

## POSTPARTUM HEMORRHAGE

### OVERVIEW

Postpartum hemorrhage (PPH) is the leading cause of maternal death globally, accounting for more than one quarter of all such deaths in low-resource regions of the world.

Gynuity Health Projects collaborates with partners to conduct programmatic and clinical research, generate and synthesize evidence to inform policy and practice, and provide technical assistance to governments and other key stakeholders to address gaps in PPH care.

We apply clinical evidence and programmatic experience to design and evaluate service delivery and program approaches to:

- a) Improve the availability and use of technologies for the management of PPH and
- b) Facilitate timely and effective PPH treatment across multiple levels of care.

We focus on simple technologies and interventions that are appropriate and useful in low-resource environments and community settings.



### LOCATIONS

The following map highlights countries where we conduct research and provide technical assistance on PPH. To date, more than 65,000 women have taken part in our studies.



### RESEARCH

#### The Role of Misoprostol in PPH Management

Uterotonic drugs stimulate contractions of the uterus after delivery and help to control bleeding caused by uterine atony, the most common cause of PPH. Misoprostol, a readily-available and inexpensive drug, comes in tablet form, is stable at room temperature, and does not require any special skills, equipment, or facilities for its use. These factors make it an important component of an integrated package of PPH interventions, especially in resource-poor and community settings. It is a valuable alternative to oxytocin (the gold standard uterotonic that requires cold storage, intravenous or intramuscular administration, and skilled providers).

## *Clinical evidence: Prevention and treatment of PPH with misoprostol*

Evidence generated through a series of clinical trials that evaluated the use of misoprostol for PPH has helped to advance knowledge about the drug's safety, efficacy and programmatic effectiveness.

**Misoprostol for PPH: Evidence-Based Regimens**  
Prevention: Single dose 600mcg oral (3 tablets)  
Treatment: Single dose 800mcg sublingual (4 tablets)

- A trial comparing misoprostol (600mcg oral) with placebo found that misoprostol reduced the incidence of measured PPH ( $\geq 500\text{cc}$ ) by a quarter when given to women prophylactically by trained traditional birth attendants following home births in a remote area of Pakistan. Another trial comparing misoprostol and oxytocin in Uniject™ for the prevention of PPH found both drugs to be safe and efficacious when delivered by auxiliary midwives in rural Senegal. Ease of use, higher acceptability and fewer logistical challenges made misoprostol a more adaptable option in this setting. Senegal has since approved the nationwide use of misoprostol for PPH prevention by auxiliary midwives in health huts.
- Two large multi-country studies comparing misoprostol (800mcg sublingual) to intravenous oxytocin (40 IU) for treatment of PPH found that 9 out of 10 women had their bleeding controlled within 20 minutes with either drug. Unexpectedly, the studies found frequent high fever after the administration of misoprostol in only one country, prompting additional research to understand misoprostol-induced side effects, specifically why the incidence of fever is higher in some places. A third multi-country study conducted in collaboration with WHO found no clinical benefits to administering misoprostol at the same time as oxytocin for treating PPH.

## *Translating the clinical evidence into practice: Models of PPH care using misoprostol*

Research is underway at the community level to clarify the different ways for integrating misoprostol into PPH programs. Models of care using misoprostol at the community level include:

- Antenatal distribution of misoprostol to pregnant women to self-administer following home birth to prevent PPH.
- Offering misoprostol for the prevention of PPH by lower level providers where access to standard injectable uterotonics is limited.
- Treatment as 'first aid' following home/community delivery using an 800mcg sublingual dose of misoprostol, administered immediately after heavy bleeding is recognized, alongside referral.
- Universal prophylaxis (600mcg oral misoprostol) followed by treatment with a single sublingual dose of 800mcg misoprostol if PPH occurs.
- Secondary prevention: early treatment with an 800mcg sublingual dose of misoprostol for women with above-average postpartum blood loss.



## *Policy and advocacy*

We work with partners to advocate evidence-based changes in policy and practice at a country and international level. Our activities include:

- Dissemination of research results through articles in peer-reviewed journals and presentations at webinars, meetings and conferences.

- Preparation and submission — resulting in subsequent approval — of applications for inclusion of misoprostol for both PPH indications on the WHO Model List of Essential Medicines.
- Development of informational and educational materials, including ‘Instructions for Use’.
- Creation of communication pieces (print and video) showcasing different delivery contexts and approaches to PPH care.
- Contribution to and support of global and national guidelines reflecting best available evidence.
- Collaboration with pharmaceutical companies to expand availability of misoprostol for PPH.

