CME

Insights for Implementation Science From 2 Multiphased Studies With End-Users of Potential Multipurpose Prevention Technology and HIV Prevention Products

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Background: Lower adherence to biomedical HIV prevention and challenges with persistence among young women underscore the need for methods to identify factors that will achieve higher adoption and use of effective prevention options and inform new approaches.

Setting: South Africa, Kenya, and Zimbabwe.

Methods: We synthesized findings from 2 multiphased studies (TRIO and Quatro) conducted with young women aged 18–30 years that included a crossover clinical study with placebo products, a discrete-choice experiment, and qualitative interviews with women, male partners, and health providers. TRIO evaluated 3 products (tablets, ring, and injections), and Quatro compared 4 vaginal products (ring, insert, film, and gel) for HIV prevention. Both were designed to assess product preferences, choice, and use.

Results: Increased experience with placebo products in the crossover study informed young women's product ratings and preferences. Over half changed their mind regarding their most preferred product after trying each one. The integrated qualitative component was vital to understanding what prompted these preference shifts. The discrete choice experiment provided insights on how features not available in placebos, like efficacy and contraception, influence choice and the tradeoffs women may be willing to make to gain a desired product feature.

Conclusion: The use of multiple research methods allowed for evaluation of varied dimensions of acceptability, preference, and choice in the context of diverse biomedical HIV prevention delivery forms. Findings elucidated the value of product choice with differences in preference within and across settings. Collectively, the 3 methodologies offered important insights about these products informative to enhanced product design development and future implementation.

Key Words: HIV prevention, women, placebo study, discrete choice experiment, implementation science

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INTRODUCTION

Despite landmark successes in preventing and treating HIV, 1.8 million new infections occurred globally in 2017.[1] Young women in sub-Saharan Africa experience particularly high infection rates. In 2017, 44% of new infections occurred in east and southern Africa, with 25% of those in young women aged 15–24 years.[1] This highlights a persistent gap in understanding how to appropriately and cost-effectively implement proven interventions[2,3] and the ongoing need to develop new approaches that address barriers experienced by young people. Early identification of factors that will ultimately influence adoption, implementation, sustained use, and high coverage of prevention options is critical to realizing their impact at a population level.

Low adherence among young women in clinical studies and challenges in persistence evidenced through oral pre-exposure prophylaxis (PrEP) demonstration projects[4–8] and routine programming in settings where PrEP is available underscore the need to engage end-users to pre-emptively understand barriers to use.[9] As demonstrated for modern contraceptives, choice improves uptake and coverage.[10,11] Thus, choice in biomedical prevention is not only just an ethical imperative but it is also critical to impacting the epidemic. An implementation science framework, such as the Practical, Robust, Implementation, and Sustainability Model (PRISM),[12] can guide research on user preferences both to optimize attributes of new biomedical interventions and to identify factors key to adoption, implementation, and continuation. In PRISM, organizational and user perspectives regarding the intervention influence recipients who are conceptualized both as health systems (providers, managers, and leaders) and clients. Recipients are affected by external environments (eg, stigma and partner support) as well as the infrastructure for implementation and sustainability. Thus, the examination of environmental factors and their roles in

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intervention adoption and use stands to offer translational lessons for implementation to achieve targets for reach and effectiveness.

Multiple research approaches offer strategies to inform implementation of biomedical HIV prevention at points along the continuum of intervention development, clinical testing, and roll-out. These approaches include discrete choice experiments (DCEs) that measure stated preferences (what individuals anticipate they would use or engage with were they presented with an opportunity to choose an intervention) and evaluate preference tradeoffs. DCE is well-suited to optimizing the design of prevention products when actual options do not exist because tradeoffs among modifiable characteristics of products in development can be evaluated. In biomedical HIV prevention, DCEs have been applied to inform the design of novel delivery forms, including multipurpose prevention technologies (MPTs) that prevent HIV, other sexually transmitted infections, and/or pregnancy.[13–16] Furthermore, DCEs have been used increasingly as a tool in HIV implementation research to integrate user preferences to guide program development, inform decisions regarding integrating multiple intervention components, and increase implementation efficiency.[17–19] Placebo crossover studies offer another approach to measure end-user "revealed" preferences through observable product choice and use. This design yields findings that extend to real-world settings more readily than those from highly controlled clinical trials that typically evaluate a single product against a placebo. To date, most acceptability studies with actual use of placebos have evaluated gel (for vaginal or rectal use)[20] or other topical delivery forms (eg, vaginal rings, films, and dissolving tablets)[21]; several have used active contraceptive products as surrogates for HIV prevention.[22] Finally, qualitative data collection nested within the crossover study design stands to explicate opinions and influences on preferences and choice.

