

Misoprostol for Prevention and Treatment of Post-Partum Hemorrhage (PPH):

Current Knowledge and Future Directions

March 11 & 12, 2009

Summary Report

More than 50 leading researchers, policymakers, program managers and advocates gathered for a two-day meeting on misoprostol for the prevention and treatment of post-partum hemorrhage at the Bill and Melinda Gates Foundation. The purpose of the meeting was to review evidence on misoprostol's use for these indications, including its safety, efficacy, and program effectiveness, and to identify unanswered questions and programmatic challenges related to expanding its use in different settings.

Highlights of the meeting included an open discussion about the potential role and limitations of misoprostol for PPH indications and the need for further research, particularly with regard to evidence of program effectiveness (versus demonstrated efficacy in clinical trials), doses and applicability of the drug for these indications in different settings. Advocates called for better guidelines regarding misoprostol use and the need to move forward with introductions while additional evidence of effectiveness and safety is gathered. There was considerable debate about when, where and how fast introductions of misoprostol for PPH should take place and, while most participants were very enthusiastic about misoprostol, concerns about safety with widespread use were also voiced.

In determining the future direction of misoprostol for PPH indications, many participants believed that while misoprostol is already being widely used in the field, more information is needed to speak about its effectiveness and safety in real world settings. There was consensus that a two-pronged approach may be practical: this would include sharing information on current guidelines and evidence on misoprostol for PPH to providers, professional associations, and communities already accessing the drug, while simultaneously addressing any research gaps. Participants also expressed the need for monitoring and evaluating programs and pharmacovigilance systems to ensure adequate follow up on drug safety and quality of care.

Session Summaries

Session 1: Development of evidence-based regimens on misoprostol for PPH Prevention and Treatment

Moderator: Richard Derman, Christiana Care Medical Systems

Presenters: Stacie Geller, University of Illinois, Chicago; Jennifer Blum, Gynuity Health Projects

Stacie Geller, University of Illinois, Chicago Misoprostol for prevention of PPH

10 IU of oxytocin administered IM or IV is the uterotonic of choice where AMTSL is practiced. If appropriate conditions cannot be met, misoprostol should be used.

Hospital-based trials have studied a range of misoprostol doses and routes in comparison to another uterotonic or placebo. A majority of these studies found non-significant differences between the groups in impacting acute and severe PPH rates.

Two of three community-based randomized controlled trials, both comparing misoprostol to placebo, showed a significant decrease in severe PPH with misoprostol use (miso: 11% v placebo: 17%, Hoj et al; miso: 0.2% v placebo: 1.2% Derman et al), suggesting that impact of misoprostol seems to be greatest in the community. Recent results from a trial in Pakistan (Gynuity/AKU/AKHSP) validate the findings of the India trial (Derman et al) which resulted in an improvement in several key outcomes after misoprostol use.

Jennifer Blum, Gynuity Health Projects Misoprostol for treatment of PPH

A Cochrane review looking at misoprostol for PPH treatment concluded that large scale randomized controlled studies were needed in light of insufficient evidence. Trials recently completed by Gynuity Health Projects, comparing misoprostol to oxytocin in two different settings, yielded the following conclusions: **misoprostol works similarly to oxytocin for PPH treatment among women given oxytocin prophylactically; oxytocin works better than misoprostol for PPH treatment among women not given oxytocin prophylactically, although misoprostol may be a suitable alternative where oxytocin is currently not available or feasible.** Shivering and fever are more likely after treatment with misoprostol, therefore delivery attendants should be trained to identify and manage high fever.

Discussion

Several possible reasons were offered by participants to explain the heterogeneity found in the PPH prevention study results. The population of women receiving misoprostol for PPH prevention may be different in these two settings. Perhaps even PPH measurement differs by health care level and women in hospitals may be over-treated Hospitals also often deal with large volumes of patients and rushed

procedures – if cord traction is undertaken, before a good uterine contraction, misoprostol may not have the same impact on PPH prevention as in the community, where the same time pressure may not exist.

