OPTIONS CONSORTIUM: Optimizing Prevention Technology Introduction On Schedule

Core Implementers: FHI 360, Wits RHI, AVAC

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The Dapivirine Ring: Key Learnings from Like-Product Introductions

Cooperative Agreement No. AID-OAA-A-15-00035
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Dapivirine Ring: Key Learnings from Like-Product Introduction

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Executive Summary

Vaginal insertion and partial efficacy are two challenges that could affect the uptake and continued use of the dapivirine ring (see Appendix 1 for explanation of the ring). Analyses of the introductions of other products that share these characteristics — vaginally inserted products such as female condoms, tampons, menstrual cups, and contraceptive rings, and partially efficacious products such as the malaria vaccine, the rotavirus vaccine, and voluntary medical male circumcision — provide useful lessons to inform planning for rollout of the dapivirine ring. This paper provides information for planners, implementers, funders, researchers, trainers, providers of technical assistance, and others to build an agenda for introducing the dapivirine ring that addresses these two challenges.

Through the analysis in this paper, we can glean key messages and approaches that have been used to convey how partially efficacious products can indeed be beneficial. We also learn not to over-promise, as this could result in a serious backlash not only for the dapivirine ring but for HIV prevention overall. Additionally, we examine products that overcame the challenges of being vaginally inserted. Few products currently in use are vaginally inserted, so knowledge of and experience with such products is valuable. Having to touch the genitals to insert the product is an added potential barrier to use, given cultural and social norms in some countries.

While product introduction processes are not analogous in all cases, we can expect that similar challenges and solutions will arise repeatedly with vaginally inserted or partially efficacious products. The results of our analysis are intended to help prepare for possible challenges faced by previous, similar products and to build on previous successes.

For the products included in this analysis, introduction planners and implementers overcame the challenges presented by partial efficacy or vaginal insertion and persuaded policymakers, identified and trained health care providers, and worked with potential end users to support and even champion the products. For the dapivirine ring, these examples offer strategies for effectively communicating product benefits and efficacy data to policymakers and funders. Additionally, the analysis led to key insights on provider training and service delivery. And finally, to reach end users of the products, guidance on consumer research and messages, message dissemination, product champions, key influencers, and gatekeepers was collected. Through consideration of these approaches, planners of ring introduction can aim to have similar positive impact with policymakers and funders, health care providers, and end users.

Topline Learnings from Partially Efficacious Products (Malaria Vaccine, Rotavirus Vaccine, Voluntary Medical Male Circumcision)

1. Presenting dapivirine ring as part of a comprehensive HIV prevention package could be a strategic way to position it as a valuable investment for policymakers. This strategy was successful in the rollout of rotavirus vaccine.

2. Cost-effectiveness studies are the most effective advocacy tool to influence ministries of health, and presenting the potential long-term impact of the ring could create a persuasive case. Finding ring cost efficiencies, either through reduction of the manufacturing cost or in provider time required to deliver the product, could improve cost-effectiveness.

3. Interpersonal communication using small groups allows for more nuanced discussion that can help overcome concerns about a complex, partially efficacious product.
Topline Learnings from Partially Efficacious Products (continued)

Focus on communicating the benefits of the ring and portraying it as a lifestyle product rather than an HIV prevention device may shift focus away from its partial efficacy.

4. Integrating the ring with other health services could draw clients in and link them to other services such as HIV testing, family planning, STI testing and treatment, and provision of prenatal vitamins.

5. A combination approach to provider training (i.e. pre-service and in-service training) would ensure provider competency. Utilizing existing mechanisms like professional associations, county/subnational health officials, and district officials to disseminate product information could enhance acceptability.

6. Task shifting delivery of the ring (e.g., counseling to peer educators), streamlining re-supply and deploying self-risk assessment tools) could reduce workload and therefore provider resistance.

7. Product champions could play an important role in driving demand for a partially efficacious ring by communicating the acceptability of the product.

Topline Learnings from vaginally inserted products (Progesterone Contraceptive Vaginal Ring, Tampons, the Menstrual Cup, and Female Condoms)

1. Evidence-based selection and training of providers who are approachable could help overcome barriers presented by vaginal insertion.

2. Peer-to-peer communications, by a product user, can be effective in recruiting new users. Trial participants who have used the ring may be effective educators and advocates who can comfortably and practically discuss vaginal insertion.

3. Detailed information, education & communication (IEC) materials with details about how the ring fits in a woman’s body can increase demand for an unfamiliar product be helpful for overcoming user and provider concerns.

4. Providing messages for partners (as well as other influencers), as well as empowering women to explain the ring to partners, will be an essential component of ring introduction.

5. Conducting research among providers will be valuable to shaping an effective training curriculum, so that they are best positioned to help clients feel comfortable and confident inserting the ring.

6. Encouraging providers to try the ring themselves can be an effective strategy for overcoming provider bias.
Introduction

This paper examines past introductions of products similar to the dapivirine ring, to inform planning for introduction of the ring. While the products have key differences (e.g., in diseases, drivers for use, contexts, single versus regular use, targeted populations), lessons are drawn from both historical product introductions (e.g., the tampon in the United States, as depicted in Figure 1) as well as ongoing learnings from products in the midst of piloting, introduction, and scale-up. The paper focuses on two characteristics of the dapivirine ring that may make it a challenging product to introduce: it is vaginally inserted, and it has been demonstrated to be only partially efficacious. We identify products that share at least one of these characteristics and explore the complexities of these challenges to highlight practical solutions for the introduction of the dapivirine ring.

