

MISOPROSTOL FOR PPH TREATMENT— WHAT WE KNOW, WHAT WE DON'T KNOW, AND WHAT THIS MEANS FOR PROGRAMS

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WHAT WE KNOW

- **Drug increasingly used & available for PPH treatment**
- **Early stigma about drug lessening; viewed as women's health drug vs. an abortion pill**
- **New supportive data from RCTs; programmatic experience internationally**
- **Some support from major institutions**
 - **RCOG, FIGO, ACOG recommend misoprostol use for PPH treatment in some circumstances**
 - **WHO “third line treatment”**
- **Need update of international recommendations to reflect evidence from 3 large RCTs published in 2010**

MISOPROSTOL FOR PPH TREATMENT: FIVE POSSIBLE SCENARIOS FOR USE

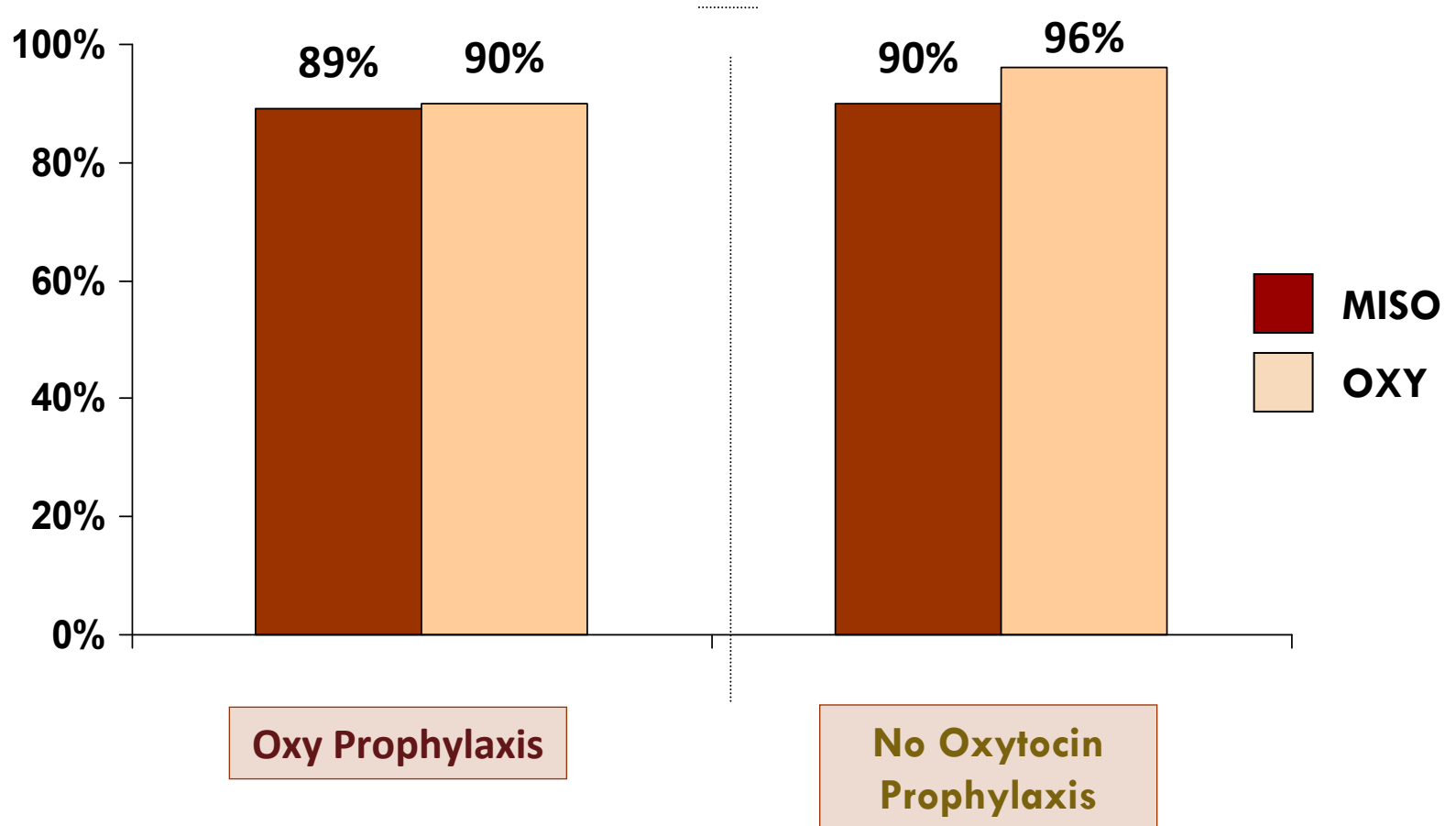
- 1. First line treatment after prophylactic uterotonic**
- 2. First line treatment after no prophylaxis**
- 3. Adjunct treatment**
- 4. Last resort**
- 5. Early liberal treatment**

