



Postpartum Haemorrhage: from Research to Practice

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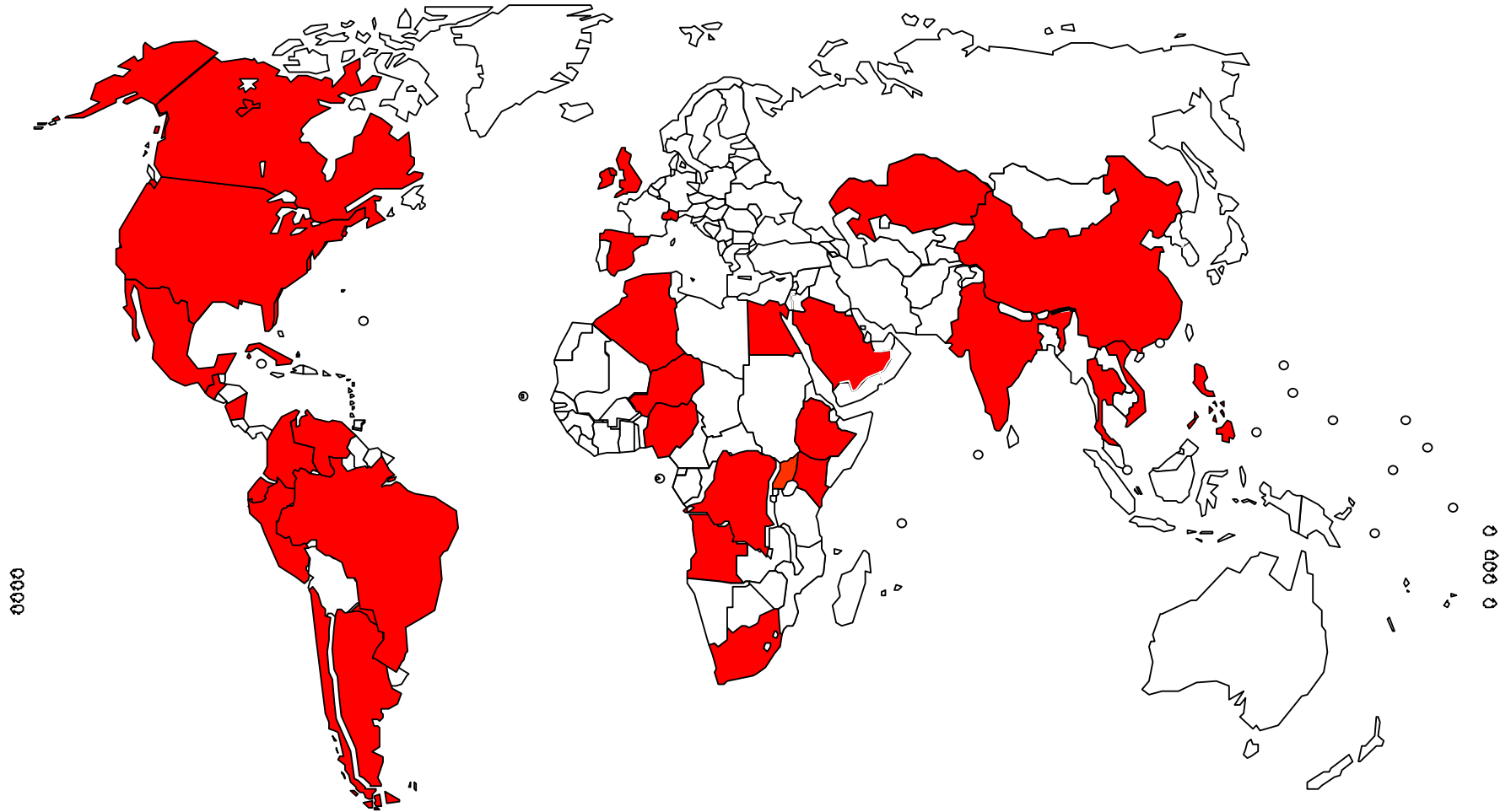
World Health
Organization

WHO Core Functions

- Articulating consistent, ethical and evidence-based **policy** and advocacy positions;
- **Managing information/monitoring** by assessing trends and comparing performance; setting the agenda for, and stimulating, research and development;
- Catalyzing change through **technical** and **policy support**, in ways that stimulate cooperation and action and help to build sustainable national and intercountry capacity;
- Setting, validating, monitoring and pursuing the proper implementation of **norms** and **standards**;
- Stimulating the development and testing of new **technologies**, tools and guidelines;
- Negotiating and sustaining national and global **partnerships**;