FIGURE 1: Lessons from Tampon Introduction in the United States

We selected two sets of products. For partially efficacious products, we sought to include products that had efficacy below 70 percent and had been or were in the process of being introduced in low- and middle-income countries. For vaginal products, we looked for products that were considered for large-scale introduction in low- and middle-income markets. Products with a third characteristic — the potential for non-clinical administration — were considered for inclusion but ultimately not included due to the likely engagement of medical professionals in the near term (e.g., through the demonstration and early introduction phases for the dapivirine ring). In consultation with members of the OPTIONS team, we included the following six products that met our criteria and shared characteristics with the dapivirine ring:

Partially efficacious:

**Voluntary Medical Male Circumcision.** Voluntary medical male circumcision (VMMC) reduces female-to-male sexual transmission of HIV by 60 percent. The World Health Organization (WHO) and the Joint United Nations Programme on HIV/AIDS (UNAIDS) recommend the implementation of VMMC programs in countries with a high HIV prevalence among the general population. By the end of 2017, more than
18.5 million men had been medically circumcised in priority countries, or about 90 percent of the 20.8 million target.\(^2\)

**Malaria Vaccine.** PATH and GSK have developed a malaria vaccine called RTS,S (a recombinant protein-based malaria vaccine with the trade name Mosquirix). A phase III clinical trial of the vaccine in seven African countries found that it reduced acquisition of clinical malaria by about 50 percent in older children (ages 5 to 17 months) and 30 percent in infants (ages 6 to 12 weeks).\(^3\) WHO is now piloting the vaccine in Ghana, Kenya, and Malawi.

**Rotavirus Vaccine.** Rotavirus is the leading cause of severe diarrheal disease in infants and young children worldwide. WHO estimates that 215,000 childhood diarrheal deaths in 2013 were due to rotavirus, with more than 90 percent of all rotavirus-related deaths occurring in resource-poor countries in South Asia and sub-Saharan Africa.\(^4\) The rotavirus vaccine proved to be 50 to 60 percent efficacious in low- and middle-income countries, though it demonstrated near-perfect efficacy in developed nations.\(^5\) Because not all diarrhea is caused by rotavirus in low- and middle-income countries, diarrheal disease is still common even with the vaccine; as a result, the product is perceived to be partially efficacious. As of August 2018, 96 countries had introduced the rotavirus vaccine.\(^6\)

**Vaginally inserted:**

**Progesterone Contraceptive Vaginal Ring.** The Population Council is currently rolling out its progesterone contraceptive vaginal ring (PVR), developed for use by breastfeeding women. It is approved and being used in several Latin American countries and is being piloted in India, Kenya, Nigeria, and Senegal. with wider rollout scheduled following these pilots. Clinical trials have demonstrated that the ring is safe for mother and child, does not affect a woman’s ability to produce breast milk, and allows for fertility to return shortly after a woman stops using the ring.\(^7\) It is inserted in the same way as the dapivirine ring.

**Menstrual Products (Tampon and Menstrual Cup).** These products are not widely used in Africa, but the introduction processes in North America and Europe — as well as their limited use in Africa — provide important lessons about trends in product uptake for novel, vaginally inserted products.

**Female Condom.** This condom is inserted into the vagina to provide barrier protection from pregnancy and sexually transmitted infections (STIs), including HIV. Today the female condom is manufactured by a number of different brands, with materials including latex, synthetic latex, and polyurethane. Some brands of the female condom (including FC2) have an inner ring which is inserted similarly to the dapivirine ring and fits close to the cervix.

Through examination of products that are either vaginally inserted or partially efficacious, this paper seeks to help prepare for challenges and expedite the successful rollout of the dapivirine ring, should it receive market authorization.

**Limitations**

Despite the shared characteristics between the dapivirine ring and the above products, there are a number of limitations to the assumptions which can be made when drawing comparisons through this analysis. For example, although VMMC and vaccines are fitting examples of partially efficacious prevention products which have been introduced in low and middle income markets, these are by nature one-time interventions which do not require continued use. Conversely, women can elect to
remove the ring at any time and could be at risk of acquiring HIV if she does not decide to use another prevention method. With regard to vaginally inserted products, many women and girls in low-income settings do not have ready access to a private place with water and light necessary to change a menstrual cup or tampon. For the dapivirine ring, this may be less of a factor because the ring will only need changing monthly.

Furthermore, the use of HIV prevention products are commonly associated with stigma and fear which must be overcome through effective, consistent and nuanced messaging and counseling. Socio-cultural perceptions surrounding the use of products for menstruation or malaria and rotavirus prevention are unique and less linked to norms around sex and sexuality. Key differences such as these are important to recognize, and this analysis aims to both acknowledge and consider the unique situation of the dapivirine ring as an HIV prevention product, while making actionable recommendations for policymakers and implementers drawing on lessons learned from the introduction of products intended to protect individuals against preventable conditions.

**Approach**

We conducted a limited literature review to identify both published and gray-literature papers that provided background information on the products and explained approaches and challenges to product introduction. We reviewed 61 papers, progress reports, and studies on 1) the dapivirine ring; 2) vaginally inserted products including female condoms, tampons, menstrual cups, and contraceptive rings; and 3) partially efficacious products including the RTS,S malaria vaccine, VMMC, and the rotavirus vaccine. Studies were categorized and themed to identify key messages and lessons learned.

To complement the literature review, we sought to interview one or two experts per product who were directly involved with the product’s introduction or a review of its introduction (Table 1). Interview guides were tailored to the product. We conducted nine key informant interviews with experts on various products, including PVR, female condom, tampon, menstrual cup, RTS,S malaria vaccine, VMMC, and rotavirus vaccine. Findings and interviews were analyzed, and lessons and conclusions were drawn based on the case studies.
Partially Efficacious Product Findings

In clinical trials, the dapivirine ring safely reduced HIV infection by 27 to 31 percent among more than 4,500 women in Malawi, South Africa, Uganda, and Zimbabwe. Among women who used it as instructed, the ring reduced the rate of new HIV infections by 37 to 56 percent. Interestingly, women older than 21 were more likely than younger women to leave the ring in place. In open-label extension (OLE) studies, researchers are trying to determine if adherence can be increased once users know the product works when it is used. At the Conference on Retroviruses and Opportunistic Infections (CROI) 2018, researchers presented initial data from one open label study (MTN-025/HOPE) showing that 90 percent of women participating in the study used the ring at least some of the time. A progression of increased efficacy and effectiveness was seen with oral pre-exposure prophylaxis (PrEP), and many are hoping the dapivirine ring will show similar increased efficacy and effectiveness with open-label use, as illustrated in Figure 2.

