Female Barrier Methods
6th International Workshop on HIV & Women

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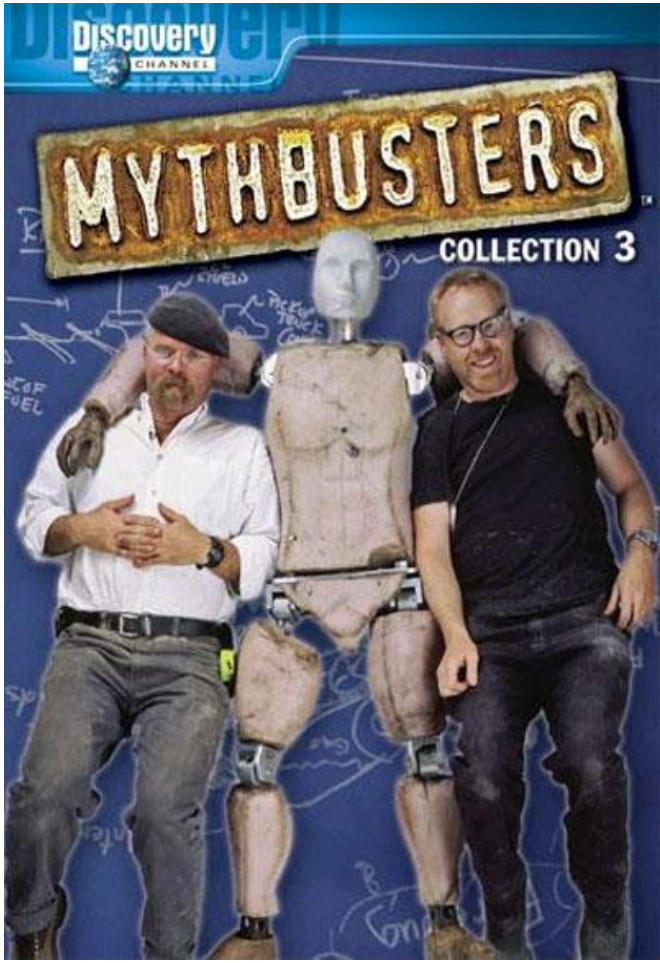
Resurgence of Interest in Barrier Methods for Dual Protection

- Recognition of the importance of dual methods that can prevent both pregnancy and sexually transmitted infections (STIs), including HIV;
- Evidence that cervical barriers provide good contraceptive protection and may reduce the risk of STIs/HIV;
- Evidence that cervical barrier use may be feasible in areas of high HIV incidence;
- The development of new cervical barrier designs that do not require clinician fitting and have other user advantages to increase accessibility.

Myths About Female Barriers (Female Condoms and Cervical Barriers)

- There is only one kind of each
- No one likes them
- No one uses them
- They don't work anyway
- There is nothing new going on



Female condom – First Generation

Reality® (FC1 – Female Health Company) – the original

- Polyurethane
- US FDA approval in 1993
- CE mark
- WHO Prequalified for international procurement (Cupid also)
- Discontinued (2010)

FC2 (Female Health Company)

- Made of synthetic latex (nitrile); automated dipping → lower cost and no seam
- US FDA approved (2009) as contraceptive and labeled for HIV/STI prevention
- CE mark (European approval); and approved/registered in many countries
- WHO Prequalified (eligible for procurement by international agencies) 2007, 2012
- Sold in drugstores in 20 countries and in global public sector in 143 countries

Female Condom Potential Advantages

- The only woman-initiated method currently available for preventing STIs/HIV
- Inserted ahead of time, unlike male condoms
- Better sensation for both partners
- Provides an option when male condom not used
- Non-hormonal; easy to start and stop using
- No need to see a provider

Female condom myths – "There is only one kind" – Other prototypes

Name	Mfr	Material	Approvals/ status	
Woman's condom (O'lavie; V Condom; Whisper)	Shanghai Dahua Medical Apparatus Co	Polyurethane with film capsule and foam shapes	CE Mark Chinese FDA South Africa Malawi; Zambia IDE filed with USFDA	
VA w.o.w., V'amour, L'amour, Reddy	HLL LifeCare Ltd. India	Latex with polyurethane sponge	CE Mark Multiple countries (incl. India, Brazil, Europe, South Africa)	
Cupid 1	Cupid, Ltd, Mubai, India	Scented latex with polyurethane sponge	CE Mark WHO Prequalified (2012) 23 countries (Europe, Asia, Africa, South America)	
Pheonurse	Condom Bao Medical Polyurethane Corp, Tianjin, China	Polyurethane with insertion tool	China	

