AIDS Behav (2010) 14:629–638
DOI 10.1007/s10461-009-9609-z

ORIGINAL PAPER

Acceptability and Use of the Diaphragm and Replens® Lubricant Gel for HIV Prevention in Southern Africa

Elizabeth T. Montgomery · Helen Cheng · Ariane van der Straten · Agnes C. Chidanyika · Naomi Lince · Kelly Blanchard · Gita Ramjee · Busisiwe Nkala · Nancy S. Padian · The MIRA team

Published online: 10 September 2009

Abstract The acceptability and use of the diaphragm and lubricant gel were assessed as part of a large randomized controlled trial to determine the effectiveness of the methods in women's HIV acquisition. 2,452 intervention-arm women were enrolled at five Southern African clinics and followed quarterly for 12–24 months. Acceptability and use data were collected by face-to-face interviews at Month 3 and Exit. Participants were "very comfortable" with the physical mechanics of diaphragm use throughout the trial, and approval of the gel consistency, quantity and the applicator was high. At Exit, consistent disclosure of use (AOR 1.97, 95% CI: 1.10–3.55); an overall high diaphragm rating (AOR 1.84, 95% CI: 1.45–2.34) and perception of partner approval (AOR 1.75, 95% CI: 1.35–2.26) were the most significant acceptability factors independently associated with consistent use. Despite being female-initiated, disclosure of use to male partners and his perceived approval of the products were factors significantly associated with their consistent use.

Keywords Diaphragm · Lubricant gel · HIV prevention · Zimbabwe · South Africa · Acceptability · Product adherence

E. T. Montgomery (✉) · H. Cheng · A. van der Straten · N. S. Padian
Women's Global Health Imperative, RTI International, San Francisco Project Office, 114 Sansome Street, Suite 500, San Francisco, CA 94104, USA
e-mail: emontgomery@rti.org

E. T. Montgomery
Infectious Diseases Epidemiology Unit, Department of Epidemiology, London School of Hygiene and Tropical Medicine, London, UK

A. van der Straten
Center for AIDS Prevention Studies, Department of Medicine, University of California San Francisco, San Francisco, CA, USA

A. C. Chidanyika
University of Zimbabwe-University of California San Francisco Research Collaborative Programme in Women's Health, Harare, Zimbabwe

N. Lince · K. Blanchard
Ibis Reproductive Health, Cambridge, MA, USA

B. Nkala
Perinatal HIV Research Unit, Johannesburg, South Africa

G. Ramjee
Medical Research Council, Kwazulu-Natal, South Africa

N. S. Padian
University of California, Berkeley, School of Public Health, Berkeley, CA, USA

Background

Globally the HIV epidemic continues to progress, with Southern Africa at the epicentre of the pandemic [1]. Within this region, women are more likely to be infected than men. Much of the exacerbated risk women face is attributed to their increased biological, socio-economic and cultural vulnerability to HIV infection [2–4]. In an attempt to address this gender imbalance, there are several ongoing investigations of female-initiated HIV prevention technologies, such as vaginal microbicides, cervical barriers, and combinations thereof. Female-initiated methods would offer women greater control over use, including undisclosed use, which may be important in relationships where women are unable to negotiate male condoms.

The Methods for Improving Reproductive Heath in Africa (MIRA) study was a phase III randomized trial

examining the effectiveness of the diaphragm, a non-contraceptive lubricant gel (Replens®) and condoms, compared to condoms alone in preventing HIV acquisition in Southern African women. As recently published, there was no additional protective benefit against HIV infection or cervical STIs, when the diaphragm and gel were provided in addition to condoms and a comprehensive HIV prevention package [5, 6]. A secondary objective of the trial was to assess the acceptability of the diaphragm and gel throughout the study period. As others have discussed, "acceptability" is a multi-dimensional concept which incorporates different meanings in different settings, and at different stages of a product lifecycle [7]. In MIRA, we focused on the clinical testing stage, and the broad domain of "acceptability" included an evaluation of user perspectives about the physical characteristics of product use (including comfort, ease of use, effect on sexual pleasure), as well as discrete use, female-initiation and partner support for use. This is the first large randomized study to examine the acceptability and use of the diaphragm and gel as a potential HIV/STI prevention method during 12–24 months of study participation.

Previous research on the diaphragm as a contraceptive has shown the device to be acceptable in several developing-country settings where historically it had not been widely available [8–10]. In a recent US contraceptive trial of the diaphragm, used with a contraceptive microbicide candidate or placebo, two-thirds of women reported strongly or somewhat liking the method [11]. In research settings where the diaphragm has been investigated as a potential HIV/STI prevention method, high user-acceptability has also been reported among diverse target groups, including reproductive health clinic attendees, sex-workers and "healthy" community-recruited women [12, 13]. Several studies in the developing world have also looked at acceptability of potential microbicidal gels, exploring issues regarding insertion, consistency, quantity, sexual pleasure and wetness among women and their male partners. Although the majority have reported the gels are acceptable, most of the studies have been small, short in duration, or have examined hypothetical acceptability [8, 9, 14–24].