<table>
<thead>
<tr>
<th>Product</th>
<th>Number of Documents Reviewed</th>
<th>Focus</th>
<th>Expert Interviews/Correspondence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraceptive Ring</td>
<td>8</td>
<td>Vaginally inserted product</td>
<td>John Townsend, Population Council</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Saumya Ramarao, Population Council</td>
</tr>
<tr>
<td>Female Condom</td>
<td>10</td>
<td>Vaginally inserted product</td>
<td>Mags Beksinska, MatCH Research Unit</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Mitchell Warren, AVAC and formerly Female Health Company</td>
</tr>
<tr>
<td>Tampon</td>
<td>6</td>
<td>Vaginally inserted product</td>
<td>Mary Aikenhead, BMGF and formerly Proctor &amp; Gamble</td>
</tr>
<tr>
<td>Menstrual Cup</td>
<td>3</td>
<td>Vaginally inserted product</td>
<td>Mags Beksinska, MatCH Research Unit</td>
</tr>
<tr>
<td>RTS,S Malaria Vaccine</td>
<td>6</td>
<td>Partially efficacious product</td>
<td>Yvette Collymore, PATH</td>
</tr>
<tr>
<td>VMMC</td>
<td>7</td>
<td>Partially efficacious intervention</td>
<td>Jason Reed, Jhpiego and formerly OGAC VMMC</td>
</tr>
<tr>
<td>Rotavirus Vaccine</td>
<td>6</td>
<td>Partially efficacious product</td>
<td>Allison Clifford, PATH</td>
</tr>
<tr>
<td>General Marketing</td>
<td>2</td>
<td>Both</td>
<td>None</td>
</tr>
<tr>
<td>General Vaccine</td>
<td>2</td>
<td>Partially efficacious product</td>
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<tr>
<td>General Vaginal Ring</td>
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<tr>
<td>General Contraceptive</td>
<td>4</td>
<td>Vaginally inserted product</td>
<td>None</td>
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</table>
Nonetheless, it seems likely that dapivirine ring efficacy will remain below that of oral PrEP and male and female condoms for HIV prevention. For this reason, learning how others have managed introduction of partially efficacious products is of critical importance for the ring. Through this analysis, we can glean key messages and approaches that were used with other products to convey how a partially efficacious product can be beneficial, and consider how these apply to the ring. We can also learn how to be positive about the product but not over-promise, as this could result in serious backlash, not only for the dapivirine ring but for HIV prevention overall.

The approaches to like-product introductions in this analysis are examined from the perspective of their impact on policymakers and funders, health care providers, and end users. We use the key below to signal the audience for each key learning and use an arrow to highlight the implications for the ring.

**Policymakers and funders**: Policymakers and donors determine if a product is introduced in the country and the scale and pace of introduction.

**Health care providers**: Providers are critical gatekeepers for new products. Their knowledge level, support of products, and interactions with clients can have a significant influence on a woman’s choice to use a certain product.

**End users**: Communications, messaging, and approaches that resonate with potential users can drive product uptake and continued use.
Product Case Study: Rotavirus Vaccine

I. **Key Learning:** The rotavirus vaccine is one of several options that can prevent severe diarrhea. At a policy level, rather than frame the product as solely about rotavirus, PATH pitched inclusion of the vaccine as part of a suite of options to help defeat diarrhea — the second leading cause of death among children under five in the world. The DefeatDD initiative aims to raise policymakers’ awareness of the burden of diarrheal disease and help increase commitments to an integrated approach to prevent and treat diarrhea that includes vaccines; oral rehydration salts and zinc; water, sanitation, and hygiene; breastfeeding; and innovative research. The message is, “We need greater investments in these solutions and in integrated policies to ensure holistic protection against diarrheal disease.”

- The ring could similarly be presented to policymakers as part of a comprehensive prevention package with a message to invest in a range of products to end HIV.

II. **Key Learning:** Cost-effectiveness studies were the most effective advocacy tool to influence the ministries of health. Such tools can have greater influence if they estimate long-term public health impact, costs, and cost-effectiveness.

- Presenting the potential long-term impact of the ring (potentially including longer-lasting ring products currently under development) could create a persuasive case. However, we know that in an era of test and treat (when antiretroviral therapy and viral suppression are highly cost-effective), cost-effectiveness alone will not make the case for the dapivirine ring (or any other prevention option). Policy positioning will therefore need to also include other persuasive arguments, such as those related to rights and the need for prevention to achieve epidemic control.

III. **Key Learning:** Mapping and using sources of information that providers already access can help deliver training information. For example, professional associations, county/subnational health officials, and district officials were respected, pre-existing mechanisms through which to disseminate the new product information.

- Identifying respected providers through whom to disseminate ring information could enhance the acceptability of the partially efficacious ring.

IV. **Key Learning:** Interpersonal communications using small groups rather than mass media allowed a more nuanced discussion that was more effective for a complex, partially efficacious product.

- Interpersonal communications for the ring could be an effective way to overcome concerns about partial efficacy.
V. **Key Learning:** While it is critical to be transparent, it is more productive to focus on the benefits of the product. Rotavirus messaging emphasizes that the vaccine greatly reduces the chances of a child having severe diarrhea, and that it will reduce childhood morbidity in conjunction with other products or interventions.

- Messaging for the ring could focus on its potential to reduce the risk of HIV infection in combination with other prevention interventions. This message could be pretested for appeal and comprehension across different target groups.

**Product Case Study: RTS,S Malaria Vaccine**

I. **Key Learning:** Formative research helped identify the need to explicitly state that the vaccine reduces malaria episodes but that a vaccinated child could still contract malaria, which is why mosquito nets (and other existing measures) are still important. In this way, consumer messaging focuses on what the product can do, while acknowledging the limitations, but does not dwell on the drawbacks.19

- Consumer messages could focus on the reduction in risk offered by the ring but also explain that HIV is still a risk, which is why other prevention options (e.g., condoms, oral PrEP) are also needed.