### *Guidance clarifying the role of misoprostol*

WHO: Recommendations for the prevention and treatment of PPH, 2012

FIGO: Prevention and treatment of PPH in low resource settings, 2012

ICM & FIGO: Misoprostol for the treatment of PPH in low resource settings, 2014

WHO Model List of Essential Medicines (19<sup>th</sup> Edition, 2015): Misoprostol listed for both PPH indications

European Medicines Agency: Approval of the first misoprostol product, Hemoprostol, for the treatment of PPH, 2014

### When Uterotonics Are Not Enough: Additional Strategies to Address Gaps in PPH Care

Uterotonics alone will not eliminate PPH morbidity and mortality. We conduct collaborative research to understand the role of additional strategies and interventions that could fill gaps in PPH care. We are evaluating:

- *The effectiveness, safety, feasibility and acceptability of introducing a low cost, locally assembled condom uterine balloon tamponade to manage PPH in referral facilities.* This treatment option could reduce the need for interventions, such as surgical procedures, which are often not immediately available or feasible outside of tertiary care centers.
- *The efficacy and safety of oral tranexamic acid (TXA) when used as an adjunct to misoprostol to treat PPH.* Use of TXA, an anti-fibrinolytic agent, could control bleeding among women who do not respond to treatment with uterotonics and/or who may have trauma-related PPH. The wide availability of TXA in tablet form and its stability at room temperature suggest feasibility for use as part of a package of PPH treatment options in lower level health facilities and home births.
- *The relationship between shock index and blood loss in order to identify new clinical measures of PPH and triggers for treatment.* PPH is most commonly defined as blood loss of 500mL or more, yet visual estimation of postpartum blood loss can be difficult. The clinical utility of the 500mL marker is also questionable. Clinical indicators of PPH that do not rely on measured blood loss could play a role in improving and simplifying how PPH is identified and managed.



- *The effectiveness of PPH care.* A better understanding of *how* care is provided may be critical to improving PPH outcomes. There is limited information, however, regarding factors central to improving effective PPH management or on how to prioritize such changes throughout a health system.

## TECHNICAL ASSISTANCE

### Evaluating What Works in National Scale-Up

We engage with governments to assist in the design, implementation and evaluation of service delivery innovations and policies. Our collaborations have allowed us to share lessons learned from national program evaluations in countries like Nepal, Niger and Senegal. In addition, our evaluations provide important guidance for other countries interested in improving the quality of their PPH programs.

## GLOBAL PARTNERS

We work in partnership with government stakeholders (including Ministries of Health), experts and agencies to achieve the goals set forth in this program. Key partners include:

- Aga Khan Health Services
- Alexandria University, Egypt
- Bijapur Liberal District Education Association, India
- Centro Rosarino de Estudios Perinatales (CREP), Argentina
- Center for Research and Consultancy in Reproductive Health, Vietnam
- ChildFund International
- Concept Foundation
- El Galaa Teaching Hospital, Egypt
- FCI Program of Management Sciences for Health
- Guttmacher Institute
- Health and Development International
- International Federation of Gynecology and Obstetrics (FIGO)
- Jawaharlal Nehru Medical College at KLE University, India
- Massachusetts General Hospital, USA
- National Committee for Maternal and Neonatal Health, Pakistan
- Population Services International (PSI)
- University of California, San Francisco
- University of Illinois, Chicago, USA
- University of Liverpool, UK
- World Health Organization (WHO)

## RELATED RESOURCES

We produce materials on PPH in multiple languages and targeted to various audiences, including policymakers, program implementers, health care providers, women's health advocates, and women. This program brief is accompanied by an insert listing over 25 articles on PPH that have been published in peer-reviewed journals since 2005. Additional resources on PPH, as well as on other women's health topics, are available from our website at [www.gynuity.org](http://www.gynuity.org) and YouTube. You can also follow us on Twitter @Gynuity.

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## Gynuity Health Projects: Peer-Reviewed Publications on Postpartum Hemorrhage (2005-2016)

Additional resources, including educational and informational materials, Instructions for Use pamphlets and meeting reports, are available from our website at [www.gynuity.org](http://www.gynuity.org)

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