Acceptability is presumed to be an important component of use, however, their relationship is inconsistent in the literature. A study in Zimbabwe preceding this trial reported an association between women's diaphragm acceptability and consistent use, while another recent trial, also in Zimbabwe, reported that partner acceptability was independently associated with consistent diaphragm use, although women's own diaphragm acceptability was not [21, 25]. Finally, a study of young women in the US that measured use under more "real life" conditions, acceptability of barrier methods was reported to be an unreliable predictor of future use [26].

This paper presents overall long-term acceptability of the diaphragm and gel, as well as acceptability of several specific attributes of their use as a potential HIV prevention method. We also examined whether these factors differed by time point, and which specific attributes of product acceptability were independently associated with consistent product use. The MIRA trial produced findings that would not warrant scale-up of the diaphragm and lubricant gel for HIV/STI prevention, but our results may have been different if use of the products had been higher [5]. Cervical barriers and microbicide gels are still under investigation for this indication, and acceptability and use results from MIRA are thus important to consider in this context.

Methods

Study Design and Participants

The MIRA trial enrolled 5,045 women HIV-negative, non-pregnant women at three sites in South Africa (2 clinics adjacent to Durban, 1 in Soweto) and Zimbabwe (2 clinics adjacent to Harare) between September 2003 and December 2006. Six participants were discontinued on the same date of randomization for not meeting inclusion criteria, or were later identified as under 18 and were excluded from the analysis dataset, resulting in an analytic sample of 5,039. Women were randomized in a 1:1 ratio to one of two study groups and received an Ortho All-Flex diaphragm, Replens® lubricant gel and male condoms (intervention group) or male condoms alone (control group). Participants were counseled to insert the diaphragm with one-applicator-full (2.5 g) in the dome at any time before sex; to insert an additional applicator-full of gel in the vagina at least 1 h prior to sex, to retain the products for at least 6 h post coitus, and to use *all* of their assigned study products for every act of sex. All women received a comprehensive package of voluntary counseling and testing for HIV, treatment for curable STIs, and intensive risk reduction counseling with health education. Participants were scheduled to attend a two-week post-enrollment visit and quarterly follow-up assessments that continued for 12–24 months, depending on the calendar date of their enrollment. Trial participants were recruited from family planning, well-baby and general health clinics, as well as through community outreach, local media and word-of-mouth (further detailed in: Padian et al. [5]). The MIRA study is registered with ClinicalTrials.gov (number NCT00121459).

This analysis focuses on the 2,521 women randomized to the intervention group. Acceptability of the intervention group products was assessed using an interviewer-

administered questionnaire delivered at the first quarterly follow-up visit (Month 3) and at the participant's last visit (Exit). To understand if general or specific aspects of product acceptability changed with duration of use, we compared acceptability responses from Month 3 and Exit. The majority (2,485, 98.6%) of women had acceptability data from at least one time point. Eighteen participants were excluded from the analytic sample because they reported non-use of the diaphragm since the start of the study, and fifteen were excluded because they were late for their Month 3 Visit, and did not have an Exit visit. Of the 2,452 women remaining, 2,208 (88%), women had a Month 3 acceptability interview, 2,317 (92%) had an Exit acceptability interview, and 2,073 (85%) had data for both Month 3 and Exit. Because of the study's staggered follow-up period, exit visits ranged in quarterly intervals from Month 12 to Month 24 (median Month 21).Thus for the exit visit data, 12% of responses were at Month 12, 16% each at Months 15 and 18, 14% at Month 21, and 42% at Month 24 (Fig. 1).