Some participants felt that if further studies are conducted to address all unanswered questions, generate new evidence where current data are unclear, and better understand the safety and effectiveness of misoprostol in randomized controlled trials, little progress will be made in moving misoprostol out to the real world over the next several years. **Instead, many participants felt that a balance should be maintained in moving forward with interventions that are practical and safe, while simultaneously addressing research gaps.**

Key questions included:

- What can explain the differences in consistency of results between hospital-based and community-based studies looking at misoprostol for PPH prevention?
- Does misoprostol save lives? Is using PPH rate a good indicator of impact or can one assess effectiveness against maternal mortality? What about other factors which may influence outcomes, resulting, for example, in a drop in PPH rate even in the placebo arm?
- How does the WHO define “trained” health workers who can offer misoprostol for PPH prevention?
- While there is a lot of evidence for efficacy of both misoprostol and oxytocin, what about their relevance in the real world, i.e. given that oxytocin is a more efficacious drug, in which setting can or should misoprostol be recommended?
- Should lower doses of misoprostol be explored for both indications?
- How do shivering and fever after either prevention or treatment with misoprostol affect breastfeeding and maternal-child bonding postpartum?
- Should oxytocin in Uniject be investigated further for efficacy and safe use in the community?
- After oxytocin prophylaxis is there evidence that use of oxytocics for treatment of PPH is better than placebo?

Session 2: Other evidence-based indications

Moderator: Matthews Mathai, World Health Organization

Presenters: Andrew Weeks, University of Liverpool; Beverly Winikoff, Gynuity Health Projects

This session provided an overview of misoprostol's use in labor induction, intrauterine fetal death (IUFD), and treatment of failed pregnancies.

Andrew Weeks, University of Liverpool

Oral misoprostol solution seems to be optimal choice for induction of labor. It is preferable to dinoprostone as it results in a 20% reduction in caesarean section rate, and also preferable to vaginal misoprostol for the reduced rate of uterine hyperstimulation.

A range of doses and routes have been studied for treatment of IUFD and recommended doses of vaginal misoprostol vary by gestational age. Caution must be taken to avoid the use of incorrect high dosages of misoprostol for labor induction and IUFD.

Beverly Winikoff, Gynuity Health Projects

Numerous studies have examined the use of misoprostol for pregnancy failure, which is a broad term that includes spontaneous abortion, anembryonic gestation, missed abortion, and unwanted pregnancy leading to termination. Misoprostol to treat pregnancy failure offers several advantages over expectant or surgical management as it does not require special surgical skills and equipment, avoids an invasive procedure, and can be offered at all levels of the health care system. Several RCTs show misoprostol has a high efficacy rate for treatment of incomplete abortion (66-100%), and recommended regimens included either a 600mcg oral or 400mcg sublingual dose of misoprostol.

Mifepristone and misoprostol are used in combination as a gold-standard regimen for termination of unwanted pregnancies. Misoprostol is used alone in places where mifepristone is not available or is too expensive.

Subsequent to this meeting, the World Health Organization announced the approval of the application for inclusion of misoprostol to the Model List of Essential Medicines for the treatment of incomplete abortion and miscarriage. The judgment was made by an expert committee that evaluated available evidence, which includes numerous randomized and comparative clinical trials for this indication.

Discussion

Uterine rupture is a serious adverse event that has been reported after high doses of misoprostol administration. A dedicated 25mcg misoprostol tablet would prove useful as it could alleviate the current practice of cutting tablets. The experience of one pharmaceutical company in India, however, suggests that there may be some reluctance among providers in using tablets of 100mcg and 25mcg strength. In addition to exploring the potential for manufacturing and marketing these lower doses, there needs to be an effort to encourage their appropriate use in the provider community.

It is not surprising that there currently exists a wide range of doses for IUD since there has been little training in this area. Information should be shared with colleagues on what regimens are acceptable.

Misoprostol for treatment of pregnancy failure is shown to be faster than expectant management and offers an additional option for treatment. It could probably lower the number of women who need to return for a follow up visit to the clinic. There is also scope for offering family planning services within the framework of postabortion care.

With increasing knowledge and awareness about misoprostol for PPH, questions will be raised about its use for other indications in obstetrics and gynecology.

- Misuse of misoprostol for labor induction is a source of concern and could negatively impact programs aimed at introducing misoprostol for PPH. Information about correct regimens of misoprostol for use for labor induction and IUD could help reduce inappropriate use of the drug. Further development of low dose pills may also prove useful.
- Misoprostol works well for treatment of failed pregnancies and its use for this indication should be considered in country programs.

