

https://dspace.org/

Higher Acceptability of the Monthly Dapivirine Ring Versus Daily Oral PreExposure Prophylaxis Among Adolescent Girls and Young Women in SubSaharan Africa in the REACH Trial

B. A Friedland; E. N Browne; S. T Roberts; K Ngure; E et al ...

https://hdl.handle.net/10539/48999
WOS

Downloaded from a DSpace repository. https://dspace.org/

OPEN

Higher Acceptability of the Monthly Dapivirine Ring Versus Daily Oral Pre-Exposure Prophylaxis Among Adolescent Girls and Young Women in Sub-Saharan Africa in the REACH Trial

Barbara A. Friedland, MPH,[a] Erica N. Browne, MS,[b] Sarah T. Roberts, PhD,[b] Kenneth Ngure, PhD,[c,d] Rita Nakalega, MBChB,[e] Pippa Macdonald, MBChB,[f] Cynthia Nombeko Mpongo, BA,[f] Siyanda Tenza, BSocSci,[g] Nomsa Mhlanga, MA,[h] Danny Szydlo, MS,[i] Sherri Johnson, MPH,[j] Tara McClure, MPH,[j] Gonasagrie Nair, MBChB,[k] Connie Celum, MD,[d] Sharon L. Hillier, PhD,[l] and Ariane van der Straten, PhD,[m,n] on behalf of the MTN-034 REACH clinical trial team

Background: Oral pre-exposure prophylaxis (PrEP) is effective for HIV prevention, yet use has been inconsistent in adolescent girls and young women (AGYW). We compared PrEP with the dapivirine vaginal ring (ring) among AGYW in MTN-034 (REACH).

Methods: We randomized 247 16–21-yr-old AGYW (South Africa, Uganda, Zimbabwe) to the sequence of using the ring and oral PrEP for 6 m each (February 2019–September 2021). Participants rated overall product acceptability (1, dislike very much to 5, like very much) after 3 m and 6 m, and product characteristics/use attributes after 3 m. We compared proportions of participants rating each product a "5" (binomial model with generalized estimating equations). We assessed associations between product characteristics/use attribute ratings at 3 m and overall acceptability after 6 m (χ^2).

Received for publication October 18, 2024; accepted July 10, 2025.

From the [a]Population Council, Center for Biomedical Research, New York, NY; [b]RTI International San Francisco Office, Women's Global Health Imperative (WGHI) Program, San Francisco, CA; [c]Jomo Kenyatta University of Agriculture and Technology, School of Public Health, Nairobi, Kenya; [d]University of Washington, Global Health, Seattle, WA; [e]Makerere University-John Hopkins University Research Collaboration, Kampala, Uganda; [f]University of Cape Town Desmond Tutu HIV Centre, Cape Town, South Africa; [g]Wits Reproductive Health and HIV Institute, Faculty of Health Sciences, Johannesburg, South Africa; [h]University of Zimbabwe Clinical Trials Research Centre, Harare, Zimbabwe; [i]Fred Hutchinson Cancer Research Center, Vaccine and Infectious Disease Division, Seattle, WA; [j]FHI 360, Durham, NC; [k]Stellenbosch University, Centre for Medical Ethics and Law, Stellenbosch, South Africa; [l]University of Pittsburgh School of Medicine, Obstetrics, Gynecology and Reproductive Sciences, Magee Womens Hospital of UPMC, Pittsburgh, PA; [m]ASTRA Consulting, Kensington, CA; and [n]Center for AIDS prevention Studies, University of California, San Francisco, San Franciso, CA.

The study was designed and implemented by the Microbicide Trials Network (MTN) of the National Institutes of Health. The MTN was fully funded by the National Institutes of Health, including the National Institute of Allergy and Infectious Diseases through individual grants (UM1AI068633, UM1AI068615, and UM1AI106707), with cofunding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the US National Institutes of Health. The National Institutes of Health was the regulatory sponsor. Oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) was donated by Gilead Sciences. The dapivirine vaginal rings used in this study were developed and supplied by the International Partnership for Microbicides (IPM). IPM's portfolio of products and other assets was acquired by the Population Council in 2022.

C.C. has received consulting fees from Gilead Sciences and Merck and has provided expert witness for Gilead. SLH has received consulting fees and funds to her institution from Merck. K.N. has received research funds from Merck (MSD). B.A.F. is employed by the Population Council that acquired IPM's portfolio of products and other assets in 2022. Oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) was donated by Gilead Sciences.

The protocol was reviewed and approved by the ethics committees at each study site. All participants provided written informed consent in their preferred language (English or their local language) before undergoing any procedures. Local regulations were followed regarding parental or guardian informed consent and adolescent assent for participants under the legal age of consent, who were reconsented as adults if they reached 18 years of age during the study.

Clinicaltrials.gov registration: NCT03593655

Data management was provided by The Statistical Center for HIV/AIDS Research & Prevention (Fred Hutchinson Cancer Research Center, Seattle, WA) and site laboratory oversight was provided by the Microbicide Trials Network Laboratory Center (Pittsburgh, PA).

Individual participant data that underlie the results reported in this article, after deidentification, are available, beginning after publication, as well as the study protocol, data dictionary, statistical analysis plan, and informed consent. Data are available for researchers who provide a methodologically sound proposal in accordance with policies of the Microbicide Trials Network (MTN).

B.A.F. conceptualized the analysis, drafted and edited the article, and oversaw development of the ACASI programming. E.B. conducted the analysis, provided figures, and contributed to drafting the article. D.S. curated and verified the data. A.v.d.S., S.R., and K.N. designed the data collection instruments and implementation plan. C.C., G.N., K.N., R.N., P.M., C.N.M., S.T., and N.M. conducted investigations, and reviewed and edited the article. S.L.H. conceptualized the trial, acquired funding, and reviewed and edited the article. S.J. and T.M. supervised the project and reviewed and edited the article. All authors had access to the data and reviewed and approved the final article for publication.