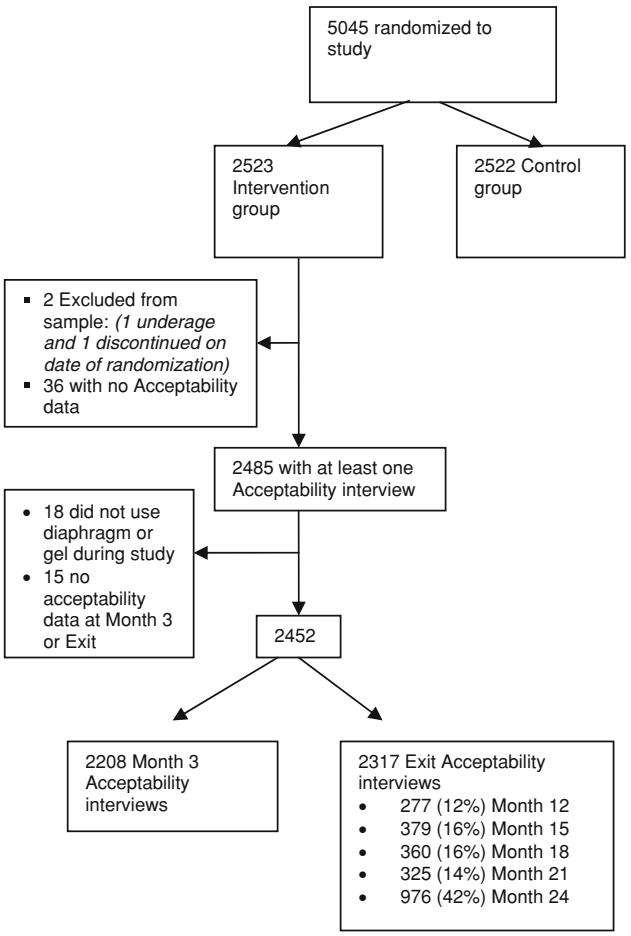

Fig. 1 Profile of MIRA acceptability and use analysis

Measures

Product Acceptability

We measured participant's general rating of the diaphragm and gel with the questions, "How would you rate the diaphragm overall?" and, "How would you rate the gel overall?" (strongly like vs. like/dislike/strongly dislike). We also focused on several specific aspects of acceptability that were relevant to use of the diaphragm and gel, and pertinent to use of female-initiated methods in general. These included women's comfort inserting, removing, and wearing a device intravaginally (very comfortable vs. somewhat/not at all comfortable); comfort with the quantity and consistency of the gel (just right vs. not just right) and the insertion of an intravaginal applicator of gel (very comfortable vs. somewhat/not at all comfortable); effects on sexual pleasure and frequency (increased vs. no effect/decreased); use of the products continuously; use for dual protection (pregnancy/disease/both) and comparisons of the ease and preference for diaphragm vs. male condoms (prefer diaphragm vs. prefer condom/the same). We also assessed partner knowledge (he knew every time vs. <every time); and acceptance of product use (he strongly likes vs. all other responses) as well as decision-making regarding use (decided jointly/he decided/she decided).

Consistent Product Use

The outcome variable of consistent use of the combination product (diaphragm and gel) was derived from responses to two questions in the Acceptability questionnaire where exposure variables were also assessed. First we asked whether the diaphragm was ever used since the start of the study (yes/no). Those who answered affirmatively were then asked, "If there have been times during the study when you did *not* use the diaphragm and gel during vaginal sex, what was the most important reason?" From among nine responses, those who chose: "Not applicable, you used them for every sex act" were categorized as "consistent users" and all other responses as "inconsistent users." Use of this "opt-in" technique which assumes participants had not been fully compliant with product use, has been shown to decrease social desirability bias in responses to sensitive behaviors [27]. Finally, the use data were collected in the same manner as the acceptability exposure variables, making associations easier to assess.

Potential Confounders

For the multivariate models evaluating the association between product acceptability and use, we considered a set

of baseline socio-demographic (e.g. age, education, marital status), clinical (i.e. baseline STI) and risk perception (e.g. impression of partner's fidelity) variables that could be associated with both acceptability and adherence and thus act as potential confounders. Those baseline characteristics that were associated in bivariate analysis at the $P \leq 0.20$ level, as well as age and site (irrespective of association level) were then included in multiple logistic regression models with the outcome of interest. Those potential confounders that remained significant at the $P \leq 0.20$ level were included in the final multivariate models.

Statistical Analysis

Measures of product acceptability were summarized for the two study time points (Month 3 and Exit) using descriptive frequencies. We ruled out multicollinearity in acceptability factors at each time by evaluating variance inflation factors and Spearman's rank correlations. To examine the association between the specific aspects of acceptability and use, we constructed two multivariate logistic regression models, one for each time point of interest. Acceptability factors significant in bivariate analyses at the $P \leq 0.10$ level, and all potential confounders previously identified as significant in multivariate analysis (described above) were retained in the final models. Because of concerns that highly correlated variables were obstructing relationships with the outcome, we used a backwards selection procedure to determine the variables independently predictive of use. All data were analyzed using SAS, version 9.1.

Results

Table 1 displays the baseline characteristics of the MIRA intervention group sample. Over three-quarters (78.1%) of the participants were under 35; 59.4% were married and 67.9% report living together with their primary male partner. The majority reported two or more live births (58.1%). Less than half (44.8%) were high-school educated. Less than a quarter (23.2%) were formally employed; although many more (56.9%) report earning income in the past year. Fewer than half (42.9%) had running tap water inside of their homes. Approximately two-thirds of participants were using hormonal or longer-term contraceptives. Only one woman had previously used a diaphragm. Thirty percent of women reported that they knew or suspected their partner had another sexual partner in the past 3 months, and a further forty percent "didn't know". The subset of participants included in this analysis (92%) did not differ significantly on any variables examined for the entire intervention group (data not shown).

General Acceptability of Diaphragm and Gel

Overall, we found high reported acceptability of the diaphragm and gel at both the Month 3 and Exit visits (Table 2). Seventy-one percent of intervention group participants reported "strongly liking" the diaphragm at both time points, and the proportion of participants "strongly liking" the gel increased from 51.9% at Month 3 to 61.6% by Exit. At the end of the trial women were asked whether they would recommend the diaphragm and gel to a friend if they were shown to be effective in preventing HIV/STIs, and almost all (96.6%) responded affirmatively.

