thailand, and Vietnam |</p>
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<tr>
<th>Organization</th>
<th>Activity</th>
<th>Countries</th>
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<tr>
<td>International Confederation of Midwives</td>
<td>Conducts global advocacy for midwives to be able to provide uterotonicics, including misoprostol.</td>
<td>Global</td>
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<tr>
<td></td>
<td>Is looking for ways to develop in-service training mechanisms at the country level (with member associations).</td>
<td>Global</td>
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<tr>
<td>Jhpiego</td>
<td>Is expanding PPH prevention at home births through advocacy, community interventions, education, and training in 20 to 30 countries as part of the MCHIP-Maternal and Child Health Integrated Program. The first approach is to train skilled providers in facilities to use AMSTL, including oxytocin where available. The second approach is to use misoprostol when there is no oxytocin or AMTSL available. Conducted misoprostol introduction studies.</td>
<td>25–30 countries</td>
</tr>
<tr>
<td>John Snow International (JSI)</td>
<td>Works with misoprostol, but detailed information was not available in time for this report.</td>
<td>Indonesia, Nepal, and Afghanistan</td>
</tr>
<tr>
<td>MacArthur Foundation</td>
<td>Awarded a $10.5 million, four-year grant to Pathfinder for PPH work, with misoprostol as one part of the overall project approach.</td>
<td>India, Mexico, and Nigeria</td>
</tr>
<tr>
<td></td>
<td>Awarded a grant to the Population Council to integrate work on misoprostol for PPH prevention in an ongoing effort in Ethiopia.</td>
<td>Ethiopia</td>
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<tr>
<td></td>
<td>Awarded a small grant through Amadu Bello University using misoprostol in community settings for prevention. Nigerian government guidelines only allow misoprostol use in facilities. The goal of the small grant is to get the Ministry of Health to change guidelines to allow misoprostol use at the community level.</td>
<td>Nigeria</td>
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<td></td>
<td>Awarded grant to the Earth Institute at Columbia University to do action-research on misoprostol for PPH prevention in the Ghana Millennium Village Cluster, with the idea that once results are available, the approach could be scaled up (a) by Ghana’s Ministry of Health and/or (b) by the Millennium Village Project in other sub-Saharan African countries where the villages are located.</td>
<td>Ghana and other sub-Saharan countries</td>
</tr>
<tr>
<td>Organization</td>
<td>Activity</td>
<td>Countries</td>
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<tr>
<td>Management Sciences for Health (MSH)</td>
<td>Through partnership with other organizations, is promoting best practices in safe motherhood and prioritizing the most effective interventions contributing to prevention of maternal deaths.</td>
<td>Nepal, Bangladesh, and Malawi; South Sudan is in the planning stage</td>
</tr>
<tr>
<td>Marie Stopes International (MSI)</td>
<td>Is working to register misoprostol in several countries for PPH (also for medical abortion and postabortion care) either as a first-time registration or re-registering it under the MSI brand name.</td>
<td>Additional information forthcoming</td>
</tr>
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<td></td>
<td>In collaboration with Venture Strategies Innovation (VSI) and Ministry of Health, managed joint research study on the use of 200 mcg misoprostol for treatment of postabortion care and treatment/prevention of PPH. The study was intended to lead to misoprostol inclusion in the Essential Medicines List for postabortion care and national protocol for PPH. The dossier has been submitted for drug registration (for postabortion care only); a decision is pending. Extensive training and supervision are provided for public sector providers.</td>
<td>Madagascar</td>
</tr>
<tr>
<td>Pathfinder</td>
<td>Is involved in introducing misoprostol in refugee camps in northern Tanzania, with trained providers during antenatal care. Women who are planning a home birth are given misoprostol for use at home.</td>
<td>Tanzania</td>
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<td></td>
<td>Introduced misoprostol as part of more general maternal and child health (MCH) project.</td>
<td>Burundi</td>
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<td>Provides training in misoprostol use at all levels (including traditional birth attendants at community level) as part of overall PPH training.</td>
<td>Nigeria</td>
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<td></td>
