Guidelines for Dapivirine Ring Pilot Implementation Studies:

Template Language for National-Level Guidance & Protocol Development

**About this Document**

The intent of this document is to provide adaptable guidelines for the design of dapivirine vaginal ring, also known as the PrEP ring, pilot implementation or post-introduction operations studies to help shape national ring guidelines. The contents here align a set of study objectives and measures to consider for use across multiple contexts to foster building an evidence base on best implementation practices for ring use. The document includes prompts for national- level consideration during the study protocol development process. Areas specifically requiring national input are highlighted in yellow.

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# Overview and how to use this tool

As new HIV pre-exposure prophylaxis (PrEP) methods become available for use, determining how best to integrate them within the existing health system will be of paramount importance. Implementation studies conducted as part of oral PrEP introduction have revealed opportunities to strengthen health system components, test new approaches to service provision, and improve provider training to optimise oral PrEP delivery and follow-up. These lessons can inform the introduction of new PrEP methods, such as the dapivirine vaginal ring (also known as the PrEP ring and referred to as “the ring” for the remainder of the document), which may have different intended user groups, and thus may require different approaches to service provision than those currently used for oral PrEP.

This template is based on a document originally developed by the dapivirine ring task force within the PrEP Technical Working Group, led by the Ministry of Health of the Government of Zambia. This template is designed for policymakers and government technical specialists to use to apply uniform objectives, study design features, and measures across pilot implementation and other operations research studies for ring introduction, in collaboration with investigator teams. These objectives, measures, and design features are proposed across countries to facilitate the generation of a body of evidence to foster regional learning and programme refinement over time and as additional PrEP methods are introduced.

# Introduction and rationale

The government of [country name], through the Ministry of Health (MOH) [or other health authority], recognises the great burden that HIV has placed on the lives and wellbeing of [nationality] families over the last four decades. The MOH [or other health authority] strives to ensure HIV prevention measures, testing, and treatment are available to and reach all citizens, including provision of oral PrEP to prevent HIV. As new PrEP methods that have the potential to expand the HIV prevention toolbox become available with sound scientific evidence of their safety and efficacy, the MOH [or other health authority] will consider whether introduction of each method in the public sector is feasible and acceptable.

The ring is a flexible silicone ring inserted into the vagina that slowly releases the antiretroviral drug dapivirine over a one month period of continuous use, after which it is replaced with a new ring. The ring protects against HIV acquisition in women only during exposure from receptive vaginal sex. This method is user- initiated and, when used in combination with other interventions to enhance HIV prevention, may present an acceptable option for clients who cannot or do not wish to take oral PrEP. Discrete choice studies (TRIO, Quatro) have been conducted in Kenya, South Africa, and Zimbabwe to determine the best way to deliver PrEP for women, with participants trying several placebo methods and documenting their preferences. The TRIO study compared oral, injectable, and ring methods and found that while injectables were most preferred, ring continuation rates were high among women willing to try the ring compared to those for other PrEP delivery methods.1 The Quatro study compared four different vaginal methods, including the ring, and found that initial preference for ring was low but increased with trial duration and product crossover with high ring adherence.2 Table 1 summarises evidence regarding ring efficacy and safety from clinical trials and open- label extension studies.

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## Table 1. Summary of dapivirine ring efficacy and safety findings from multi-country trials and open-label extension studies

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| --- | --- | --- | --- | --- |
| **Study lead author, name of study; sites; sample size** | **Study design** | **Main safety finding(s)** | **Main effectiveness finding(s)** | **Key limitations reported by authors** |
| Nel *et al*.,3 The Ring Study; South Africa & Uganda; 1959 women ages 18–45 years | Placebo- controlled, double-blind randomised controlled trial (RCT) (Phase III) | Serious adverse events were rare but more common in women randomised to ring (2.9% vs. 0.9%), with no detected pattern. Rates of adverse events were similar between groups, and product- related events were rare (0.4% for ring and 0.3% for placebo) and mild. No significant differences were detected in rates of non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance mutation amongwomen with new infections. | Women receiving the ring had a 31% lower incidence of HIV infection (4.1 vs. 6.1 infections/100 person- years [p-y]); there was no significant difference in efficacy for women <21 years compared to those >21 years. | Limitations include the lack of standardised criteria for measuring ring use based on dapivirine concentrations. |
| Baeten *et al*.,4 ASPIRE trial; Malawi, South Africa, Uganda, & Zimbabwe; 2629 women ages 18–45 years | Placebo- controlled, double-blind RCT (Phase III) | Rates of serious adverse events, adverse events overall, and NNRTI resistance in women with new HIV seroconversions were similar between study arms. | Overall, women receiving the ring had a 27% lower HIVincidence (3.3 vs. 4.5 infections/100 p-y); women ages >21 years had significantly higher (56%) protection compared to those <21 years (27%), correlated to reduced adherence. | Ring use as measured by plasma levels and residual drug in used rings may not have perfectly correlated with use patterns based on variability in both measures |