Also Cupid 2, Velvet, Panty and Origami 

Female condom myths – "no one likes them"

FC1 vs. FC2 in pivotal clinical trial:

- 276 women used at least 10 of each
- Participants did like them - highly acceptable without major differences between condom types:
  - ~95% of women reported good or satisfactory experience
  - ~65% said insertion was easy or moderately easy
  - >90% had no problems with removal
  - 29% preferred FC1, 37% FC2, 34% no difference
  - Most liked and least liked feature was lubricant
  - Appearance and noise not major issues

Smit, *Contraception* 2006

Female condom myths – "no one likes them"

- FC2 vs. Woman's Condom vs. Reddy
  - 180 participants in South Africa also liked them, especially Woman's Condom

Liked somewhat or very much:	Woman's condom	FC2	Reddy
Ease of use	92%	86%	69%
Overall fit	88%	85%	72%
Feel	82%	76%	68%
Appearance	81%	73%	66%
Preferred	**48%**	**36%**	**16%**

Joanis, *Contraception* 2011

Female condom myth – "no one uses them"

- 60 million female condoms distributed in 2012[1]
  - Primarily in low resource countries; 98% of the market is public sector distribution for HIV prevention
- South Africa:[2]
  - Reality/FC1 introduced in 1998
    - FC2 now provided free in 4000 public health clinics
    - 5.1 million distributed in 2010[3] - one of the highest #s in the world
      - But <2% of 350 million male condoms
- US: ~2% of reproductive aged women report ever use

1 *AccessRH's RH Interchange database* 2012 .
2 Beksinska *Sexual Health* 2012
3 Eva Murumo, South Africa Department of Health, 2011.

What would increase female condom use?

- Create positive environment to support use:
  - Support market development for female condoms similar to male condoms (promotion, counseling, access and supply)
  - Educate consumer and providers:
    - Awareness of risk
    - Dispel myths about use
    - “Practice makes perfect”
  - Involve partners and multiple delivery sites:
    - Promote to both men and women
    - Have available at STI clinics and HIV prevention programs
  - Portray in positive light:
    - Point out advantages (non-disruptive, better sensation, STI protection)
    - Use humor: The Condom Project
    - Promote pleasure: The Pleasure Project

Female condoms – Use in anal sex

Not well studied or approved for anal sex

- In men
  - US: 5-20% of MSM have used[1,2,3]
  - Promoted to MSM by Population Services International in Myanmar and Philippines
- In women:
  - No data on female condom use in anal sex, but women practice receptive anal sex [4]
- Potentially very important use:
  - Research needed on safety and efficacy as well as how best to use

[1] Kelvin, *Am J Pub Hlth* 2011
[2] Renzi ,*AIDS* 2003; Wolitski, *AIDS Educ Prev* 2001; Gross, *Am J Pub Hlth* 1999
[3] Mantell *AIDS Care* 2010
[4] Halperin, *AIDS Patient Care* 1999

Female condom myths - “they don’t work anyway”- Slippage, breakage, etc.

	Woman's Condom	Woman's Condom	FC1	FC1	FC2	FC1	Phoenurse	FC2, Woman’s Condom, Reddy, Cupid—China & SA
Reference	Zirong 2012	Schwartz 2008		Beksinska 2006		Hou 2010		Beksinska 2013
N (condoms)	234	287	285	127	106	291	291	2800
% of condoms failing due to:								
Clinical breakage	0	1.1	0	0.5	0.4	2.9	3.6	0.08-0.25
Misdirection	2	2.2	2.6	1.3	0.6	12.9	11.8	0.60-1.22
Invagination	1	9.9	9.9	3.1	3.0	7.1	8.0	0.47-1.21
Complete slippage	1	1.5	3.7	0.2	0.1	9.1	10.9	0.53-1.48
Total clinical failure	4.3	13	15	5.2	4.3	25.1	24.6	2.49-3.87

Variability between studies: population, prior experience, instructions, definitions.