Correspondence to: Barbara A. Friedland, MPH, Population Council Center for Biomedical Research 1230 York Avenue NY, NY 10065 (e-mail: bfriedland@popcouncil.org).

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Results:Overall, 65% and 41% of participants rated the ring versus PrEP a "5" (adjusted risk difference [aRD] 24%, 95% CI: 15%, 32%; $P < 0.001$). For both products, high overall acceptability was associated with "excellent" self-rated adherence (ring, $P < 0.001$; PrEP, $P = 0.03$), product appearance (ring, $P = 0.005$; PrEP, $P < 0.001$), and ease of use (ring, $P = 0.001$; PrEP, $P = 0.003$). Not worrying about/or experiencing side effects were also associated with high acceptability of oral PREP.

Conclusions: The dapivirine ring was highly acceptable to substantially more individuals than oral PrEP, although a significant minority rated oral PrEP highly, even after using the ring. As has been found in the contraceptive field, offering AGYW a choice of PrEP products is likely to increase the use of any HIV prevention method in this vulnerable population.

Key Words: PrEP, HIV prevention, adolescent girls and young women, Africa < Region, acceptability, dapivirine ring

(*J Acquir Immune Defic Syndr* 2025;100:415–424)

INTRODUCTION

HIV incidence has been declining globally, yet 15–24-year-old adolescent girls and young women (AGYW) continue to be disproportionately affected, particularly in sub-Saharan Africa (SSA).[1–3] In 2021, 250,000 AGYW globally, 82% living in SSA, were newly infected with HIV—a rate 3 times higher than males of the same age. AGYW are particularly vulnerable because many of the biologic, psychologic, and cultural factors that increase their risk also limit their ability to access and use existing HIV prevention strategies.[2–6]

Tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) used as oral pre-exposure prophylaxis (PrEP) is highly effective in reducing HIV transmission;[7] however, uptake, adherence, and persistence have been suboptimal among AGYW because of the anxiety or burden of daily pill-taking, and the possible (or experienced) side effects of PrEP.[8–10] Stigma is also a key factor limiting oral PrEP use; AGYW worry that community members will think they are living with HIV if they are seen taking the same drugs used for treatment, or that they will be labeled as promiscuous or sex workers if they seek PrEP.[10–12] AGYW also fear violence or potential relationship dissolution if partners suspect them of mistrust or infidelity.[13]

New PrEP methods are being developed and introduced to expand the HIV prevention options, because no single product will work for all users.[14] The 1-month dapivirine vaginal ring (ring), which was approved by the European Medicines Agency (EMA) and received WHO prequalification in 2020,[15] was shown to reduce HIV risk by approximately 30% among 18–45-year-old women.[16,17] However, although not powered to do so, subanalyses showed no protection in 18–21 year-old AGYW because of low adherence.[16–18]

Recognizing that acceptability influences product uptake and adherence, many researchers have sought to develop frameworks to assess acceptability within clinical trials of oral PrEP and microbicides.[19–21] In a conceptual model by Mensch et al,[21] acceptability is a proximal determinant to product choice and adherence. Acceptability is conceived of as an individual's perceptions of a product's characteristics and use attributes that may act as facilitators or barriers to adherence, and is situated within a socio-ecological framework that incorporates individuals' characteristics (such as age, marital status, education, worry about HIV) and contextual factors (such as community norms) that may also influence acceptability and, in turn, adherence. Regulatory agencies have also begun to require acceptability data as a critical component of new drug applications.[22,23]

To inform the continued roll out of oral PrEP and the introduction and scale-up of the dapivirine ring in SSA, we evaluated product acceptability among 16–21-year-old AGYW in South Africa, Uganda, and Zimbabwe participating in MTN-034, or "REACH" (Reversing the Epidemic in Africa with Choices in Prevention). Primary objectives of REACH were to evaluate and compare adherence with and safety of oral PrEP and the ring; assessing and comparing the acceptability of the 2 products were a secondary objective, and the focus of this article.

METHODS

Study Design and Population

REACH was a randomized, 2-arm, open-label, crossover trial comparing oral PrEP and the ring (Clinicaltrials.gov registration: NCT03593655). Detailed methods have been described previously.[24] In brief, we implemented REACH between February 2019 and September 2021 among 247 healthy, sexually active, HIV seronegative nonpregnant cisgender AGYW at 4 sites: Cape Town and Johannesburg, South Africa; Kampala, Uganda; and Harare, Zimbabwe.[24,25] We randomized (1:1) participants to 1 of 2 sequences of study product use: the ring used continuously for 6 months (with a new ring each month) followed by daily PrEP for 6 months, or vice versa (Fig. 1). After completing the 12-month crossover period, participants could choose PrEP, the ring, or neither for an additional 6-month Choice period. We compared overall acceptability of oral PrEP and the ring during the randomized crossover period, and assessed how specific components of product acceptability were associated with overall acceptability of each product, based on the Mensch model.[21]

Data Collection Procedures

Participants attended monthly clinic visits with clinical evaluations, pelvic examinations, adherence assessments (tenofovir diphosphate levels in dried blood spots, residual dapivirine in used rings), and counseling to encourage adherence by providing drug level feedback.[24] Participants completed behavioral questionnaires, including acceptability assessments, at baseline and quarterly thereafter through audio computer-assisted self-interviewing (ACASI) on tablet computers in private in their choice of English or the local language (Luganda, Uganda; Shona, Zimbabwe; isiXhosa and isiZulu, South Africa).

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

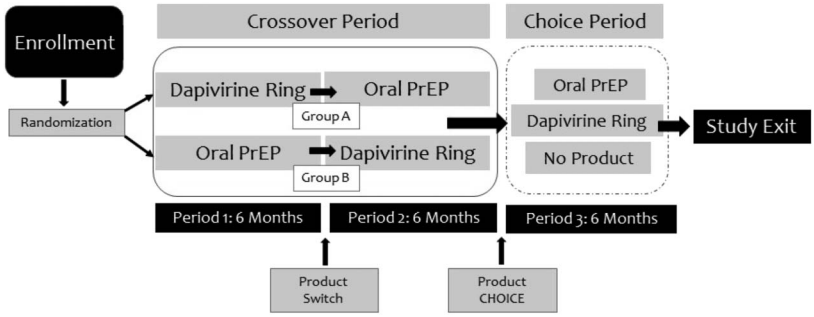


FIGURE 1. Study schema.