<td>Is planning a PPH project (with misoprostol for facility and community use as one component) as part of an integrated family health project.</td>
<td>Ethiopia</td>
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<td></td>
<td>Conducts PPH work as part of a large maternal and child health project, including training traditional birth attendants.</td>
<td>Mozambique</td>
</tr>
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<td>Trains all levels of providers in using misoprostol for prevention and treatment as part of overall management of PPH.</td>
<td>India</td>
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<td></td>
<td>Is conducting a study on use of misoprostol for treatment of PPH at the facility level.</td>
<td>Peru</td>
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<td>Distributes a misoprostol birth kit given to women by community health agents, which includes three tablets of misoprostol and a blood collection mat to measure blood loss. Provides counseling and training of staff at facilities that treat women with pregnancy-related complications.</td>
<td>Bangladesh</td>
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<td>Organization</td>
<td>Activity</td>
<td>Countries</td>
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<tr>
<td>PATH/POPPHI</td>
<td>Is working with Gynuity Health Projects on operations research.</td>
<td>Vietnam</td>
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<td></td>
<td>Is studying use of oxytocin in Uniject®.</td>
<td>Guatemala, Honduras, Indonesia, Ghana, India, and Mali; interest in Argentina and Nicaragua</td>
</tr>
<tr>
<td>Population Council</td>
<td>Works with Ministry of Health and Venture Strategies to distribute misoprostol through youth groups.</td>
<td>Ethiopia</td>
</tr>
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<td></td>
<td>Works with VSI and JSI to include misoprostol and instructions in safe delivery kits that are given to midwives (who also receive training).</td>
<td>Pakistan</td>
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<td></td>
<td>With VSI, is developing plan to provide magnesium sulfate for preeclampsia that will be bundled with misoprostol.</td>
<td>Northern Nigeria</td>
</tr>
<tr>
<td></td>
<td>Is working with MSI on misoprostol for medical abortion and postabortion care.</td>
<td>Ghana and Bangladesh</td>
</tr>
<tr>
<td>Population Services International (PSI)</td>
<td>Is working with VSI to get drug registered in country.</td>
<td>Additional information forthcoming</td>
</tr>
<tr>
<td></td>
<td>Distributes misoprostol, including purchasing and importing the drug, vouching for quality, overbranding (sometimes), detailing, and distributing only to providers.</td>
<td>Zambia</td>
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<td></td>
<td>Provides training for health care providers.</td>
<td>Nigeria and India</td>
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<td></td>
<td>Develops and distributes materials for detailers, providers, and consumers.</td>
<td>Additional information forthcoming</td>
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<td></td>
<td>Conducts situation analysis, monitoring, and evaluation.</td>
<td>Additional information forthcoming</td>
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<tr>
<td></td>
<td>In partnership with Gynuity, is designing a research study to gather more information on the market and use of misoprostol in Uganda.</td>
<td>Uganda</td>
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<tr>
<td>University of California, San Francisco</td>
<td>Is conducting Millennium Development Villages research in Ghana in partnership with University of Illinois (see above).</td>
<td>Ghana</td>
</tr>
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<td></td>
<td>Is acting as a consultant to Pathfinder on its clinical and community actions project to address PPH.</td>
<td>Nigeria and India</td>
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<td>Organization</td>
<td>Activity</td>
<td>Countries</td>
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<tr>
<td>University of Illinois, Chicago</td>
<td>Plans to implement a study of the cost effectiveness and safety of use comparing two regimens – 400 mcg for prevention versus 600 mcg for treatment. Is working with Pathfinder on Continuum of Care for PPH project, which includes community education, AMTSL, provision of anti-shock garments, transport to higher level facilities when needed, and provision of misoprostol in areas where oxytocin and ergometrin are not available.</td>
<td>India</td>
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<td>Nigeria and India</td>
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<td></td>