WHO Maternal and Perinatal Research Network



PPH: from research to practice

POPPHI Meeting, Nov 20, 2009



World Health
Organization

Clinical Trials

- WHO multicentre randomized trial of misoprostol in the management of the third stage comparing oxytocin with misoprostol *Lancet 2001: 358: 689-95*
 - 600 mcg misoprostol vs 10 IU oxytocin IV or IM
 - Over 18000 participants in Argentina, China, Egypt, Ireland, Nigeria, South Africa, Switzerland, Thailand, Vietnam
 - "10 IU oxytocin (intravenous or intramuscular) is preferable to 600 mcg oral misoprostol in the active management of the third stage of labour in hospital settings where active management is the norm"
- WHO-Gynuity RCT of misoprostol as an adjunct for treatment of PPH trial
 - 1400 women in Argentina, Egypt, South Africa, Thailand, Vietnam
 - 600 mcg misoprostol + routine treatment
 - Awaiting publication



Synthesis of research findings

- WHO Systematic review of maternal morbidity and mortality: the prevalence of severe acute maternal morbidity (near miss)
 - Say L, Pattinson RC, Gülmezoglu AM. *Reproductive Health*, 2004;1:3 (17 August 2004).
- WHO analysis of causes of maternal death: a systematic review.
 - Khan KS, Wojdyla D, Say L, Gülmezoglu AM. *Lancet*, 2006; 367:1066-74



WHO analysis of causes of maternal death: a systematic review
Lancet 367: 1066-1074, 2006

	Africa	Asia	LAC	Developed countries
Data sets	8	11	10	5
Maternal deaths	4508	16089	11777	2823
Haemorrhage	33.9% (13.3-43.6)	30.8% (5.9-48.5)	20.8% (1.1-46.9)	13.4% (4.7-34.6)
Hypertension	9.1% (3.9-21.9)	9.1% (2.0-34.3)	25.7% (7.9-52.4)	16.1% (6.7-24.3)
Sepsis	9.7% (6.3-12.6)	11.6% (0.0-13.0)	7.7% (0.0-15.1)	2.1% (0.0-5.9)



Synthesis of research findings

- Systematic reviews
 - prostaglandins in the third stage management
 - misoprostol for prevention and treatment of PPH
 - dose related effects and maternal mortality related to misoprostol

- Safety of misoprostol (ongoing)



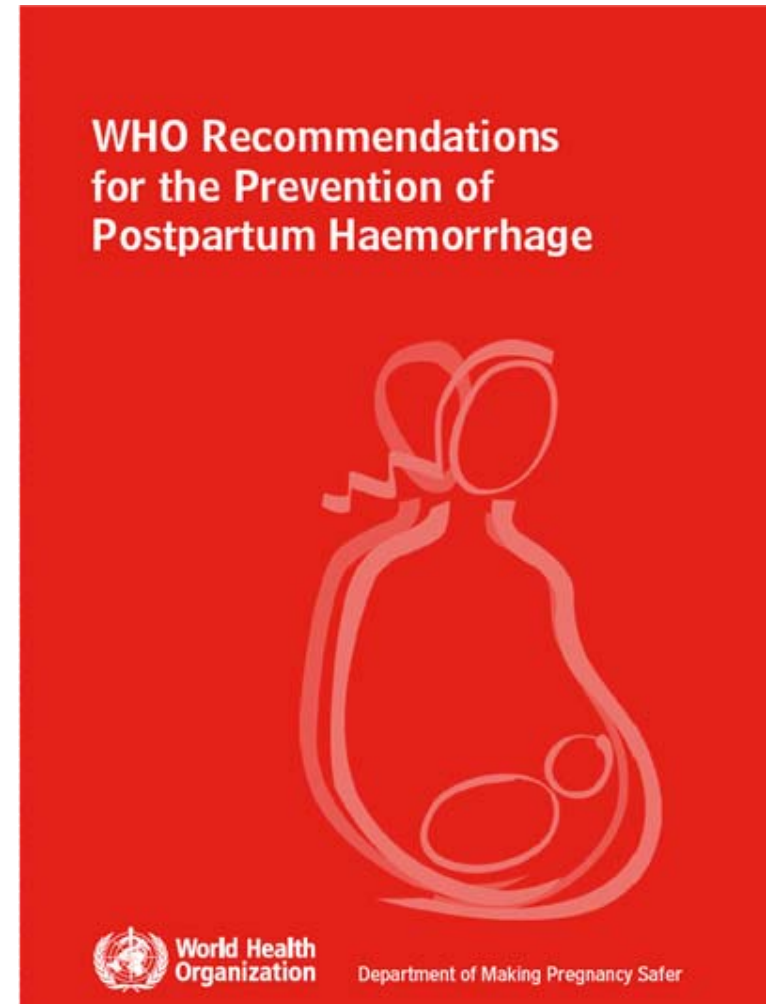
Research to practice

- **Technical support to countries to implement PPH prevention programmes - promoting evidence based guidelines and policies**
 - Clinical practice guidelines (IMPAC)
 - Training modules
 - Essential medicines list
 - Costing
 - Monitoring and evaluation