Physical Characteristics of Products and Their Use

At Month 3, the majority of participants reported feeling very comfortable inserting (88.9%), removing (90.1%), having the diaphragm in situ (88.2%), and retaining the diaphragm intravaginally for 6 h post-coitus (82.5%). Attitudes towards these components of use remained relatively constant or increased slightly between Month 3 and Exit (Table 2). Many felt that the quantity and consistency of the gel (83.6 and 89.2%, respectively) were "just right" at Month 3, and reported being very comfortable inserting the gel applicator (78.7%). Favorable attitudes towards these gel factors increased by Exit. A smaller proportion of women reported strongly liking the guideline to insert the gel within an hour of sex (41.8% at Month 3, 50.4% at Exit).

When asked to compare diaphragms to condoms, more women started out reporting that they preferred diaphragms to condoms (57.2%), and found them easier to use (55.1%). However, by exit, more women found them equivalent, or favored condoms.

Effect on Sex

An increased effect of the diaphragm and gel on sexual pleasure and frequency was minimal. Approximately one-third (33.1%) of participants at Month 3 reported that the diaphragm and gel increased their sexual pleasure, and 21.4% said it increased their sexual frequency. Both of these proportions declined by Exit to 23.5 and 16.6%, respectively.

Female-Initiation and Use Patterns

An important attribute of the diaphragm and gel is that it is female-initiated. Just under two-thirds of our study participants reported that they were the primary decision maker in the use of the products at both time points (59.7 and 63.2%, respectively: Table 2). While almost half of the women agreed at Month 3 that it was "very important" that

Table 1 Baseline characteristics of MIRA intervention group participants, for the acceptability analysis sample ($n = 2,452$)

		n	%
Socio-demographic			
Age	24 years old or younger	969	39.5
	25–34 years old	945	38.6
	35 years old or older	537	21.9
Education	Less than high school education	1,352	55.2
Marital status	Married	1,457	59.4
Earned income in past year	Yes	1,392	56.9
Employed	Employed	569	23.2
Source of water	Tap water inside premises	1,050	42.9
	Tap water outside premises	956	39.1
	Well water	365	14.9
	River/stream/rain water and other	77	3.2
Site (main language used in trial)	Harare, Zimbabwe (Shona)	1,230	50.2
	Durban, South Africa (Zulu)	732	29.9
	Johannesburg, South Africa (Zulu, Sotho)	490	19.9
Parity	0 births	217	8.9
	1 birth	811	33.1
	2+ births	1,424	58.1
Current contraceptive use at screening	Long term/user independent[a]	736	30.0
	Pill[b]	900	36.7
	Barrier[c]	507	20.7
	Other/none	309	12.6
Ever used diaphragm	No	2,451	99.9
Sexual & risk behavior			
Lifetime # of sexual partners, mean (range)		2.2 (1–20)	
Age at first sex, mean (range)		18 (10–29)	
Number of sexual partners in the past 3 months	0	152	6.2
	1	2,094	85.6
	2 or more	201	8.2
Know or suspect partner had other sexual partners in past 3 months	Yes	734	30.0
	No	723	29.6
	Don't know	990	40.5
Baseline STI[d]	Yes	377	15.4
Baseline HSV-2	Yes	1,402	57.2
Coital frequency	3 times per week or less	1,586	64.7
High behavior risk[e]	Yes	687	28.1
High partner risk[f]	Yes	1,679	68.6

[a] Long term/user independent methods include tubal ligation, vasectomy, injectables, IUD, implants such as Jadelle & Norplant

[b] Pill methods includes combined oral contraceptive and progestin only pills

[c] Barrier methods include male or female condoms and diaphragm

[d] Includes Chlamydia (CT), Gonnorhea (GC), Trichomoniasis (TV) and Syphilis (TP)

[e] At least one indicator (vs. none) of: Any exchange of sex for money, food or shelter; sex under the influence or 2 or more sex partners in the past 3 months; ever had anal sex; and/or ever used a needle for injectable drug use

[f] At least one indicator (vs. none) of: Ever had a known HIV-positive partner, know or suspect partner has multiple partners, had sex under the influence in the past 3 months and/or partner away from home >1 month

they could use the diaphragm and gel without their partners knowing, this proportion declined to 40.7% at Exit, and throughout the study period, the majority (range 70.5–71.8%) of participants disclosed use of the diaphragm to their partner(s) every time they had sex. The majority of women reported the perception that their partner felt use of the diaphragm was a good idea (71.0% at Month 3, 68.9% at Exit).

Participants were offered free hormonal contraceptives through the trial. Nonetheless, over half (53% at both time points) reported using the diaphragm for both disease and pregnancy prevention (although not necessarily their sole contraceptive method).

Association Between Product Acceptability and Use

At the Month 3 visit, 66.4% of women reported using the diaphragm and gel every time they had sex since the start of the study. This proportion decreased to 51.6% at Exit.

