

FEATURED RESEARCH

Evidence-Based Planning of a Randomized Controlled Trial on Diaphragm Use for Prevention of Sexually Transmitted Infections

Behets F, Van Damme K, Turner A, Rabenja N, Ravelomanana N, Raharinivo M, Zeller K, Rennie S, Swezey T.

Sexually Transmitted Diseases. 2008; 35(3): 238-242.

Objectives: We conducted formative research to evaluate the acceptability and feasibility of continuous diaphragm use among low-income women highly exposed to sexually transmitted infections (STIs) in Madagascar.

Goal: To identify potential obstacles to researching the effectiveness of diaphragm use for STI prevention in a randomized controlled trial.

Study Design: Mixed methods to collect complex information. In a quantitative pilot study, women were asked to use diaphragms continuously (removing once daily for cleaning) for 8 weeks and promote consistent male condom use; they were interviewed and examined clinically during follow-up. Focus group discussions (FGDs) were conducted pre-/post-pilot study. Audio-taped FGDs were transcribed, translated, coded, and analyzed.

Results: Ninety-three women participated in pre-pilot FGDs, 91 in the pilot study, and 82 in post-pilot FGDs.

Diaphragm use was acceptable and feasible, but participants reported lower condom use in FGDs than during interviews. Most participants reported in interviews that they used their diaphragms continuously, but FGDs revealed that extensive intra-vaginal hygiene practices may impede effective continuous diaphragm use. Despite counseling by study staff, FGDs revealed that participants believed the diaphragm provided effective protection against STIs and pregnancy.

Conclusions: Mixed methods formative research generated information that the prospective pilot study alone could not provide and revealed contradictory findings. Results have methodological and ethical implications that affect trial design including provision of free hormonal contraceptives, and additional instructions for vaginal hygiene to avoid displacing the diaphragm. Mixed methods formative research should be encouraged to promote evidence-based study design and implementation.

A Phase I Study of the Functional Performance, Safety and Acceptability of the BufferGel Duet

Ballagh SA, Brache V, Mauck C, Callahan MM, Cochon L, Wheellessd A, Moench TR.

Contraception. 2008; 77(2):130-137.

The purpose of this study was to assess the functional performance of the BufferGel Duet, a buffering microbicide and spermicide gel applied to the cervix and vagina by a novel applicator that also serves as a mechanical barrier. This was a noncomparative Phase I safety trial in 30 healthy couples, aged 20-50 years, at low risk for sexually transmitted infections, who agreed to use the gel-device combination twice in 1 week and respond to detailed questionnaires about their experience. The female participants were examined with colposcopy before and 6-18 hours after using the second device. Based on written instructions alone, 25 women successfully placed and 28 women successfully removed the device. Three women reported feeling the device dislodge around the time of intercourse. The product was equally acceptable to both men and women. Most users concluded that intercourse was the

same or better with the device than with no product. About 73% would choose Duet over male condoms, and no one preferred the standard diaphragm. Colposcopic findings were noted in 79% of women with external genital findings (9) or cervicovaginal peeling (18) predominating. Only one finding breached the epithelium. Most product-related adverse events were mild (10/11) and confined to the genitourinary tract. The successful placements and acceptability suggest that further product development is warranted and could target over-the-counter use. During increased duration of use or more frequent dosing, cervicovaginal monitoring is advised based on the extent of peeling and external colposcopic findings in this short-term study.

Analyzing Direct Effects in Randomized Trials with Secondary Interventions

Rosenblum M, Jewell N, van der Laan M, Shiboski S, van der Straten A, Padian N.
U.C. Berkeley Division of Biostatistics Working Paper Series. 2007; Working Paper 223.

The Methods for Improving Reproductive Health in Africa (MIRA) trial is a recently completed randomized trial that investigated the effect of diaphragm and lubricant gel use in reducing HIV infection among susceptible women. 5,045 women were randomly assigned to either the active treatment arm or not. Additionally, all subjects in both arms received intensive condom counseling and provision, the "gold standard" HIV prevention barrier method. There was much lower reported condom use in the intervention arm than in the control arm, making it difficult to answer important public health questions based solely on the intention-to-treat analysis. We adapt an analysis technique from causal inference to estimate the "direct effects" of assignment to the diaphragm arm, adjusting for condom use in an appropriate sense. Issues raised in the MIRA trial apply to other trials of HIV prevention methods,

some of which are currently being conducted or designed.