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| --- | --- | --- | --- | --- |
| **Study lead author; name of study; sites; sample size** | **Study design** | **Main safety finding(s)** | **Main effectiveness finding(s)** | **Key limitations reported by authors** |
| Nel *et al.*,5 DREAM open-label extension (OLE) study; South Africa & Uganda; 941 women who had participated in The Ring Study | OLEobservational cohort | Serious adverse events (2.1%) and product-related adverse events (0.6%) were rare. Serious adverse events were not deemed product- related and adverse events related to product use were mild, such as vaginal itching. NNRTI resistance was detected among 29% of thoseseroconverting. | 18 incident infections (1.8/100 p-y) were detected, with a modelled 62% lower infection rate than the simulated placebo rate. | Lack of a placebo group and the time lag between parent trial and OLE with differences in background HIV incidence rates may have affected placebo estimates. Another limitation is possible selection bias of having only participants who remained HIV-negative in the parent trial, as they were older and had lower rates of sexually transmitted infection. |
| Baeten *et al*.,6 HOPE OLE; Malawi, South Africa, Uganda, & Zimbabwe; 1456 women participating in the ASPIRE trial | OLEobservational cohort | 22 serious adverse events occurred, with none deemed related to product use. Two adverse events were related to product use (abdominal pain and pelvic pain with ring insertion) and were graded as mild in nature. Seven women seroconverting had NNRTI resistance mutations that differed, suggesting no distinct pattern related to dapivirine. | 35 incident infections (2.7/100 p-y) were detected, with a modelled 39% lower infection rate than predicted mean incidence rate of 4.4/100 p-y from parent trial. 89% of returned rings had dapivirine levels reflecting some degree of use and drug release; 77% of par- ticipants had evidence of use across each 3- month period. Ring acceptance and use rates in the OLE werehigher than in the RCT. | Limitations included lack of a placebo group, quarterly follow-up limiting precision of estimates, low inclusion of women ages 18– 21 years, and greater participant experience and comfort with ring use or lack of widely available oral PrEP as an alternative, resulting in higher adherence rates. |

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The trials found higher HIV prevention efficacy of the ring among women who had greater drug release from their rings, reflecting more consistent use.7 The open-label extension studies added data to support the association between consistent, correct ring use and lower HIV acquisition.5,6 All studies noted no product-related severe adverse events. Less than 5 percent of women experienced side effects related to ring use, which were mainly urinary tract infections, pelvic pain, and vaginal discharge or itching and resolved within a few weeks.

In light of these data, the European Medicines Agency provided a positive scientific opinion in July 2020 supporting ring use for women at significant risk of HIV infection. In January 2021, the World Health Organization (WHO) recommended that the ring be offered as an additional prevention choice for women at substantial risk of HIV infection as part of combination prevention approaches, and the ring was included in the revised WHO Consolidated HIV Guidelines for Prevention, Treatment, Service Delivery & Monitoring released in July 2021.

The ring is currently approved for women 18 years and older because younger adolescents were not included in the original trials. The available data regarding safety in pregnant and breastfeeding women are sparse yet reassuring: among 169 trial participants who became pregnant, no congenital, maternal, or infant adverse outcomes were observed among those exposed to dapivirine.8 Studies assessing the safety and acceptability of ring use among adolescent girls and young women ages 16–21 years (REACH), pregnant women (DELIVER), and breastfeeding women (B-PROTECTED) are ongoing, with the potential for changes in product labelling consistent with study results. Interim results from the REACH study, being conducted at four clinical research sites in Uganda, South Africa, and Zimbabwe, demonstrated that the vast majority (97 percent) of the study’s 247 participants used the ring and daily oral PrEP some or all of the time. Fewer than 3 percent of participants used neither of the products, according to laboratory tests for adherence.9

At this time, ring use data are largely based on clinical trials rather than “real world” implementation. Moreover, discrete choice experiments measuring interest in use can inform our understanding of feasibility but not our understanding of acceptability because they do not capture user experience with the actual product. These studies also may not measure or anticipate the impact of specific barriers and facilitators to method access and use, such as partner perceptions or provider counselling and attitudes, that can be measured in implementation evaluations.