II. **Key Learning:** Integration of RTS,S with other services for children can increase demand for both. PATH aims to integrate RTS,S with the Second Year of Life initiative (for sustaining adequate immunization and other health services through 24 months of age).20 Bringing children in for new vaccination visits for the malaria vaccine could help to catch children up on other health measures like vitamin A supplementation, the second dose of the measles vaccine, and weight measurements.21 In this way, the RTS,S vaccine has the potential to increase uptake of potentially underused services for this age cohort.

- Similarly, curiosity about and interest in a new product like the ring could draw clients in and provide an opportunity to engage them with other services such as HIV testing, family planning, STI testing and treatment, and provision of prenatal vitamins. It would be beneficial for implementers to consider possible avenues for service integration early on and explore issues of feasibility and scalability. Improving overall health outcomes is a strategic way for partially efficacious products to gain buy-in from key stakeholders.

**Context for RTS,S Communications:** PATH’s formative consumer research identified two factors that made RTS,S introduction a challenge. At the community level, understanding of efficacy was linked to perceptions of whether the vaccine “works.” For example, if children continued to get malaria following vaccination, the vaccine would not be perceived to be good or working. It was also evident that community members were accustomed to using multiple measures for preventing malaria (e.g., mosquito nets, spraying). (Source: Y. Collymore Interview)

**Background on RTS,S Policy:** At a policy level, PATH’s Malaria Vaccine Program recognized the challenge of gaining a commitment to a partially efficacious vaccine and sought ways to show additional benefit from the vaccine introduction.
Product Case Study: Voluntary Medical Male Circumcision

I. Key Learning: Surgical circumcision for HIV prevention was a skill that providers learned through pre-service training, though in-service training was needed and used extensively to ensure competency.22
   - This combination approach to training offers a useful model for the ring and other HIV prevention interventions. Though not unique to partially efficacious products, the quality of the intervention needs to be high to ensure no further reduction in efficacy.

II. Key Learning: Much of the provider resistance seemed to be about workload. Task shifting and sharing, as well as orchestration of high-throughput models, persuaded some that VMMC scale-up could be achieved more efficiently than first thought. A motivator among providers was the additional pay for overtime in the evenings and weekends by many programs. While compensation can help, it is useful to note that effective use of providers’ time can alleviate concerns about new interventions.23
   - Identifying efficiencies in providers’ delivery of the ring (e.g., shifting some of the counseling to peer educators, streamlining re-supply, deploying self-risk assessment tools) could reduce provider resistance.

III. Key Learning: Messages can progress over time. VMMC demand-creation strategies were anchored heavily to HIV risk and HIV prevention for the first five years or so of introduction and evolved to focus on benefits unrelated to HIV (e.g., hygiene, modernity, responsibility, preferences of partners). Therefore, partial protection was a central theme initially, and later messaging was less related. Of course, clients still received counseling about the partially protective nature of circumcision against HIV infection and the need to still use condoms, but the public messages were less directly about HIV.24
   - Ring messages can and should evolve over time. Messages could portray the ring as more of a lifestyle product than an HIV prevention device, which might shift focus away from the partial efficacy. Implementers can monitor whether users like other features of the ring (e.g., pleasure, cleanliness, peace of mind).

Context for VMMC Providers and Communications: Introduction of VMMC required two changes: clinics had to add a new health service, and men had to go to health clinics. Adding another product or service to the plethora of provider responsibilities was a potential barrier to VMMC introduction, particularly as the product is partially efficacious and providers did not fully buy in to the solution.

Policymaker Data for VMMC: VMMC modeling estimated that approximately one HIV infection would be averted for every 10 men circumcised over 15 years, and scale-up was predicted to be cost-effective in all countries and cost saving in most. Showing infections averted and cost-effectiveness over 15 years demonstrated that the potential epidemic and economic impact outweighed concerns about partial efficacy. For costs, it was important to show at a granular level the cost to roll out the product at scale, though this can demonstrate too high an upfront cost to be feasible. Global VMMC modeling has shown that increasing coverage to 80 percent in 14 priority countries among men ages 15-49 would save US$16.5 billion in treatment costs, but it would cost US$2 billion to reach that point. (Sources: S.K. Sgaier et al. “Achieving the HIV Prevention Impact of Voluntary Medical Male Circumcision: Lessons and Challenges for Managing Programs” & J. Reed Interview.)
IV. Key Learning: VMMC programs found product champions to be an effective strategy for creating demand. Champions included prominent citizens, politicians, traditional leaders, sports figures, and leading artists (e.g., musicians) who engaged in activities to support VMMC, including advocacy, public education, and motivation of potential VMMC clients. While this strategy is certainly not unique to partially efficacious products, a prominent product champion can be a powerful influence for a product that may evoke skepticism or doubt.

- Product champions could play an important role in driving demand for a partially efficacious ring by communicating the acceptability of the product.

V. Key Learning: Modeling is critical for partially efficacious products. Positive cost-effectiveness and impact data helped make the case to ministries by tangibly demonstrating what an investment would return, and in turn the data made it easier for a ministry to justify its support. Strong data, via cost-effectiveness and health-impact modeling, will be attractive to ministries and can mitigate worry that accompanies a product of partial efficacy. However, any cost-effectiveness modeling produced today would need to reflect the impact of universal test and treat in the context of 90-90-90, making it more difficult now than at the time of VMMC introduction to demonstrate the cost-effectiveness and impact of any new prevention intervention.

- Although ring modeling will appear less effective than VMMC modeling at the introduction stage, presenting the relative impact of the ring in the context of impact modeling of other products may help to make a compelling case for the ring.

VI. Key Learning: Cost reductions can mitigate concerns about partial efficacy. VMMC research identified cost-saving opportunities, including task sharing, bundling of surgical instruments, and electrocautery for surgical efficiency, without compromising quality. Discovering mechanisms through which costs could be reduced decreased the risk that poor cost-effectiveness would restrict rollout.

- Finding ring cost efficiencies, either through reduction of the manufacturing cost or in the provider time required to deliver the product, could be helpful for improving cost-effectiveness.

### Vaginally Inserted Product Findings

A potential challenge for the dapivirine ring is that it is vaginally inserted. Few products currently in use are vaginally inserted, so knowledge of and experience with such products is limited and therefore valuable. Having to touch the genitals to insert the product is an added potential barrier to use given cultural and social norms. The experience of introducing other vaginally inserted products can provide useful guidance for the dapivirine ring.

