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Preference of Oral Tenofovir Disoproxil Fumarate/Emtricitabine versus Rectal Tenofovir Reduced-Glycerin 1% Gel Regimens for HIV Prevention Among Cisgender Men and Transgender Women Who Engage in Receptive Anal Intercourse With Men

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Compliance with Ethical Standards

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Informed consent: Informed consent was obtained from all individual participants included in the study.

Abstract

Oral pre-exposure prophylaxis (PrEP) can prevent HIV transmission. Yet, some may prefer not to take systemic daily medication. MTN-017 was a 3-period, phase 2 safety and acceptability study of microbicide gel applied rectally either daily or before and after receptive anal intercourse (RAI), compared to daily oral tablet. At baseline, cisgender men and transgender women who reported RAI (N=187) rated the daily oral regimen higher in overall liking, ease of use, and likelihood of future use than the gel regimens. After trying all three, 28% liked daily oral the least. Gel did not affect sexual enjoyment (88%) or improved it (7–8%). Most partners had no reaction to gel use. Ease of gel use improved significantly between the first and the last few times of daily use. A rectal gel used before and after RAI may constitute an attractive alternative to daily tablet. Experience with product use may increase acceptability.

Keywords

acceptability; gel; PrEP; microbicide; rectal

Introduction

The effectiveness of HIV oral pre-exposure prophylaxis (PrEP) and other PrEP technologies in development (e.g., vaginal rings, topical microbicide gels, rectal inserts, rectal douches, long-acting injectables and implants) is contingent on consistent and correct use. To some extent, such use hinges on product acceptability, i.e., its appeal and tolerability to the user.

Several studies have assessed the acceptability of oral PrEP. Although its definition varies among studies, acceptability in general is high [1] and may be affected by cost [2–8], perceived effectiveness [3–5], potential side effects [4,5,7], risk perception [1,7–10], dosing regimen (i.e., daily or intermittent) [2,11], and stigma (i.e., user being perceived as promiscuous) [7].

Other studies have focused on the acceptability of rectal PrEP to be used in association with receptive anal intercourse (RAI). They showed that the acceptability of potential rectal microbicides is affected by product formulation (i.e., gel, suppository, or douche) [12–17], attributed lubrication capacity of gels [18,19], anticipated product effectiveness [17,20,21], application method [19,22,23], packaging and portability of the product [22,24], dosing regimen (i.e., daily, before receptive anal intercourse (RAI), or before and after RAI) [16,17,24], side effects [21,24], type of partner with whom the rectal microbicide will be used [19,24,25], frequency of RAI [26], accessibility of product (i.e., prescription versus over-the-counter) [17,21], ease of use of the product [16], and product's effect on sexual pleasure [13,15]. However, these findings stem from studies that were either hypothetical (participants expressed their opinions without actually using a product), placebo trials (the products used did not contain agents that could potentially have microbicide properties) or Phase 1 safety trials in small numbers of low-risk participants.

This manuscript is the first to report in detail the acceptability findings from a Phase 2, expanded safety rectal microbicide trial. It focuses on the acceptability of a rectal

microbicide gel used daily or in association with RAI in comparison to the acceptability of daily oral tablet.

Methods

MTN-017 was a phase 2 randomized sequence open label crossover study of expanded safety and acceptability of reduced-glycerin 1% tenofovir (RG-TFV) gel formulated for intrarectal delivery by an applicator (an investigational product) compared to emtricitabine/TFV disoproxil fumarate (FTC/TDF) formulated as an oral tablet. The two products were studied in three regimens: 1) daily oral tablet (i.e., daily oral), 2) daily rectal gel (i.e., daily rectal), and 3) rectal gel applied within 12 hours before and 12 hours after RAI (i.e., RAI rectal). In this third regimen, consistent with the study's safety objective, participants were asked to apply the gel intrarectally at least twice a week if RAI did not occur. After enrollment, participants were randomly assigned to one of six possible 3-regimen sequences. Each regimen period lasted eight weeks. All participants were provided condoms and lubricants and were counseled on the unproven efficacy of the study gel and the consequent need to use protection. The main outcomes of the study and adherence to product use have been reported elsewhere [27, 28]. In this manuscript, we explore product acceptability in further detail.

