New Approaches using Misoprostol for the Management of Postpartum Hemorrhage at the Community Level

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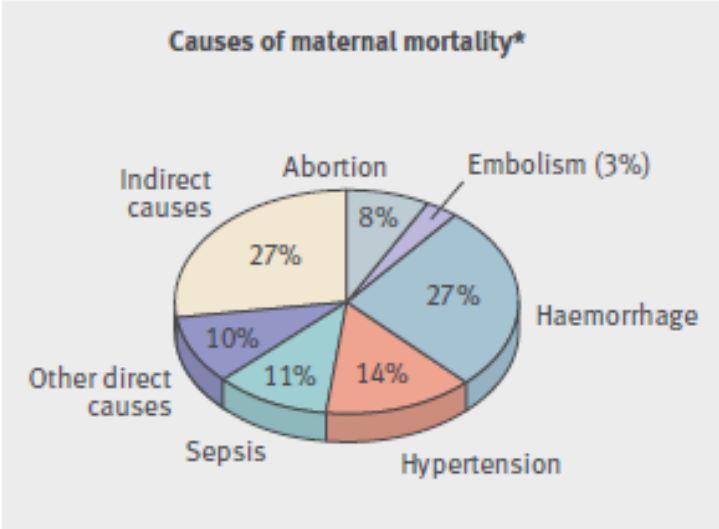
Inequities in Access to Services

- Since 1990, 45% reduction in maternal mortality
- Leading single direct cause of maternal death globally: **hemorrhage**
- Risk of death far higher in resource-poor community settings
- Most cases of postpartum hemorrhage can be prevented or effectively treated



Say et al. 2014

Women & providers need access to essential life-saving health care interventions, regardless of delivery site

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International Consensus: Misoprostol for PPH

- **WHO Model List of Essential Medicines**
  - Prevention of PPH* : 2011
  - Treatment of PPH* : 2015
- **WHO, FIGO, ICM & UNCoLSC**
  - Recommend misoprostol for PPH care*
- **Evidence-Based Regimens**
  - Prevention of PPH : 600mcg oral dose (3 tablets)
  - Treatment of PPH : 800mcg sublingual dose (4 tablets)

An important uterotonic option in community settings

Low-cost, easy to use, available in tablet form, stable at room temperature

*where oxytocin (gold standard) is not available or cannot be safely used

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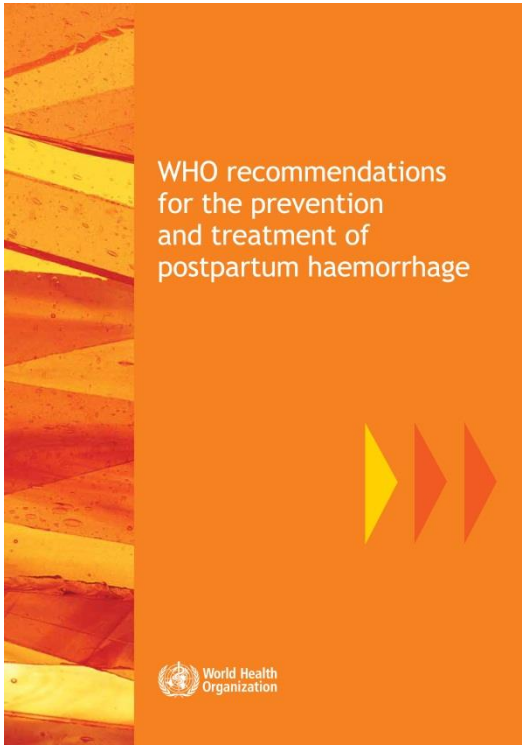
WHO PPH Guidelines (2012): Prevention with Misoprostol in the Community

- Support its use by lay health workers if no skilled birth attendant present
- Call for additional research of antenatal distribution of misoprostol to women for self-administration



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Self-Administered Misoprostol for PPH Prevention

- **Experience from rural Uganda**
  - Advance distribution of misoprostol given to women to self-use following home deliveries
  - 600 mcg oral misoprostol vs placebo
- **Our research revealed**
  - 97% of women took the study medicine
  - No adverse events
  - High acceptability
  - Evidence of misoprostol (ie study medicine) use in clinics when oxytocin unavailable

