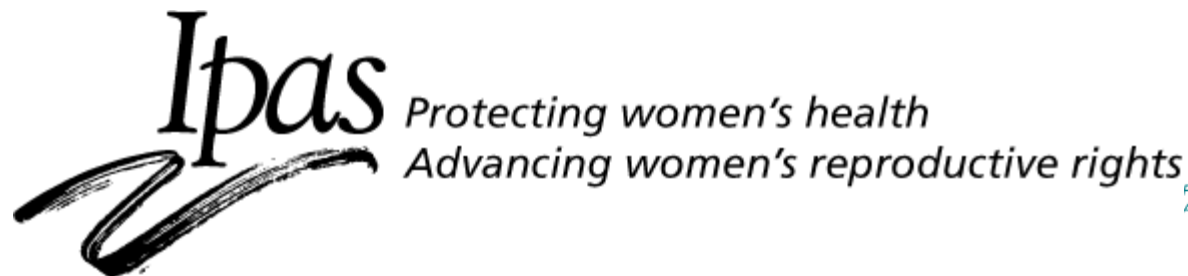


Medical Abortion- Overview of the *Clostridium* infections and American practice

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Protecting women's health
Advancing women's reproductive rights

Context

These data were collected when I worked for Planned Parenthood Federation of America.

The global context is not the same as the US context since there have been no reports of infection-related deaths outside the U.S.

Review of quality data is local to your population.

Clostridia sordellii

Clostridium sordellii is a gram-positive anaerobic spore-forming Bacillus that typically resides in soil. It colonizes the gastrointestinal and genital tracts of approximately 0.5% of healthy humans.

Immediately after childbirth or abortion, the rate of *C. sordellii* colonization may be as high as 29%.¹

Goplerud, Ohm, Galask. Aerobic and anaerobic flora of the cervix during pregnancy and the puerperium. Am J Obstet Gynecol 1976; 126:858-68.

Clostridium sordellii

The virulence and clinical manifestations of *C. sordellii* are determined by two cytotoxins: lethal toxin and hemorrhagic toxin.

Some *C. sordellii* strains are more lethal than others.

Fatal Toxic Shock Syndrome associated with *Clostridium sordelli* after medical abortion in the U.S.

- 8 deaths in the U.S. (4 from California)
- Young, previously healthy women; death within 7 days after medical abortion (one case after 12 days)

Fisher M et al. *NEJM* 2005, 353:22

Cohen et al. *Obstet & Gynecol* 2007, 1027-1033

Ho et al. *Am J Obstet & Gynecol* 2009, 459e1-7

Mietes, Zane, Gold. *NEJM* 2010, 1382-1383.

Clostridium deaths –U.S.

<u>Organism</u>	<u>misoprostol route</u>	<u>antibiotics</u>
1. <i>C. sordellii</i>	vaginal	no
2. <i>C. sordellii</i>	vaginal	no
3. <i>C. sordellii</i>	vaginal	no
4. <i>C. sordellii</i>	vaginal	no
5. <i>C. perfringens</i>	vaginal	no
6. <i>C. sordellii</i>	buccal	no
7. <i>C. sordellii</i>	vaginal	no
8. <i>C. sordellii</i>	vaginal	no

C. Sordellii Fatal TSS

Notable clinical features

- absence of fever and rash
- Woman feels very ill (nausea, vomiting abdominal pain, diarrhea)
- dramatic leukemoid reaction (WBC 45-120,000)
- marked edema of infected tissues without gas
- Absence of retained POC

Fisher M et al *NEJM* 2005, 353:22

C. Sordellii Fatal TSS

Toxin cascade causes profound capillary leak syndrome:

Essentially, fluid leaks out of the blood stream through the capillaries. "And all that's really left are circulating red blood cells and elevated white count".

Results in:

- Low BP, high hematocrit, tachycardia
- Third-spacing (abdominal pain)
- Adult respiratory distress syndrome
- Multi-organ failure

Rate of Serious Infection at Planned Parenthood Clinics when misoprostol was administered vaginally and no antibiotics were given

Serious infections 1/1000 (0.1%)

Definition of serious infection:

- Fever with pelvic pain- treated with I.V. antibiotics in ER
- Inpatient admission for treatment of infection
- Sepsis (+ blood culture) or organ removal due to infection
- Death caused by infection