Male condom breakage 0.4% to 6.7%, slippage 0.6-5.4%*

* Rosenberg, *Contraception* 1997

FC1 Contraceptive Efficacy

Site, N*	Pregnancy probability		Reference
	Typical Use	Perfect Use	
UK: 106	12-month: 15%		Bounds 1992
US: 221 Latin America:107	6-month: 12.4% 6-month: 22.2	6-month: 2.6% 6-month: 9.5%	Farr 1994
Japan:190	6-month: 3%	6-month: 0.8%	Trussell 1998

FC1 and FC2 label: 12-month typical use: 21%, perfect use: 5%

Male condom:* 12-month typical use: 18%, perfect use: 2%

*Contraceptive Technology 20th edition, 2011

FC: HIV/STI prevention

- Female condom covers the cervix, lines the vagina, and protects the vulva and perineum
- Preclinical data on effectiveness comes from in vitro permeability and water leakage studies
- Hypothetical impact modeling: Female condom may ↓ risk of HIV by >90%[1]
- Studies in STI clinics and brothels
  - Female condoms appear to be as good as male condoms.

[1] Trussell, *Fam Pl Per* 1998

FC: HIV/STI prevention

Study	Population	Results
Impact on STIs		
Soper, 1993	104 women at STI clinic	Consistent use of FC protects against recurrent Trichomoniasis
Feldblum, 2001	1,752 women Kenya provided FC & MC or MC alone	25% decline in STIs in both groups
Fontanet, 1998	548 CSW in Thailand used MC backed up by FC or MC alone	24% reduction in STIs in MC/FC group, 17% reduction in unprotected sex acts
Hoke, 2007	1,000 CSW in Madagascar addition of FC to MC	>10% reduction in STIs with addition of FC

Female condom myths – "There is nothing new going on"

- Comprehensive Condom Programming (CCP)* - UNFPA initiative to raise awareness, increase demand, overcome taboos, ensure supply
- 2005, UNFPA launched Global Condom Initiative
    - Works in 86 countries
        - Global female condom distribution tripled between 2005 and 2009
    - Zimbabwe:
        - Sales in public sector increased from 400,000 to >2,000,000
        - Sales through social marketing rose from 900,000 to >3,000,000 (2000 hairdressers and 70 barbers)
    - Other success stories in Malawi, Nigeria, Ethiopia, Swaziland

*UNFPA Report 2011 HIV Prevention Gains Momentum: Successes in Female Condom Programming."

Female condom myths – "There is nothing new going on"

- Universal Access to Female Condoms (UAFC) - 2008
  - Goals:
    - Decrease unwanted pregnancies, maternal deaths, and STIs/HIV
    - Promote gender equality and women empowerment
  - Strategy:
    - Research and development of new female condoms to expand choice
    - Large-scale country programs in Nigeria, Cameroon & Mozambique
    - International advocacy
  - Successes:
    - Financed comparative functionality studies to generate data for product dossiers.
    - Provided assistance to female condom manufacturers to prepare for WHO Prequalification reviews.
    - Developed markets for multiple female condoms in Cameroon, Mozambique and Nigeria; more than 3 million units sold/distributed in 2014

Female condom myths – "There is nothing new going on"

- FC2 launched in selected US cities ~ 2010
- Washington DC + DC Dept of Health + Washington AIDS Partnership + FHC + CVS drugstores
  - Education and distributing female condoms
  - Results:
    - Education reached 38,000 people
      - Knowledge increased from 2.9 out of 5 on pretest to 4.6
    - 200,000 condoms given out
    - Cost: $400,000
      - Lifetime cost of HIV medical care per person is $367,000
      - 23 cases of HIV were averted, **$8 million saved**

Holtgrave *AIDS Behav* 2012

Female condom myths – "There is nothing new going on"

- Ongoing effort advocating change in US regulatory pathway:
  - Currently, FDA classifies female condoms as a Class III medical device—requires contraceptive efficacy study
  - New studies using detection of PSA in the vagina after sex as a marker for barrier effectiveness:
    - More sensitive measure than pregnancy or STIs
    - Faster and less expensive
  - Woman's Condom in two such trials
    - CONRAD: PSA + slippage/breakage, etc
    - NIH: Nested PSA within efficacy study
    - Data could help FDA accept performance and failure mode/PSA data rather than requiring contraceptive effectiveness