#### The Importance of Providers:
Providers are critical gatekeepers for new products. This tends to be particularly true for products that are differentiated in some manner from well-known or already existing products. A vaginally inserted ring will be less familiar than other product modalities such as an oral pill or an injection. Similarly, it will likely be harder to persuade providers to prescribe a product that does not demonstrate extremely high efficacy than one that demonstrates perfect efficacy.
**Product Case Study: Female Condom**

I. **Key Learning:** Provider counseling and training programs can be used to address bias and select appropriate trainees. While not unique to the female condom, client comfort with the provider is especially important for intimate products like the female condom and ring. The curriculum of the female condom training of trainers was informed by interviews with various stakeholders including health care administrators, clinicians, advocates, and clients. Engagement of health care workers who are not physicians may help women feel more comfortable discussing sex and vaginally inserted products. Research needs to inform which providers are trained, and the delivery channels more broadly, to ensure that the ring is available at sites where women would like to obtain it.

- Evidence-based selection and training of providers who are approachable by potential ring users could be an important way to overcome barriers presented by vaginal insertion.

II. **Key Learning:** Peer-to-peer communications, by a product user, can be effective in recruiting new users of the product. Having individuals who use and advocate for the product as the face of campaigns was important and crucial in Zimbabwe. For a product like a female condom or ring, a provider who has never tried it may struggle to explain how it feels to use it. A peer champion, on the other hand, is relatable and can bring credibility as someone who has actually used the product. Trial participants who have used the ring may be effective educators and advocates who can comfortably and practically discuss vaginal insertion.

III. **Key Learning:** Detailed information, education, and communication (IEC) materials are critical to increasing demand for an unfamiliar product. Posters and manuals that demonstrated with granularity how the female condom is inserted and removed, how it remains secure in place, and how it interacts with a woman’s body were crucial for initial introduction.

**Experience of Provider Training and the Female Condom:** In South Africa, prior to the launch of the wide-scale government female condom program, 3,000 health care workers, mostly female nurses, were trained under the “Training of Trainers” model, which generated a “cadre of knowledgeable health care workers for training others and provided a support structure at the service delivery level for ensuring potential users’ access to the female condom within each province.” These trainers were thought to be more approachable and relatable and therefore more able to help younger women try the female condom. Qualitative research demonstrated that this effort both promoted positive attitudes about the female condom and expanded the repertoire of problem-solving approaches, which made the trainees feel more confident recommending the product. During rollout of the product, implementers also trained more intimate influencers of women such hairdressers and other female leaders in the community.

Today, the female condom program is well established in South Africa and female condoms are available in every public health sector facility. Data indicate that providers remain key gatekeepers and with proper training can help drive uptake.

(Source: J.E. Mantell et al. “Introducing the Female Condom through the Public Health Sector: Experiences from South Africa”, M. Beksinska et al. “Twenty Years of the Female Condom Programme in South Africa: Past, Present, and Future” & M. Warren Interview)
IEC materials with details about how the ring fits in a woman’s body can be helpful for overcoming concerns about an unfamiliar vaginal product.

**Female Condom Communications:** Like the dapivirine ring, the female condom is not familiar or intuitive to many women. The initial marketing and communications plan recognized this and focused on explaining the product. Creating demand among patients, providers, and other influencers for a new global health product or intervention typically receives less focus and investment than getting the product through trials and regulatory processes. Marketing and communications planning are often left until the last minute, or are completely neglected, during planning for product introduction. A vaginal ring, like the female condom, is not a familiar product and will take additional literacy and communications to garner interest and acceptance. *Source: M. Warren Interview*

IV. **Key Learning:** Strong consideration must be given to men as well as other influencers of women contemplating the product. Targeting these gatekeepers and getting them to accept and understand the technology and nature of the product will enable stronger uptake among women. A female condom framed to “empower women” had the unintended effect of disempowering male partners, so the product was reframed as a benefit to everyone (including male partners who would not need to wear a condom). Branding and positioning can also help engage men.

- Like the female condom, partners may be able to feel the ring. Although most women in an ASPIRE trial sub-study reported that partners did not feel the ring during sex, many reported that they felt they had to “manage their partner’s interaction with or reaction to the ring.”

  - Providing messages for partners, as well as empowering women to explain the ring to partners, will be an essential component of ring introduction.

**Product Case Study: Progesterone Contraceptive Vaginal Ring**

The introduction process for the Progesterone Vaginal Ring (PVR) was planned to be a phased approach, which focused first on gauging demand for the product, followed by formative research on markets and users, an acceptability study, early engagement with regulators, and finally, developing a clear plan for introduction. This approach not only maximized efficiency, but led to the development of an effective strategy for engaging providers and leveraging their influence to communicate the benefits of the PVR and help overcome stigma. As a vaginal ring, the experience of introducing the PVR has also illustrated a number of key insights into strategic positioning of vaginal rings for users, policymakers, and donors.
I. **Key Learning:** The product acceptability study fed directly into the development of the provider training curriculum for the PVR. The results provided insights on concerns providers may have and offered positive ways providers could communicate the challenges.³⁴

- Similar research among providers could shape the dapivirine ring training curriculum and communications for providers. While this is not unique to vaginal products, it is especially important for them given the role providers have in helping clients feel comfortable and confident inserting the ring.

II. **Key Learning:** Formative research in Central America found that among users, “the acceptance rate was higher in sites where providers themselves used the ring.” In one PVR training, one of the providers tried the ring at home and then reported it back to the group thereby adding some real-life and real-time experience to the training.³⁵

- Encouraging providers to try the ring themselves can be an effective strategy for overcoming provider bias against the ring.

III. **Key Learning:** The research and pilot programs highlighted the importance of having at least one influencer provider at each implementing site. The influencer possesses a comprehensive understanding of the product, is supportive, and is willing to share knowledge with other providers and health care workers at the site.

- Where other products may have influencer who advocate among users, for a vaginally inserted product that requires provider support, having an influencer among providers can also offer helpful support for overcoming concerns about the product, including acceptability of vaginal insertion.