<td>Is working with Earth Institute’s Millennium Villages Project doing operations research on misoprostol provided to women who are delivering at home. The use of misoprostol during home births will be documented by external observers—the auxiliary birth midwives. The project includes up-front policy work with the government to get buy-in for replication/expansion if research shows feasibility.</td>
<td>Ghana</td>
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<td></td>
<td>Is working with Gynuity Health Projects on a comparison of universal prophylaxis with 600 mcg oral misoprostol versus secondary prevention (women who bleed &gt;350 ml postpartum receive a dose of 800 mcg sublingual misoprostol). This includes a cost-benefit analysis.</td>
<td>India</td>
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<tr>
<td>university_of_liverpool</td>
<td>Is updating the FIGO guidelines based on new data within next two years. Is researching uterine contractility with misoprostol doses of 200, 400, and 600 mcg, as well as looking at genetic factors and how they relate to side effects of misoprostol. Results are expected by 2012. With Gynuity Health Projects, conducting a randomized controlled trial of 5,000 women who receive either misoprostol or a placebo at antenatal care to be self-administered. The outcome measure is hemoglobin level. The study will be under way by spring/summer 2011.</td>
<td>Global</td>
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<td></td>
<td>Is involved in ongoing advocacy through publications and <a href="http://www.misoprostol.org">www.misoprostol.org</a>.</td>
<td>Global</td>
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<td></td>
<td></td>
<td>Uganda</td>
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<td>Organization</td>
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<td>Countries</td>
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<td>USAID</td>
<td>Helps countries to evaluate their need for community-based solutions for decreasing deaths from PPH, and where appropriate, supports countries to pilot-test community-based distribution/use of misoprostol with rigorous evaluation to provide data and lessons learned to governments. The data collected will assist governments to make decisions about whether to scale up the national program. If governments make the decision to scale up, USAID will support this decision with technical assistance. The model is to give misoprostol to women in their last trimester during a visit to antenatal care or to communities via community health workers.</td>
<td>Pilots in Afghanistan and Nepal, possibly expanding to Malawi, Honduras, Senegal, and Ghana</td>
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<td></td>
<td>Funded WHO to develop PPH prevention and treatment guidelines and also provided funding for WHO to make these guidelines more clear. USAID will hold another Expert Committee meeting on this within the next year. Provided support to get misoprostol on the WHO Essential Medicine List (EML) for PPH prevention in 2009 (not successful). Will continue to support reapplication to EML for PPH prevention.</td>
<td>Global</td>
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<td></td>
<td>Is working with the Ministry of Health to gain acceptance for misoprostol.</td>
<td>Additional information forthcoming</td>
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<tr>
<td></td>
<td>Is working with manufacturers to establish distribution strategies and pricing for misoprostol.</td>
<td>Additional information forthcoming</td>
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<tr>
<td></td>
<td>Trains providers and users of misoprostol.</td>
<td>Additional information forthcoming</td>
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<tr>
<td></td>
<td>Conducts operations research to explore feasibility of home use of misoprostol.</td>
<td>Additional information forthcoming</td>
</tr>
<tr>
<td>Women on Waves/Women on Web</td>
<td>Trains women’s organizations and nonmedical individuals in using misoprostol for PPH prevention and safe abortion in targeted countries in Africa and Asia.</td>
<td>Tanzania, the DRC, Kenya, Indonesia, Sri Lanka, and Pakistan (training also for Burundi)</td>
</tr>
<tr>
<td>World Health Organization</td>
<td>Is updating guidelines for PPH prevention and treatment in 2011 (Reproductive Health Division).</td>
<td>Global</td>
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<tr>
<td></td>
<td>Conducting research to evaluate misoprostol program implementation (Reproductive Health Division).</td>
<td>Global</td>
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</tbody>
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**ORGANIZATIONS WORKING WITH MISOPROSTOL BUT NOT FOR PPH INDICATION**

ABT Associates
BPAS
Ibis Reproductive Health
Ipas