

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

**Beverly Winikoff
Addis Ababa
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Why miso for PPH ?

- ❖ PPH is leading cause of maternal death
- ❖ Conventional uterotonics for PPH often unavailable, not feasible or not properly stored, particularly in rural settings
- ❖ Misoprostol offers several advantages:
 - Safe, evidence-based potent uterotonic
 - Affordable, often easily available
 - Easy administration
 - No refrigeration required

WHAT WE KNOW

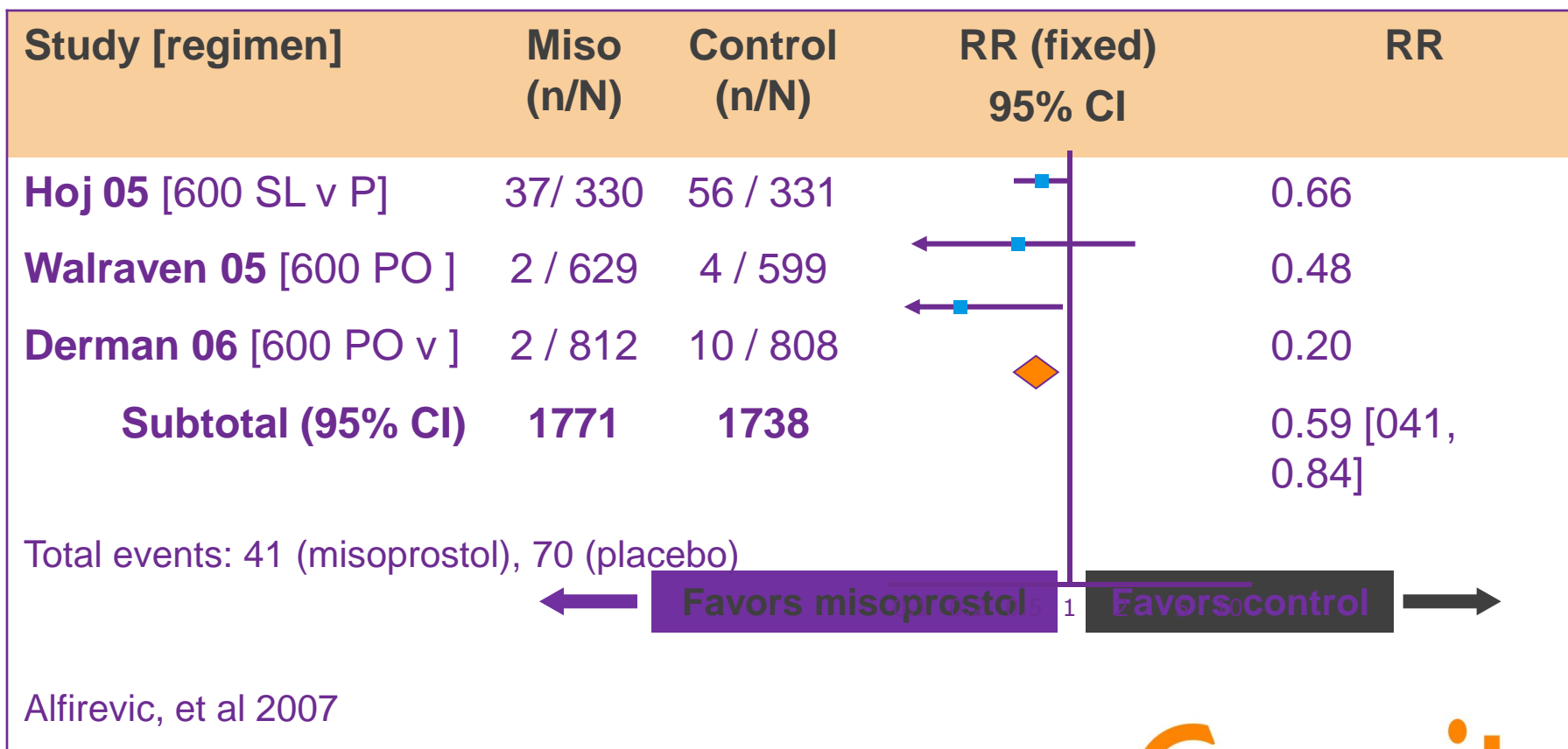
- **Drug is increasingly used and available for treatment of PPH**
- **Now seen more as a women's health drug vs an abortion drug**
- **New body of supportive data from RCTs and programmatic experience internationally**
- **Support from major institutions including FIGO, RCOG, ACOG**
- **WHO “third line treatment”**

