Female-controlled physical barrier methods

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Female Condoms

Biological plausibility:

- Covers cervix, vagina,vulva
- Polyurethane sturdier than latex
- Impermeable (*in vitro* data on passage of HIV, bacteria, sperm)
- Pregnancy rates comparable to male condoms

Reality

Status of research:

- 3 STI prevention RCT * : no effect
- No HIV trials conducted
- Novel designs:

PATH

Reddy

* Fontanet, 1998; Feldblum, 2002; French, 2002

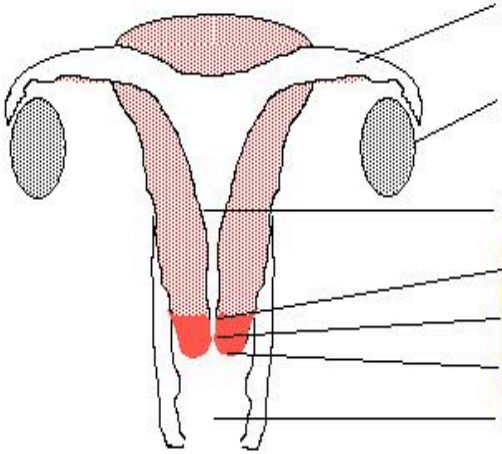
Protecting the cervix should reduce infection risk

The cervix is:

- The initial site of many STIs
- Likely site for most HIV infections
- Fragile columnar epithelium
- Guarding the upper genital tract

Hussain et al., Immunology 1995; Pudney et al., 1997; Zhang et al., J.Virol. 1998; Patterson et al., AIDS Intl. Conf. 1998; Wira, C. WHIN symposium, UCSF, May 24, 2004

HIV-1 INFECTABLE CELLS ARE CONCENTRATED IN THE CERVIX[1]



	HIV-1 Host Cells[2]			*HIV-1 Coreceptors*	
	T	Mϕ	LC	CCR-5	CXCR4
Fallopian Tube	+	+	-	+	+
Ovary	+	+++	-	±	±
Endometrium	++	++	-	+	+
Endocervix	++	++	-	+++	+
Transformation Zone	+++	+++	+	+++	++
Ectocervix	++	++	+	++	+
Vagina	+	+	+	±	+

[1]Healthy women without evident genital tract infection

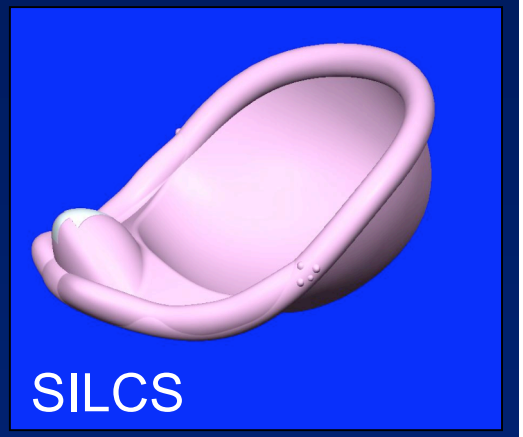
[2]T-CD4+ T lymphocytes, Mϕ -Macrophages, LC-Langerhans Cells

Cervix

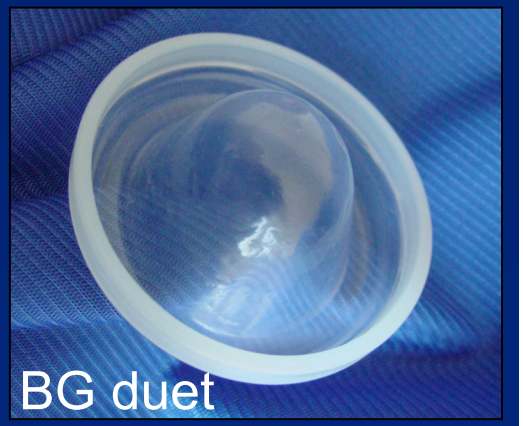
Not all cervical barrier methods are created equally…

Commercially available, approved methods

Novel designs:



SILCS



BG duet

Current status of research on CB

Number	Devices	Gel	Study design / endpoint	Status	Location
1	Diaphragm	Replens	Phase III HIV/STI	Ongoing	RSA, Zimbabwe
2	Diaphragm	none Acidform	Phase III STI	Planned(07) Planned(07)	Madagascar
4	Diaphragm	none Acidform Acidform/Bgel CS	Safety	Completed	Kenya RSA US Zimbabwe
1	BG duet	BufferGel	Safety	Completed	US, Dom. Rep
2	SILCS SILCS/Ortho	K-Y Jelly	Acceptability	Completed Completed	RSA, Thailand Dom. Rep.
3	Diaphragm (+ female condom)	K-Y Jelly	Acceptability	Completed Completed Ongoing	Kenya Zimbabwe Dom. Rep.
1	Diaphragm SILCS FemCap	-	pilot feasibility/ acceptability	Ongoing	Zimbabwe
Contraceptive studies					
1	Diaphragm	Buffergel	Phase III Contraceptive	Completed	US
1	SILCS	CS or N9	Phase III Contraceptive	Planned(07)	US

Outstanding research questions:

Cervical barrier research should not hinge on 1 product & 1 study

Basic science

- Role of cervix and upper genital tract in HIV acquisition
- Effect of cervical barrriers on innate vaginal immunity

Clinical/behavioral sciences

- Role of cervical barriers in decreasing F → M transmission?
- Test different devices: all physical barriers, yet effectiveness may vary
- Test in different populations (i.e. youth, Asia/ latin America)
- Examine issues related to fit, duration of use, episodic vs continuous use

More research on combination methods (CB+ microbicide)

- Enhanced efficacy
- Delivery and retention of gel (dosage; cervical side vs vaginal side)
- Acceptability and feasibility of use

Challenges in Design and Analysis: (1) male condom promotion

- Effects study incidence in all studies
- Women most in need of FCM are likely not to participate, because condom use is part of study intervention

Especially problematic in open-label design:

- Intensity of condom counseling (Same across arms? Same as country-level standards?)
- Need to consider a range of designs and analytic techniques, which take into account:
  - Condom use may not be independent from use of the test product
  - Both condom an product use are time dependant
  - The estimate of the direct effect of the product, which has key public health significance, is complicated by condom use
  - How to measure the relative effect of the product compared to that of condoms, which is another essential public health message.

Challenges in Design and Analysis: (2) Product adherence and measurement

- Most challenging in open-label designs
- Coital dependency (could decrease adherence)
- Varies over time
- No DOP (directly-observed prevention) for condoms or test products: rely on self-report of private behavior
  - Biological markers of adherence
  - Novel methods of self-report (electronic diaries, etc..)
  - Devices with computer chips that register use (e.g. body Temp, pH)

Thank you!