Session 3: Bringing misoprostol into programs: evidence & lessons learned from the field

Moderator: Paul Blumenthal, Stanford University

Presenters: Jeffrey Smith, JHPIEGO; Temple Cooley, Population Services International; Ndola Prata, University of California, Berkeley; Erin Gainer, HRA Pharma; Rasha Dabash, Gynuity Health Projects

Jeffrey Smith, JHPIEGO

JHPIEGO has implemented successful programs in several countries to distribute misoprostol directly to women via trained community health workers. Women are given information on side effects, follow up if PPH occurs after taking the medication, safety and correct timing for misoprostol intake. JHPIEGO's research has indicated that no women took the drug prior to delivery in their intervention areas; there was a drop in expected versus actual maternal deaths in the intervention areas although whether this change can be attributed to use of misoprostol alone is unknown; more women in the intervention area used midwives during their delivery compared to control areas which was attributed to a greater awareness among women.

Temple Cooley, Population Services International

PSI is launching PPH prevention programs in 7 countries and exploring various channels for distribution of misoprostol. The largest channel will be the direct distribution of misoprostol to providers in private and public sector clinics. Community-based channels and pharmacies will also be utilized. Challenges include trying to reach the most vulnerable women and geographic coverage, particularly in places where pharmacies and clinics may be clustered in urban centers. Another issue

relates to developing pill-packs and informational materials that respond to the needs and requests of the country government and determining how to handle the monitoring and evaluation.

Ndola Prata, University of California, Berkeley

Venture Strategies is introducing misoprostol for PPH treatment and prevention in home birth settings. In one study in Tanzania, TBAs were trained to identify PPH and administer 1000mcg misoprostol rectally for PPH treatment in the intervention area. Women in the non-intervention area were referred to the nearest facility. A reduced need for referrals and interventions was recorded in the intervention area. In Ethiopia, Ventures is introducing misoprostol for PPH using TBAs who are able to successfully administer misoprostol for prevention. Based on their research, the presenter shared strategies for community-based distribution of misoprostol which include training TBAs to identify women with PPH using context-specific and culturally appropriate blood loss measurement techniques, involving CHWs and health extension workers for distribution of misoprostol at delivery for PPH prevention, utilizing antenatal care clinics for misoprostol distribution, and partnering with the private sector.

Erin Gainer, HRA Pharma

HRA Pharma works within the regulatory framework for drug approval, focusing on safety and efficacy, security, and helping speed innovations through the approval process. Countries lacking the infrastructure for their own approval process wait for proof of “first-world” approval. Based on current data, the presenter felt some of the findings were inconclusive and indicated that this type of registration for misoprostol for PPH prevention and treatment will be a challenge. Beyond registration, once a drug is on the market, there is an important need to continually monitor the safety of the product. A risk-management plan needs to be developed which includes a post-marketing surveillance/pharmacovigilance system to ensure product security. Other measures should include the ability to perform batch recalls, audit ongoing manufacturing, and conduct agency inspections.

Rasha Dabash, Gynuity Health Projects

In scaling up misoprostol for PPH there are several programmatic issues that need to be considered, including drug supply, service delivery options and models, provider training at all levels, and monitoring and evaluation. Drug supply is a critical issue and ultimately the responsibility of governments where there is little commercial interest but high potential public health benefit. How misoprostol is approved and registered also facilitates other key processes needed to create drug and program sustainability. Operations research can help bridge the gap between clinical research and program effectiveness, ideally with countries integrating several prevention and/or treatment models within the healthcare system, including the community level. Program effectiveness will need to be assessed more broadly within implementation and scale-up. Potential evaluation indicators could include measures of program uptake, reduction in PPH rates, morbidity outcomes and mortality, however collecting these data present particular challenges in the context of real life settings and program and needs to be considered.

Discussion

There seemed to be two schools of thought among participants on the need for further research on misoprostol for PPH prevention and treatment. One group was convinced by the current evidence on misoprostol and eager to embark on operations research to determine programmatic effectiveness, which would include developing a monitoring and evaluation component. The second group remained unconvinced by available data and felt the need for cluster design studies to determine the effectiveness in real world settings.

Key questions included:

- Is a randomized trial needed to demonstrate effectiveness of misoprostol at the community-level? Is there a need to provide more definitive evidence on misoprostol's benefits and answer questions about safety and effectiveness before launching programs?
- If a cluster randomized study on misoprostol is considered, what is the comparison group? Should such a study investigate use of oxytocin in Uniject (as the comparison arm) at the community level? What outcomes should be monitored? If evaluated against maternal mortality, would the logistics, money, and effort be worth it?
- Who is the target population for use of misoprostol – women who do not deliver in a health center (whether or not they have access), or population groups of women with very limited access to health centers?
- What are the critical components of scaling up misoprostol programs and evaluating service delivery models?