PPH PREVENTION: MISOPROSTOL

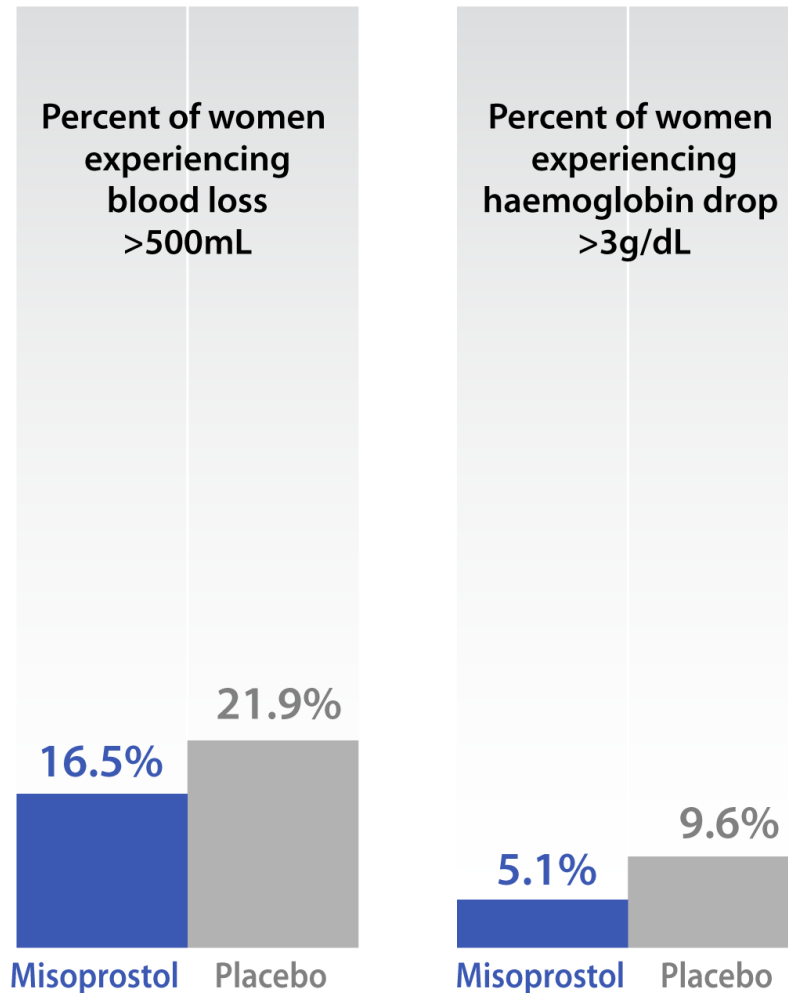
- ❖ Hospital-based RCT data show that misoprostol prophylaxis results in 4% rate of blood loss ≥ 1000 mL & oxytocin results in 3% rate (Gulmezoglu 2001)
- ❖ Four community-based trials show a reduction of 24-50% in PPH (blood loss ≥ 500 mL) with misoprostol prophylaxis



Misoprostol for PPH prevention: Community-based RCTs



PPH PREVENTION



Misoprostol compared to nothing reduces bleeding after childbirth.

Summary

- ❖ Safe and effective for PPH prevention in community settings
- ❖ Providers at all levels can be trained to use it
- ❖ Logistical advantages in community settings
- ❖ Oxytocin is preferred but misoprostol can fill gaps, particularly in rural areas
- ❖ To date, no comparative studies on misoprostol vs. oxytocin in PHCs or home delivery settings

SCENARIOS FOR USE OF MISO FOR PPH TREATMENT

- ❖ First line treatment after prophylactic uterotonic
- ❖ First line treatment after no prophylaxis
- ❖ Adjunct treatment
- ❖ Last resort
- ❖ Secondary prevention/Early liberal treatment

Is 800 mcg s/l miso as efficacious as 40 IU oxy IV for the treatment of PPH ?