The study took place at eight sites in four countries: Peru (Lima), South Africa (Cape Town), Thailand (Bangkok and Chiang Mai), and the United States (Boston, Pittsburgh, San Francisco, and San Juan, Puerto Rico). Participants were men who have sex with men (MSM), and transgender women (TGW, individuals born with male genitalia who identified as women), recruited from the Internet, primary health clinics, community-based organizations, and referrals from other research projects and local health providers. To be eligible, study candidates had to be HIV-1 uninfected at enrollment, available to return for all study visits, in general good health, and have had consensual RAI at least once in the three months prior to screening. Full inclusion and exclusion criteria are available at https://clinicaltrials.gov/ct2/show/NCT01687218. The Institutional Review Boards/Ethics Committees of all participating entities approved the conduct of this study, and all participants signed informed consent.

Instruments

Upon enrollment, participants completed a baseline behavioral questionnaire via web-based computer assisted self-interview (CASI) available in English, Spanish, Thai, Xhosa and Afrikaans. Besides demographic information, the baseline CASI included questions on likelihood of future use of either oral PrEP or a rectal microbicide gel if available to the participant and protective against HIV acquisition. For each product, and prior to first use, we inquired how likely the respondent would be to use it every day or within 12 hours before and 12 hours after RAI. Participants were also asked whether daily use or use before and after RAI was their preferred choice for each product.

At the end of each eight-week study period, participants completed a follow-up behavioral CASI. It included questions on the participant's sexual behavior during the preceding 8-week study period and on product acceptability, including overall liking of the products;

preferences for thicker or thinner gel (viscosity), preference for more or less gel volume in the applicator; overall ease of use, and ease of use the first few times and the last few times in the study period; liking the applicator and experiences using it; and overall likelihood of product use considering the positive and negative experiences the participant had using each product during the study period. In separate dichotomous (Yes/No) questions, participants were asked if they experienced any positive or negative reactions to product use from a sex partner. After completing all three study periods, the CASI Follow-up Behavioral Questionnaire asked participants to select the most and least liked of the three regimens.

Statistical Analysis

A primary objective of the study was to evaluate and compare the acceptability of daily oral, daily rectal, and RAI rectal regimens. The acceptability endpoints were participants' self-reports evaluating overall product liking, overall ease of use, and overall likelihood to use the product if shown effective. Descriptive statistics were generated for participants' baseline demographic characteristics and for acceptability endpoints at baseline and follow up. Acceptability endpoints were compared between study regimens using a generalized linear model (GLM) with identity link function for continuous variables and logit link function for dichotomous outcomes; the model included product regimen indicators (daily rectal vs. daily oral and RAI rectal vs. daily oral) as covariates and adjusted for study period to account for the cross-over design. The generalized estimating equations method was employed with exchangeable correlation structure to account for within subject correlation due to repeated measures. The associations between measures of sexual behavior and product acceptability were also explored using linear regressions and adjusting for study period. We report the regression coefficients β corresponding to product regimen indicators that represent the adjusted mean difference (amd) on the outcome between each of the two study regimens (daily rectal and RAI rectal) and the reference regimen (daily oral). A similar analytic approach was employed to compare the rating of ease of gel use between the first few times and the last few times. As exploratory analyses, we have elected to note all associations at the .05 level. We report exact p-values in the tables to alert the reader that many are very close to that cut-point and would not be significant if adjustments for multiple comparisons were made. SPSS Statistics software, version 23, Armonk, NY: IBM Corp. was used for all analyses.

Results

Sample Description

Table I presents the demographic characteristics of participants as per CASI responses. Mean age was 31 years, and on average, they had completed 12 years of schooling. Four-fifths were employed. While the majority identified as men, 12% did not (e.g., transgender, gender non-conforming, women) and were reclassified by the research team as TGW. Nine out of 10 participants identified as gay/homosexual.

Acceptability at Baseline

At baseline, similarly high proportions of participants anticipated being likely or very likely to take the daily oral tablet (FTC/TDF) (88%), take the tablet before and after RAI (92%), or

use a RG-TFV gel before and after RAI (89%) for HIV prevention. Fewer participants (76%) anticipated likelihood of daily use of RG-TFV gel rectally. Given a choice between taking a tablet daily or with RAI, 55% preferred daily vs. 45% with RAI. Given a choice between using RG-TFV gel daily or with RAI, there was clear preference for the latter (27% vs. 73%, respectively). For the tablet, there were no significant differences by age concerning regimen preferences. A greater proportion of TGW preferred the daily tablet compared to those who identified as men (76% vs. 51%, p=.031). No other significant differences in product preference were associated with gender. Fewer U.S. respondents reported likelihood to use RG-TFV gel daily compared with respondents in other countries (59% vs. 90%, p<.001). For the gel, more U.S. participants preferred use with RAI than those from other countries (84% vs. 67%, p=.009).