Feasibility of a RCT of antibiotics and serious infection

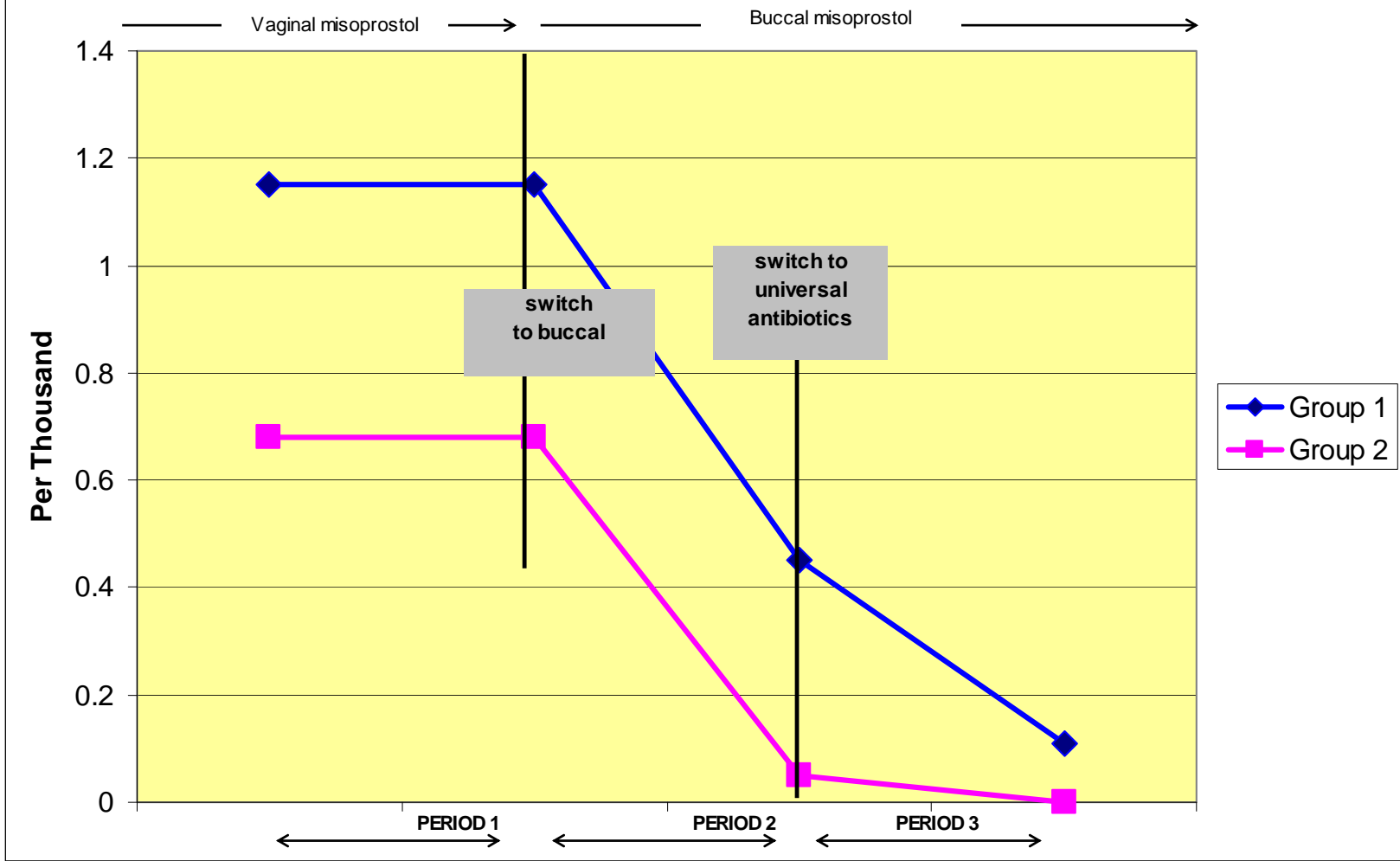
- PPFA met with scientists for two years
- Formally consulted with CDC
- RCT was not feasible

Planned Parenthood Changes in Regimen for Medical Abortion

	Period			
	1	2	3	4
	Jan '05 – Mar '06	Apr '06 – Jun '07	Jul '07 – Dec '07	Jan '08 – June '08
Misoprostol Route	Vaginal	Buccal	Buccal	Buccal
Maximum days of gestation	63	56	56	63
Number of infections/ Rate per 1000	67 0.93	20 0.25	2 0.06	3 0.07
Infection prevention	No standardized approach- no antibiotics	STI screen and treat <u>or</u> Doxy x7d	Doxy x7d	Doxy x7d
N =	72,195	78,794	33,468	43,366