IV. **Key Learning:** Framing the product in a way that demonstrates how it will make a provider’s life easier is recommended to convince providers to support the product.³⁶ For example, demonstrating how a PVR may reduce the time a provider needs to spend with a client after the initial consultation was quite attractive. Similarly, users can insert PVR without provider assistance, thus reducing the number of clinic visits needed. Like the PVR, a longer-term, non-systemic monthly product like the dapivirine ring might require less continuation counseling than oral PrEP, and can reduce the burden placed on users and providers.³⁷

- Acknowledging the length of the initial counseling required while also highlighting the decrease in counseling required once the product is in use can be a compelling case for providers to offer
the ring. Additionally, communicating the benefits of a self-administered vaginal ring may increase uptake among potential users.

V. Key Learning: Use of the PVR appears to increase its acceptability. The dapivirine ring produced similar findings — that initial apprehensions resolved with use.  
- Recruitment and communications strategies that encourage women to try the ring can help to overcome their initial physical concerns with the ring and its vaginal insertion.

VI. Key Learning: Proving that the addition of the PVR to the existing suite of contraception options would increase the number of women choosing to use contraception, not just switching between products, was important. All methods are imperfect, but some women will find the PVR to be right for them. Some women may have an issue with a ring in their vagina, some men may not allow their partners to use the ring, and some women may prefer other technologies; however, there will be some women for whom the product is the best option. 
- Demonstrating a similar uptick in demand for HIV prevention options through choice may prove to be a critical driver in approval of ring policy and subsequent uptake of the device.

VII. Key Learning: Analysis demonstrated that the PVR would actually reduce the burden on the health system by reducing the time health care workers need to spend with a client. The rationale was that the product could eventually be provided outside clinical settings (e.g., in pharmacies) or by community health care workers, reducing the burden on medical staff. Additionally, PVR use supported women to breastfeed their children longer, which provides a health benefit to the child. 
- Identifying and conveying the dapivirine ring’s added benefits to the broader health system may encourage policymakers to consider dapivirine ring introduction. For example, clearly outlining the cost efficiencies that dapivirine ring will provide to the health system, in addition to identifying the final costs to the end-user,

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Consumer Perception of the PVR: The Population Council’s progesterone PVR faced challenges at initial rollout in sub-Saharan Africa. A survey of women regarding their first impressions of the product found that “the size of the ring and its texture seemed to be of importance, as there were variations in perceptions. For example, about half the women thought its size and texture was fine (50% and 53%, respectively), 46% thought it was too big and one-third perceived it to be too soft.” After using the product for two ring cycles, those same perceptions changed significantly: “There was a greater increase in the proportion who reported that the size, color and texture of the ring were just fine” as compared with women who had not used the product. The Population Council compared a woman using the ring for the first time with a woman breastfeeding for the first time; both become more familiar and comfortable after first experience. (Source: J. Townsend Interview)

Policy Experience with the PVR: When introducing the progesterone PVR and working with ministries, the Population Council found several compelling approaches. Demonstrating that an investment in their product was going to reduce unintended pregnancies was simple, straightforward, and convincing. But the Population Council also had to demonstrate that the new PVR would have advantages over existing family planning products and interventions, such as bringing new users into the system who were not previously accessing contraceptives. The contraceptive literature has found that increasing choice increases contraceptive use. (Source: J. Ross and K. Hardee. “Access to Contraceptive Methods and Prevalence of Use”)
providers, procurers, and donors is critical for decision-makers.

Product Case Study: Tampon and Menstrual Cup

I. **Key Learning:** Provider acceptability of a new technology, especially of a vaginally inserted product, will likely improve over time. Advocacy by even a small but vocal minority of providers can change provider perceptions. Following the introduction of tampons in the 1930s, their use in the United States increased fivefold from 1937 to 1943. One survey taken in 1940 and 1944 found that approximately one-quarter of women regularly used them. 42

- Acceptability of the ring among even a small group of vocal providers can influence uptake nationally, so those providers need to be found, supported, and encouraged to be vocal. However, it is important to note that tampons (similar to menstrual cups) are hygienic and not medical products – for this reason, there isn’t an explicit need for them to be provided by a clinician or nurse. Additionally, medical products including active drugs can face unique user concerns related to safety and side effects.

**Provider Influence on Tampon Uptake:** When the tampon was introduced in the United States in the early- to mid-twentieth century, providers were very skeptical that the product would ever take off. Eventually providers led research that advocated for its widespread use, but not until well after initial approval and availability. In one early provider survey about the tampon, 74 percent of providers “definitely opposed” the use of the tampon and only 14 percent were “completely favorable.” The authors of the study (who themselves were providers) concluded, “It is our opinion that inefficacy of the method, common sense, and fear would limit the use of this procedure to a relatively small number, and that the fad should soon die of its own weight, were it not for the constant new crop of neophytes in schools and colleges gullible to attractive advertising and sampling.” (Sources: J. Farrell-Beck and L.K. Kidd. “The Roles of Health Professionals in the Development and Dissemination of Women’s Sanitary Products, 1880-1940” & J.M. Singleton and H.F. Vanorden. “Vaginal Tampons in Menstrual Hygiene”)

II. **Key Learning:** Comprehensive training on reproductive anatomy is likely to be an appropriate starting place for the introduction of a vaginally inserted product like the ring. Experience with menstrual cup introduction in South Africa indicates that such training can help adolescent girls and women learn where their cervix is and overcome nervousness of “inserting things too far.” 43
As with the menstrual cup, training that focuses on anatomy and includes pictures showing exact product placement and pelvic models showing how the ring fits may be helpful.\textsuperscript{44}

III. Key Learning: In some countries, a limitation to tampon and menstrual cup use has been the taboo against inserting products into the vagina. This may be related to concerns about product use during menses. In other countries, health providers have discouraged the insertion of products such as herbs or stones, and this may deter insertion of any vaginal product.

- Finding culturally acceptable messages about inserting the dapivirine ring into the vagina will be critical. A former tampon marketer suggested testing a message about the ring as part of “purification” to see if it would resonate with potential users.\textsuperscript{45} It will be essential to understand the perceptions and concerns around insertion of the dapivirine ring.