Acceptability at Follow-up

Table II presents the average ratings of experiences using all three regimens: daily oral, daily rectal, and RAI rectal. Participants liked the daily oral regimen significantly more than either gel regimen. Twenty-two percent of participants expressed preference for a different gel viscosity (18% thicker, 4% thinner in daily regimen; 19% thicker, 2% thinner in RAI rectal regimen) and a quarter preferred a different volume in the applicator (13% more, 12% less in daily rectal regimen; 15% more, 11% less in RAI rectal regimen).

Table II also shows scores for ease of product use. Overall, the daily oral regimen was rated significantly easier to use than both rectal regimens, whereas there were no significant differences in ease of use between daily rectal and RAI rectal regimens. On average, participants reported that gel use was easy and became easier with experience, as reflected in the improvement of scores between the first few times used and the last few times used (data not shown in table). Ratings for the daily rectal regimen improved from 3.04 to 3.33 (amd between the first few times and the last few times = 0.29, $p < .001$) and they improved from 3.07 to 3.38 (amd between the first few times and the last few times equals 0.31, $p < .001$) for the RAI rectal regimen. All ease of use ratings were collected at the end of the study period.

Concerning the applicator used to deliver the gel, mean scores correspond to the “liked a little” point of the scale. Not shown in the table, 67% of participants liked the applicator (very much or a little).

In terms of likelihood of future use, Table II shows that the daily oral regimen received significantly higher scores than either rectal regimen. Furthermore, the RAI rectal regimen score was statistically significantly higher than that of daily rectal regimen.

Acceptability Endpoints

Table III summarizes the overall favorable responses of the three acceptability endpoints. In terms of liking the products and overall ease of use, most participants preferred the daily oral regimen (91% and 92% respectively), followed by the RAI rectal regimen (79% and 90%); their least preferred was the daily rectal regimen (74% and 87%). Likelihood of future product use showed the same ranking expressed at baseline. The largest proportion of participants (87%) would be likely to use the daily oral regimen, followed by those likely to

use the RAI rectal regimen (82%); the least favorite option was daily rectal regimen (72%). Cranston et al.[27] report that participants liked the daily oral regimen significantly more than either rectal regimen and that their likelihood of using it was significantly higher than daily rectal. Not included in Table III, when the three acceptability endpoints were compared across country of residence adjusting for product order, there were three significant differences, with U.S. participants providing the lowest rating in each case: overall liking of daily rectal (liked by 85%, 82% and 86% in Thailand, South Africa, & Peru, respectively, compared to 59% in the U.S.; $p = .002$) overall liking of RAI rectal (liked by 91%, 73% and 86% in Thailand, South Africa, & Peru, respectively, compared to 70% in the U.S.; $p = .027$), and intentions to use daily rectal (likely to use by 80%, 88% and 89% in Thailand, South Africa, & Peru, respectively, compared to 55% in the U.S.; $p < .001$).

Association of Acceptability with Sexual Behavior

During the 24 weeks of product use (three 8-week periods), participants reported a median of seven sexual partners (range 0–113), four occasions of insertive anal intercourse (IAI) (range 0–90; 65% > 0), and 10 occasions of RAI (range 0–107; 98% > 0). Thirty (16%) of participants reported transactional sex (paid or received money or other goods in exchange for sex). We analyzed the association between these three sexual behavior measures and ease of use, overall liking, and likelihood to use for all three products. The results of the nine regressions (adjusted for study period) for each measure are shown in Table IV. Those with more sex partners expressed higher likelihood to use the daily oral regimen. More frequent IAI was associated with lower overall liking scores for both daily rectal and RAI rectal regimens. Those with more RAI occasions were more likely to find the daily oral and daily rectal regimens easy to use, overall liked the daily rectal and RAI rectal regimens more, and would be more likely to use both the daily oral and daily rectal regimens. Transactional sex was significantly associated with only 1 acceptability measure. Those who reported transactional sex found the pill *less* easy to use compared to those who did not report transactional sex.