Several factors related to product acceptability were independently associated with consistent use of the device at both time points. At Month 3, women who "strongly

Table 2 Diaphragm and gel acceptability: overall and specific attributes at Month 3 and Exit

	Month 3 (n = 2,208)[a]		Exit (n = 2,317)[a]	
	n	%	*n*	%
Overall acceptability				
Diaphragm				
Strongly likes	1,583	71.7	1,646	71.1
Likes	577	26.1	574	24.8
Dislikes/strongly dislikes	48	2.2	95	4.1
Gel				
Strongly likes	1,138	51.9	1,417	61.6
Likes	903	41.2	731	31.8
Dislikes/strongly dislikes	153	7.0	151	6.6
Would recommend to a friend if proven effective	NA	NA	2,263	96.6
Physical characteristics of products and use				
Very comfortable inserting diaphragm	1,962	88.9	2,150	92.8
Very comfortable removing diaphragm	1,988	90.1	2,170	93.7
Very comfortable waiting 6 h after sex before removing diaphragm	1,821	82.5	1,906	82.3
Very comfortable having diaphragm in situ	1,946	88.2	2,103	90.8
Very comfortable inserting gel applicator	1,732	78.7	1,901	82.6
Amount of gel is just right	1,839	83.6	2,074	89.9
Consistency of gel is just right	1,961	89.2	2,183	94.7
Strongly like inserting gel before sex	918	41.8	1,162	50.4
Prefers diaphragm to condoms	1,262	57.2	943	40.7
Thinks diaphragms easier to use than condoms	1,215	55.1	880	38.0
Effect on sex				
Diaphragm and gel increases sexual pleasure	730	33.1	544	23.5
Diaphragm and gel increases sexual frequency	472	21.4	384	16.6
Female-initiation and use patterns				
Very important you can use diaphragm without partner knowing	1,099	49.8	944	40.7
Partner knew diaphragm in use every time	1,584	71.8	1,633	70.5
Partner thinks diaphragm is a good idea	1,555	71.0	1,579	68.9
She decides when to use diaphragm	1,309	59.7	1,457	63.2
Uses diaphragm for disease and pregnancy prevention	1,177	53.4	1,240	53.6

[a] Responses and proportions do not always correspond to full sample because of missing information

liked" the diaphragm (AOR 1.69, 95% CI: 1.34–2.12), or reported that their partners reactions were favorable (AOR 1.59, 95% CI: 1.19–2.13), and those who made a joint decision with their partner to use the products (AOR: 1.53, 95% CI: 1.02–2.28) were more likely to consistently use the diaphragm and gel (Table 3). Women who felt the consistency of the gel was "just right" (AOR 1.54, 95% CI: 1.12–2.12), or that the diaphragm and gel increased sexual pleasure (1.36, 95% CI: 1.08–1.69), and those that preferred diaphragms to condoms (AOR 1.36, 95% CI: 1.11–1.67), were also more likely to consistently use (Table 3).

By Exit, several different characteristics of the diaphragm and gel emerged as independently associated with consistent use. The strongest association with consistent use occurred among those reporting that their partner knew about diaphragm use at every sex act (AOR: 1.97, 95% CI: 1.10–3.55). A somewhat complementary finding related to female-initiation and disclosure was that women who felt that it was "very important" to be able to use the products without the partner's knowledge were less likely to consistently use them (AOR: 0.73, 95% CI: 0.60–0.89). Women's own strong liking of the diaphragm, and the perception that her partner's reactions were favorable remained independently associated with use (AOR 1.84, 95% CI: 1.45–2.34 and AOR 1.75, 95% CI: 1.35–2.26, respectively). Joint decision-making regarding diaphragm use also remained independently associated with use (AOR 1.52, 95% CI: 1.02–2.25). Those who were "very comfortable" waiting 6 h before removing the diaphragm were more likely to consistently use the diaphragm and gel

Table 3 Multivariate logistic regression model for the association between acceptability and consistent use of the diaphragm and gel at month 3 and exit*

	Month 3 (n = 2,145)**		Exit (n = 2,247)***	
	AOR	95% CI	AOR	95% CI
Physical characteristics of products and use				
Very comfortable waiting 6 h after sex before removing diaphragm	NA		1.45	1.12–1.88
Prefers diaphragm to condoms	1.36	1.11–1.67	NA	
Thinks diaphragms are easier to use than condoms	NA		1.23	1.01–1.50
Strongly likes diaphragm overall	1.69	1.34–2.12	1.84	1.45–2.34
Diaphragm and gel increases sexual pleasure	1.36	1.08–1.69	NA	
Consistency of gel is just right	1.54	1.12–2.12	NA	
Strongly likes male condoms	NA		1.31	1.04–1.66
Female-initiation and use patterns				
Thinks it very important diaphragm can be used without partner's knowledge	NA		0.73	0.60–0.89
Partner knew diaphragm in use every time	NS		1.97	1.10–3.55
Partner's general reactions to using diaphragm good (vs. neutral or bad)	1.59	1.19–2.13	1.75	1.35–2.26
Both partners have final word on diaphragm use (vs. HE does alone)	1.53	1.02–2.28	NS	
Both partners have final word on diaphragm use (vs. SHE does alone)	NS		1.52	1.02–2.25

