



# **Misoprostol for PPH: Current evidence & future directions**

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# Misoprostol for PPH: Current evidence

## Misoprostol in obstetrics and gynecology

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Indication	Dosage	Notes
PPH prophylaxis	600 mcg oral	<i>Not as effective as oxytocin or ergometrine</i>
PPH treatment	600 mcg oral	<i>Limited evidence – use conventional oxytocics first</i>

# Misoprostol for PPH: Current evidence



## Cochrane Database of Systematic Reviews

### Prostaglandins for preventing PPH




*“If conditions for oxytocin use cannot be met then misoprostol could be used based on current evidence...”*  
*(Gulmezoglu AM et al. Cochrane Systematic Review 2007)*

### Treatment for primary PPH

*“The current evidence is not robust enough to recommend replacing the combination of oxy/ergo with misoprostol for the first-line treatment of primary PPH ...”*  
*(Mousa et al. Cochrane Systematic Review 2007)*

# Misoprostol for PPH prevention: Community-based evidence

Published studies on 600mcg oral/sublingual misoprostol

Study	Context	Methodology	Outcomes
Derman et al 2006	India Midwives/ANMs PHCs/homebirths	RCT (n=1620)  oral vs. placebo	↓ Acute PPH in miso ↓ Severe PPH in miso ↓ Need for transfer, blood transfusion, surgery w/ miso
Hoj et al 2005	Guinea-Bissau Midwives Rural health facility	RCT (n=661)  SL vs. placebo	NS BL $\geq$ 500ml w/ miso ↓ BL $\geq$ 1000ml in miso arm
Walraven et al 2005	The Gambia TBAs homebirths	RCT (n=1229)  oral vs. oral ergo	NS ↓ BL in miso arm ↓ drop in PP Hb w/ miso

# Misoprostol for PPH prevention: Recently completed research

**Purpose** Determine if 600mcg oral misoprostol reduces rate of PPH when given by trained TBAs during 3<sup>rd</sup> stage of labor

**Community-based study** Double-blinded, placebo controlled, randomized controlled trial (n=1395)

**Study arms** After childbirth, trained TBAs administered either 600 µg oral misoprostol or placebo

**Context** Remote villages in Chitral District, NWFP, Pakistan

**Primary outcomes** rate of PPH  $\geq 500$ ml; change in hemoglobin drop pre- to post-delivery

# Misoprostol for PPH prevention: Future directions

- Operational research to bridge gaps between clinical research and programmatic realities
- Prioritize development of monitoring & evaluation tools
- Bolster evidence on its use/integration among various levels of health systems and providers
- Investigate cost-effectiveness of various PPH prevention strategies
- Compare use of misoprostol vs. oxy/Uniject at the community-level
- Investigate lower doses of misoprostol to minimize side effects/costs

# Misoprostol for PPH treatment: Current published evidence

- Fewer than 600 women have received misoprostol for PPH treatment in published literature
- Data show that misoprostol causes rapid uterine contractions that reduce postpartum blood loss
- Side effects dose dependent; mostly mild and transient; non-life threatening reported cases of high fever infrequent

*Insufficient data to support a specific misoprostol regimen for treatment of primary PPH, either following or in absence of prophylactic uterotonics or as adjunct to standard treatment (Blum, IJGO 2007)*

# Misoprostol as first-line treatment: Recently completed research

**Purpose** Determine if misoprostol alone is a safe and effective treatment option for primary PPH (due to uterine atony)

**Study design** Two hospital-based, double-blinded, placebo controlled, randomized controlled trials

**Study arms** After PPH diagnosis, 1787 women randomized to either 800 µg sublingual misoprostol or 40 IU oxytocin IV

**Context** Burkina Faso, Egypt, Ecuador, Turkey, and Vietnam:

**Study 1:** oxytocin prophylaxis given during 3<sup>rd</sup> stage of labor

**Study 2:** no oxytocin given during 2<sup>nd</sup> or 3<sup>rd</sup> stages of labor

# Misoprostol as adjunct treatment: Recently completed research

**Purpose** Determine if misoprostol is an effective adjunct treatment for primary PPH (due to uterine atony)

**Study design** Hospital-based, multi-center, double-blinded, placebo controlled, randomized controlled trial

**Study arms** After PPH diagnosis, standard uterotonic treatment (IV oxytocin) plus either: A) 3 tablets of misoprostol 200 $\mu$ g or, B) matching placebo

**Enrollment** 1,400 women from July '05 – July '08

**Participating countries/agencies:** Argentina, Egypt, South Africa, Thailand and Viet Nam, RHR Division of World Health Organization, Gynuity Health Projects

# Misoprostol for PPH: Future Directions

## Misoprostol for Prevention and Treatment of PPH: Current Knowledge and Future Directions

March 11 & 12, 2009

The Bill & Melinda Gates Foundation

### Meeting purpose

- Review current evidence, identify unanswered questions, and discuss programmatic challenges related to expanding its use

### Discussions called for ...

- More comprehensive approach to managing PPH
- Better guidelines on appropriate use of misoprostol
- Evidence of the program effectiveness vs. demonstrated efficacy in clinical trials
- Further research with regard to doses and applicability in different settings