- ❖ Two double-blind RCTs in hospitals with
 1. oxytocin prophylaxis in 3rd stage of labor
 2. no oxytocin prophylaxis
- ❖ Primary outcomes: bleeding cessation in 20 min and additional blood loss after treatment
- ❖ > 40,000 women screened

Study Treatments

800 mcg misoprostol
sublingual

40 IU oxytocin IV

Active drug

Placebo

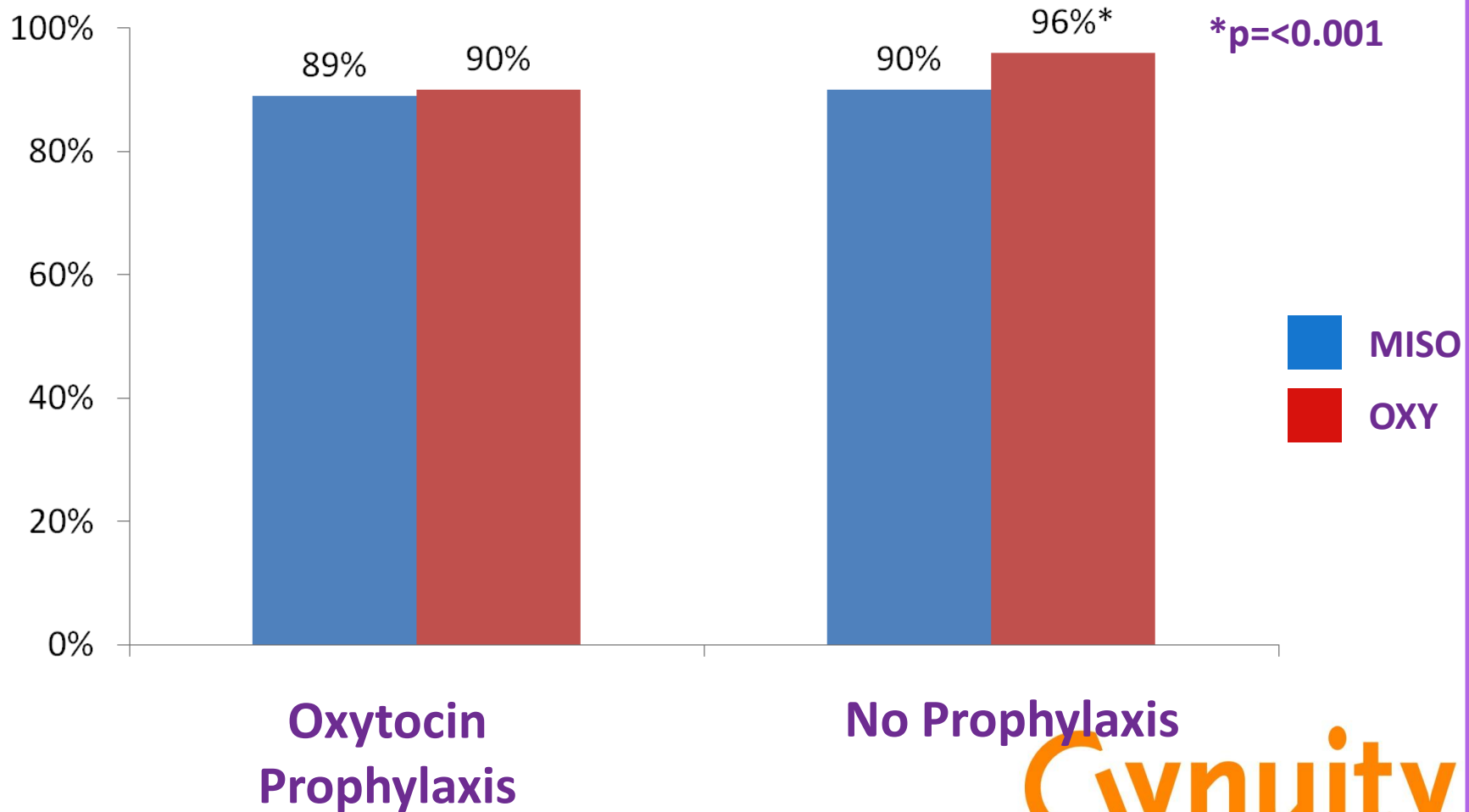


Placebo

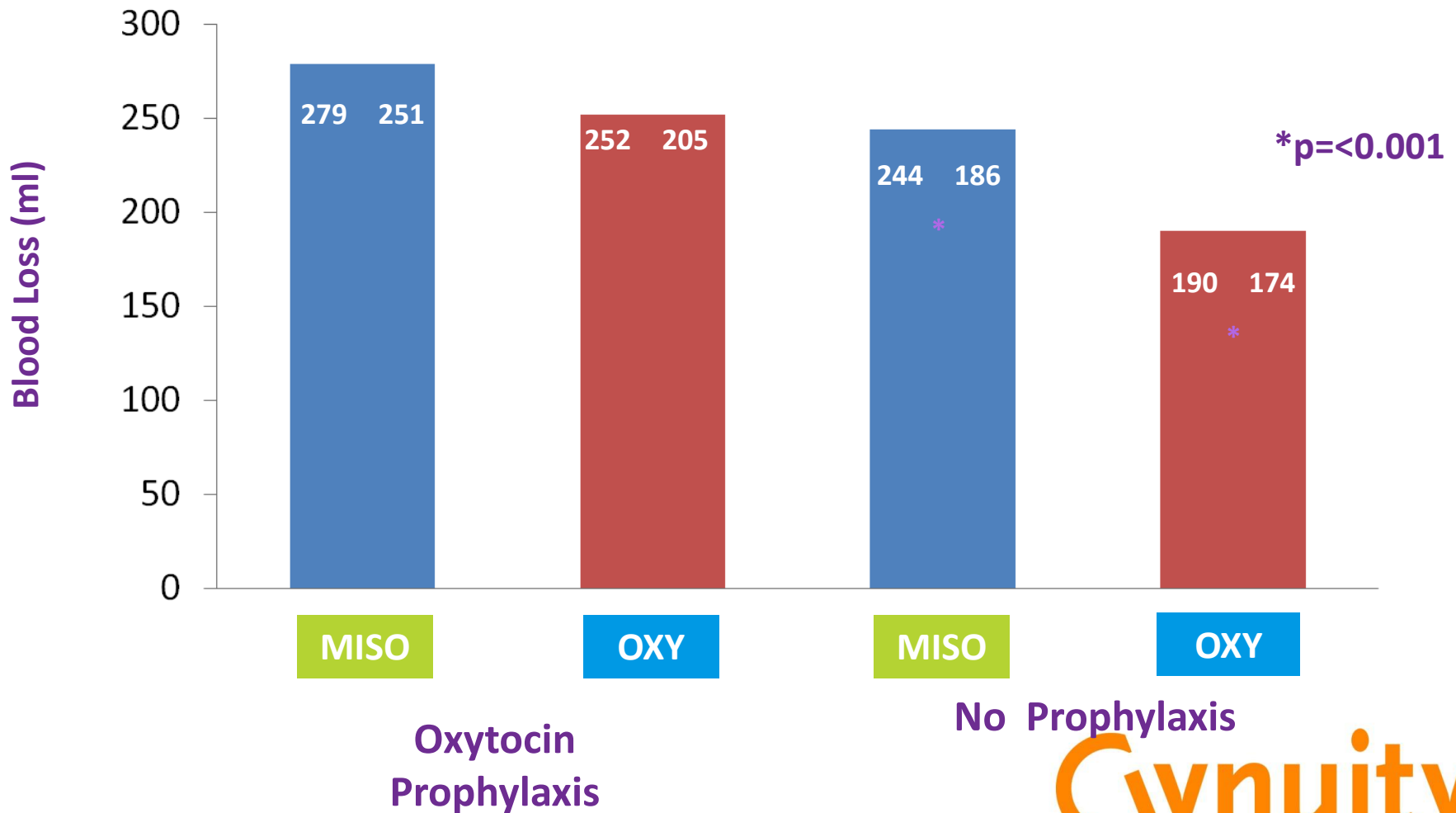
Active drug



Bleeding Controlled with Initial Rx Alone



Blood Loss (mL) After Rx



Summary of Results

- ❖ Oxytocin prophylaxis: Misoprostol worked similarly to IV oxytocin
- ❖ No oxytocin prophylaxis: Oxytocin worked slightly better than misoprostol (96% vs. 90%)

Misoprostol is a good alternative when oxytocin is unavailable or not feasible to use

SERVICE DELIVERY IMPLICATIONS

	Model 1 – No prophylactic uterotonics	Model 2 – Oxytocin prophylaxis
Deliveries	1000	1000
PPH prophylaxis	None	10 IU OXY
Women with PPH (#) PPH rate (%)	100 10%	30 3%
Treatment options	IV OxyMiso	IV OxyMiso
Bleeding controlled	9690	2727
Additional interventions	410	33

MISOPROSTOL AS ADJUNCT TREATMENT

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 when miso added to oxy

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

Widmer et al, 2010

LAST RESORT TREATMENT

- ❖ Approx 9 case reports in the literature: little science on efficacy 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

Secondary Prevention, Early Treatment

- ❖ Is universal prevention needed? Do the costs outweigh the potential benefit?
- ❖ Does universal prevention save lives?
- ❖ Would early treatment for some women be more effective both clinically and programmatically than prophylaxis for all?