The truth about female condoms

- FC2 is most widely available product; multiple regulatory approvals, available in 140+ countries.
- Other FC products already marketed outside the US; additional designs in development & clinical studies.
- Multiple studies show women and men like using female condoms.
- Additional market development needed to “mainstream” this product (similar to how male condoms have been promoted since 1980s)
- Both male and female condoms are effective in preventing the transmission of HIV
- Anal use is happening and should be further studied
- Requirements for market approval in the US may become more reasonable if FDA agrees that performance and failure mode study with PSA is sufficient.
- The female condom landscape is rapidly evolving --there is plenty “going on”

Cervical barriers

Myths about cervical barriers

- There is only one kind of cervical barrier
- No one likes them
- No one uses them
- They don’t work
- There is nothing new going on

Cervical barriers

Name	Material	Sized?	Approval/status
Currently available			
Milex	Silicone	Yes, 8	CE, US, Canada, Asia, Middle East
Semina	Silicone	Yes, 6	Brazil
FemCap	Silicone	Yes, 3	CE, US
SILCS	Silicone	No	CE, US FDA , Canada, Australia,
Discontinued			
Ortho All-Flex:	Silicone	Yes, 4	US, Canada, Europe Discontinued 2014
Prentif Cap	Latex	Yes, 4	US –Discontinued 2007
Oves	Silicone	Yes, 3	CE – dc'd. US as conception device
Lea's Shield	Silicone	No	CE, US Discontinued 2008

Cervical barrier myths – "No one likes them"

Device	Site, N*	% liking strongly/ somewhat	Definitely/ probably would use	Would recommend to friend:	Reference
FemCap + N-9	US, 398		50%		Mauck, 1999
All-Flex diaphragm + N-9	US, 401		63%		
All-Flex diaphragm + N-9	US, 300	72%	70%		Barnhart, 2007
All-Flex diaphragm + BufferGel	US, 621	68%	68%		
Flat or arcing spring + N-9	Turkey, Colombia, & Philippines, 550	73%			Behets, 2001
All-Flex diaphragm + Replens (MIRA)	S. Africa 5045	96%		97%	Montgomery 2010
All-Flex diaphragm + cellulose sulfate or placebo gel	Zimbabwe, 117	99%		97%	Van der Straten 2008
Latex diaphragm (mfd by CMD, the Netherlands)	Kenya, 185	95%	96%		Luchters 2007
SILCS pivotal study	**US, 500**				**Schwartz, 2015**

Cervical barrier myths – No one uses them

- 17% of US women had ever used diaphragm in 1982 but decreased to 3.1% in 2006-2010 (National Health Statistic Report 2013)
- Providers stopped promoting diaphragms in favor of more effective methods, can't use method that is unavailable and not promoted
- Women remain interested in nonhormonal, user initiated methods

Cervical barrier myths – "they don't work anyway"

For contraception:

Device	Site, N	6-month Pregnancy probability		Reference
		Typical Use	Perfect Use	
Lea's Shield + N-9	US, 185	8.7	NA	Mauck, 1996
FemCap + N-9	US, 398	13.5	11.1	Mauck, 1999
All-Flex diaphragm + N-9	US, 401	7.9	7.4	
All-Flex diaphragm + N-9	US, 300	12.3	4.7	Barnhart, 2007
All-Flex diaphragm + BufferGel	US, 621	10.1	6.1	
SILCS +BG or N-9	US, 450	10.4		Schwartz, 2015

Cervical barrier myths – "They don't work anyway"

For STIs:

- MIRA study :*
  - Endpoint: HIV incidence
    - 4.1% in condom + diaphragm + Replens group; 54% used condoms
    - 3.9% in condom-only group; 85% used condoms
    - Diaphragm use may have compensated for the difference in condom use
  - Similar results for gonorrhea and chlamydia

*"Methods for Improving Reproductive Heath in Africa" Study, Padian, *Lancet* 2007

Diaphragms—STI Prevention

There have been several observational studies that report that using the diaphragm is associated with a reduced risk of STIs.