The objectives of this article are twofold. First, we synthesize findings from 2 mixed-method studies that integrated a DCE, a randomized, crossover study with placebo products, and qualitative methods to examine multiple aspects of choice, preference, and acceptability across diverse delivery forms for HIV prevention.[23,24] We implemented these studies using strategies to engage end-users as codesigners. Second, we examine the utility of these approaches in guiding intervention design and implementation for young women in a landscape of expanding choices.

METHODS

The TRIO and Quatro Multisite Studies: Design Overview

TRIO (Kenya and South Africa, 2015–2017) and Quatro (Zimbabwe and South Africa 2016–2017) evaluated the acceptability of multiple drug delivery forms among young women aged 18–30 years with a focus on the outcomes of preference, choice, and use.[25] All participants were sexually active, HIV-negative, not pregnant, and microbicide and PrEP naïve. Details of both studies have been published elsewhere; however, key methods are described here to inform interpretation of the results synthesis.[13,23,24,26–28] In TRIO, 3 delivery forms for both HIV and pregnancy prevention were evaluated: daily oral tablets, a monthly vaginal ring, and monthly dual injections. Quatro evaluated 4 vaginally delivered product forms for HIV prevention: a monthly ring, gel, inserts, and film, inserted precoitally. All products evaluated in the clinical study components were placebos. This decision was made to permit focus on attributes of the delivery forms free from drug-related side effects or varying (or unknown) efficacy that might influence acceptability.

The multiphased studies were designed to include a crossover clinical study with placebos, a DCE, and qualitative research with women, male partners, and health providers (Fig. 1 and Table 1). In the clinical study, at enrollment, women viewed an educational video that introduced the products, then used each product for 1 month in a randomized order (crossover period), and, at the end of the crossover period, chose their preferred product to use for an

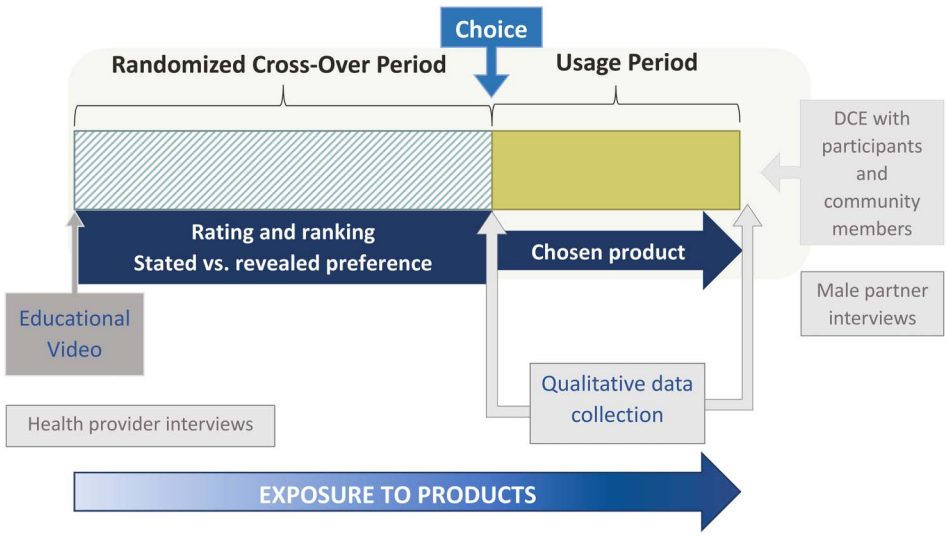

FIGURE 1. TRIO and Quatro study design overview. TRIO evaluated 3 products during the randomized crossover period, with women randomized to a sequence in which they used each product for 1 month. Women chose their preferred product to use during the subsequent 2-month usage period. Quatro followed the same overall design to evaluate 4 products during the crossover period, followed by choice of their preferred product for a 1-month usage period.