*To be explored by Gynuity and partners at
UIC, UCSF, Egypt and India*

Total Cohort

1,000

Scenario 1

600 mcg of
misoprostol
prophylaxis

Scenario 2

No PPH
prophylaxis

Blood loss

700 mls expected¹

4.7%

n= 47

9.5%

n= 95

PPH Treatment

women expected to stop bleeding with
800 mcg miso

90%²

n= 42

90%³

n= 86

**Additional care to stop
bleeding**

(e.g. uterotonics, referral, hysterectomy)

10%

n= 4

10%

n= 9

**Additional care to manage
fever/chills**

?

Expected to be
manageable

1,000 women given
misoprostol
4 may need additional care
3,288 pills administered

95 women given misoprostol
9 may need additional care
380 pills administered

1. Pakistan Prevention Trial, unpublished

2. Blum, et al 2010

3. Winikoff, et al 2010

Knowledge Gaps Remain

- ❖ Do miso and oxy-in-Uniject provide equal benefit for equal cost in field programs?
- ❖ Is IM oxy as effective as IV oxy for prophylaxis and treatment?
- ❖ Is 800 mcg sublingual miso appropriate for lower-level health facilities/ home births?
- ❖ Would a lower sublingual treatment dose be as effective as 800 mcg with fewer side effects?
- ❖ Will misoprostol work well for PPH treatment if it was used prophylactically?

WHAT ALL THIS MEANS FOR PROGRAM NEEDS

- ❖ New recommendations based on recent evidence
- ❖ Broader consensus to minimize confusion on recommended dose, routes, and ideal role
- ❖ Operational research to demonstrate programmatic effectiveness of misoprostol for PPH care including self-administration
- ❖ Investigation of alternative ways to use misoprostol, minimizing side effects, cost, overtreatment

New Activities

Gynuity Health Projects is implementing a 5-year grant from the Bill & Melinda Gates Foundation to answer remaining scientific questions around PPH and misoprostol and to develop the policy approaches best suited to making this technology available to women

PROJECT FRAMEWORK

Implementation of policy models
that will lower maternal mortality



OUR PARTNERS

- ❖ Aga Khan Development Fund
- ❖ Family Care International
- ❖ U of Liverpool
- ❖ PATH
- ❖ Population Services International
- ❖ FIGO
- ❖ University of Illinois, Chicago/UCSF
- ❖ Guttmacher Institute
- ❖ Hospitals, providers, advocates & networks globally
- ❖ Research advisory group members

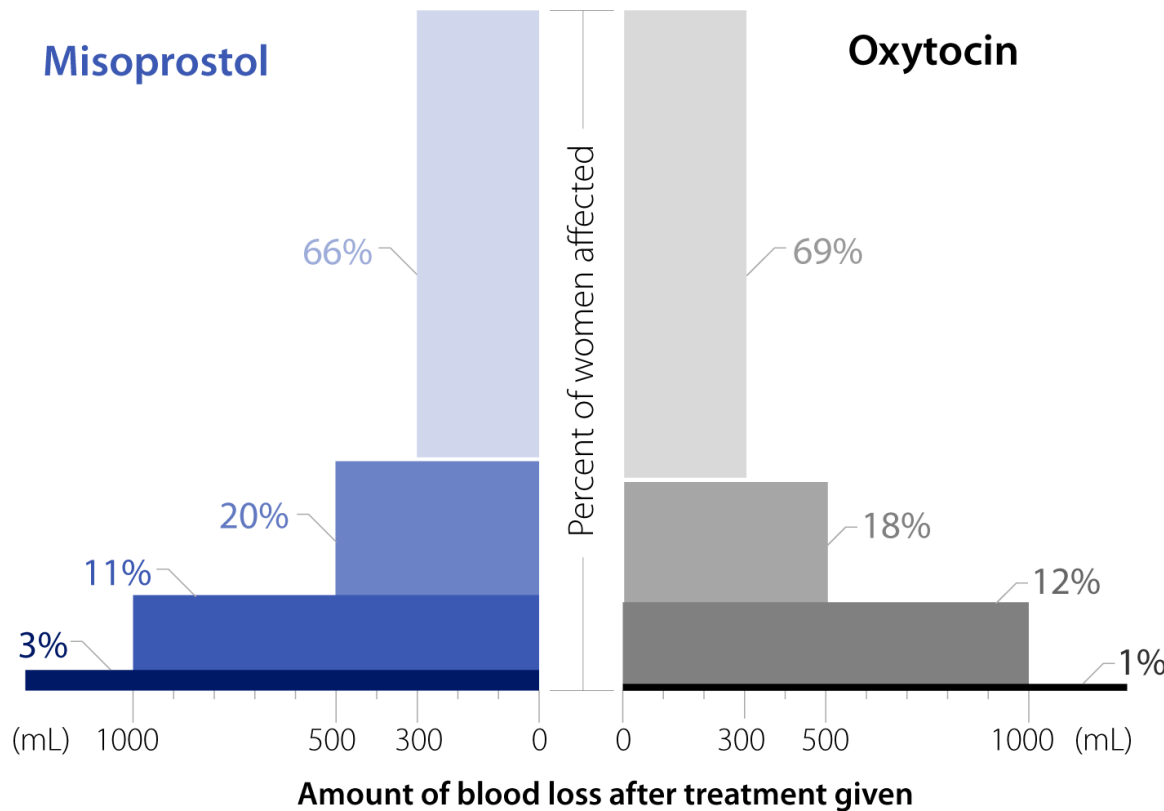
Thank you!