Day 2

Session 1: Program Delivery: Designing Appropriate Programs

Moderator: Rajeev Venkayya, The Bill & Melinda Gates Foundation

Presenters: Deborah Armbruster, PATH; Pierre Buekens, Tulane University, School of Public Health and Tropical Medicine & Fernando Althabe, Institute of Clinical Effectiveness and Health Policy, Argentina; Suellen Miller, University of California, San Francisco; Gretel Pelto, Cornell University

Deborah Armbruster, PATH

Success of program scale-up is dependent on funding, political leadership, sustainability, technical consensus on program approach, good on-the-ground management, and effective use of information for action. The presenter evaluated AMTSL programs and the potential for scale-up with misoprostol within this framework. Lessons learned from USAID-supported long running AMTSL programs were shared, with commitment from leaders, providers, and partner organizations proving to be the key to

success. Scale-up for PPH prevention in hospitals is influenced by the WHO guidelines which recommend use of oxytocin over misoprostol when possible. Given these guidelines, the presenter indicated that a PPH prevention strategy should include oxytocin for AMTSL and misoprostol for community-based care where oxytocin is unavailable or where there are challenges to its use.

Pierre Buekens, Tulane University, School of Public Health and Tropical Medicine & Fernando Althabe, Institute of Clinical Effectiveness and Health Policy, Argentina

Passive diffusion of information has not been successful in influencing medical practice, however, behavioral intervention strategies to improve obstetrical care in Argentina and Uruguay has resulted in lower rates of episiotomies and increased use of oxytocin in the third stage of labor. A cluster RCT with 24 hospitals was conducted to study the effect of a behavioral intervention on the use of two evidence-based birth practices – selective use of episiotomies and increase in use of AMTSL. Field teams were trained and post-intervention, there was a 2 to 84% increase in use of oxytocin prophylaxis in the intervention group and no change in the control group. There was a decrease in the rate of episiotomies in the intervention group although this was not a significant difference. The behavioral change model involved training for opinion leaders, training early adopters of practice to convert late adopters, and using techniques employed by pharmaceutical representatives to sell medical products in hospitals.

Suellen Miller, University of California, San Francisco

Cost-effectiveness models using data and assumptions based on available literature, despite their weaknesses, indicate that PPH treatment with misoprostol is more cost-effective than prevention. In settings where use of oxytocin is not possible, and given the limitation of misoprostol use for both prevention and treatment per the WHO guidelines, is prevention or treatment the more effective strategy? The presenter shared what she acknowledged were potentially controversial results from a working simulation model where cost per life saved with the prevention strategy was \$378 versus \$84 with a strategy promoting treatment alone. These data raise questions about whether it makes sense to move forward with programs offering prevention for all or treatment for some.

Grete Pelto, Cornell University

Program Impact Pathways (PIP) can help plan, implement, and monitor programs to bridge the gap between clinical efficacy and program effectiveness. Program failure can result from inadequate resources, skills, and motivation. PIP, a new model based on experience, involves formative research to assess the delivery system and identify gaps in best-practice and barriers to change. Process evaluation and operations research will help identify emerging bottle-necks in the pathways and determine ways to resolve them; outcomes and impact evaluation will assist in the quantitative assessments needed for decision-making.

Discussion

- Misoprostol is already available in many hospitals settings around the world. The question isn't how to scale up-services, necessarily, but how to ensure that appropriate guidelines are available and used for PPH indications.

- Behavioral interventions to influence providers in adopting new practices can be managed in a simple and inexpensive manner. One successful model involves getting the key actors and opinion leaders on board and using their influence to effect change.
- Cost-effectiveness models, while increasingly comprehensive and robust, are still incomplete and may not reflect the true costs and benefits of PPH prevention and treatment with misoprostol.
- Programs dedicated to treatment of PPH versus universal prevention for PPH may prove more cost-effective in the long term. Further research is needed to determine how to best allocate resources for the prevention and treatment of PPH.
- Program monitoring is an important component in transitioning from clinical studies to programs. PIP is a useful model to help identify gaps in the delivery systems and strategies to resolve them.