TABLE 1. Synthesis of the Main Results From Each Component of the TRIO and Quatro Studies, Organized by a Methodological Approach

Crossover clinical study with placebo products (N = 277 TRIO; N = 200 Quatro)*	
Design: Two-staged study with a randomized, crossover period during which participants tried each placebo product for 1 month, followed by a usage period when they used the product of their choice (Fig. 1).	
Crossover (CO) period	
Experiences with placebo products shifted acceptability and preferences (illustration in Fig. 2).	
TRIO	Proportion ranking tablets as most preferred decreased from 29% to 17% from baseline to after product use in the CO phase, ($P < 0.001$).
	Overall, 50% of women changed their mind about the most preferred product; for example, 34% of injections choosers preferred a different product at enrollment (25% preferred tablets, 9% rings).
	Product ratings increased significantly for all products, with greatest increase for the ring (0.97 point increase in product rating after CO, $P < 0.001$).
Quatro	Proportion ranking the gel as most preferred decreased from 33% to 16%, ($P < 0.001$). The proportion ranking the film as most preferred increased from 17% to 29%.
	Overall, 81% of women changed their mind about the most preferred product; for example, 69% of ring choosers had preferred another product at enrollment.
	All products were well liked; at least 50% rated each product a 4 or 5 on a 5-point scale after CO.
Usage period	
Chosen product provided "revealed" preference; use offered preliminary insights into intervention persistence	
TRIO	100% of those who completed CO chose to use a study product.
	91% chose to use the product they had ranked as most preferred.
	Adherence highest for injections (100%).
Quatro	100% of those who completed CO chose to use a study product.
	96% chose to use the product they had ranked as most preferred.
	Adherence highest for the ring (88% self-reported use most or all the time with sex); corroborated with biomarkers of use.
Educational video shown at enrollment	
Modest exposure to products through an educational video shifted acceptability for more novel (less familiar) products.	
TRIO	The rating for the ring increased significantly from 2.4 before video to 2.8 after video ($P < 0.05$).
Quatro	The proportion ranking the ring most preferred increased from 15% before video to 25% after video ($P < 0.05$).
Multicountry enrollment	
Some product preferences differed significantly by country.	
TRIO	More women in South Africa chose to use the injections (71% versus 57% in Kenya; $P = 0.01$).
Quatro	More women in Zimbabwe chose to use the film (45% versus 13% in South Africa, $P < 0.001$).
Participants engaged as codesigners	
Satisfaction ratings, although generally high, were more nuanced than previously reported in studies of similar products. In Quatro, participants reported considerable levels of product nonuse. We hypothesize this is because of messaging on the importance of candid feedback and as role as a codesigner.	
Discrete choice experiment (N = 536 TRIO; N = 395 Quatro)†	
Efficacy was a main driver of preference for a product, although other attributes also influenced choice.	
TRIO	In South Africa, product form (ring, tablet, or injection) was just as important as efficacy. Some women in Kenya also strongly preferred a monthly injection over a monthly vaginal ring.
Quatro	All attributes influenced choice; only 11% of women always chose the product with highest efficacy (level of HIV protection).
Multipurpose prevention technologies (MPT) were preferred.	
TRIO	In South Africa, 72% were estimated to choose an MPT ring or MPT tablets over an injection that only protected against HIV.
Quatro	A large share of the sample (73%) was estimated to trade some level of efficacy for more desirable other product features.
Qualitative	
Women in clinical study	N = 87 TRIO; N = 41 Quatro

TABLE 1. (*Continued*) Synthesis of the Main Results From Each Component of the TRIO and Quatro Studies, Organized by a Methodological Approach