IV. Key Learning: The mechanics of inserting and removing a tampon or menstrual cup are a barrier to use. Women and girls in low-income settings do not have ready access to a private place with water and light necessary to change a cup or tampon.\textsuperscript{46} Water and sanitation experts are only beginning to consider these factors, particularly for girls in school.\textsuperscript{47} For the ring, this may be less of a factor because the ring will only need changing monthly; nonetheless, these logistical factors need to be considered.

- Providing guidance to ring users to help them identify a private place with water and light where the ring can be inserted and removed is a possible way to overcome potential logistical constraints. Likewise, guidance on product disposal will be important.

V. Key Learning: As we saw with female condoms, the appeal of the tampon and its attributes varies considerably among users. According to one tampon market analyst, U.S. tampon users prefer tampons with applicators (they “will tell you it’s a hygienic thing — they don’t want to gunk up their fingers”) and European tampon users prefer tampons without applicators (they will say “it’s a hygienic concern — that they don’t trust the applicator being inserted inside their bodies)...

Consumer Perception of Vaginal Products: Although the tampon has not been widely marketed in Africa, a rubber menstrual cup is starting to be made more available alongside sanitary napkins. Like the tampon, the menstrual cup is vaginally inserted. An important factor in the acceptability of menstrual products is body awareness, particularly of the vaginal area. “Many girls and women lack adequate knowledge of reproductive health in general and menstrual hygiene in particular, leaving them susceptible to myths and misconceptions.” Women are unfamiliar with inserting vaginal products such as tampons. In one Ugandan study, “Despite being curious, most girls stated that they would not use insertion products even if they became more widely available for fear they would ‘get stuck,’ be difficult to insert or painful. Insertion materials generally were seen as culturally inappropriate, with girls questioning their effects on fertility and health.” (Sources: World Bank Group. “Changing the Lives of Women and Girls through Affordable Feminine Hygiene Products” & T. Crofts and J. Fisher. “Menstrual Hygiene in Ugandan Schools: An Investigation of Low-Cost Sanitary Pads”)

Tampons and menstrual cups also touch on taboos surrounding menstrual blood and vaginal products. In some cultures, wearing something in the vagina is not considered hygienic, and there are taboos against capturing menstrual fluids and keeping them inside. Training sessions with young women have shown that the insertion of a device into the vagina is a new concept for many. Over the years, some countries have tried to convince women not to insert items in their vaginas. (Sources: M. Aikenhead Interview, M. Beksinska Interview, & N. Mgodi Interview)
Consumers develop very strong opinions on usage habits — polar opposites, for the same reason. The nuance and complexity of a consumer’s relationship to a vaginally inserted product cannot be overlooked. Understanding the consumer and recognizing that users may find different aspects of a product appealing is critical for tampon marketing.

- Continuing to learn what aspects of the ring are attractive to women and how women interact with the product will be important for developing messages that appeal to potential dapivirine ring users.

### Conclusion

The analysis of like-product introductions provides actionable guidance for planning dapivirine ring introduction. Table 2 summarizes potential messages, approaches to research and training, reasons for engagement, mechanisms for communication, and ideas for data collection relevant to the introduction of partially efficacious and vaginally inserted products. Potential implementers of the dapivirine ring can consider the relevance of these strategies when planning for introduction. These ideas can help introduction planners efficiently and effectively engage decision makers, consumers, providers, influencers, and other stakeholders.

These findings are presented to encourage all those engaged in planning and leading product introduction to consider them. Researchers can consider what issues may merit further study to generate data for policymakers and others. Communications experts can consider how critical issues can be further explored and developed. Training specialists can build on the experience of training plans for other products and on other strategies to gain provider buy-in.

As the field prepares for potential market introduction of the dapivirine ring for HIV prevention, it is critical to learn from barriers and facilitators of similar past product introductions. Embedding the lessons from past introductions in the access plan for the dapivirine ring will not guarantee success, but it will put the field on the right path for an efficient and effective introduction.

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**Consumer Uptake of Tampons:** While the tampon is now commonly used in higher-income countries (e.g., used by approximately 80 percent of U.S. women), a 2017 World Bank paper reported that only a small fraction of women in low- or middle-income countries use sanitary products during menstruation. A 2012 study in Durban, South Africa, found that 20 percent of women surveyed had ever used tampons, and not quite 11 percent used them regularly. Lack of uptake of the tampon in lower-income markets may also provide insights for the dapivirine ring. (Sources: A. Feters. “The Tampon: A History” & World Bank Group. “Changing the Lives of Women and Girls through Affordable Feminine Hygiene Products” & V. Hoffman. “Menstrual Management and Sanitation Systems”)
<table>
<thead>
<tr>
<th>Aim</th>
<th>Partially Efficacious Products</th>
<th>Vaginally Inserted Products</th>
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<tr>
<td></td>
<td>Message</td>
<td>Example</td>
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<tr>
<td>Policymakers and funders</td>
<td>Make the case</td>
<td>Make the ring part of a comprehensive package of prevention The ring can help attract clients for other sexual and reproductive health services (family planning, STI treatment, HIV testing, prenatal vitamins)</td>
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<tr>
<td>Present the data</td>
<td>Over time, the ring can have an impact similar to that of other prevention products in the context of 90-90-90 With introduction and scale-up, cost efficiencies can be identified to improve the ring’s cost-effectiveness</td>
<td>Rotavirus &amp; VMMC</td>
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<tr>
<td>Aim</td>
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<td>Message</td>
<td>Example</td>
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<td><strong>Health care providers</strong></td>
<td>Ensure providers are knowledge-able supportive of the product</td>
<td>Respected providers can enhance ring acceptability and help overcome efficacy concerns</td>
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<td></td>
<td>High-quality training is critical to avoid a decrease in effectiveness</td>
<td>VMMC</td>
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<td></td>
<td>The ring will bring some efficiencies for health systems</td>
<td>VMMC</td>
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<td></td>
<td>Identify and highlight ways the ring can create/support efficiencies, such as shifting some of the counseling to peer educators, streamlining re-supply, or deploying self-risk assessment tools</td>
<td>PVR</td>
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<tr>
<td>End users</td>
<td>Use appropriate means and channels for message dissemination</td>
<td>Interpersonal communications are ideal for dissemination of an efficacy message</td>
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<tr>
<td>Conduct consumer research</td>
<td>Over time, the ring could become more of a lifestyle product than an HIV prevention device</td>
<td>VMMC</td>
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<tr>
<td>Convey appropriate consumer messages</td>
<td>The ring can reduce an individual's risk of HIV in combination with other prevention interventions</td>
<td>Rotavirus RTS,S</td>
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<td>Pretest messages about ring use in the context of other prevention products for appeal and comprehension</td>
<td>Women need safe, private places to go to change the ring</td>
<td>VMMC</td>
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<tr>
<td>Product champions can convince users of the product’s acceptability</td>
<td>A champion among providers can provide helpful support</td>
<td></td>
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<tr>
<td>Use product champions</td>
<td>Engage gatekeepers/influencers</td>
<td>Ring users need to be counseled and empowered so they may choose to provide ring information to their partners</td>
</tr>
</tbody>
</table>
Endnotes