Measures

We collected baseline data on ***individual characteristics***, such as marital status, education, income, partnership status, sexual behaviors, and HIV risk perception. At 2 time points—after ***3 and 6 months*** of product use (and at the Early Product Use End Visit [EPUEV] for those who discontinued early)—we asked participants to rate how much they liked using each product, overall, on a 5-point Likert scale (1–5, "dislike very much" to "like very much"). After 3 months of using each product, we asked participants detailed questions about specific components of product acceptability, including *product characteristics* (such as overall look, size, smell of the ring/PrEP), *use attributes* (such as comfort wearing the ring/swallowing PrEP tablets daily, side effects, potential for discreet use), *effects on sex* (such as partner attitudes, sexual pleasure for participants and their partners), *product-associated norms* (such as future negative health effects, worry about incorrect use, hygiene), and *product efficacy*. We also asked participants to rate their adherence, framed as how well they had followed product use instructions in the past month (very poor, poor, fair, good, very good, excellent), a measure that has been used to assess antiviral treatment adherence.[26]

Statistical/Analytical Considerations

Our analytical sample included all participants who provided an overall acceptability rating after 6 months of use for at least 1 product. We used summary statistics (counts, proportions) to describe the participants and the acceptability measures. We described the overall acceptability of products and compared the proportion who found each product acceptable at each time point (after 3 and 6 months of use), rating it a 4 (liked) or 5 (liked very much). Because most participants found both products acceptable (rated 4 or 5), and a minority rated either product lower than a 4 ($n < 20$), we grouped neutral ratings ("neither like nor dislike") with lower ratings ("dislike" or "dislike very much") to account for potential social desirability bias.[27] Further analyses considered the outcome of "high overall acceptability" (rating the product 5, "like very much") versus all other ratings (1–4) after 6 months of use. We estimated and compared the proportions of participants rating each product as highly acceptable (rating of 5) using a binomial model, adjusting for site and period, and used generalized estimating equations with identity link and unstructured correlation to account for repeated measures. The model included 2 interaction terms: 1 between product and site and another between product and period. We assessed the impact of specific acceptability components rated after 3 months of use on high overall acceptability at the end of each product use period (6 months) using Chi-square tests. We used Stata 16.1 (StataCorp LLC, College Station, TX) for all analyses; *P*-values were uncorrected for multiple comparisons.

RESULTS

Nearly all (237/247; 96%) REACH participants provided an overall acceptability rating for at least 1 product after 6 months of use (Table 1) and 210 (85%) rated both products. Median age was 18 years old (IQR 17–19 years), most were single (88%), had completed secondary school (86%), and had a primary sex partner (89%). Almost half were somewhat or very worried about getting HIV in the next year, 36% had 2 or more partners in the 3 months before screening, 26% did not know their primary partners' HIV status, and 76% knew or suspected that their primary partners had other partners.

Overall Acceptability

The ring and PrEP were both rated a 4 or 5 (like/like very much) by most participants (Fig. 2). Overall acceptability of the ring was high and stable over time; 91% and 88% of participants reported liking or liking it very much (rated 4 or 5) after 3 and 6 months, respectively. Oral PrEP was also rated a 4 or 5 by most participants. However, between 3 and 6 months, the proportion of those rating it a 4 or 5 declined significantly from 76% to 64% (adjusted risk difference −12%, 95% CI: −19% to −6%) and the proportion who disliked it (rated a 1 or a 2) increased from 17% to 23%. The ring was rated as highly acceptable (5, liked very much) by 65% of participants versus 41% who rated PrEP a 5 (adjusted risk difference 24%, 95% CI: 15 to 32%; $P < 0.001$). Participants who were randomized to use the ring first were more likely to rate it a 5 compared with those who used it second (75% versus 54%; $P = 0.003$), whereas period did not have a significant impact on overall acceptability of oral PrEP. A higher proportion of women at all 4 sites liked the ring very much (rated a 5) compared with oral PrEP, with the greatest differences at the 2 South African sites (71% ring versus 30% PrEP, Johannesburg; 69% ring versus 39% PrEP, Cape Town). Of those who rated overall acceptability for both products, 57% rated both 4 or 5 (liked/liked a lot), and 28% rated both a 5. Approximately one-third of participants who

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

TABLE 1. Background Characteristics of Participants Who Provided an Overall Acceptability Rating for at Least One Product (N = 237)

	N	(%)
Age—mean, median (interquartile range)	18.2–18	17–19
Completed secondary school	205	86
Currently in school	89	38
Earns income	49	21
Marital status		
Single	206	87
Married or cohabitating	28	12
Separated or divorced	3	1
Parous	95	40
Primary sex partner		
Has a primary sex partner	211	89
Age difference > 5 yrs	75	36
Partnership for at least 1 yr	128	61
Primary partner provides financial support	130	62
Partner's HIV status		
Positive	3	1
Negative	154	73
Unknown	54	26
Partner has other partners		
Yes (knows or suspects)	47	22
No	51	24
Do not know	113	54
Sexual behavior and HIV risk		
Number of sex partners in past 3 mo		
0	11	5
1	140	59
2 or more	86	36
Any vaginal sex in past 3 mo	197	83
Condom use during last sex act	107	54
Any anal sex in past 3 mo	19	8
Condom use during last anal sex	16	84
Diagnosed with STI at enrollment	84	35
Received goods or money for sex in past 6 mo	61	26
Experienced physical intimate partner violence in past 6 mo	33	14
Perceived risk of HIV in next yr		
Very worried	68	29
Somewhat worried	28	12
A little worried	66	28
Not at all worried	75	32
Site		
Cape Town, South Africa	56	24
Johannesburg, South Africa	67	28
Kampala, Uganda	56	24
Harare, Zimbabwe	58	25
Product sequence (arm)		
A: Ring → Tablets	121	51
B: Tablets → Ring	116	49

rated the ring 4 or 5 (liked/liked a lot) rated PrEP 1, 2, or 3 (disliked a lot, disliked, neutral), and 7% who rated PrEP a 4 or 5 rated the ring a 1, 2, or 3 (data not shown).