In TRIO, in-depth interviews conducted after the CO period and focus group discussions and in-depth interviews conducted after the clinical study exit. In Quatro, in-depth interviews conducted after the clinical study exit.	
Women's preferences focused on "peace of mind," discretion, and low user burden.	
TRIO	Women's choices were influenced more so by the unfavorable attributes of other products; preferences were closely linked with expressed dislike of another product's attributes.
Quatro	The ease of use and lack of interference with daily life were more salient to product satisfaction and choice than were physical features of the products. Female-initiation, product invisibility, and nonreliance on male cooperation were appreciated for all product options.
Male partners	N = 39 TRIO; N = 17 Quatro
Preferences centered on lack of interference with sex.	
TRIO	Favored a product that has a neutral effect on sex; desired involvement with (control over, for some) their partner's product use decisions.
Quatro	Favored a product that made sex feel more natural.
Health care providers‡	N = 24 TRIO; N = 24 Quatro
Considerations of product introduction focused on healthcare system capacity and provider burden.	
TRIO	Providers eager to offer MPT; emphasized importance of user ease and discreteness, alongside low provider burden. Demand for products could burden system and present supply challenges; products with high user adherence demands (ie, oral PrEP) present challenges for health system as well.
	Stigma regarding provision of HIV prevention to young women as signaling approval of sexual freedom.
Quatro	Desire to be able to offer female-initiated HIV prevention products that offer women control. Concern that insertion of products intravaginally conflicts with messaging about hygiene and disease control.

*Enrollment sample sizes are indicted for each study component. Retention for the crossover period in TRIO and Quatro was 89.9% and 90.0%, respectively; 88.8% and 88.0% completed the full study (CO and usage period).

†The DCE survey was conducted at the final clinical study visit. The product-experienced sample was complemented with a product-naïve community sample of women from the target population. The community sample size was 301 in TRIO and 222 in Quatro. The DCE was developed through formative research that included in-depth interviews with women from the target populations, with the final design informed by this formative research and our team's past work in biomedical prevention.

‡In TRIO, health care providers included nurses, doctors, and counselors who were influential stakeholders representing diverse roles and settings within the health care system, with a focus on those directly providing services to young women. In Quatro, health care providers were key informants from job categories including health care providers, pharmacists, Department of Health representatives, and clinical trialists.

additional one (Quatro) or 2 (TRIO) months (usage period). Recruitment and engagement messaging during pre-enrollment workshops and throughout study participation emphasized women's roles as product "codesigners" of the delivery forms giving them opportunity to inform new prevention tools for women. Messaging focused on the critical importance of honest feedback about the products, underscoring the value in communicating dislikes. We highlighted past biomedical prevention trials where women did not, in fact, find products in clinical testing easy to use or suitable in their contexts. TRIO and Quatro, then, afforded an opportunity to partner with women as end-users to shape the future of HIV prevention for women like them in their communities. Primary endpoints of the crossover period included product ranking, choice (for the usage period), and acceptability ratings. TRIO and Quatro were not designed to measure adherence over a sustained time period; however, we did assess use of the chosen product during the usage period. We integrated multiple measurements of adherence to capture initiation, persistence, execution, and completion. These included direct observation, pelvic examinations, self-report, Wisepill electronic monitoring of opening events, and counts of returned, unused products. In Quatro, biomarkers for use of the placebo products were available and had good reliability with self-reported use.[29]

A DCE was conducted with clinical study participants at their final visit, and it was supplemented by a product-naïve, community sample that viewed only the educational video before completing the DCE survey. In TRIO, attributes included efficacy, side effects, product form, pregnancy prevention, and duration of protection.[13] In Quatro, attributes included timing of insertion (before or after sex, daily, and monthly), how product is inserted, whether it causes added vaginal wetness, discreteness of use (ie, whether partner will notice), efficacy, and pregnancy prevention.[30]

In TRIO, women were randomly selected to complete an in-depth interview after the crossover period, with a focus on likes and dislikes of each product as well as contextual factors influencing preferences and use. In both studies, after the clinical study exit, women were purposively selected for qualitative interviews based on their product choice at the end of the crossover period. Health care provider in-depth interviews included influential stakeholders representing diverse roles and settings within the health care system. These interviews focused on product reactions (after handling) and infrastructure considerations with introduction of new

prevention tools. Male partner interviews, conducted after women exited the study, focused on product perceptions, use experiences and relationship-based attitudes regarding HIV prevention decision-making.

Statistical Analysis

We used logistic regression models to estimate product choice by country, controlling for randomization sequence. Mixed-effect logistic regression models were used to estimate the proportion ranking each product as most preferred (rank #1) at baseline, after watching the brief educational video, and after crossover. The models controlled for country and included a random participant effect to account for the longitudinal structure of the data. We also examined changes in ratings at baseline and after crossover using a 2-sample *t* test. Preference data from DCEs were analyzed with random parameter logit models. All analyses were conducted using Stata 15.0 (StataCorp LLC, College Station, TX). For qualitative analyses, we coded in-depth interview transcripts using a codebook informed by past work and a conceptual model of HIV prevention product acceptability. A team of analysts coded all transcripts using qualitative analysis software Dedoose.

