
Diaphragm Renaissance Meeting – The Role of Cervical Barriers

Research/Trials

Our goals

- ◆ Provide acceptable level of protection against cervically-acquired HIV/STIs
- ◆ Provide acceptable (or at least known) contraceptive effect

What is the research question?

- ◆ Are we testing the effect of adding a mechanical barrier to a microbicide; or
- ◆ Are we testing the effect of adding a microbicide to a mechanical barrier?

Possible arms

		Microbicide	
		Yes	No
Mechanical barrier	Yes	Barrier + microbicide	Barrier "alone"*
	No	Microbicide alone	"Nothing"***

* Barrier "alone" = nothing vs. saliva/household product vs. marketed lubricant?

** "Nothing" = nothing vs. saliva/household product vs. marketed lubricant vs. condoms only?

Is a barrier “alone” likely to “work?”

- ▶ Advantage: barriers are available
- ▶ Barriers probably move around, especially those held in place by “wedge fit” or cling
 - PSA results
- ▶ Spermicide probably augments contraceptive effect of barriers
 - Barrier with non-spermicide results
- ▶ Mechanical barrier may best function as “holder” for chemical barrier
 - Increases the complexity of trial, use, and supply

Is microbicide alone likely to “work?”

- ◆ Mechanical barrier will almost certainly improve effectiveness

Possible arms

		Microbicide	
		Yes	No
Mechanical barrier	Yes	Barrier + microbicide	Barrier "alone"*
	No	Microicide alone	"Nothing"***

Test barrier + microbicide against nothing?

Effectiveness endpoints

- ◆ Non-HIV STIs
- ◆ HIV

Non-HIV STIs HIV

Male-to-female only?

Safety endpoints

- ◆ UTI
- ◆ BV
- ◆ TSS - use in menses bad or helpful, effect of prolonged wearing and difficult cleaning
- ◆ Mechanical trauma and resulting epithelial damage and inflammation
- ◆ Interference with lubrication of lower tract and delivery of immune defense products to it

Acceptability

- ◆ Will women at high risk of HIV use mechanical barriers?
 - ▶ Promising results in
 - 3-country study
 - Nairobi
 - Zimbabwe
 - Mombasa

Acceptability questions

- ◆ Effect of need to add chemical barrier
- ◆ Effect of living conditions and amenities
- ◆ Effect of sexual frequency on acceptability
- ◆ Effect of partner ability to detect

Unknowns (need to be studied?)

- ◆ Effect of preexisting infection/inflammation (BV, STIs) on safety and effectiveness
- ◆ Lack of protection of urethral orifice
- ◆ Effect hormonal status (cycle phase, menopausal status, use of exogenous hormones)
- ◆ Effect of age (adolescents)
- ◆ Effect of general health of woman and her living conditions

Which barrier?

◆ Desirable features:

- ▶ Available - simplifies regulatory process
- ▶ One size - simplifies trial, provider training, use, and supply. Makes OTC possible.
- ▶ Non-latex - reduces risk of allergy, improves durability, allows for greater variety of lubricants
- ▶ Easy to clean - more convenient, safer
- ▶ Reusable - reduces cost, logistics, and environmental impact
- ▶ Discreet both in use and not in use

Scorecard (all are reusable, none are totally discreet)

	Std	Milex	Lea	Cerv cap	Fem Cap	PATH/SILCS	Oves
Available	✓	✓	✓	✓			
One size	Poss*		✓			✓	
Non-latex		✓	✓		✓	✓	✓
Easy to clean	✓					✓	

* CONRAD/FHI study should shed light on this

Trial design issues in common with microbicide studies

- ◆ Sample size
- ◆ Expected attrition
- ◆ Length of follow-up
- ◆ How to assess compliance (with use of 2 products?)
- ◆ Need for multiple trials
- ◆ Cost, funding

Issues unique to mechanical barrier studies

- ◆ Insertion of gel:
 - ▶ With insertion of barrier
 - On one or both sides?
 - ▶ Additional amount if first coital act is delayed?
 - ▶ With additional acts?
 - ▶ How much to use at each time point?
- ◆ How long to leave in? Minimum for effectiveness (3 days?), maximum for safety
- ◆ How to clean and store?

Summary

- ◆ Decide on research questions -- > #arms
- ◆ Decide on endpoints (effectiveness, safety, acceptability)
- ◆ Decide whether to study unknowns
- ◆ Decide which barrier
- ◆ Address usual questions of sample size, duration of follow-up, compliance, etc.
- ◆ Address use issues unique to mechanical barrier studies