Participant's Sexual Enjoyment and Partner's Reaction by Regimen

Table V shows that most participants (84% in daily oral, and 88% on both daily and RAI rectal) felt sexual enjoyment was not affected by product use. Among the few who felt otherwise, more reported increased sexual enjoyment; however, this difference was not statistically significant.

Partner reaction questions were answered by 96% (daily tablet), 95% (daily gel), and 98% (RAI gel) of the 187 participants. Most participants reported that partners had no reaction to product use. Positive partner reactions were reported by 27% of participants in the daily tablet regimen, 17% in the daily gel regimen, and 19% in the RAI gel regimen; negative reactions were reported by only 4% of the participants in each regimen (Table V).

Most and Least Liked Regimens

After trying all three regimens and responding to the acceptability questions for each regimen as presented above, thus having had a chance to reflect on different aspects of acceptability, participants were asked which regimen they liked the most and the least.

Table V shows that 73% of participants preferred the daily oral. Nonetheless, 28% of participants said that daily oral was the regimen they liked the least. The next preferred regimen was RAI rectal (19%), and only 8% of participants liked the daily rectal best.

Discussion

This was the first Phase 2 trial in which a rectal microbicide gel with HIV prevention potential was studied in at-risk MSM and TGW. A primary study objective was to determine the acceptability of RG-TFV gel. We found that RG-TFV gel was acceptable to MSM and TGW who, on average, liked the gel, found it easy to use, and reported being likely to use it in the future. Of the two gel regimens, RAI rectal was preferred over daily rectal. This comes as no surprise, given that the logistics of daily delivery of a rectal gel are more cumbersome than its use in association with RAI, a practice for which many habitually use lubricant gels.[29–31] Even at baseline, participants anticipated that daily use of the gel would be their least favorite choice. Yet, given the need to evaluate safety in an early phase study, daily use was required.

Comparing acceptability of the rectal gel to a daily oral tablet, the latter was preferred by three-quarters of participants after having tried both. This may be due to the high familiarity that most people have with pill-taking, plus the public knowledge that oral PrEP could confer a very high level of HIV protection if used consistently.[32] Yet, a nonnegligible 28% of participants declared that daily oral was their least preferred regimen, choosing gel (especially in the RAI rectal regimen) over the tablet. Similar results have been seen in other studies of hypothetical acceptability[33]; in particular, people concerned about potential side effects of a systemic HIV-prevention regimen may choose not to take a daily tablet.[4,5,7] Therefore, some people at risk for HIV due to RAI practices could benefit from an alternative to oral PrEP. Condoms have proved insufficient to stop the HIV epidemic due to lack of acceptability and inconsistent use among many at risk for HIV. This led to the exploration of other strategies such as male circumcision and oral PrEP. Evidence that such methods may still present acceptability barriers for some warrants the continuation of research on other options.

Participants reported that gel use became easier with experience. This may be important for future trials. Participants may require some degree of encouragement or incentives to overcome initial barriers to product use before achieving a stage of increased familiarity and comfort. Also, microbicide gel acceptability could be increased if it were available in at least two different viscosities, as some participants preferred a thicker product.

In prior studies, the gel applicator used in this study elicited criticism from users[22,23], especially in qualitative evaluations. In this study, which used only quantitative measures for applicator evaluation, participants were less critical. Nevertheless, research is warranted on improved rectal delivery methods that may not require applicators, such as rapidly dissolving tablets, suppositories or rectal inserts.

Geographical differences were observed in terms of product acceptability, with US being significantly less favorable to gels than non-US participants. As other studies have noted

[16,21,24], there may be sociocultural contexts that influence rectal microbicide acceptability. In addition, the promotion of oral PrEP in the US and publicity on its effectiveness in preventing HIV may have influenced responses. Conversely, if effective rectal microbicides could be produced at low cost, they could be an attractive alternative to oral PrEP outside the US.

Participants with higher numbers of sexual partners were more likely to prefer tablets over gel. This may be an issue of practicality. Someone who anticipates a high frequency of partners may want to be ready for unplanned sexual occasions, which may be achieved more easily taking a tablet daily than using a rectally applied gel, especially if the sexual episode does not take place in the home of the respondent. Sexual role, whether insertive or receptive, also appeared to influence acceptability, as those with more receptive occasions expressed higher acceptability of all three regimens than respondents with more insertive occasions. This may be related to heightened awareness of the increased risk of HIV transmission during RAI and the fact that those who primarily engage in RAI are at a relative disadvantage in the use of male condoms, which is dependent on the insertive partner's willingness. These factors may have motivated those engaging in RAI to be more tolerant of discomforts in order to be protected.