Components of Acceptability

A total of 215 AGYW rated specific acceptability components after 3 months, and overall acceptability after 6 months of use (Tables 2 and 3).

Ring

After 3 months, most participants (74%) said the size of the ring was fine and 34% liked how it looked very much (Table 2). Most said the ring was easy to insert (72%) and remove (80%), and that it usually felt comfortable to have the ring inside the vagina every day (74%). Fewer participants did not mind wearing the ring for an entire month (29%) or during menses (36%). Two-thirds said they minded wearing the ring during sex, yet 61% said they never felt it during sex and 88% said the ring had increased or had no impact on their sexual pleasure. About half reported that their primary partner had ever felt the ring during sex (53%), though few partners asked participants to remove it during sex (9%) or at other times (7%). More AGYW thought the ring could be used without family members (68%) than sex partners (44%) knowing. About half of the participants were bothered by a change in vaginal scent (51%) or were worried about the cleanliness of the ring (53%). Most participants (81%) perceived the ring could provide "a lot of protection" from HIV and did not experience bothersome side effects (82%), although 54% were worried about negative health effects. Half rated themselves as "excellent" at keeping the ring in the vagina as instructed in the past 30 days (before the 3-month visit).

Oral PrEP

After 3 months of oral PrEP use, 56% said the size of the tablets was fine, 51% liked or were neutral about the sound the tablets made when carrying them, 69% liked or were neutral about how the tablets tasted, 75% liked or were neutral about the tablets' smell, and 23% liked the look of the tablets very much (Table 3). Although two-thirds of participants said it was easy or very easy to swallow the PrEP tablets (67%) or take them every day (68%), 86% said they minded (a little or a lot) taking PrEP daily. Most participants (91%) said PrEP had no impact on their sexual pleasure. Fewer than half thought it could be used without a sex partner (43%) or family member (38%) knowing. Most participants (82%) thought PrEP can provide a lot of protection against HIV, although 71% were worried about forgetting to take the tablets, and while 56% had not experienced bothersome side effects, 62% were a little, somewhat, or very worried about negative health effects. Twenty percent rated themselves as "excellent" in taking the "tablets" (PrEP) in the way that they were supposed to in the past 30 days (before the 3-month visit).

Impact of Acceptability Components on Overall Acceptability

Self-reported adherence was the factor that was most strongly associated with overall acceptability after 6 months (Table 2); 61% of participants who rated the ring a 5 versus (vs) 32% who rated it 1–4 reported being "excellent" at keeping the

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

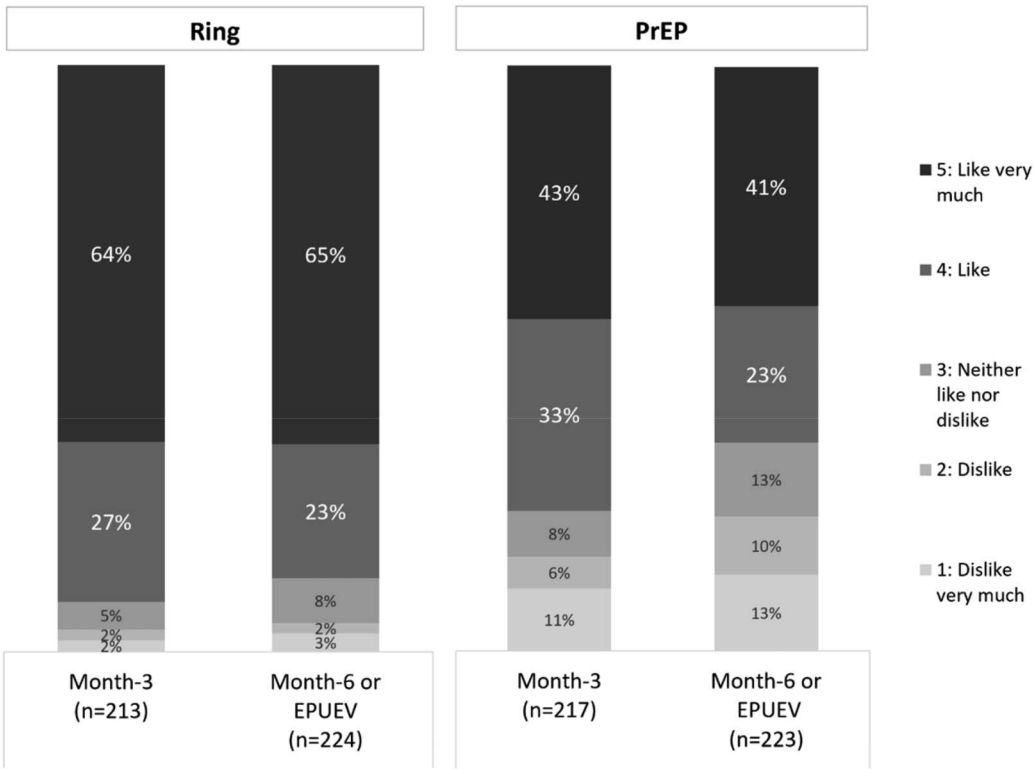


FIGURE 2. Acceptability of the ring and oral PrEP, crossover period (n = 237).

ring inserted for 30 days ($P < 0.001$). Other factors associated with high overall acceptability included being comfortable having the ring inside every day (82% vs 61%, $P = 0.001$) and liking the look of the ring (41% vs 22%, $P = 0.005$) after 3 months. More women with high overall acceptability did not mind wearing the ring for an entire month (33% with high acceptability did not mind at all vs 22% with lower acceptability, $P = 0.06$) and rated the size of the ring as "fine" (78% vs 66% with lower acceptability, $P = 0.05$), however, these differences were not statistically significant. Effect on sex, partner attitudes, beliefs, and worries about the ring and ability to use the ring discreetly were not associated with overall acceptability.