Empowering women to deliver their own care

Read more: Weeks et al. BMC Pregnancy and Childbirth (2015). The MamaMiso study of self-administered misoprostol to prevent bleeding after childbirth in rural Uganda: a community-based, placebo-controlled randomised trial

Strategies Using Uterotonics for PPH Management at the Community Level

Prevention

Administration after delivery to lower incidence of PPH

- Effectively reduces average blood loss
- Most popular approach adopted by programs

Limitations:

- Unclear if prevention alone "saves lives"
- Does NOT eliminate need for PPH treatment
- Few current misoprostol programs address treatment options for when women fail to respond to prophylaxis (6-16%)

Treatment

Administration after PPH diagnosis to stop bleeding

- Integration into programs has been slower
- Stops bleeding in 20 minutes in 9/10 women*
- Treatment interventions often limited to referral only
- Recognition that treatment options are urgently needed in all settings where women deliver

*Winikoff et al. Lancet 2010; Blum et al. Lancet 2010 (hospital-based trials)

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Integrating PPH Treatment into Models of Care

- Misoprostol can be of greatest use in settings where:
  - IV oxytocin is not feasible
  - Referral not always possible
- Barriers to using misoprostol in these settings:
  - Unknown safety of misoprostol for treatment following its prophylactic use
  - Concern about capacity of non-physician providers to diagnose & treat PPH
  - Focus on universal prophylaxis

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New Approaches to PPH Treatment

Building the evidence base for misoprostol for PPH management & its safe integration into programs at the community level:

1. Treatment as “First Aid” (along with referral)
2. Treatment following Prevention
3. Secondary Prevention / Early Treatment

Considerations: Cost per woman, sustainability, provider training, exposure to side effects, potential for ‘over-use’, reaching women most in need of interventions, acceptability among providers & women, rarity of severe PPH event…

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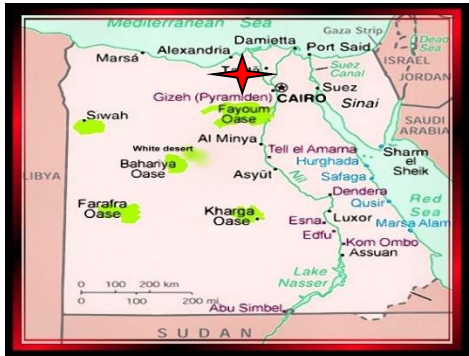
1. Treatment as “First Aid” with Referral

Assess impact of adding misoprostol given to women as ‘first aid’ to standard of care, referral to higher level facility	
Location	Egypt: El Beheira governorate
Birth Attendant	Midwife or Nurse-Midwife
Context	Home births or births in Primary Health Units
Protocol	If PPH diagnosed: Referral + 4 tablets of misoprostol OR of placebo

Our research revealed

- No instances of providers using misoprostol at inappropriate time
- No serious adverse events or maternal deaths associated with misoprostol
- Side effects (shivering): short-lived & easily managed
- Transfer levels low



2. Treatment following Prevention

Key Question Is it safe to administer a treatment dose of misoprostol for PPH after prophylaxis ? (800mcg SL + 600mcg oral misoprostol)	
Location	Pakistan: Chitral district (Khyber-Pakhtunkhwa province)
Birth Attendant	Traditional Birth Attendant
Context	Home births
Protocol	Prophylactic dose (3 tablets) given by TBA If PPH diagnosed, referral + 4 tablets of misoprostol or of placebo (TBA)

Our research revealed

- 800mcg SL misoprostol for treatment + 600 mcg oral misoprostol prophylaxis is safe
- No serious adverse events
- Side effects: transient, easily managed, & acceptable
- Transfers levels low

Similar trial ongoing in Afghanistan (Badakhshan) where prophylactic dose of misoprostol is self-administered.