Summary of Results

Though both point estimates are in the direction of assignment to the diaphragm arm being protective in these scenarios, neither is close to statistical significance. Also, based on the bootstrap estimates of standard errors, both of the direct effects relative risk point estimates are within one standard error of the value corresponding to no effect of assignment to the diaphragm arm. We therefore conclude that the direct effects analysis provides no evidence in support of, nor in refutation of, diaphragms providing a protective effect against HIV infection.

See full text: <http://www.bepress.com/ucbbiostat/paper223>

Female Condom Uptake and Acceptability in Zimbabwe

Napierala S, Kang MS, Chipato T, Padian N, van der Straten A.
AIDS Education and Prevention. 2008; 20(2):121-134.

As the first phase of a two-phase prospective cohort study to assess the acceptability of the diaphragm as a potential HIV/STI prevention method, we conducted a 2-month prospective study and examined the effect of a male and female condom intervention on female condom (FC) use among 379 sexually active women in Harare, Zimbabwe. Reported use of FC increased from 1.1% at baseline to 70.6% at 2-month follow-up. Predictors of FC uptake immediately following the intervention

included interest in using FC, liking FC better than male condoms, and believing one could use them more consistently than male condoms. Women reported 28.8% of sex acts protected by FC in the 2 weeks prior to last study visit. Though FC may not be the preferred method for the majority of women, with access, proper education, and promotion they may be a valuable option for some Zimbabwean women.

Members of U.K. Parliament Call for Women-Centered HIV/AIDS

Approximately 175 members of parliament in the United Kingdom have signed a motion for the United Kingdom's Department of International Development to put women at the center of the new global HIV/AIDS strategy and to encourage other international agencies to follow suit, the [Herald Express](#) reports (April 7, 2008). The motion

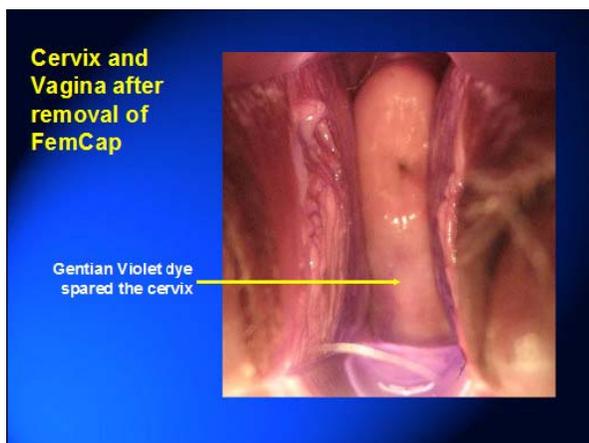
is part of the "[Women Matter](#)" campaign run by the international development charity VSO (Voluntary Service Overseas). This campaign seeks to highlight the fact that women in sub-Saharan Africa are more likely than men to become infected with HIV due to violence, discrimination, and inequality.

FemCap as a Novel Delivery System for Microbicides

The FemCap cervical barrier was featured in "A Novel Delivery System for Microbicides," a poster presented by Dr. Alfred Shihata at the National HIV Prevention Conference in Atlanta, Georgia, in December 2007. Dr. Shihata's research highlights the role of the FemCap in protecting the cervix while serving as an applicator for a microbicide designed to prevent HIV infection. Given that irritation to the cervix that can occur from contact with microbicides causes immune cells to migrate to the cervix, and that immune cells are the primary targets for HIV invasion, deleterious effects of microbicides as demonstrated in trials of Non-oxynol-9 and Cellulose Sulphate could possibly be avoided by protecting the cervix from contact with the microbicide.