RESULTS

A synthesis of main results from each component of the TRIO and Quatro studies is provided in Table 1. Here, we highlight and illustrate thematic findings across the studies, drawing on pertinent data from each one.

Experiences With Placebo Products Shifted Product Ratings and Preferences

The opportunity to use multiple placebo delivery forms during the crossover period informed young women's product ratings and preferences. In TRIO, product ratings increased significantly from enrollment for all products. However, the increase was greatest for the least familiar product, the vaginal ring.[27] Even modest exposure to the TRIO products through the educational video shown at enrollment shifted ring acceptability slightly toward a more favorable rating.[26] Nonetheless, the mean rating only shifted above neutral to a positive rating after use, highlighting the added value of the opportunity to gain experience with this unfamiliar delivery form. Similarly, in Quatro, exposure through an educational video shifted baseline preferences in a more favorable direction for the ring. In contrast to TRIO, however, there was little change in mean ratings of the 4 vaginally delivered forms after actual use.[31]

Across the population of young women in each study, the proportions ranking each product as their most preferred were generally consistent between enrollment and the end of the crossover period. However, on an individual level, there was substantial change in rankings with half or more of women shifting their top-ranked product after using each one (Fig. 2). Rankings at the end of the crossover period aligned well with product choice, with nearly all women choosing their top-ranked product to use during the second stage of the study. In TRIO, 34% of women who chose the injection after trying each of the 3 products (N = 160) had preferred another product at enrollment (25% tablets, 9% rings). Nearly all (84%) of those who chose the ring had indicated a different preference at enrollment (57% injections, 27% tablets). Likewise, in Quatro, 69% of the ring choosers indicated preference for another product at enrollment (25% insert, 19% film, 25% gel). As noted in Table 1, in both studies, some preferences did vary by country.

Adherence Measures Provided Insight on Actual Use

Despite no prevention benefit in using a placebo product, all participants accepted doing so. In the qualitative component, women highlighted their comfort with the minimal risk of using a "drug-free" product. As may be expected, adherence was lower for the on-demand and daily dosage products, compared with those used monthly. In TRIO, the injection achieved the highest adherence, which was also the most popular delivery form, whereas oral tablets achieved the lowest (by Wisepill measurement). In Quatro, despite the ring being chosen by only 28% of women, it was

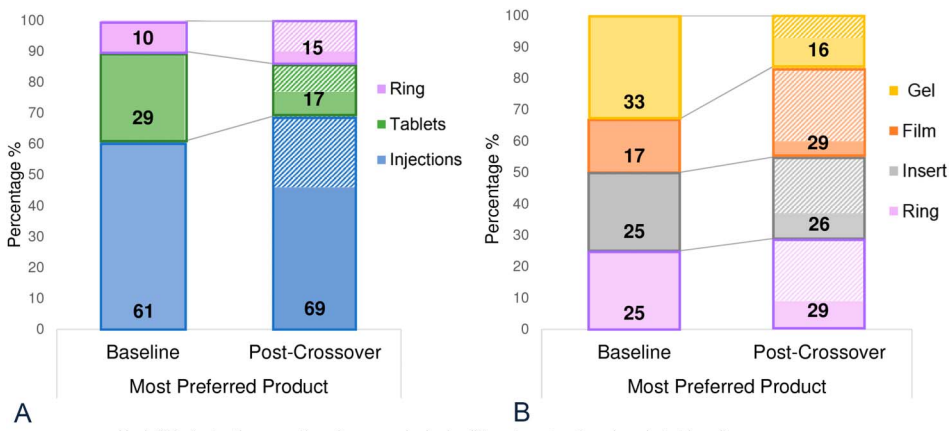

FIGURE 2. Shifts in product preferences from baseline to after crossover. In A, TRIO (N = 249), and B, Quatro (N = 180), studies, the overall distribution of the products ranked as most preferred at baseline and after crossover. The hash fill indicates the proportion of women who indicated a different product was most preferred at baseline.

used more consistently than the other vaginally delivered products by virtue of its continuous-use design.