Observational studies reporting the association between diaphragm use and STIs

Design	Sample	STI	Odds Ratio	95% C.I.	Author
Case control	STI clinic	Gonorrhea	.45	.15-1.3	Austin et al
Cross sectional	STI clinic	Gonorrhea	.8		Madger et al
Cross sectional	STI clinic	Gonorrhea Trichomonis Chlamydia	.32* .24* .25	.16-.45 .12-.48 .05-1.36	Rosenberg et al
Case control	STI clinic	Cervical neoplasia (CIN I, II)	.3*	.1-.8	Becker et al
Case control	STI clinic	Pelvic Inflammatory Disease (PID)	.3	.09-.75	Wolner-Hanssen et al
Case control	Hospital	Pelvic Inflammatory Disease (PID)	.4	.2-.7	Kelaghan et al

*Also significantly protective when compared to condom users

(adapted from Moench, Chipato, and Padian, 2001)

Cervical barrier myths: "There's nothing new going on"

Consider other ways of using :

- "Continuous use" (take out; wash daily; then reinsert) rather than "episodic use"
  - Few studies (Brazil and Madagascar), but seems acceptable and safe and more effective than episodic use
- Omit contraceptive gel -logical that contraceptive gel improves effectiveness, but clinical data is weak
- Eliminate sizing
  - -Exact size probably doesn't matter (Mauck 2009)
- Educate users and providers about effectiveness and acceptability
- Come up with a truly exciting design

Cervical barrier myths – "There is nothing new going on"

- Caya® contoured diaphragm:
  - Single size, simplifies supply/provision
  - Silicone—long lasting and soft
  - Contoured spring; removal dome
  - Developed with user-centered approach
  - CE Mark approved in 2013
  - US FDA market clearance in 2014, US launch June 2015
  - First design innovation in product category in 50 years
  - Currently marketed in 25+ countries
- Pivotal trial of safety and effectiveness
  - 450 couples
  - 6 months
  - Randomized to BufferGel (300) or N-9 (150)
  - Design similar to All-Flex+N-9 vs BufferGel trial