Amphora (ACIDFORM) is a microbicide that protects the mucous membrane from HIV invasion

and preserves vaginal acidity, while also killing sperm and HIV organisms. Dr. Shihata's poster featured a test with ten women in which he mixed five grams of ACIDFORM with ten drops of Gentian violet (a dye) and applied the mixture to the storage groove on the vaginal side of the FemCap. The cervix and vagina were photographed before insertion, upon insertion, six hours after insertion, and upon removal of the FemCap. In all women, no staining was detected over the cervix while the vaginal walls were lightly stained with Gentian violet (see photo). These findings highlight the potential for FemCap to protect the cervix from possible irritation by microbicides. Dr. Shihata encourages this novel use of a cervical barrier in clinical trials to show microbicides' success in reducing the risk of transmission of HIV.



Photograph highlighting the protective effect of the FemCap as a vehicle for microbicides.



FemCap with microbicide and dye.

Prevention Now! Campaign

Led by the Center for Health and Gender Equity (CHANGE) in partnership with global advocates, the Prevention Now! Campaign aims to prevent the spread of HIV, reduce unintended pregnancy, and advance the sexual and reproductive health and rights of all people worldwide. Specifically, the campaign calls on governments and donor agencies to increase their investment in efforts to improve access to female condoms and other existing HIV prevention options. The campaign works towards this goal by building partnerships among national and international efforts and through education and advocacy.

As part of the Prevention Now! Campaign, CHANGE has developed a resource entitled, "Saving Lives Now: Female Condoms and the Role of US Foreign Aid," that documents US investment in global female condom procurement, distribution, and programming and provides recommendations for removing barriers to access to female condoms and ensuring US support for female condoms in the future, given that female condoms still represent less than 2% of the total US international condom procurement. For more information on the campaign and to download this report, visit: <http://www.preventionnow.net>.

Implementation of Female Condom Programs Worldwide

According to the [Female Health Company](#) website, 40 countries around the globe are currently implementing female condom programs. These initiatives are part of the worldwide effort to place female-initiated HIV/STI prevention and family planning methods into the hands of women. Several countries have recently begun to launch new programs, and we highlight a few of these new and exciting initiatives below.

The [Times of India](#) (March 6, 2008) and *Kaiser Network* (March 7, 2008) report that the Indian National AIDS Control Organisation (Naco) plans to scale up an acceptability and feasibility pilot project completed in 2006 that demonstrated that 98% of users found the female condom comfortable and 60% re-purchased the female condom after receiving it as part of the pilot project. The initiative will include training for women on how to use the female condom and distribution of five-rupee female condoms (about 12 cents) in four states to sex workers and married women, the two groups of women in India at highest risk for HIV infection. The project also will include the manufacture of 10 million female condoms annually in Kochi, India, which, although each one will cost 40 rupees to manufacture, will continue to be available for five rupees through 200 NGO-led interventions. Another article in the [Times of India](#) (April 21, 2008) reports that the manufacturing company Hindustan Latex Ltd. has begun to place female condom machines in wash rooms of elite urban night clubs in an effort to target upper-class women as well.

The [Jamaica Gleaner](#) (April 21, 2008) and *Kaiser Network* (April 22, 2008) report that the new female condom, the FC2, will be the focus of a workshop put on by Jamaica's National Family Planning Board to promote its use and address the negative stigma surrounding the contraceptive,

such as its association with prostitution and its perceived high cost. The workshop will highlight the improved features of the FC2, which include being less noisy, stronger, hypoallergenic, and able to be used for five years with no special storage conditions.