* Only acceptability factors significant at the $p < 0.05$ level presented. NA = variable not included in final model; NS = variable included in final model but not significant

** Also controlling for: site, age, source of water in the home, education, knowledge of other partners

*** Also controlling for: site, age, source of water in the home, education, contraceptive use, parity, number of sexual partners in the last 3 months

(AOR 1.45, 95% CI: 1.12–1.88). Finally, while women who reported "strongly liking" condoms were more likely to consistently use the diaphragm and gel (AOR 1.31, 95% CI: 1.04–1.66), those who found diaphragms easier to use than condoms were also more likely to be consistent product users (AOR 1.23, 95% CI: 1.01–1.50).

Discussion

This study highlights several important findings that are relevant to the acceptability and introduction of novel female-initiated methods of HIV prevention. Diaphragms and gels for either contraceptive or disease prevention purposes were hardly known, available, or distributed prior to this study in these Southern African communities. Despite this fact, the majority of the study population found them easy and comfortable to insert, wear and remove over the entire study period, suggesting that women are receptive and capable of easily adopting new intravaginal technologies. The overall proportion of women strongly liking the diaphragm remained high (71%) over the 2 year study period, and improved over time for the gel. That said, fewer than 60% reported consistent use of the diaphragm throughout the course of the study, and while more than half the women preferred and found diaphragms easier to use than condoms in the early period, by Exit, more women found diaphragms and condoms equally preferable and equally easy to use. Since the acceptability of many specific attributes of the diaphragm and gel increased at Exit, the latter finding may be a result of successful condom counseling and condom use, rather than a decreased enthusiasm for the diaphragm and gel.

In this study, women's report of strongly liking the diaphragm overall was associated with its consistent use in both the early and late time periods. This finding supports the association between acceptability and use, and corroborates findings reported from two smaller and shorter duration cervical barrier studies in Zimbabwe [21, 25]. Insofar as acceptability is linked to product use and ultimately effectiveness, and keeping into consideration that an important component of acceptability may be duration of use, there is a continued need for formative and ongoing evaluation of product acceptability in the pre-clinical, clinical testing and in roll-out/marketing stages of the development of other new female-initiated HIV prevention methods. Further it is important to consider that consistent use may not be associated with acceptability of *each individual* attribute of a given product, for example one may not like the feel or required negotiation of male condoms, but may use them because of their protective effect.

Several measures of male partner attitudes, support and communication between couples were also identified in

this study to be associated with consistent use. This underscores several opinion articles and evidence from other studies that even with female-initiated HIV prevention methods, the role of the male partner is critical for women's uptake and continuous use [28]. Here, women's perceptions that their male partner supported use of the study products was associated with consistent use at both time periods, as has been reported in other studies [21, 25]. Three indicators of couples communication measured in this study suggest important relationships with use: joint decision-making and full disclosure of product use were associated with consistent use, while valuing the importance of clandestine use was associated with inconsistent use. Thus, efforts to gain male partner support for study product use may improve adherence in similar trials of female-initiated methods. This might be accomplished through early involvement of male partners in trial enrollment procedures and product counseling. More research into the identification of innovative strategies for including male partners while still ensuring women's autonomy is needed, and female trial participants may help inform this research.

One strategy for enlisting greater male partner support and potentially improving adherence to female-initiated methods might be to emphasize ways in which study products might enhance sexual pleasure. At Month 3, women who felt the diaphragm and gel made sex more pleasurable were more likely to be consistent users, although by the Exit Visit, this was no longer independently associated with use. The benefit of eroticizing disease prevention methods, or highlighting their potentially pleasurable attributes has been discussed by others, but perhaps still needs more emphasis in individual or couples-based counseling [7, 29, 30].

While the relationship and contextual dynamics regarding the use of intravaginal devices and gels are essential components of women's acceptability, as many have argued [28, 31, 32], it is also important to continue to measure basic attitudes towards the physical properties of investigational products, even well past their developmental stage in phase III clinical trials. As described above, women in this study were very comfortable using the diaphragm and gel, and in particular, those who were "very comfortable" wearing the diaphragm for 6 h post-coitus were more likely to consistently use the products. This finding has implications for use of other female-initiated methods in coitally-dependent and continuous use regimens. A study in Madagascar has reported that continuous use of the diaphragm was acceptable in a sex worker population [16], and a safety and acceptability study comparing continuous use vs. pre-coital use of a diaphragm-like device (Duet®) for 14-days in a general population will further address these issues [33]. In the MIRA trial, participants were advised to use the diaphragm, gel and condoms for every act of sex. Nonetheless, substitution of products (i.e. use of the diaphragm and gel instead of condoms or vice versa) was a concern, which we explored in separate quantitative and qualitative analyses. In the former, 83.1% of women reported use of the diaphragm instead of condoms at least some of the time [34]. In this study, at Exit, both women who reported an overall "strong liking" of the diaphragm and gel and those reporting the same for male condoms were more likely to be consistent diaphragm and gel users, suggesting that a strong liking of male condoms does not necessarily preclude consistent diaphragm and gel use.