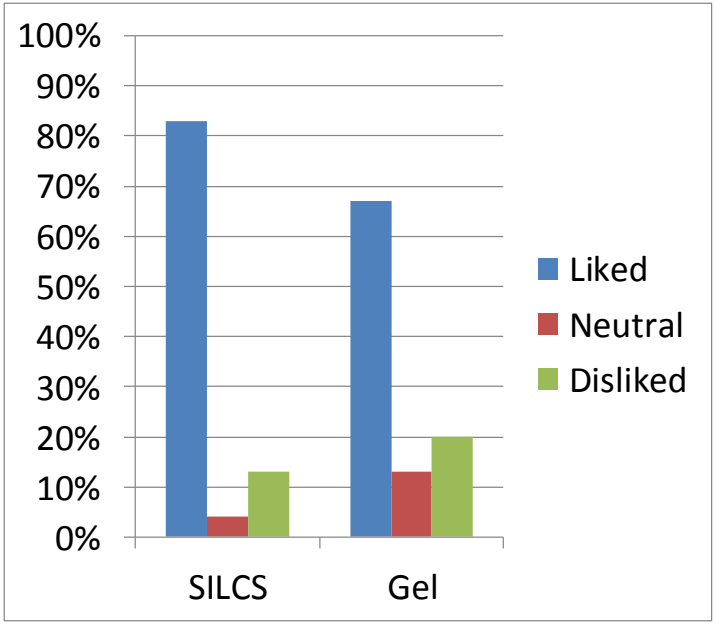
Schwartz, Obstetrics & Gynecology, 2015

SILCS Diaphragm: 6-month Typical Use Pregnancy Rates

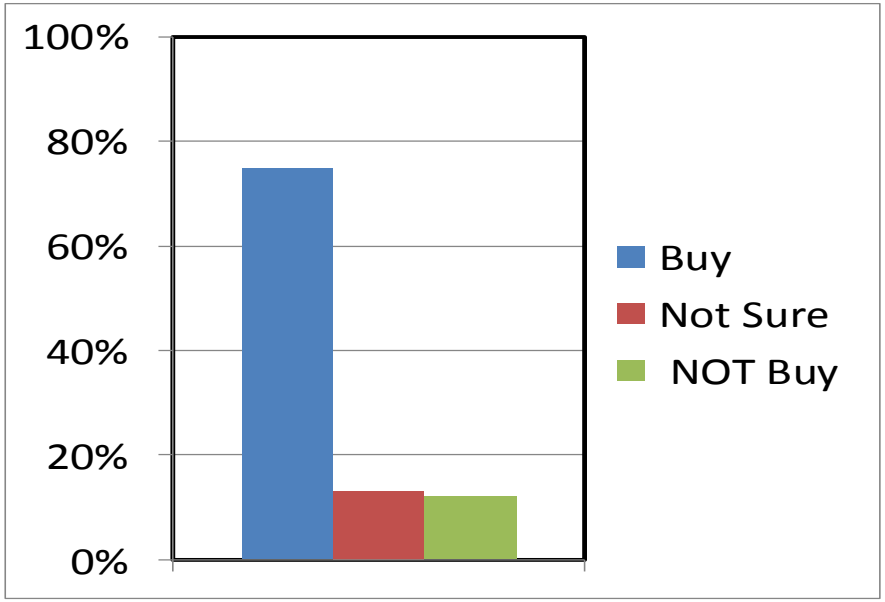
Device	6-month typical use pregnancy probability	Reference
SILCS + N-9	12.5	Schwartz, *Obstetrics & Gynecology* 2015
SILCS + BufferGel	9.6	
SILCS + either	10.4	
All-Flex+ N-9	12.3	Barnhart, *Obstetrics & Gynecology* 2007
All-Flex+ BufferGel	10.1	

SILCS Diaphragm – acceptability and fit

Liked/Disliked SILCS



If SILCS were available in drugstores…



80% correctly positioned the device on the first try after reading instructions
98% were a good fit after more than one try, and/or with coaching

Caya® Contoured Diaphragm

- PATH licensed the SILCS technology to Kessel medintim GmbH of Germany in 2010 for manufacturing/marketing.
- Kessel achieved regulatory approvals in Europe, Canada, US, and Australia. Caya now launched in 25+ developed and middle income countries for OTC use or by Prescription.
- HPSRx, markets the Caya diaphragm in the US. (http://caya.us.com/), launched in 2015.
- Introduction in developed countries used to build developing country introduction.

Caya Experience in Europe

- Two and one half years into introduction of Caya
  - >31,000 women use it as a daily method
- 2015 consumer survey of 140 users
  - 45% previously used OCP
  - 45% had no children
  - 35% surveyed say sex has became better, 60% the same
  - 40% of partners don't notice device, 60% liked that their partner was using it

https://www.medintim.de/assets/Caya/rzfrauenarztbeilegeren150925WEB.pdf

Caya Diaphragm and Contraceptive Gel

- Diaphragms recommended for use with contraceptive gel
- Contraceptive gel availability:
  - N-9 gel currently the only product available in the US
  - Contragel/CayaGel available in Europe/Canada/Australia and 25 other countries (lactic acid based gel);
  - Amphora gel (another lactic acid based gel) being reviewed by the USFDA as a contraceptive gel, so could become available in future.
- Contraceptive gel a recurring cost, and also impacts consumer access and acceptability.
  - CONRAD looking at the barrier effectiveness of SILCS with no gel.

Multi-purpose technology: Prevention of HIV/STIs *and* pregnancy

- Caya as a delivery system for **microbicide gel**:

  Multiple studies demonstrate feasibility and acceptability of Caya as a delivery system for microbicide gel (US; South Africa)

  Advantages: reusable/lower cost, more discreet than gel from a vaginal applicator; potentially less stigma since Caya introduced as a FP method not an HIV prevention method.

- In market research, women more interested in the SILCS + microbicide than in either SILCS alone or microbicide alone.
- Feasibility studies suggest Caya diaphragm spring can be loaded with ARV drug for long-term drug release.

The truth about cervical barriers

- Caya introduction is reinvigorating interest in barrier methods.
- Cervical barriers are acceptable to many women, and provide an important option.
- Advantages are similar to those of female condoms, but diaphragms are more discreet.
- They have not been promoted or made easily available in recent decades, so awareness and usage is low.
- They are effective in preventing pregnancy and may help reduce STIs/HIV (especially when used with microbicide)
- There are exciting new developments.

Thank you

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