The *Daily Times* (April 30, 2008) and the *International Planned Parenthood Federation* (May 2, 2008) report that Population Services International (PSI), with support from the Ministry of Health in Malawi and the United Nations Population Fund (UNFPA), have launched a social marketing program for the Care female condom in up to 2,800 hair salons in the four major urban centers of Malawi. According to the *Daily Times*, PSI Malawi says that experiences in Zimbabwe and Zambia, countries that have sold a total of over 7 million female condoms since the mid-late 1990's, indicate that hair salons are an effective venue for creative, targeted marketing programs that build upon existing social networks in gathering places for women. PSI Malawi trains promoters who in turn educate hair salon workers on how to explain to women the correct use of female condoms and encourage them to protect themselves against unplanned pregnancies, STIs, and HIV. According to one promoter, "The salon is a place where most women throw away any inhibitions and are able to talk to fellow women on a lot of important issues including sexual health." The same promoter also reported to the *Daily Times* that she was making a good profit from sales of the female condom, which she is able to buy at K23 (approximately 16 cents) from PSI and sell for K35 (approximately 24 cents) to customers. PSI currently has 15 country programs worldwide distributing female condoms through creative approaches that integrate peer education, mass media communications, and innovative strategies for distribution.

UPCOMING EVENTS

Event: Implementing Best Practices (IBP) in Reproductive Health Knowledge Gateway Diaphragm Forum

Date: June 2-6, 2008

Location: Online

Website: www.ibpinitiative.org/knowledge_gateway.php

Description: The Knowledge Gateway is an electronic tool that helps IBP members to communicate, share, and work together more effectively. The week of June 2-6 will feature an international forum on the diaphragm. Visit the website above to sign up to participate in this week-long online discussion about diaphragm programs worldwide.

Event: Reproductive Health in Emergencies Conference

Date: June 18-20, 2008

Location: Kampala, Uganda

Website: www.raiseinitiative.org/conference

Description: Reproductive Health (RH) in Emergencies Conference 2008 will bring together a wide range of actors from the fields of RH in emergencies, global RH, humanitarian assistance, and development to contribute to the expansion of comprehensive RH services in crisis settings.

Event: XVII International AIDS Conference

Date: August 3-8, 2008

Location: Mexico City

Website: www.aids2008.org

Description: AIDS 2008 will provide many opportunities for the presentation of important, new scientific research and for productive, structured dialogue on the major challenges facing the global response to AIDS.

Event: Women's Global Network for Reproductive Rights (WGNRR) Regional Consultation Meeting

Date: November 11-13, 2008

Location: Cape Town, South Africa

Website: www.wgnrr.org

Description: The WGNRR is a membership organization whose annual regional consultation meeting seeks to strengthen linkages and facilitate networking between members. This year's meeting will address African reproductive and sexual health and rights issues. For information on how to join the network and participate in this meeting, please contact Irina Otmakhova at membership@wgnrr.org.

Event: Association for Women's Rights in Development (AWID) XI International Forum on Women's Rights and Development

Date: November 14-17, 2008

Location: Cape Town

Website: www.awid.org/forum08

Description: The largest recurring event of its kind, the AWID Forum brings together women's rights leaders and activists from around the world every three years to strategize, network, celebrate, and learn in a highly charged atmosphere that fosters deep discussions and sustained personal and professional growth.

CBAS Steering Committee

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What are cervical barriers?

Most people think of cervical barriers primarily as the diaphragm and cervical cap but a broader definition would encompass Lea's shield, female and male condoms, the sponge and microbicides. For more information about the range of cervical barrier methods, go to <http://www.cervicalbarriers.org/information/methods.cfm>.

Mission of CBAS

Established in 2004, the Cervical Barrier Advancement Society (CBAS) aims to raise the profile of cervical barrier methods for pregnancy prevention and provide information about research on the potential of cervical barriers to prevent sexually transmitted infections, including HIV.

Membership

CBAS membership is free and open to all who are interested in joining. CBAS's goal is to create an international, professional networking organization including clinical and social science research groups, academic institutions, advocacy groups, trade associations, and pharmaceutical, biotech, and medical device companies. As a member, you will have the opportunity to network and collaborate with other professionals in the field; keep abreast of new research; share information and ideas; and receive a semi-annual newsletter.

CBAS Contact Information: For more information, contact Kelsey Otis, CBAS Executive Director at kotis@cervicalbarriers.org. CBAS is hosted by Ibis Reproductive Health and based in Cambridge, Massachusetts.

To comment on anything you read in the CBAS newsletter or to contribute a story, event, or news item, please email info@cervicalbarriers.org.