Session 2: Unanswered questions and debates affecting program delivery for PPH

Moderator: Jeff Spieler, USAID

Presenters: Gijs Walraven, Secretariat of High Highness the Aga Khan; Carine Ronsmans, London School of Hygiene & Tropical Medicine; Jill Durocher, Gynuity Health Projects & Wilfrido León, Hospital Gineco Obstétrico Isidro Ayora, Ecuador; Justus Hofmeyr, University of Witwatersrand, Eastern Cape Department of Health, South Africa

Gijs Walraven, Secretariat of High Highness the Aga Khan

While there is scope to use misoprostol at different levels of the health care system, it is important to think beyond misoprostol alone in addressing PPH. The presenter shared data and experiences of misoprostol use in various low resource settings, including Afghanistan, Pakistan and Tajikistan, in the context of why women die of PPH and what can be done to reduce such deaths. The need for investigations of lower dose regimens of misoprostol for prevention and treatment of PPH at the community level was raised as potentially meaningful in addressing safety concerns around widespread misoprostol use.

Carine Ronsmans, London School of Hygiene & Tropical Medicine

Evidence shows that delivery in a health care facility with a skilled attendant is the best way to promote maternal survival. All efforts should be put towards increasing health center deliveries. There is a need to determine whether community-level use of misoprostol complements this strategy. In 2006, the Lancet series on maternal mortality raised critical questions about where women deliver and who attends to them, recommending that a health center strategy may best promote maternal survival. The presenter questioned whether misoprostol at the community-level complements the

health center strategy, emphasizing the need to first define the target population for this intervention as well as assess the role of CHWs and TBAs in achieving high coverage.

Jill Durocher, Gynuity Health Projects & Wilfrido León, Hospital Gineco Obstétrico Isidro Ayora, Ecuador

Fever and shivering are common side effects after misoprostol administration and are typically transient and non life-threatening. Rates of fever and shivering are dose and route related. In the Gynuity PPH treatment study, an unusually high number (over one-third of women), experienced high fevers ($\geq 40^{\circ}\text{C}$) in the site in Ecuador. These symptoms did not last beyond a few hours or result in prolonged hospitalization. Hospital staff was able to diagnose and treat all cases. Policy questions include whether other populations are prone to experiencing high fevers, whether the benefits of misoprostol outweigh disadvantages of high fevers in some or all settings, what level of training is needed, and what type of health care provider can adequately manage high fevers.

Justus Hofmeyr, University of Witwatersrand, Eastern Cape Department of Health, South Africa

An increase in misoprostol's popularity has been accompanied by increased clinical risks and adverse events, underscoring the importance of proper training and steps to minimize risk. Most of the risks documented were of ruptured uterus especially with high doses for induction in term pregnancies before delivery of the baby, not for prevention or treatment of PPH. The presenter advocated use of a lower dose of misoprostol, although comparisons of 600mcg to 400mcg dose of misoprostol for prevention of PPH are inconclusive. Recommendations to minimize risks include changing the global focus from misoprostol-centered to PPH prevention-centered efforts. Steps should be taken to make oxytocin available to all, with efforts put into basic research on non-injectable administration of oxytocin, perhaps in tablet form.

Discussion

- How can programs reconcile the important and immediate needs of women delivering at home without access to health facilities, with long-term plans for sustainable, facility-based care?
- Research is needed to investigate lower doses of misoprostol for PPH indications. If a 400mcg dose is effective for PPH prevention, the same dose may work well for treatment and reduce frequency of many of the associated side effects.
- There is a need to broaden inquiry into risks of uterotonics beyond just misoprostol.
- It is important to collect information from women on their perspectives after they experience a high fever.

Session 3: Barriers to Implementation, Delivery and Sustainability

Moderator: André Lalonde, Society of Obstetricians and Gynaecologists of Canada

Presenters: Cynthia Stanton, Johns Hopkins Bloomberg School of Public Health; Metin Gulmezoglu, World Health Organization; Dorothy Shaw, FIGO; Lester Coutinho, Packard Foundation

Cynthia Stanton, Johns Hopkins Bloomberg School of Public Health

Misuse of uterotonics in low resource settings can affect expansion of its use for PPH prevention. The presenter suggested that for misoprostol, the greatest policy concern is overuse of misoprostol particularly before delivery given the potential for uterine rupture. For oxytocin, induction or augmentation is of concern, particularly at non-surgical facilities at home-based births. Despite limited data on oxytocin use for labor induction and augmentation, experience with oxytocin use can be useful in developing strategies for misoprostol expansion, and efforts can be made to better document misoprostol use for a range of indications. Collaborative efforts to develop a tool kit or questionnaire to assess delivery practices will yield important data on use of misoprostol and oxytocin in different contexts.