Given that a primary barrier to condom use is interference with sexual enjoyment, it is reassuring that a large majority of participants felt that sexual enjoyment was not affected by any of the regimens or that it was enhanced. Equally important is that most partners' reactions, when they occurred, were positive.

This study has several limitations. First, it was designed mainly to test the safety of RG-TFV gel. As a result, in one regimen gel had to be used daily regardless of likelihood of RAI, and in another gel had to be used at least twice a week in absence of RAI. These are hardly conditions under which a rectal microbicide would be used in the real world. Second, the sample consisted of less than two hundred, not-randomly recruited individuals who acknowledged engaging in sexual risk behavior. As such, they may have already been predisposed to have higher tolerance for potential discomforts involved in applying a gel rectally in exchange for HIV protection. Yet, this potential bias may also help us understand rectal microbicide gel acceptability by the population for whom the product is being developed. Relatedly, partner reactions in the context of a self-selected sample of MSM who opt to participate in a time-limited clinical trial may be different to those in the real world. In addition, the sample of transgender women was small, which may have limited our ability to detect gender-based differences in acceptability. Furthermore, we were unable to differentiate product preferences by sociodemographic and behavioral characteristics, but our work indicates that this could be a direction for further research. Finally, oral PrEP efficacy is known whereas gel efficacy is not, and this may have biased respondents to favor oral tablets. This study was designed before results documenting the effectiveness of intermittent oral PrEP were published [34] and it did not include an arm with such regimen. Yet, at baseline our respondents indicated that slightly more than half preferred a daily pill over a pill taken in association with RAI.

Despite these limitations, this study highlights the potential for non-systemic, topical HIV prevention methods. Future work should explore in-depth the barriers and facilitators of rectal microbicide acceptability to orient developers towards increasing product acceptability.

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Table I

Demographical characteristics of MTN-017 participants (N=187) recruited from September 2013 to November 2014

	Mean (SD)	Range
Age	31.4 (9.3)	18–64
Education (years)	12.3 (1.9)	0–13
	N*	%*
Currently working full- or part-time	144	79%
Currently in school full- or part-time	52	28%
Country of residence		
Peru	36	19%
South Africa	18	10%
Thailand	54	29%
United States (including Puerto Rico)	79	42%
Gender		
Cisgender Man	163	88%
Transgender Woman	23	12%
Sexual identity		
Gay/homosexual	164	91%
Bisexual	13	7%
Straight/heterosexual	3	2%
Sexual behavior during 24 week follow-up period	Median	Range
Number of sexual partners	7	0–113
Frequency of insertive anal sex	4	0–90
Frequency of receptive anal sex	10	0–107

* Ns may not sum to 187 due to missing data; percentages are of those with non-missing data. SD= standard deviation.

Table II

Acceptability by regimen at end-of-period follow-up visit among transgender women and cisgender men who have sex with men in MTN-017 (N=187) recruited from September 2013 to November 2014 in the US, Thailand, Peru and South Africa

		Scale	Daily oral unadjusted mean	Daily rectal unadjusted mean	RAI rectal unadjusted mean	Adjusted mean difference/ odds ratio	p[1]
Liking the product							
	Overall	1=disliked very much, 2=disliked a little, 3=liked a little, 4=liked very much	3.51	3.05	3.14	−0.46 −0.37	<.001 <.001
	Prefer gel thicker/thinner (% Yes)[2]			22%	22%	0.99	.969
	Prefer more/less gel in applicator (% Yes)[2]			25%	25%	0.99	.974
Ease of use							
	Overall	1=very difficult, 2=difficult, 3=easy, 4=very easy	3.54	3.19	3.19	−0.35 −0.35	<.001 <.001
	Ease of gel use first few times			3.04	3.07	−0.03	.559
	Ease of gel use last few times			3.33	3.38	−0.05	.306
Liking of applicator							
	Overall	1= disliked very much, 2= disliked a little, 3= liked a little, 4= liked very much		2.92	2.98	−0.03	.591
	Bothered by…						
	-size of applicator	1=not bothered at all, 2=bothered a little, 3=bothered a lot		1.36	1.37	−0.01	.759
	-wrapper			1.22	1.17	0.05	.171
	-assembly process			1.41	1.40	0.03	.518
	-lack of tip lubrication			1.84	1.82	0.02	.667
	-finding position to insert applicator			1.51	1.47	0.04	.390
	Pain or trauma due to insertion	1=none, 2=some, 3=a lot		1.39	1.29	0.09	.035
	Portability	1=very difficult, 2=difficult, 3=easy, 4=very easy		2.86	2.93	−0.09	.144