[Please add paragraph reflecting ring use or experience within specific country. For example, ring Phase III and OLE trials were conducted in Kenya, Malawi, South Africa, Uganda, and Zimbabwe, so these countries have documented acceptability and safety data within their contexts, which should be featured in this paragraph. For countries not included in these trials or in the Quatro study (which included South Africa and Zimbabwe), here is some example text from the Zambia ring pilot implementation guidelines: “The ring has not been previously used or tested in Zambia, and further information is needed regarding the feasibility and acceptability of this method among clients, providers, and administrators in the public sector health system. Furthermore, MOH administrators will require data regarding ring safety with any pilot use of the ring in Zambia. Prior to considering introduction of the ring as part of the PrEP method mix within Zambia, the MOH requires evidence regarding ring acceptability among key end-user groups and health care providers, the feasibility of ring service provision in a variety of clinical and community-level settings, and anticipated barriers and facilitators to ring introduction and implementation from the

perspective of health system infrastructure, cost, and community and provider-level demand.”]



The MOH [or other health authority] has requested pilot ring implementation studies to address this need for data to shape ring decisions. The MOH [or other health authority] mandates that the pilot studies include a set of common features as well as conform to guidelines regarding geographic and end-user group distribution to ensure the resultant data are comparable, robust, and provide sufficient detail to guide decisions about adding the ring to the PrEP method mix and any associated policy, strategy, and guideline development.

# Study objectives

1. To measure the feasibility, including cost projections, of adding the ring to available PrEP methods in [country name] among clients and service providers. [For countries that have already conducted ring feasibility assessments but desire costing analyses, please reword this objective to measure cost projections and move it to the final position in the list of objectives, as it will be informed by measures from those feasibility studies as well as from existing health systems data.]
2. To measure the acceptability of ring use among clients and service providers through PrEP method selection/uptake and continuation (ring vs. oral PrEP).

2a. To measure product safety through described side effects and adverse events with either the ring or oral PrEP.

2b. To measure and explore responsive actions by service providers for social harms attributed to PrEP use.

1. To measure the fidelity of ring and oral PrEP service delivery against minimum service standards, including service quality, and document adaptations and the rationale for these changes.

# Study design considerations

[These design considerations are illustrative from Zambia’s experience; each country can adapt the considerations based on its specific priorities. For example, in countries for which feasibility and safety data already exist, health authorities and investigator groups may agree that having a single dissemination event that reports uptake, acceptability, and safety measures is preferable to the two-prong approach described below.]

The MOH [or other health authority] requests that all investigator teams include these design features in their protocols:

* + Study sites should include those currently either directly providing oral PrEP or linked to oral PrEP provision (e.g., primary care sites providing family planning and sexual and reproductive health services) with representation of urban, peri-urban, rural, and remote settings, as possible. Each investigator team will complete a mapping matrix to specify the site and primary end-user group for the proposed study to maximise coverage and prevent duplication (Annex 1).
	+ The MOH [or other health authority] requests that studies include and identify clients who have

used and discontinued oral PrEP as a separate arm/group from PrEP-naïve participants in the sample. The rationale for this differentiation is that users who have tried and discontinued oral PrEP (inclusive of periods of resuming use) may have different perspectives on the tolerability of

side effects or product access/use, and those perspectives may influence ring continuation or switching. Because the ring is indicated predominantly for women who cannot or do not wish to use oral PrEP, it is important to capture the perspectives of experienced users who have discontinued oral PrEP as a primary client group for the ring. This number may be limited relative to new PrEP clients and can be considered an exploratory analysis.