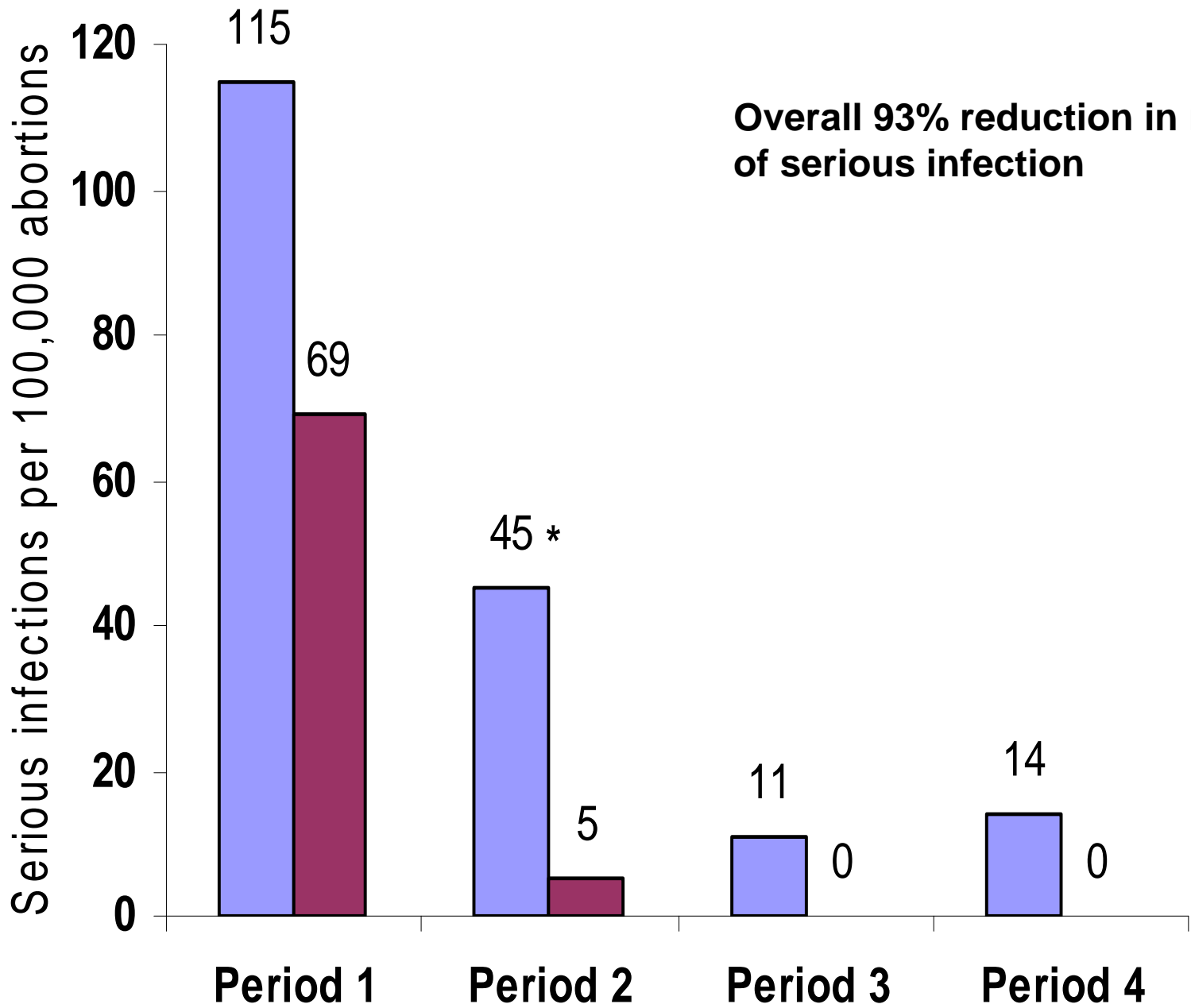


Rate of Serious Infection



Group 1- STI testing in Period 2

Group 2- antibiotic coverage in Period 2



Overall 93% reduction in rate of serious infection

Group 1
Group 2

What was the contribution of change in route from vaginal to buccal misoprostol versus antibiotics?

Minimum effect Maximum effect

Buccal	0%	67%
Antibiotics	33%	100%

Why have *Clostridium* deaths been reported only in North America?

- Unknown
- Hypothesis that the lethal toxin of *Clostridium* has mutated in North America

Why do Planned Parenthood data show a higher rate of serious infection following medical abortion than previously reported?

- Active surveillance
- Rigorous reporting system
- Clear definition of serious infection



Conclusions

We don't know if 7 days of doxycycline will prevent a future *Clostridium* death.

Gynuity study underway will provide more evidence about *Clostridium* colonization and whether doxycycline is protective.

There has not been a death or surgery to remove infected organ among >310,000 women who have received the new regimen.

Each country/ organization has to analyze its data and provide the regimen they find to be the safest and most effective.

There is no evidence elsewhere in the world that the vaginal route of misoprostol contributes to a higher rate of serious infection or that antibiotics are warranted.