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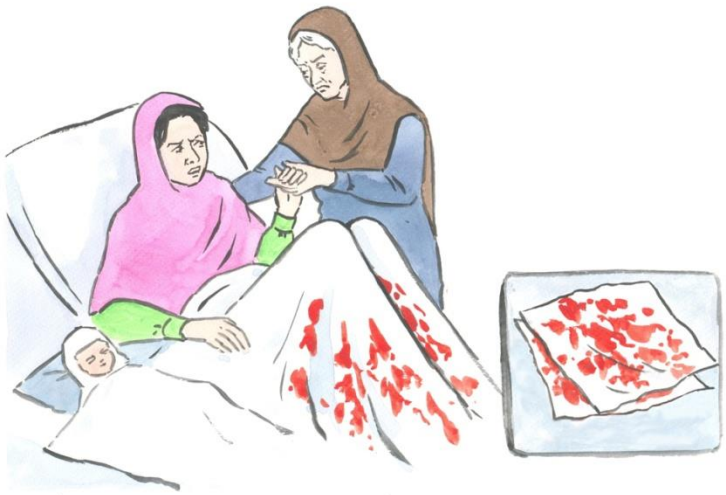
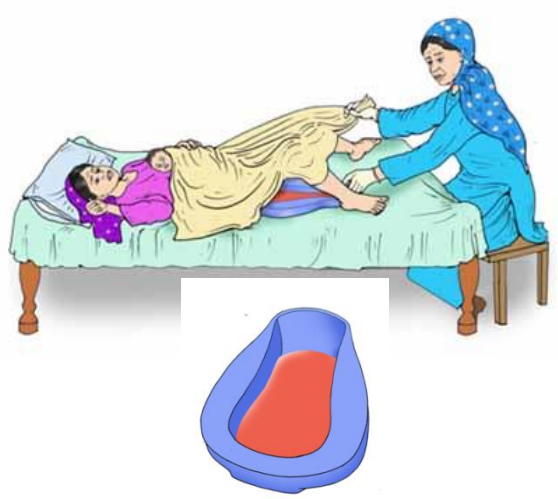
PPH Diagnosis In Community Deliveries



Two cloths to help diagnose PPH (~500ml)

Marked bedpan ~500ml to trigger diagnosis



Visual estimation of blood loss or other clinical signs or symptoms may also trigger diagnosis in some cases

3. Secondary Prevention/Early Treatment

Compare Universal Prophylaxis to Secondary Prevention	
Location	India: Bijapur, Karnataka
Birth Attendant	Auxiliary Nurse Midwife
Context	Home births or births at health sub-centres
Protocol	600mcg oral misoprostol to all women **OR** 800mcg sublingual misoprostol only to women who bleed ≥ 350mL

- Innovative early intervention approach:
  - Uses treatment dose to provide early treatment only to women with above average blood loss
- Several potential advantages over universal prophylaxis:
  - Medicates fewer women
  - Reduces cost
  - Improves acceptability (fewer side effects)
- May alleviate concerns about late diagnosis at community level

3. Secondary Prevention continued…

Our research revealed

- Secondary prevention is no worse than (non inferior to) universal prophylaxis
- Substantially fewer women medicated – **5% compared to 99%**
- Providers successfully administered both regimens & easily managed side effects
- Women willing to use misoprostol in future deliveries & recommend to others

Acceptable & feasible alternative strategy to universal prophylaxis

Practical way to address simultaneously prevention & treatment

Equips providers with a timely & fitting strategy to manage bleeding before point of emergency

Read more: Raghavan S et al, 2015, British Journal of Obstetrics & Gynaecology

Misoprostol for primary versus secondary prevention of PPH: a cluster-randomised non-inferiority community trial

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What The Evidence Tells Us

- Community providers can be trained to recognize heavy bleeding & to offer misoprostol treatment
- Low transfer rates highlight importance of treatment options as part of basic EmOC at delivery site
- Offering misoprostol for PPH treatment at community level is safe – no serious adverse events associated with misoprostol
- High acceptability, tolerability of side effects
- Women can be involved in their own care

800mcg sublingual misoprostol is a safe and effective treatment option at ALL levels of care, irrespective of prophylaxis strategies

What Next?…

- **Clear evidence-based policies and guidelines**
  - Integration of misoprostol for PPH indications in to national essential medicines lists
  - Development of clinical guidelines
- **Train/support health providers & community health workers**
  - on appropriate use & administration of misoprostol for PPH.
- **Quality assured product**
  - Eg European Medicines Agency approval of first misoprostol product (Hemoprostol, Linepharma) for treatment of PPH in low resource settings (2014)
- **Public sector engagement**
  - Scaled up models of successfully piloted misoprostol service delivery programs

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Thank you

on behalf of our many partners & collaborators

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