Metin Gulmezoglu, World Health Organization

The WHO guidelines and Essential Drugs List are two resources based on rigorous evaluation that outline a role for misoprostol in PPH prevention and treatment. PPH prevention guidelines were published in 2007 and indicate the following: oxytocin recommended over misoprostol; in the absence of AMTSL, health workers should be trained to offer a uterotonic alone (including misoprostol). For PPH treatment, the WHO is working to develop guidance which would recommend oxytocin as a first-line treatment, followed by ergometrine, failing which misoprostol can be used. Results of the recent PPH treatment trials will be presented to the Guidelines Review Committee in April 2009. There are currently 2 submissions to get misoprostol on the EDL, one for prevention of PPH and the other for treatment of incomplete abortion.

Dorothy Shaw, FIGO

There is a need for agreement among regional and international professional organizations to adapt best-practice and evidence-based guidelines. Professional organizations such as FIGO should develop guidance for comprehensive PPH care with public and private systems, and also focus on education and training of all levels of personnel. The presenter felt that essential interventions and recommendations for maternal health are needed that are more “friendly” to low resource countries as an alternative to the gold-standard WHO recommendations.

Lester Coutinho, Packard Foundation

Medical knowledge, in whatever form, often becomes community practice, and advocates and policy-makers are lagging behind in evaluating what this means. Mifepristone and misoprostol are being used widely in India, with staggering sales figures and indications that there is misinformation related to their use. Development of adequate guidelines will help address some of these issues although registering a product for a specific indication depends largely on evidence to support the registration. In terms of

program development, there is an important need to understand present patterns of use of misoprostol in communities on both a quantitative and qualitative level. The presenter felt this would help in designing programs that match the present use and needs of communities.

Discussion

Key questions included:

- It is important to conduct large-scale evaluations of health outcomes. Is it possible to conduct programs while simultaneously employing rigorous evaluations?
- How can drug quality be ensured?
- How can anecdotal information on use of oxytocin and misoprostol be better documented?
- How can companies be helped in meeting pre-qualification needed for misoprostol registration for PPH?
- How do colleagues and communities stay informed of guidelines on PPH, and how will new data and information be managed?

Summary Session – Looking Forward: Next Steps

Participants offered their thoughts on the future direction of misoprostol for PPH prevention and treatment, which largely fall under the themes of strategies to move forward, the need for further research and evidence on misoprostol, need for development of guidelines, and the important role of monitoring and evaluating programs and putting in place pharmacovigilance systems to monitor safety.

Strategies for moving forward

- Develop a comprehensive approach to managing PPH. There is not one solution and no short-term solutions.
- Work with communities to develop appropriate interventions and solutions.
- Integrate misoprostol into broader service delivery packages with practical solutions to address maternal mortality.
- Oxytocin is the most effective drug – more effort should be placed on enabling oxytocin to be used for PPH.
- Misoprostol is available and being used - there is a need to understand the market better, including distribution channels, prescribing factors, and attitudes of women and providers.

More evidence needed

- There is still a need for research to parallel any implementation of misoprostol programs.

- An RCT at the community level will provide much needed evidence comparing oxytocin in Uniject with misoprostol for PPH prevention.
- There is a need for development of evidence demonstrating the safety/efficacy of misoprostol at the community level.
- A step-wise design for implementation may be a good way forward to collect baseline and outcome data.
- Lower dosages (with possibly reduced side effects) of misoprostol should be studied
- The cost-effectiveness of various PPH prevention and treatment strategies should be investigated.
- A heat stable/non-injectable preparation of oxytocin could provide critical in addressing PPH at the community-level.

Development and dissemination of guidelines

- Clear guidance on dosages is needed along with an understanding of what it means for health workers to be trained to offer to misoprostol.
- There is a need for simple and concise guidelines that are updated regularly and disseminated widely as the research and programmatic experience continues to evolve.
- Online guidelines that can be easily updated could be very useful.
- Pharmaceutical companies are hoping for more specific recommendations with respect to PPH so that they can develop specific packaging on misoprostol for PPH

Monitoring & Evaluation

- There is a call for rigorous evaluation of the impact of misoprostol use for PPH indications.
- There is a need for proper monitoring and evaluation – what are the dangers? What are the side effects? What are the risks?
- Development of monitoring & evaluation tools and cost-effectiveness studies should be prioritized.
- Distribution of misoprostol at the community level is easy, but its safe distribution may not be so easy and should be monitored.
- Programs should be monitored to evaluate whether they are doing more good than harm.
- Pharmacovigilance is critical for moving forward.