		Scale	Daily oral unadjusted mean	Daily rectal unadjusted mean	RAI rectal unadjusted mean	Adjusted mean difference/ odds ratio	p[1]
Likelihood to use							
	Overall	1=very unlikely, 2=unlikely, 3=likely, 4=very likely	3.38	2.91	3.16	−0.47 −0.22	<.001 .016

[1] p-values are in the following order: for 3-group comparisons: Daily Gel vs. Daily Tablet then RAI Gel vs. Daily Tablet; for 2-group comparisons: Daily Gel vs. RAI Gel.

[2] Percentages are rounded.

Table III

Proportion of favorable responses by product regimen among transgender women and cisgender men who have sex with men in MTN-017 (N=187) recruited from September 2013 to November 2014 in the US, Thailand, Peru and South Africa

	Daily oral	Daily rectal	RAI rectal
Overall liked the product[1]	91%	74%	79%
Found product easy to use[2]	92%	87%	90%
Likely to use product in future[3]	87%	72%	82%

[1] Original 4-point response scales were dichotomized into Liked (very much or a little) vs. Disliked (very much or a little);

[2] Easy to use (easy or very easy) vs. Difficult to use (difficult or very difficult);

[3] Likely to use (likely or very likely) vs. Unlikely to use (unlikely or very unlikely).

RAI= receptive anal intercourse.

Table IV

Association between sexual behavior and product acceptability among transgender women and cisgender men who have sex with men in MTN-017 (N=187) recruited from September 2013 to November 2014 in the US, Thailand, Peru and South Africa

	Daily oral						Daily rectal						RAI rectal					
	Ease of use		Overall liking		Likelihood to use		Ease of use		Overall liking		Likelihood to use		Ease of use		Overall liking		Likelihood to use	
	β*	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p	β	p
Sex partners	.13	.084	.13	.074	.15	.043	.03	.669	−.06	.405	−.00	.975	−.02	.803	−.02	.810	−.05	.500
Insertive anal sex	.13	.078	.08	.291	.10	.193	−.05	.468	−.16	.037	−.05	.508	−.04	.637	−.18	.015	−.04	.574
Receptive anal sex	.15	.048	.08	.270	.16	.033	.22	.002	.24	.001	.18	.017	.05	.497	.20	.007	−.04	.632
Any transactional sex	−.19	.012	−.08	.263	−.05	.498	−.01	.895	.01	.881	.09	.205	−.08	.269	.09	.246	−.04	.641

*β coefficients and p-values from linear regressions adjusting for study period. Associations with p≤ .05 have been highlighted.

RAI= receptive anal intercourse

Table V

Participant's sexual enjoyment, partner's reaction, and final preference per regimen among transgender women and cisgender men who have sex with men in MTN-017 (N=187) recruited from September 2013 to November 2014 in the US, Thailand, Peru and South Africa

	Daily oral	Daily rectal	RAI rectal
	N (%[2])	N (%[2])	N (%[2])
Participant's sexual enjoyment[1]			
More	23 (13%)	12 (7%)	13 (8%)
Less	5 (3%)	9 (5%)	8 (5%)
Not affected	149 (84%)	157 (88%)	152 (88%)
Partner's reactions[1]			
Negative	7 (4%)	7 (4%)	7 (4%)
Positive	45 (27%)	29 (17%)	32 (19%)
Participant's final preference			
Liked the most	130 (73%)	14 (8%)	33 (19%)
Liked the least	50 (28%)	76 (43%)	50 (28%)

[1]Differences in participant's sexual enjoyment and partner's reactions were not statistically significant across the 3 regimens.

[2]Percents are of those with non-missing data. N varied question-by-question ranging from 166 to 180.