5 Clifford, A. (2018, April 16). Rotavirus Vaccine [Interview].


15 Collymore, Y. (2018, April 19). RTS,S Malaria Vaccine [Interview].


17 Clifford, A. (2018, April 16). Rotavirus Vaccine [Interview].

18 Clifford, A. (2018, April 16). Rotavirus Vaccine [Interview].

19 Collymore, Y. (2018, April 19). RTS,S Malaria Vaccine [Interview].


21 Collymore, Y. (2018, April 19). RTS,S Malaria Vaccine [Interview].
22 Reed, J. (2018, April 26). Voluntary Medical Male Circumcision [Interview].
23 Reed, J. (2018, April 26). Voluntary Medical Male Circumcision [Interview].
24 Reed, J. (2018, April 26). Voluntary Medical Male Circumcision [Interview].
31 Beksinska, M. (2018, May 19). Female Condom [Interview].
40 Townsend, J. (2018, April 3). Progesterone PVR [Interview].
41 Townsend, J. (2018, April 3). Progesterone PVR [Interview].
43 Beksinska, M. (2018, May 19). Female Condom [Interview].
44 Beksinska, M. (2018, May 19). Female Condom [Interview].
Appendix 1: Introduction to the Dapivirine Ring (Source: International Partnership for Microbicides)

The first microbicide to be submitted for regulatory approval is a monthly vaginal ring, developed by the nonprofit International Partnership for Microbicides (IPM). Made of flexible silicone, the long-acting ring releases dapivirine, an antiretroviral drug, slowly over the course of one month. It is user-controlled (the woman inserts the ring herself each month) and is designed to offer protection locally at the site of potential infection (inside the vagina) rather than systemically (affecting the whole body).

Between 2012 and 2016, IPM and the Microbicide Trials Network (MTN) conducted two large-scale Phase III studies (called IPM-027/The Ring Study and MTN-020/ASPIRE) among more than 4,500 female volunteers in Malawi, South Africa, Uganda, and Zimbabwe to evaluate the ring’s effectiveness and long-term safety. Together, the studies found that the ring reduced HIV risk by approximately 30 percent overall. Participants who used the ring at least some of the time saw their HIV infection risk cut by 45 percent across both studies. Women older than 21 were more likely than younger women to leave the ring in place. Research is underway to learn more about how younger women perceive the ring and what might increase their interest in using it.

Two OLE studies — IPM-032/DREAM and MTN-025/HOPE — were conducted between 2016 and 2018 to provide additional data on the ring. Both studies were launched in July of 2016, with HOPE completed in October 2018 and DREAM completed in January 2019. Final results for HOPE and DREAM indicate that rate of HIV infection among participants in the open-label studies (which have no placebo arms for comparison) was reduced by 39% and 63% respectively.

The MTN-034/REACH study is evaluating how adolescent girls and young women use the monthly dapivirine ring and daily oral PrEP, and their preferences for both approaches. Additional ring studies are planned among pregnant and breastfeeding women in Africa. IPM is also developing a three-month dapivirine-only ring and a three-month dapivirine contraceptive ring, both of which are in Phase I studies being conducted in partnership with the MTN.

The monthly dapivirine ring is currently under review by the European Medicines Agency (EMA) under a procedure called Article 58. That procedure allows the EMA, in cooperation with WHO, to provide a scientific opinion on the safety, efficacy, and quality of medicines that would be marketed exclusively outside of the European Union — specifically in low- and middle-income countries — for diseases of major public health interest.
Appendix 2: Resources


Clifford, A. (2018, April 16). Rotavirus Vaccine [Interview].


Collymore, Y. (2018, April 19). RTS,S Malaria Vaccine [Interview].


Reed, J. (2018, April 26). Voluntary Medical Male Circumcision [Interview].


Townsend, J. (2018, April 3). Progesterone PVR [Interview].


Warren, M. (2018, April 10). Female Condom [Interview].


Appendix 3: List of Abbreviations

ASPIRE – A Study to Prevent Infection with a Ring for Extended Use
BMGF – Bill & Melinda Gates Foundation
CROI – Conference on Retroviruses and Opportunistic Infections
PVR – Contraceptive Vaginal Ring
DREAM – Dapivirine Ring Extended Access and Monitoring
EMA – European Medicines Agency
HIV – Human Immunodeficiency Virus
HOPE – HIV Open Label Prevention Extension
IEC – Information, Education, and Communication
IPM – International Partnership for Microbicides
MatCH – Maternal, Adolescent, and Child Health
MTN – Microbicide Trials Network
OGAC – Office of the U.S. Global AIDS Coordinator
OLE – Open Label Extension
PrEP – Pre-Exposure Prophylaxis
REACH – Reversing the Epidemic in Africa with Choices in HIV Prevention
STI – Sexually Transmitted Infection
UNAIDS - Joint United Nations Programme on HIV/AIDS
VMMC – Voluntary Medical Male Circumcision
WHO – World Health Organization