Side effects following oral misoprostol

- ❖ Shivering and fever most common side effects
- ❖ Reported rates of shivering and fever vary greatly – e.g. shivering 18-71%, fever 1-38%
- ❖ High fevers ≥ 40.0 infrequent following its prophylactic use (0.1%; 10/10,000)
- ❖ Studies show side effects are transient, easily managed by providers and tolerated by women
- ❖ No adverse effects on misoprostol on breastfed neonate have been reported

What We Know

PPH TREATMENT

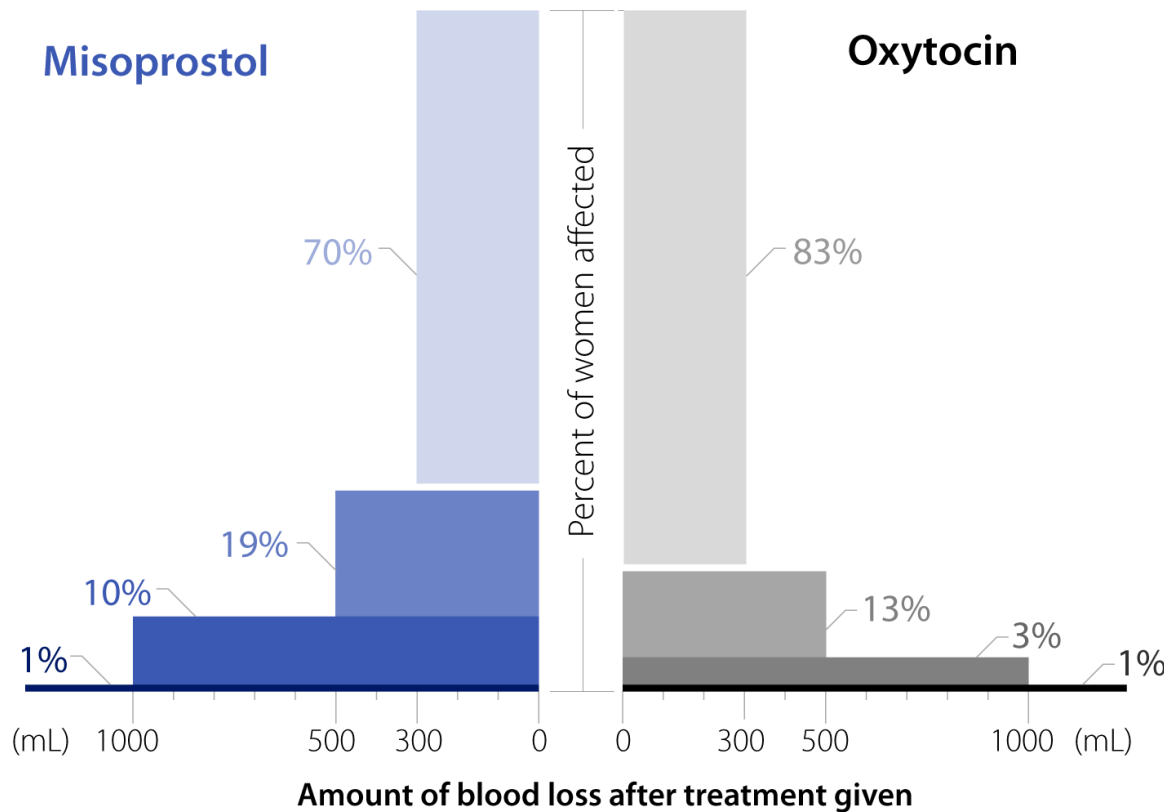