EVIDENCE FROM TWO RCTS: SCENARIOS 1 & 2

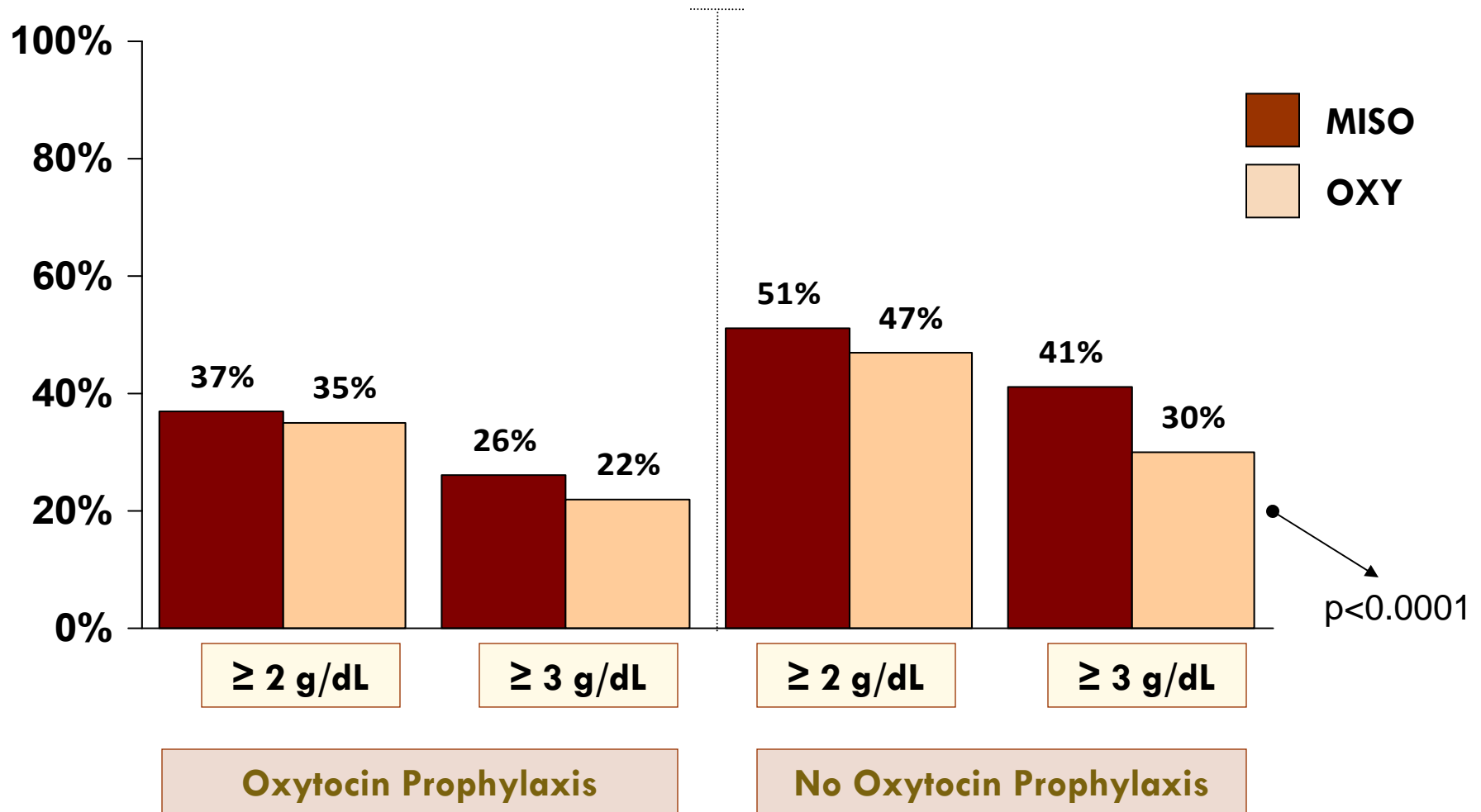
- To determine if 800 mcg sublingual misoprostol **is similarly efficacious to 40 IU oxytocin delivered IV** for the treatment of primary postpartum hemorrhage (PPH)
- Double-blinded, placebo-controlled, RCTs in 2 settings:
 - where women **given oxytocin** in third stage of labor
 - where women **not given oxytocin** in third stage of labor
- More than 40,000 women screened (1,800 enrolled) in 5 countries from February 2005 – January 2008