Qualitative Research Elucidated the Value of Choice and Factors Influential to Preferences

Qualitative data collected at the end of each of the 2 study stages provided in-depth understanding of women's experiences trying the products and considerations regarding which one(s) they would choose to use over a more sustained period, if active products were available. Participants valued trying different products and making an informed choice after having direct experience with each one. In discussing likes and dislikes of each product, women emphasized the importance of choice, recognizing that preferences will vary, with attributes deemed unfavorable differing based on personal preferences and contextual factors.[28] These views confirmed the crossover study and DCE findings that highlighted differences in preferred delivery forms by country and within site. Qualitative data also deepened understanding of possible challenges with use: In Quatro, Zimbabwean women confirmed the quantitative preferences favoring the film; however, many also had difficultly inserting it because it stuck to fingers or had sharp corners.[31] These perspectives were complemented by male partners, who underscored the importance of choice and discreteness given gender-power imbalances in relationships whereby men expressed a desire to "approve" and control women's reproductive decisions.

DCE Augmented Preference Findings

DCE results in both studies demonstrated the value placed on product efficacy, with this being the most important attribute among those evaluated. However, most women were willing to trade some level of efficacy to gain their preferred choices among other product attributes. Among Quatro participants, 11% chose the product with higher efficacy across all choice questions, underscoring the importance of other attributes, including non-daily use, insertion with an applicator, and pregnancy prevention.[30] Likewise, in TRIO, DCE results highlighted the importance of MPTs. Although injections were the favored delivery form in all components of TRIO, DCE data estimated that a larger proportion of participants would choose an MPT ring or MPT tablets over injections that prevented only HIV. In South Africa, for example, 55% were estimated to choose an MPT ring and 17% MPT tablets when presented alongside an HIV-only injection.[13]

Codesigner Approach Enhanced Participant Experience and Honesty

Efforts to engage participants as codesigners resonated and promoted sharing of perceived disadvantages and barriers to use. As 1 participant expressed, she gave "*true feedback because it is going to help other women. So when I was given a product and returned, I made sure I gave honest answer"* (TRIO, focus group, Kenya). The opportunity to choose their preferred product for the usage period engaged women who felt like they were "*part of the team*" (TRIO, dissemination workshop, Kenya). Women also commonly expressed a sense of empowerment during qualitative interviews about being able to select the product of their choice. The placebo design allowed them to experience multiple products in a relatively compressed time frame, make determinations about their preferences, and provide important insights in their decision-making process when presented with multiple options—information instructive to future implementation and roll-out.

Providers Reflected on Health Care System Capacity and Burden

Health care providers interviewed for both studies were eager to consider opportunities to have additional biomedical prevention tools to offer women, including those that are female-initiated and give women control over their use. They emphasized the importance of user ease and discreteness, alongside low provider burden, and noted that demand for products could strain an already-taxed health system and present supply challenges. Products with high demands for user adherence (ie, oral PrEP) were regarded as presenting challenges for the health system as well as owing to increased need for counseling and patient monitoring.

DISCUSSION

HIV prevention is increasingly shaped by the opportunity for choice and the need to integrate complementary interventions to achieve UNAIDS targets to reduce the burden of the epidemic.[3] The use of multiple research methods in the TRIO and Quatro studies allowed for evaluation of varied dimensions of acceptability, as well as preference, choice, and use in the context of diverse biomedical HIV prevention delivery forms. Use of a randomized crossover clinical study with placebos permitted consideration of products free from drug-related side effects, including novel delivery forms in development. This design afforded efficiency and lower cost, relative to use of active products, and supported examination of implementation-relevant considerations, including the benefit of early standardized education tools to increase familiarity (eg, video) and product-specific challenges young women experienced. The DCE allowed consideration of tradeoffs among product attributes, such as efficacy, MPT indication, and side effects that could not be evaluated with placebo products. Furthermore, it extended the study into a product-naïve community sample, allowing for comparison of findings in a more real-world situation in which women had not had the opportunity to try the product forms on which the DCE was based. The integrated qualitative component was vital to understanding what prompted women to change their preferences after trying the products and the considerations they identified when selecting their preferred option. Taken collectively, these methods offered important insights that are informative to enhanced product design development and future implementation.