Guidelines: PPH prevention (2007)

- 9 questions related to management of the 3rd stage of labour
- 3 critical outcomes
 - Maternal death
 - Blood loss \geq 1000 ml
 - Blood transfusion
- Subgroup by skilled and non-skilled attendants
- GRADE system for quality of evidence and strength of recommendations



Active management and the uterotonic

- Active management should be offered to all women delivering with skilled attendants
- Oxytocin 10 IU IM or IV is preferred to ergot alkaloids or misoprostol
- In the absence of active management a uterotonic drug (oxytocin or misoprostol) should be offered by a health worker trained in its use for PPH prevention



Timing of cord clamping and cutting

- Because of the benefits for the baby, the cord should not be clamped earlier than is necessary for applying cord traction in active management of the third stage of labour
 - *For the sake of clarity, it is estimated that this will take around 3 minutes*
 - *Early clamping may be required if the baby requires immediate resuscitation*



Controlled cord traction

- Given the current evidence for active management includes cord traction, no change to the current practice is recommended
 - *Further research into the effects of individual components of active management is needed*



AMTSL trial:

**ACTIVE MANAGEMENT OF THE THIRD STAGE OF
LABOUR WITHOUT CONTROLLED CORD
TRACTION:
A RANDOMIZED NON-INFERIORITY CONTROLLED
TRIAL**

HRP Trial: A65554

Objective

- To determine whether the simplified package without CCT, *with the advantage of not requiring training to acquire the manual skill to perform this task*, is not less effective than the full AMTSL package with regard to reducing blood loss in the third stage of labour.



Trial interventions

1. Management of the third stage of labour WITH controlled cord traction (CCT)
2. Management of the third stage of labour WITHOUT controlled cord traction (CCT)



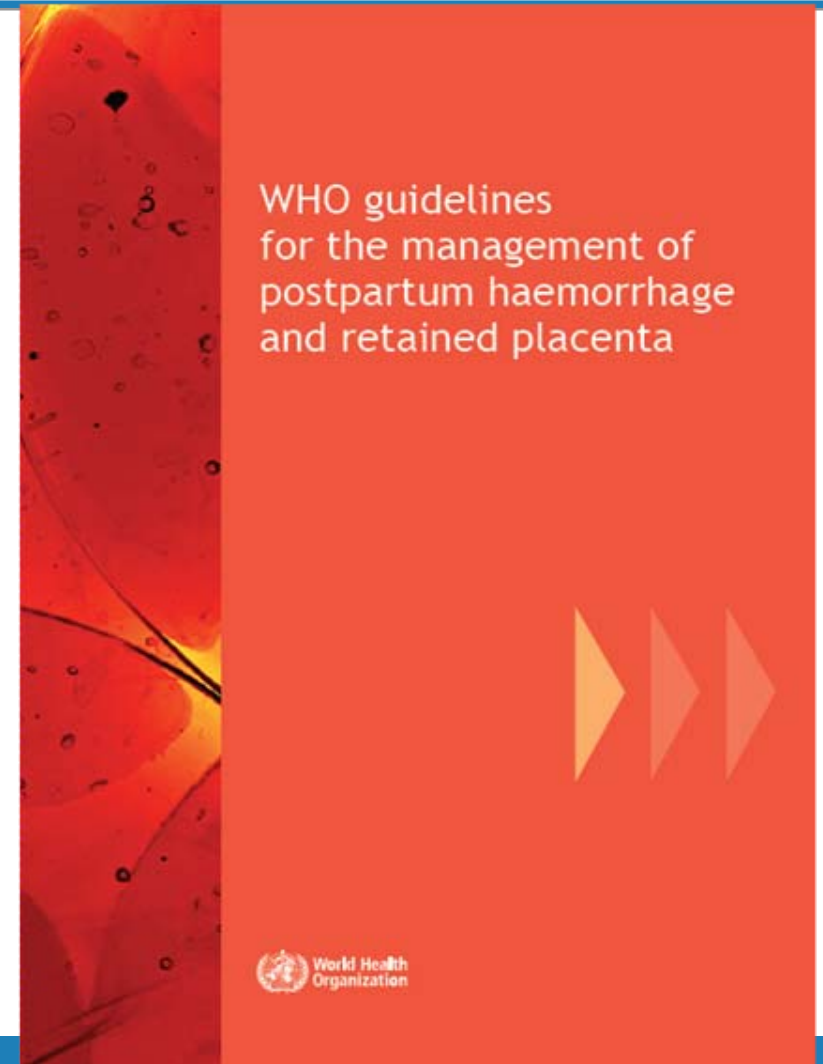
Trial progress

- As of 9 November 2009
 - All 8 countries have started recruitment
 - Egypt started first in July, Argentina last in mid October
 - 5693 Women screened
 - 4045 Women randomized
- Target sample size 24,000