Misoprostol vs. Oxytocin for PPH Treatment When Prophylactic Oxytocin is Administered

If oxytocin has been administered for prophylaxis, oxytocin and misoprostol are clinically equally effective for treating PPH.

What We Know

PPH TREATMENT



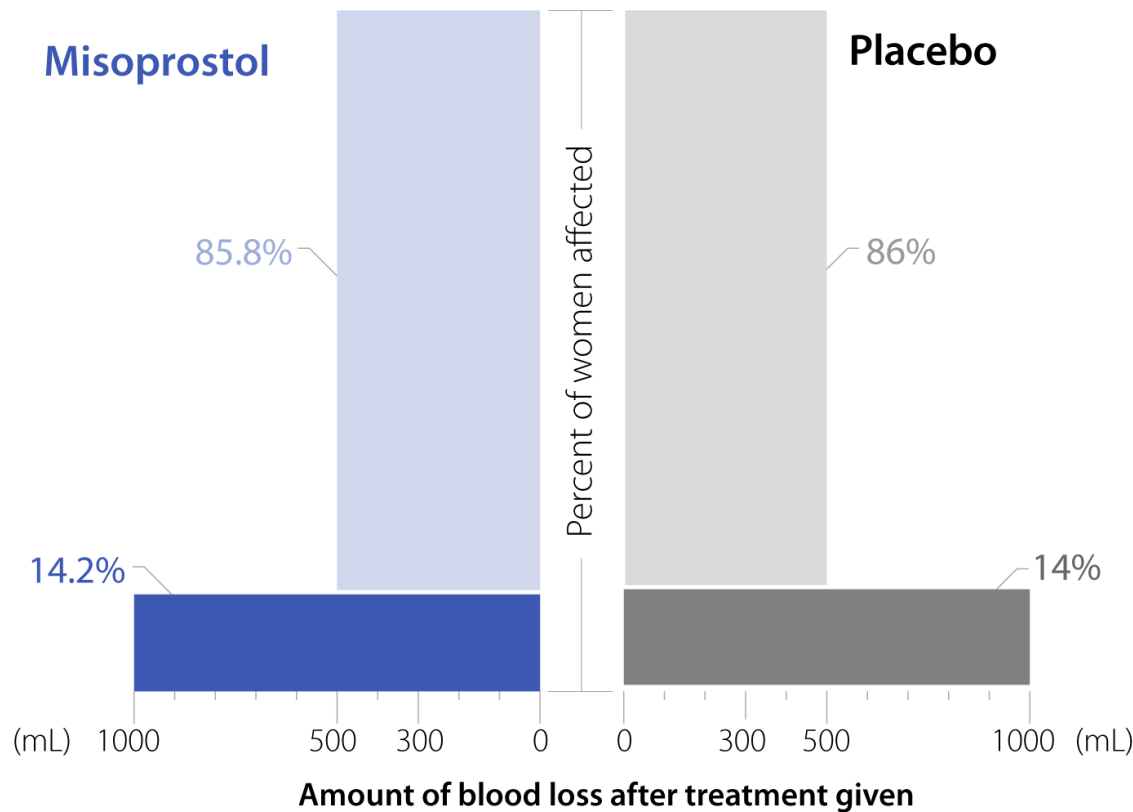
Misoprostol vs. Oxytocin for PPH Treatment When No Prophylactic Oxytocin is Administered

If no prophylactic oxytocin has been administered, oxytocin is the preferred treatment for PPH.

Misoprostol is almost as effective as oxytocin, and can be used if oxytocin is not available.