As shown in Table 3, participants were more likely to rate oral PrEP as a 5 (like very much) after 6 months if after 3 months they liked or were indifferent to the tablets' taste (80% vs 62%, $P = 0.009$), found the tablets easy or very easy to swallow (79% vs 59%, $P = 0.003$), felt like it was easy or very easy to take the tablets every day (77% vs 51%, $P = 0.01$), did not experience bothersome side effects (66% vs 50%, $P = 0.03$), or were not concerned about negative health effects (51% vs 30%, $P = 0.003$). In addition, liking the look of the tablets (37% vs 13%, $P< 0.001$) and rating oneself as "excellent" taking the tablets daily (27% vs 15%, $P = 0.03$) were associated with high overall acceptability.

DISCUSSION

In the 12-month randomized, crossover portion of the REACH trial, both the ring and oral PrEP were acceptable to most participants in South Africa, Uganda, and Zimbabwe. After 6 months of using each product, more than half of the participants rated both products as a 4 or 5 (liked/liked very much), and more than one-quarter rated both as a 5. However, approximately two-thirds of participants reported liking the ring very much (rating 5) versus less than half liking oral PrEP very much. Overall acceptability of the ring was consistently high for the entire 6-month use period, whereas oral PrEP's acceptability declined significantly between 3 and 6 months of use. Furthermore, more than one-third of the participants reported liking the ring a lot and disliking PrEP, while a small minority liked oral PrEP a lot and disliked the ring. The proportions who liked each product a lot (rated a 5) align with the proportions of women who chose each product for the 6-month Choice period (65% ring, 30% PrEP).[24]

Self-reported ratings of "excellent" at following instructions for product use were significantly associated with high acceptability for both products, although more than twice as many participants rated themselves as "excellent" for the ring versus PrEP. This finding underscores the importance of incorporating the construct of self-efficacy within acceptability assessments, as conceptualized by Sekhon et al[28] in the Theoretical Framework of Acceptability (TFA). In the TFA, "self-efficacy," defined as an individual's "confidence that they can perform the behavior(s) required to participate in the intervention," is 1 of 7 distinct constructs of acceptability. The significant association between one's ability to be adherent and acceptability also aligns with participants' selections for the Choice period, in which the strongest

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

TABLE 2. Associations Between Components of Ring Acceptability at 3 Months and High Overall Ring Acceptability After 6 Months of Use (n = 203)

	Highly Overall Acceptability After 6 months (rating 5: Like Very Much)						
	Yes		No		Total		*P*
Acceptability Components (Rated After 3 months)	**N**	**(%)**	**N**	**(%)**	**N**	**(%)**	
Total	129	100	74	100	203	100	
Product characteristics							
How the ring looks							**0.005**
Like very much	53	41	16	22	69	34	
Like, neither like/dislike, dislike, dislike very much	76	59	58	78	134	66	
Size of the ring							0.05
Size is fine	101	78	48	66	149	74	
Too big or too small	28	22	25	34	53	26	
Use attributes							
Ring insertion							0.30
Easy or very easy	96	74	50	68	146	72	
Neither easy/difficult, difficult, or very difficult	33	26	24	32	57	28	
Ring removal							0.46
Easy or very easy	103	81	56	77	159	80	
Neither easy/difficult, difficult, or very difficult	24	19	17	23	41	21	
How it felt to have the ring inside every day							**0.001**
Usually comfortable	105	82	45	61	150	74	
Sometimes/usually uncomfortable	23	18	29	39	52	26	
Minded wearing the ring for an entire month							0.06
Not at all	43	33	16	22	59	29	
A little or a lot	86	67	58	78	144	71	
Aware of ring during normal daily activities							0.10
Never	79	61	36	49	115	57	
Most of the time or some of the time	50	39	37	51	87	43	
Minded wearing during menses*							0.74
Not at all	39	35	23	38	62	36	
A little or a lot	72	65	38	62	110	64	
Had bothersome change in vaginal scent							
No	64	50	36	49	100	49	0.90
Yes—bothered a little or a lot	65	50	38	51	103	51	
Experienced bothersome side effects							0.09
No	110	85	56	76	166	82	
Yes—a little or a lot	19	15	18	24	37	18	
Ring can be used without family knowing							0.85
Yes	87	68	48	67	135	68	
No or do not know	41	32	24	33	65	32	
Ring can be used without sex partner knowing							0.92
Yes	56	44	31	43	87	44	
No or do not know	72	56	41	57	113	57	
Product efficacy							
Perceived level of protection ring can provide							0.11
A lot	108	84	54	75	162	81	
A little, some, or none	20	16	18	25	38	19	
Effect on sex†	123	95	70	95	193	95	
Felt the ring during sex							0.16
Never	79	65	37	54	116	61	
Sometimes/often	43	35	31	46	74	39	
Minded wearing the ring during sex							0.26
Not at all	45	37	20	29	65	34	
A little/a lot	78	63	50	71	128	66	

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

TABLE 2. (*Continued*) Associations Between Components of Ring Acceptability at 3 Months and High Overall Ring Acceptability After 6 Months of Use (n = 203)