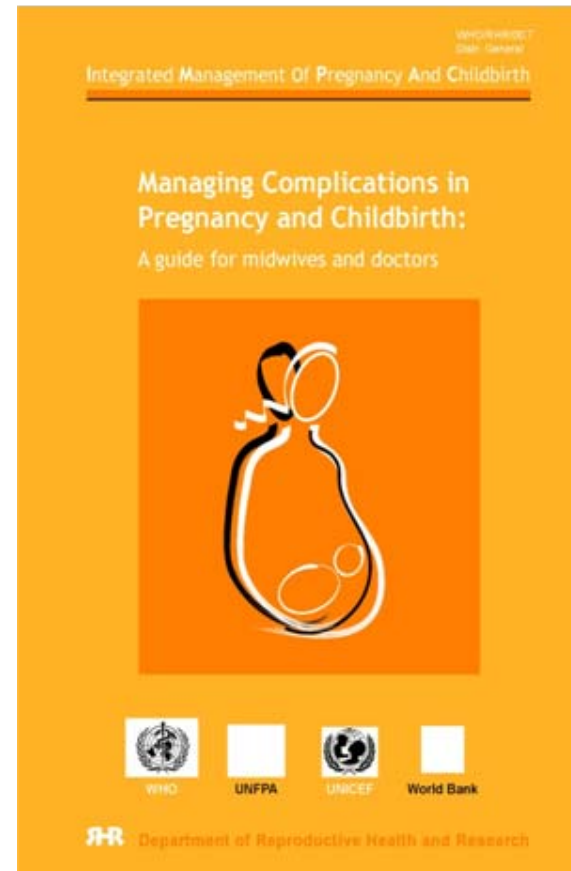
WHO Guidelines for Management of PPH

- 2007-2009
- Following WHO guidelines for guideline development
 - Scoping (Q & outcomes)
 - Search, review
 - Critical appraisal
 - GRADE
 - Guideline panel meeting (18-21 November 2009)
- Published 2009



WHO's Recommendations 2000 - Treatment

- Rapid assessment – IV infusion
- **Oxytocin IM stat + IV infusion**
- Other uterotonics
 - Ergometrine
 - Prostaglandins
- Identify cause of PPH
- Provide appropriate treatment



Misoprostol as an adjunct

- Four trials – over 1800 women who had AMTSL with oxytocin – given adjunct misoprostol 600 – 1000 mcg
- Outcomes
 - Addl blood loss \geq 500 ml (RR 0.83; 95% CI 0.64-1.07)
 - Addl blood loss \geq 1 L (RR 0.76; 95% CI 0.43-1-34)
 - Blood transfusion (RR 0.96; 95% CI 0.77-1.19)
- Recommendations:
 - No added benefit of misoprostol as adjunct treatment in women who have received oxytocin during third stage of labour.
Oxytocin alone should be used (Moderate-high quality; strong)



Misoprostol for treatment

- One large trial – unpublished – 800 mcg misoprostol compared to 40 IU oxytocin – NO AMTSL
- Misoprostol associated with
 - Addl blood loss \geq 500 ml (RR 2.66; 95% CI 1.62-4.38)
 - Receiving addl uterotonics (RR 1.79; 95% CI 1.19-2.69)
 - Temp $>$ 40° C over 13% of women; none in oxytocin
- Recommendation:
 - In women who have not received oxytocin for PPH prevention, oxytocin alone should be offered for treatment (Moderate-high quality; strong)



Additional points

- Oxytocin – higher effectiveness with fewer side effects
- Make oxytocin available where not currently available
- Misoprostol may be used if no other uterotonic is available but safest dose not clear
 - WHO will commission a review on safety of misoprostol



WHO statement on misoprostol for PPH prevention and treatment - 1

- Active management of third stage of labour (AMTSL) with **oxytocin** recommended for PPH prevention
- In the absence of personnel to offer AMTSL, trained health worker should offer 600 mcg misoprostol orally immediately after birth of baby. In such cases **no** active intervention to deliver placenta should be carried out



WHO statement on misoprostol for PPH prevention and treatment - 2

- Misoprostol not included in WHO Model List because:
 - Estimates of efficacy compared with placebo are not consistent across trials
 - Significant risk of increased shivering and fever
 - Unresolved concern about possible increase in risk of maternal mortality
- Not recommended for treatment of PPH – no additional protection
 - Offer only in the absence of other uterotonics or as a last resort
 - Higher temp over 40° C and altered consciousness observed with 800 mcg doses



WHO statement on misoprostol for PPH prevention and treatment - 3

- WHO does not recommend distribution of misoprostol to community level health workers or women and their families for routine or emergency use.
- WHO recommends research at the community-level to investigate how PPH can be managed effectively at this level