(Lancet 2010)

ACTIVE BLEEDING CONTROLLED WITH INITIAL UTEROTONIC ALONE



CHANGE IN HEMOGLOBIN



ADDITIONAL INTERVENTIONS & SIDE EFFECTS

INTERVENTIONS:

□ No difference: bimanual compression, hysterectomy, blood transfusion

Oxytocin prophylaxis: No difference in use of addit' uterotonics (10% vs. 12%, NS)

No oxytocin prophylaxis: Misoprostol users more likely to receive addit' uterotonics (13% vs. 6%, $p=0.003$)

SIDE EFFECTS:

Oxytocin prophylaxis: all minimal, no differences between 2 treatments with exception of fever & shivering

No oxytocin prophylaxis: all minimal, vomiting significantly more common with misoprostol, fever & shivering also more common with misoprostol

IMPLICATIONS OF RESULTS

Scenario 1:

- **Misoprostol is clinically equivalent to oxytocin for treatment of primary atonic PPH among women receiving prophylactic oxytocin in 3rd stage of labor**

Scenario 2:

- **Oxytocin is significantly better than misoprostol as 1st line treatment of primary atonic PPH among women *not* receiving prophylactic oxytocin in 3rd stage of labor**
- **In settings in which oxytocin is not feasible, misoprostol might be a suitable alternative 1st line treatment for PPH**

SCENARIO 3: MISOPROSTOL AS ADJUNCT TREATMENT

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

Four studies: Hofemyer, Zuberi, Walraven, Widmer

Summary of results:

- Data show no benefit of simultaneous administration of IV oxytocin + 600 mcg sublingual misoprostol over IV oxytocin alone for treatment of PPH
- Significantly more fever in misoprostol arm

Implication of results: No reason to combine the two drugs as there is no added benefit, but more side effects

SCENARIO 4:

LAST RESORT TREATMENT

- **Little scientific data on efficacy of use of misoprostol as last ditch effort to save woman's life**
- **Not feasible/ethical to do RCTs**
- **Summary of results:** Possible positive effect probably outweighs limits, particularly in low resource settings

IMPLICATIONS

	PROPHYLACTIC OXYTOCIN GIVEN	NO PROPHYLACTIC OXYTOCIN GIVEN
Immediate Treatment of PPH		
IV OXYTOCIN FEASIBLE (1)	Either Drug	Oxytocin Preferred
IV OXYTOCIN NOT FEASIBLE (2)	Misoprostol	Misoprostol
Adjunct PPH Treatment (3)		
	No beneficial effect of Misoprostol	??
Last resort (4)		
	All Drugs++	All Drugs++

SCENARIO 5:

EARLY LIBERAL TREATMENT

- **Is universal prevention needed? Do the costs outweigh the potential benefit?**
- **Does universal prevention save lives?**
- **Would early or “liberal” treatment for some women be more effective both clinically and programmatically?**
- **Data:** To be explored in current grant by Gynuity and partners at UCSF, UIC, in Egypt and India

WHAT WE KNOW

NEW RESEARCH QUESTIONS

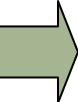
- Miso use is associated with fever.
- Miso has been shown to be effective in hospital settings.
- Miso has been shown to work for prevention or txt of PPH.
- Miso, Uniject®/oxy and components of AMTSL have been shown effective in PPH prevention.

- Can a lower dose maintain efficacy & lower side effects?
- Can miso be effective in community-based settings?
- Can miso be used for both prevention & txt of PPH?
- What is the relative impact of each of these interventions?

GAPS IN EVIDENCE

- **Is misoprostol's safety profile acceptable for widespread to treat PPH?**
- **More information/service delivery models to ensure functioning/timely referral systems for women needing additional care after misoprostol txt**
- **Better guidance/evidence on training & monitoring to ensure correct use of drug More programmatic experience**
- **Data showing that misoprostol programs save lives**

WHAT THIS MEANS FOR PROGRAMS

- **Providers have evidence supporting use of sublingual misoprostol (800 mcg) for txt in certain circumstances other non-evidence based regimens still being used advocacy efforts should educate providers/policy makers on evidence-based regimens** 
- **More OR/completion of ongoing research to understand safety of self-administration/community use of misoprostol for PPH**

WHAT THIS MEANS FOR PROGRAMS

- **Program managers and policymakers need to be prepared to respond to questions as to why misoprostol recommended by some and not others**
- **Providers and policymakers should advocate for making both oxytocin and misoprostol more widely available, as they both have their advantages under certain circumstances**
- **New recommendations for use and for best regimens likely to emerge in consideration of recent evidence**



Thank you.