	Highly Overall Acceptability After 6 months (rating 5: Like Very Much)						
	Yes		No		Total		*P*
Acceptability Components (Rated After 3 months)	**N**	**(%)**	**N**	**(%)**	**N**	**(%)**	
Impact on sexual pleasure							0.54
Increases/does not change	107	87	63	90	170	88	
Decreases	16	13	7	10	23	12	
Product-associated norms							
Concerned about negative health effects‡							0.30
Not at all worried	63	49	30	42	93	47	
A little, somewhat, or very worried	65	51	42	58	107	54	
Concerned about cleanliness‡							0.40
Not at all worried	63	49	31	43	94	47	
A little, somewhat, or very worried	65	51	41	57	106	53	
Partner attitudes§ (subtotal w/partner)	109	84	61	82	170	84	
Primary partner ever felt ring during sex							0.46
No	49	45	31	51	80	47	
Yes	60	55	30	49	90	53	
Partner ever asked to remove the ring during sex							0.59
No	100	92	54	89	154	91	
Yes	9	8	7	12	16	9	
Partner ever asked to remove the ring aside from during sex							0.35
No	103	95	55	90	158	93	
Yes	6	6	6	10	12	7	
Self-reported adherence							
How well you used the ring in the way you were supposed to in the past 30 d							**<0.001**
Excellent	78	61	24	32	102	50	
Very poor, poor, fair, good, or very good	51	40	50	68	101	50	

Bold indicates $P < 0.05$.
*Had menses in the past 3 months.
†Sexually active in the past 3 months.
‡Using as directed for 6 months or more.
§Those with a primary sex partner in the past 3 months.

predictor of choosing oral PrEP was having received drug level feedback, indicative of high adherence during the crossover period—concrete evidence that participants were able to be adherent.[24] In addition, the most significant correlate of adherence to oral PrEP throughout the entire REACH trial was rating it as highly acceptable.[29]

For both products, acceptability was also significantly associated with opinions about how the products looked and ease of using the regimens (such as keeping the ring inserted for 30 days or swallowing the tablets daily). Other studies of the dapivirine ring and rings, in general, have demonstrated, not surprisingly, that comfort is associated with acceptability.[30,31] However, although some studies have found, as we did, that how a ring looks affects acceptability, there is also evidence that women may be apprehensive about using a ring when they first see it, but that acceptability improves with actual use.[32,33] In contrast, although other studies have noted the impact of partner disclosure and feeling the ring during sex on acceptability,[34,35] we found no associations between impact on sex or ability to use the ring discreetly and high overall acceptability in this study. Acceptability of oral PrEP was significantly associated with concerns about negative health effects and experiencing bothersome side effects, which has been seen in other PrEP studies.[10,36]

Acceptability varied significantly by country. In South Africa, approximately twice as many participants rated the ring highly compared with oral PrEP, whereas acceptability of oral PrEP was higher in Uganda and Zimbabwe, although not significantly different than the ring. The differences between sites and countries highlight the impact of context on acceptability, as articulated by Mensch[21] and others.[28] These differences may be attributable to the varying models of oral PrEP introduction and roll-out in each country or other factors, such as differences in predominant contraceptive methods.

REACH is the first study where AGYW in SSA have had the opportunity to try both oral PrEP and the ring for 6 months each before choosing which method they prefer to use. Our findings show that the ring is highly acceptable to a higher proportion of AGYW than PrEP, indicating that

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

TABLE 3. Associations Between Components of Oral PrEP Acceptability at 3 Months and High Overall PrEP Acceptability After 6 Months of Use (n = 203)

	Highly Overall Acceptability at 6 Months (rating 5: Like Very Much)						
	Yes		No		Total		*P*
Acceptability Components (Rated After 3 Months)	**N**	**(%)**	**N**	**(%)**	**N**	**(%)**	
Total	84	100	119	100	203	100	
Product characteristics							
How tablets look							**<0.001**
Like very much	31	37	15	13	46	23	
Like, neither like/dislike, dislike, dislike very much	53	63	104	87	157	77	
Size of the tablets							0.09
Size is fine	53	63	61	51	114	56	
Too big or too small	31	37	58	49	89	44	
Sound when carrying tablets							0.50
Like or neither like nor dislike	45	54	58	49	103	51	
Dislike	39	46	61	51	100	49	
Taste of tablets							**0.009**
Like or neither like nor dislike	66	80	74	62	140	69	
Dislike	17	21	45	38	62	31	
Smell of tablets							0.75
Like or neither like nor dislike	63	76	88	74	151	75	
Dislike	20	24	31	26	51	25	
Use attributes							
Swallowing the tablets							**0.003**
Easy or very easy	66	79	70	59	136	67	
Difficult, very difficult, or neither easy/difficult	18	21	49	41	67	33	
Storing the tablets at home							0.43
Easy or very easy	72	86	97	82	169	83	
Difficult, very difficult, or neither easy/difficult	12	14	22	19	34	17	
Mind taking the tablets every day							0.29
Not at all	9	11	19	16	28	14	
A little or a lot	75	89	100	84	175	86	
Ability to take tablets every day							**0.01**
Easy or very easy	65	77	72	61	137	68	
Difficult, very difficult, or neither easy/difficult	19	23	47	40	66	33	
Interfere with regular daily activities							0.12
Never	52	62	60	51	112	55	
Most/some of the time	32	38	58	49	90	45	
Tablets can be used without sex partner knowing							0.89
Yes	36	43	50	42	86	43	
No or do not know	47	57	68	58	115	57	
Tablets can be used without family knowing							0.95
Yes	32	38	45	39	77	38	
No or do not know	51	62	73	61	124	62	
Experienced side effects that were bothersome							**0.03**
No	55	66	59	50	114	56	
Yes—a little or a lot	29	35	60	50	89	44	
Product efficacy							
Perceived protection tablets can provide							0.06
A lot	73	88	91	77	164	82	
A little, some, or none	10	12	27	23	37	18	
Effect on sex (sexually active, past 3 months)	83	99	111	93	194	96	
Impact on sexual pleasure							0.71
Increases or does not change	75	90	102	92	177	91	
Decreases	8	10	9	8	17	9	

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

TABLE 3. (*Continued*) Associations Between Components of Oral PrEP Acceptability at 3 Months and High Overall PrEP Acceptability After 6 Months of Use (n = 203)