What We Know

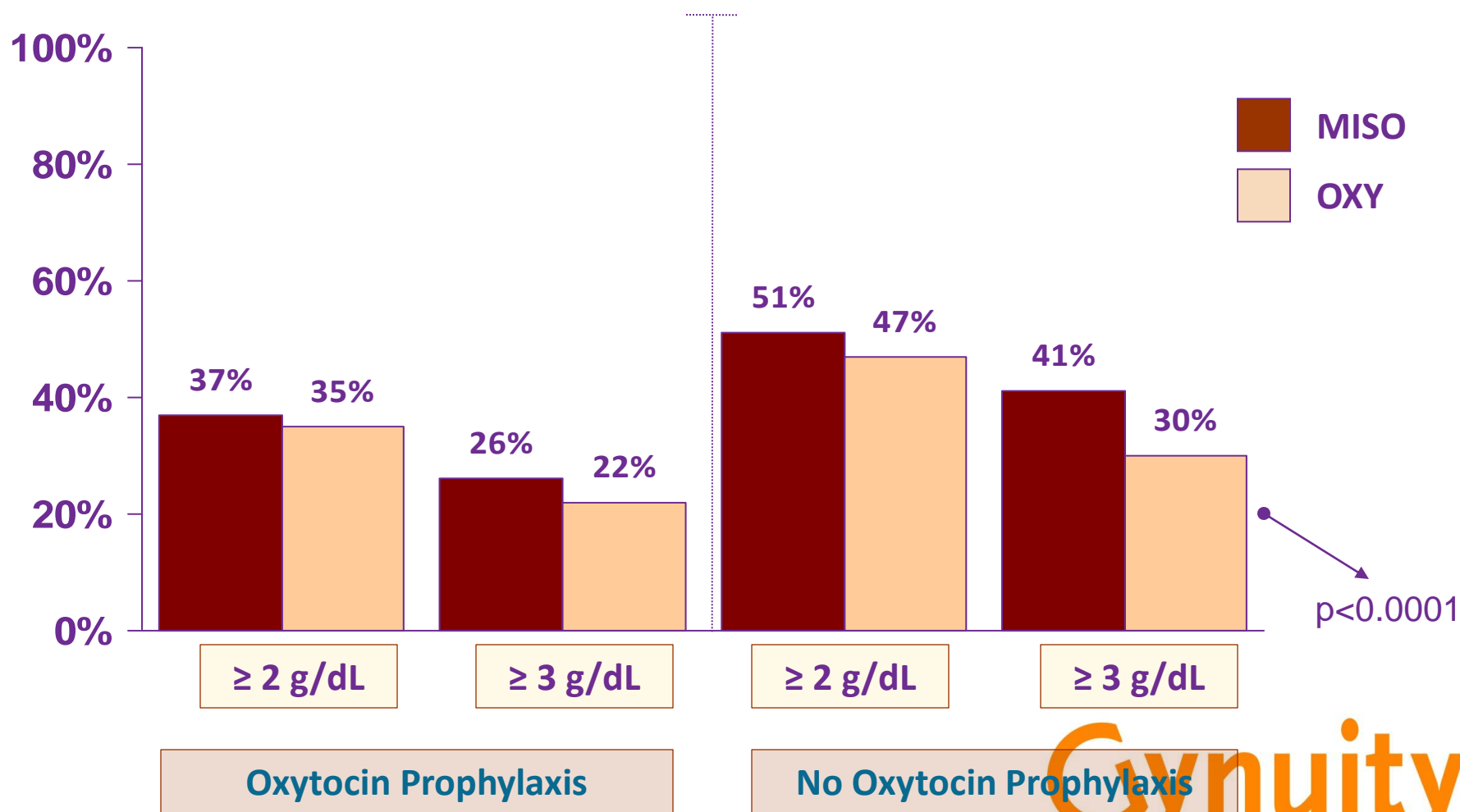
PPH TREATMENT



Misoprostol as Adjunct to Standard Uterotonics for Treating PPH

For treatment of PPH, use oxytocin or misoprostol, not both.

CHANGE IN HEMOGLOBIN



IMPLICATIONS

	PROPHYLACTIC OXYTOCIN GIVEN	NO PROPHYLACTIC OXYTOCIN GIVEN
Immediate Treatment of PPH		
IV OXYTOCIN FEASIBLE	Either Drug	Oxytocin Preferred
IV OXYTOCIN NOT FEASIBLE	Misoprostol	Misoprostol
Adjunct PPH Treatment		
	No beneficial effect of Misoprostol	Gynuity HEALTH PROJECTS
Last ditch effort		