There are several potential limitations to this study. First, the measures of acceptability and adherence relied on self-report of participants' attitudes and behaviors that may have been subject to social desirability and recall bias. This limitation is true of most studies of this nature, and underscores the need for better measures (including biomarkers) and techniques for eliciting honest reporting. Participants who were lost-to-follow-up did not receive an Exit acceptability assessment and may have missed a Month 3 assessment; and these participants may have been less likely to like the study products. We chose an outcome measure for consistent product use from the acceptability form that may have been less reliable than the Computer-based self-administered (ACASI) variables, however, we confirmed that the overall rate of consistent use reported by FTFI was congruent and virtually identical with our ACASI data which collected consistent use in the past 3 months [5, 35].

In summary, we found high acceptability of a combination method as a potential HIV/STIs preventative in the MIRA trial. The overall rating of the diaphragm remained consistently high and that of gel increased with time. However, attitudes towards several specific attributes of the products changed with time, and in both directions. It is important for trials of female-initiated methods, particularly those with longer follow-up periods, to conduct multiple assessments of product acceptability, as some attitudes may change with sustained use. It is also important to measure several different aspects of investigational products (physical attributes, effect on sex, partner's support, etc.) to understand the relative importance of each within the context of a given population, and over time, and this will be particularly important as products transition from clinical studies to the general public. Despite high levels of reported acceptability, the proportion of women that reported consistent use was only moderate ($\sim$50% at Exit). As a recent modeling paper highlighted, these suboptimal levels of adherence, as we observed in the MIRA trial, would dramatically decrease the measured efficacy of an intervention, thus eliminating the power of the study to

detect an effect, if true biological efficacy existed [36]. This underscores the importance of understanding factors that promote or discourage consistent use. Here, several acceptability factors were independently associated with consistent use, most notably, partner approval/liking of the study products and open disclosure and joint decision-making around use. Thus, our results suggest that even though the diaphragm and gel are female-initiated, the role of the male partner is critical for product acceptance and use among women in stable partnerships participating in a clinical trial. Future studies of this nature might consider strategies to more actively engage male partners as a way to optimize product adherence. Nonetheless, women's control over use of these products remains important: if female-initiated methods are proven effective and become widely available, women- and particularly select sub-populations such as unmarried women, those with casual or multiple partners or sex workers- might need or want to use them more autonomously than was observed in this study.