	Highly Overall Acceptability at 6 Months (rating 5: Like Very Much)						
	Yes		No		Total		*P*
Acceptability Components (Rated After 3 Months)	**N**	**(%)**	**N**	**(%)**	**N**	**(%)**	
Product-associated norms							
Concern about negative health effects*							**0.003**
Not at all worried	42	51	35	30	77	38	
A little, somewhat, or very worried	41	49	83	70	124	62	
Worried about forgetting to take the tablets							0.11
Not at all worried	29	35	29	25	58	29	
A little, somewhat, or very worried	54	65	89	75	143	71	
Self-reported adherence							
How well you took the tablets in the way you were supposed to in the past 30 d							0.03
Excellent	23	27	18	15	41	20	
Very poor, poor, fair, good, or very good	61	73	101	85	162	80	

Bold indicates $P < 0.05$.
*Using as directed for 6 months or more.

introducing the ring is likely to expand the proportion of AGYW using an effective HIV prevention method. However, we also found that oral PrEP is highly acceptable for a substantial number of AGYW, even after trying the ring. As has been the case with contraception,[37] it is likely that as the number of PrEP options increase, better coverage will ensue.[38]

Limitations

Our research had several limitations. First, our results are not generalizable because of a relatively small sample size that yielded small numbers for certain comparisons that might be significant in larger populations. In addition, REACH had strict eligibility criteria because of the lack of safety data for the ring in AGYW and was implemented in research centers where participants received extensive counseling and support —a level of care that may be unrealistic in typical service delivery settings. Second, there were several methodological limitations. Participants were asked about overall acceptability twice (at 3 and 6 months of use), but about specific components of acceptability only once (at 3 months), which may have compromised our ability to understand how opinions about product characteristics and use attributes influence overall acceptability over time. In addition, all behavioral data were self-reported, which is subject to social desirability bias.[27] However, the use of ACASI, which has been shown to improve reporting of sensitive behaviors,[39] likely reduced the impact of social desirability bias, given the variability of responses, overall, and the significantly different ratings of the ring and oral PrEP that aligned with product selection in the Choice period.[24] Finally, oral PrEP had been available in all 3 countries for several years before REACH began,[40] while the ring had not yet been approved or introduced. It is possible that existing PrEP programs may have negatively influenced opinions about PrEP, whereas the ring was a novel product that did not yet have negative associations in the communities. Yet, it is also possible that acceptability of the ring was diminished given it was an unfamiliar device.

CONCLUSIONS

The dapivirine ring was highly acceptable to twice as many AGYW than oral PrEP, although a significant minority rated oral PrEP highly, even after using the ring. As has been found in the contraceptive field, offering AGYW a choice of PrEP products is likely to increase the use of any HIV prevention method in this vulnerable population. Future research should evaluate whether or not the addition of new HIV prevention options increases the number of AGYW using any method.

ACKNOWLEDGMENTS

The authors thank the study participants and the teams at each of the sites for study implementation.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). In *DANGER: UNAIDS Global AIDS Update 2022 [Internet]. Geneva*; 2022. Available at: https://www.unaids.org/sites/default/files/media_asset/2022-global-aids-update-summary_en.pdf Accessed January 4, 2024.
2. Howard AL, Chiang L, Picchetti V, et al. Population estimates of HIV risk factors to inform HIV prevention programming for adolescent girls and young women. *AIDS Educ Prev*. 2023;35(suppl A):20–38.
3. Murewanhema G, Musuka G, Moyo P, et al. HIV and adolescent girls and young women in sub-Saharan Africa: a call for expedited action to reduce new infections. *IJID Reg*. 2022;5:30–32.
4. Celum CL, Delany-Moretlwe S, Baeten JM, et al. HIV pre-exposure prophylaxis for adolescent girls and young women in Africa: from efficacy trials to delivery. *J Int AIDS Soc*. 2019;22:e25298.
5. Lewis L, Kharsany ABM, Humphries H, et al. HIV incidence and associated risk factors in adolescent girls and young women in South Africa: a population-based cohort study. *PLoS One*. 2022;17:e0279289.

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.