Both TRIO and Quatro revealed differences in product preference within and across geographic settings, emphasizing the need for health care delivery systems to prepare for

and offer multiple options to women. Preferences changed over time with increased levels of exposure to the products—from educational videos, in which only visual representations were available, to one experiential month with each product and finally an informed choice of a product for an additional short period of use. These findings underscore the value to building in opportunities for individuals to gain experience with different intervention options in a short-term, low-risk manner and then to use these experiences to refine intervention design (eg, product development and messaging regarding making choices among multiple product options) and future implementation. The diverse approaches integrated in TRIO and Quatro could be applied to testing different intervention implementation strategies. A DCE survey may be sufficient when the personal experience with the options may be less critical to informing preferences, when the actual options do not readily exist, or to focus or fine-tune intervention directions. The crossover study with placebos provided opportunities for women to gain tangible experience with each product and reflect on how they integrated into their lives. This design offers promise for future evaluation of new product forms and with other user groups (eg, MTN-035). It could also be leveraged to assess health systems'relevant implementation barriers.

In addition to synthesis of results across the different research methods, insights pertinent to implementation can also be gained through triangulation of different sources of data. In TRIO and Quatro, comparisons of qualitative data between young women, male partners, and health providers highlighted possible challenges from users and other stakeholders alike. Women wanted discretion; male partners wanted to "approve" and control women's reproductive decisions. Health providers were mostly concerned with ease of administration and minimized burden in an overstretched health care system. These interviews also illuminated strongly held stigma beliefs regarding provision of HIV prevention to young women as signaling approval of increased sexual freedom. As reflected in the PRISM framework, health systems constitute critical recipients of a biomedical prevention intervention, and relevant considerations are central to successful rollout of products, both in terms of infrastructure, training, and capacity, as well as addressing stigma directly. Adapting the other approaches used in TRIO and Quatro to understand provider preferences and optimize models for offering choice in biomedical HIV prevention could offer insightful direction for implementation of interventions as more biomedical tools become available. Likewise, recognizing that HIV prevention needs and preferences will vary over a woman's life-course, research designed to understand how preferences and choices are informed by developmental and normative transitions could be important to successful integration and alignment with reproductive needs and choices.

Limitations

Evaluation of preference and choice in the context of placebo product options does not allow assessment of how efficacy and drug-related side effects will ultimately affect acceptability and use. The short duration of product use limits our conclusions, particularly regarding persistence and discontinuation, both of which are essential to address in achieving population effectiveness. However, we were able to evaluate novel biomarkers of adherence to placebo products for feasibility. Future studies could use these methods in the context of extended use, recognizing that a prolonged use period with a placebo product may still fail to achieve high adherence, given lack of protection, unless user burden is extremely low (eg, with the use of a fully "invisible" product).[32] The inclusion of efficacy as an attribute in the DCE limited, somewhat, our ability to examine the role of other factors known to be important to product choice as maximizing efficacy dominated women's choices among product alternatives. This was particularly the case in the product-naïve community samples, suggesting, perhaps, less comprehension of the other attributes or the complexity of this study design. These findings have prompted us to conduct more thorough cognitive testing in designing a DCE survey, including the attribute descriptions and accompanying illustrations.

Conclusion

Efficacious biomedical interventions can only realize their prevention impact when behaviors and systems-level influences support their adoption and use. TRIO and Quatro offer multiple methodological insights for evaluating choice and for engaging communities and populations at high risk of HIV to contribute to the design of new HIV prevention interventions. The engagement of women as codesigners constituted a defining feature of TRIO and Quatro with the goal of soliciting candid and critical input to inform choices for women in their communities during downstream implementation stages. The methodologies further enhanced understanding of factors that will be influential to women's and other stakeholders' choices during real-world implementation. Findings from several study components have implications for attaining high real-world HIV prevention coverage: decreased user burden may yield higher adherence, even if the method is not the most preferred. Although TRIO and Quatro focused primarily on women as end-users, we explored 2 stakeholder groups, male partners and providers, to gain preliminary insights into their opinions, given their critical roles in supporting access to new tools for women. Similar methods could be applied to understand more systematically the values and preferences of these or other groups (eg, family members or policy makers), with systems-level implications for ultimately achieving successful roll-out, adoption, and scale-up of new prevention technologies.

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