References

1. UNAIDS. AIDS epidemic update 2007, regional summary: sub-Saharan Africa. Geneva: UNAIDS; 2008.
2. UNAIDS/WHO. 2004 Report on the global AIDS epidemic, July 2004.
3. Gray R, Wawer M, Brookmeyer R, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Lancet. 2001;357(9263):1149–53.
4. European study group on heterosexual transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. Brit Med J. 1992;304:809–13.
5. Padian NS, van der Straten A, Ramjee G, et al. Diaphragm and lubricant gel for prevention of HIV acquisition in southern African women: a randomised controlled trial. Lancet. 2007;370(9583):251–61.
6. Ramjee G, van der Straten A, Chipato T, et al. The diaphragm and lubricant gel for prevention of cervical sexually transmitted infections: results of a randomized controlled trial. PLoS ONE. 2008;3(10):e3488.
7. Elias C, Coggins C. Acceptability research on female-controlled barrier methods to prevent heterosexual transmission of HIV: where have we been? Where are we going? J Womens Health Gend Based Med. 2001;10(2):163–73.
8. Bulut A, Ortayli N, Ringheim K, et al. Assessing the acceptability, service delivery requirements, and use-effectiveness of the diaphragm in Colombia, Philippines, and Turkey. Contraception. 2001;63(5):267–75.
9. Ortayli N, Bulut A, Nalbant H, Cottingham J. Is the diaphragm a viable option for women in Turkey? Int Fam Plan Perspec. 2000;26(1):36–42.
10. Ravindran TKS, Rao S. Is the diaphragm a suitable method of contraception for low-income women: a user-perspective study, Madras, India. *Beyond acceptability: user's perspectives on contraception—out of print—a World Health Organization Monograph.* 1997.
11. Barnhart KT, Rosenberg MJ, MacKay HT, et al. Contraceptive efficacy of a novel spermicidal microbicide used with a diaphragm: a randomized controlled trial. Obstet Gynecol. 2007;110(3):577–86.
12. Luchters S, Chersich MF, Jao I, et al. Acceptability of the diaphragm in Mombasa Kenya: a 6-month prospective study. Eur J Contracept Reprod Health Care. 2007;16:1–9.
13. Guest G, Johnson L, Burke H, et al. Changes in sexual behavior during a safety and feasibility trial of a microbicide/diaphragm combination: an integrated qualitative and quantitative analysis. AIDS Educ Prev. 2007;19(4):310–20.
14. Moon M, Khumalo-Sakutukwa G, Heiman J, Mbizvo M, Padian N. Vaginal microbicides for HIV/STI prevention in Zimbabwe: what key informants say. J Transcult Nurs. 2002;13(1):19–23.
15. Pool R, Whitworth JA, Green G, et al. An acceptability study of female-controlled methods of protection against HIV and STDs in south-western Uganda. Int J STD AIDS. 2000;11(3):162–7.
16. Behets F, Turner A, Van Damme K, et al. Acceptability and feasibility of continuous diaphragm use among sex workers in Madagascar. Sex Transm Infect. 2005;81(6):472–6.
17. Ramjee G, Gouws E, Andrews A, Myer L, Weber A. The acceptability of vaginal microbicide among South African men. Int Fam Plann Perspec. 2001;27(4):164–70.
18. Bird S, Harvey S, Maher J, Beckman L. Acceptability of an existing, female-controlled contraceptive method that could potentially protect against HIV: a comparison of diaphragm users and other method users. Women Health Iss. 2004;14(3):85–93.
19. Buck J, Kang MS, van der Straten A, et al. Barrier method preferences and perceptions among Zimbabwean women and their partners. *AIDS Behav.* 2005;9(4):1–8.
20. Harvey S, Bird S, Maher J, Beckman L. Who continues using the diaphragm and who doesn't: implications for the acceptability of female-controlled HIV prevention methods. Women Health Iss. 2003;13(5):185–93.
21. van der Straten A, Kang M, Posner S, et al. Predictors of diaphragm use as a potential sexually transmitted disease/HIV prevention method in Zimbabwe. Sex Transm Dis. 2005;32(1):64–71.
22. Bentley ME, Fullem AM, Tolley EE, et al. Acceptability of a microbicide among women and their partners in a 4-country phase I trial. Am J Public Health. 2004;94(7):1159–64.
23. Coggins C, Blanchard K, Friedland B. Men's attitudes towards a potential vaginal microbicide in Zimbabwe, Mexico and the USA. Reprod Health Matters. 2000;8(15):132–41.
24. van de Wijgert J, Khumalo-Sakutukwa G, Coggins C, et al. Men's attitudes toward vaginal microbicides and microbicide trials in Zimbabwe. Int Fam Plan Perspec. 1999;25(1):15–20.
25. van der Straten A, Moore J, Napierala S, et al. Consistent use of a combination product versus a single product in a safety trial of the diaphragm and microbice in Harare, Zimbabwe. Contraception. 2008;77(6):435–43.
26. Minnis A, Shiboski S, Padian N. Barrier contraceptive method acceptability and choice are not reliable indicators of use. Sex Transm Dis. 2003;30(7):556–61.
27. Catania JA, Binson D, van der Straten A, Stone V. Methodological research on sexual behavior in the AIDS era. In: Rosen RC, Davis CM, Ruppel JHJ, editors. Annual review of sex research, vol. 6. Mt. Vernon, IA: Society for the Scientific Study of Sexuality; 1995. p. 77–125.
28. Mantell JE, Stein ZA, Susser I. Women in the time of AIDS: barriers, bargains, and benefits. AIDS Educ Prev. 2008;20(2):91–106.

29. Philpott A, Knerr W, Maher D. Promoting protection and pleasure: amplifying the effectiveness of barriers against sexually transmitted infections and pregnancy. Lancet. 2006;368(9551): 2028–31.
30. Hammett TM, Mason TH, Joanis CL, et al. Acceptability of formulations and application methods for vaginal microbicides among drug-involved women: results of product trials in three cities. Sex Transm Dis. 2000;27(2):119–26.
31. Woodsong C. Covert use of topical microbicides: implications for acceptability and use. Int Fam Plan Perspec. 2004;30(2):94–8.
32. Woodsong C, Alleman P. Sexual pleasure, gender power and microbicide acceptability in Zimbabwe and Malawi. AIDS Educ Prev. 2008;20(2):171–87.
33. Montgomery E, Musara P, Chandipiswa A, et al. Safety of the Duet® used continuously or pre-coitally in Zimbabwean women *International AIDS society conference on HIV pathogenesis, treatment and prevention.* Vol Cape Town, South Africa 2009.
34. van der Straten A, Cheng H, Moore J, et al. The use of the diaphragm instead of condoms in a phase III diaphragm trial. *AIDS Behav.* 2009;13:564–572.
35. van der Straten A, Shiboski S, Montgomery ET, et al. Patterns and predictors of adherence to diaphragm use in a phase III trial in sub-Saharan Africa: a trajectory analysis. J Acquire Immune Defic Syndr. 2009;50(4):419–26.
36. Weiss HA, Wasserheit JN, Barnabas RV, et al. Persisting with prevention: the importance of adherence for HIV prevention. Emerg Theme Epidemiol. 2008;2008(5):9.