6. Mathur S, Pilgrim N, Patel SK, et al. HIV vulnerability among adolescent girls and young women: a multi-country latent class analysis approach. *Int J Public Health*. 2020;65:399–411.
7. Eakle R, Venter F, Rees H. Pre-exposure prophylaxis (PrEP) in an era of stalled HIV prevention: can it change the game?. *Retrovirology*. 2018;15: 29.
8. Eakle R, Weatherburn P, Bourne A. Understanding user perspectives of and preferences for oral PrEP for HIV prevention in the context of intervention scale-up: a synthesis of evidence from sub-Saharan Africa. *J Int AIDS Soc*. 2019;22(suppl 4):e25306.
9. Heck CJ, Abdool Karim Q. Enhancing oral PrEP uptake among adolescent girls and young women in Africa. *J Int AIDS Soc*. 2022;25: e25876.
10. Kayesu I, Mayanja Y, Nakirijja C, et al. Uptake of and adherence to oral pre-exposure prophylaxis among adolescent girls and young women at high risk of HIV-infection in Kampala, Uganda: a qualitative study of experiences, facilitators and barriers. *BMC Womens Health*. 2022;22: 440.
11. Calabrese SK, Dovidio JF, Tekeste M, et al. HIV pre-exposure prophylaxis stigma as a multidimensional barrier to uptake among women who attend planned parenthood. *J Acquir Immune Defic Syndr*. 2018;79:46–53.
12. Corneli A, Perry B, McKenna K, et al. Participants' explanations for Nonadherence in the FEM-PrEP clinical trial. *J Acquir Immune Defic Syndr*. 2016;71:452–461.
13. Jani N, Mathur S, Kahabuka C, et al. Relationship dynamics and anticipated stigma: key considerations for PrEP use among Tanzanian adolescent girls and young women and male partners. *PLoS One*. 2021; 16:e0246717.
14. Henderson M, Schmidt HMA, Chitembo L, et al. The future of pre-exposure prophylaxis (PrEP) for HIV prevention: a global qualitative Consultation on provider perspectives on new products and Differentiated service delivery. *AIDS Behav*. 2023;27:3755–3766.
15. European Medicines Agency (EMA). *Approval of the Dapivirine Ring for HIV Prevention for Women in High HIV Burden Settings [Internet]*. World Health Organization; 2020. Available at: https://www.who.int/news/item/24-07-2020-european-medicines-agency-(ema)-approval-of-the-dapivirine-ring-for-hiv-prevention-for-women-in-high-hiv-burden-settings. Accessed July 23, 2023.
16. Nel A, van Niekerk N, Kapiga S, et al. Safety and efficacy of a dapivirine vaginal ring for HIV prevention in women. *N Engl J Med*. 2016;375: 2133–2143.
17. Baeten JM, Palanee-Phillips T, Brown ER, et al. Use of a vaginal ring containing dapivirine for HIV-1 prevention in women. *N Engl J Med*. 2016;375:2121–2132.
18. Browne EN, Brown ER, Palanee-Phillips T, et al. Patterns of adherence to a dapivirine vaginal ring for HIV-1 prevention among South African women in a phase III randomized controlled trial. *J Acquir Immune Defic Syndr*. 2022;90:418–424.
19. Coly A, Gorbach PM. Microbicide acceptability research: recent findings and evolution across phases of product development. *Curr Opin HIV AIDS*. 2008;3:581–586.
20. Morrow KM, Ruiz MS. Assessing microbicide acceptability: a comprehensive and integrated approach. *AIDS Behav*. 2008;12:272–283.
21. Mensch BS, van der Straten A, Katzen LL. Acceptability in microbicide and PrEP trials: current status and a reconceptualization. *Curr Opin HIV AIDS*. 2012;7:534–541.
22. Stegemann S, Klingmann V, Reidemeister S, et al. Patient-centric drug product development: acceptability across patient populations - science and evidence. *Eur J Pharm Biopharm*. 2023;188:1–5.
23. Desai N, Edwards AJ, Ernest TB, et al. "Big Data" informed drug development: a case for acceptability. *Drug Discov Today*. 2021;26:865–869.
24. Nair G, Celum C, Szydlo D, et al. Adherence, safety, and choice of the monthly dapivirine vaginal ring or oral emtricitabine plus tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis among African adolescent girls and young women: a randomised, open-label, crossover trial. *Lancet HIV*. 2023;10:e779–e789.
25. Ngure K, Friedland BA, Szydlo DW, et al. Baseline preferences for oral pre-exposure prophylaxis (PrEP) or dapivirine intravaginal ring for HIV prevention among adolescent girls and young women in South Africa, Uganda and Zimbabwe (MTN-034/IPM-045 study). *PLoS One*. 2023;18: e0287525.
26. Wilson IB, Lee Y, Michaud J, et al. Validation of a new three-item self-report measure for medication adherence. *AIDS Behav*. 2016;20:2700–2708.
27. Nederhof AJ. Methods of coping with social desirability bias: a review. *Eur J Social Psychol*. 1985;15:263–280.
28. Sekhon M, Cartwright M, Francis JJ. Acceptability of healthcare interventions: an overview of reviews and development of a theoretical framework. *BMC Health Serv Res*. 2017;17:88.
29. Ngure K, Browne E, Reddy K, et al. Correlates of adherence to oral and vaginal pre-exposure prophylaxis (PrEP) among adolescent girls and young women (AGYW) participating in the MTN-034/REACH Trial. *AIDS Behav*. 1. 2024 Jun 9. doi: 10.1007/s10461-024-04382-3. Epub ahead of print. PMID: 38852114.
30. Ridgeway K, Montgomery ET, Smith K, et al. Vaginal ring acceptability: a systematic review and meta-analysis of vaginal ring experiences from around the world. *Contraception*. 2022;106:16–33.
31. Boyd P, Merkatz R, Variano B, et al. The ins and outs of drug-releasing vaginal rings: a literature review of expulsions and removals. *Expert Opin Drug Deliv*. 2020;17:1519–1540.
32. Baker Z, Javanbakht M, Moore J, et al. Qualitative study on the acceptability of and adherence to a vaginal ring for HIV prophylaxis among adolescent girls. *J Acquir Immune Defic Syndr*. 2021;87:944–950.
33. Roberts ST, Hawley I, Luecke E, et al. Acceptability and preference for 3-month versus 1-month vaginal rings for HIV-1 risk reduction among participants in a phase 1 trial. *J Womens Health (Larchmt)*. 2022;31: 1029–1039.
34. Laborde ND, Pleasants E, Reddy K, et al. Impact of the dapivirine vaginal ring on sexual experiences and intimate partnerships of women in an HIV prevention clinical trial: managing ring Detection and Hot sex. *AIDS Behav*. 2018;22:437–446.
35. Montgomery ET, van der Straten A, Chitukuta M, et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial. *AIDS*. 2017;31: 1159–1167.
36. Smit F, Masvawure TB. Barriers and facilitators to acceptability and uptake of pre-exposure prophylaxis (PrEP) among Black women in the United States: a systematic review. *J Racial Ethn Health Disparities*. 2024;11:2649–2662.
37. Ross J, Stover J. Use of modern contraception increases when more methods become available: analysis of evidence from 1982-2009. *Glob Health Sci Pract*. 2013;1:203–212.
38. Bekker LG, Pike C, Hillier SL. HIV prevention: better choice for better coverage. *J Int AIDS Soc*. 2022;25:e25872.
39. Gorbach PM, Mensch BS, Husnik M, et al. Effect of computer-assisted interviewing on self-reported sexual behavior data in a microbicide clinical trial. *AIDS Behav*. 2013;17:790–800.
40. PrEPWatch. PrEPWatch [Internet]. PrEPWatch; An initiative of AVAC. Available at: https://www.prepwatch.org/. Accessed January 4, 2024.

Copyright © 2025 The Author(s). Published by Wolters Kluwer Health, Inc.