* + The MOH [or other health authority] recommends inclusion of broad community-level ring sensitisation sessions prior to and during study implementation, with qualitative assessment of planned materials to guide national adaptation. Sensitisation sessions shall feature the nature of the study (i.e., implementation assessment rather than safety/efficacy trial) and plans for inclusion of community oversight within the study’s Advisory Committee.
	+ The MOH [or other health authority] recommends developing/adapting and testing draft provider

training packages with minimum service delivery standards and coaching of providers on offering ring users instruction on and motivation for self-insertion at initial use and subsequent visits.

Training and coaching should be provided prior to and during study implementation, with qualitative assessment of planned materials to guide national adaptation. Illustrative questions to aid in refining these packages are provided in Tables 3 and 4.

* + For acceptability outcomes, the MOH [or other health authority] requests that all studies measure whether clients opt for either oral PrEP or the ring in addition to other HIV prevention measures (e.g., condom use) at study entry and include PrEP method discontinuation/switching and reported use of other HIV prevention methods as part of required acceptability outcome measures (please see Table 3). Although this differentiation may present statistical power concerns for an individual study if conducted as a pilot, we anticipate that a pooled analysis will be possible in scenarios where there are multiple studies or a multisite study, permitting greater power to detect true differences in initial and longer-term acceptability for each PrEP method.
	+ To contextualise acceptability outcomes, the MOH [or other health authority] requests that studies conduct qualitative interviews with a subsample of clients to explore the acceptability of ring use, including reasons for selecting or switching to the ring and reasons for continuing or discontinuing its use. These interviews should also address disclosure of ring use and discussions about ring use with partners and peers. Interviews would ideally include representatives across the age span and by group, such as sex workers. Interviews may also include key influencers, such as male partners to whom partners have chosen to disclose their ring use, other family members, or community leaders. These interviews may focus on exploring communication and demand creation strategies and adherence support strategies.
	+ To contextualise acceptability outcomes, the MOH [or other health authority] requests that studies include qualitative interviews with a subsample of health care providers to explore ease of ring counselling and provision, including preferences for ring insertion by providers vs. teaching self- insertion at initial and follow-up visits, perceived time investment, utility of draft provider training materials/job aids, and factors motivating or dissuading providers from counselling or providing the ring. Interviews may also explore provider-targeted strategies for communication, demand creation, and adherence support. Interviews will ideally include providers representing different cadres, sexes, years in practice, and service areas (e.g., HIV service sites vs. family planning clinics vs. mobile/community/DREAMS services).
	+ The MOH [or other health authority] requests inclusion of measures to inform ring cost modelling across studies (Table 5); these measures are germane to feasibility outcomes and centre on supply side considerations.
	+ Study duration should be at least six months of follow-up overall with a proposed two-phase analysis of results: at one to three months (at the end of cohort recruitment) to focus on feasibility and early acceptability (e.g., uptake) and at six months to focus on acceptability outcomes.
	+ A member of the subnational-level health authority in the area of pilot implementation should be included in the implementation as a co-investigator with funding for routine oversight visits to the study site.
	+ The MOH requests the inclusion of an MOH [or other health authority]-convened Advisory Committee to include inputs from potential end-user groups (e.g., adolescent girls and young women, sex workers, and gender-diverse individuals) and their communities in the design (upon investigator or MOH request) and oversight of research (please see Advisory Committee section). Please ensure that study budgets include costs for monthly site visits by one member of the Advisory Committee.

# Inclusion and exclusion criteria

## Facility or care site features

All study sites should meet the following criteria:

* + Have experience providing oral PrEP counselling and/or services
	+ Have links to the public sector supply chain and service quality oversight to ensure minimum service standards are met for oral PrEP
	+ Have authorisation from local authorities to expand service delivery to include oral PrEP provision (e.g., reproductive health care sites)

## End-user participants

All studies should have the following inclusion criteria for end-user participants:

* + At least 18 years of age [Can consider revising this if and when data on ring product safety among adolescents older than 15 years become available and international guidelines are adapted accordingly]
	+ Assigned female sex at birth — eligibility questions will need to ask potential participants about their sex assigned at birth and gender identity and to help those who are unfamiliar with these terms to answer easily
	+ Sexually active and wishing to prevent HIV acquisition during receptive vaginal sex
	+ Able to provide informed consent
	+ Member of priority groups for HIV prevention: sexually active adolescent girls and young women; sex workers or other women engaged in transactional sexual partnerships; clients with a partner of unknown or positive HIV status; or any client who meets other eligibility criteria and requests access to PrEP
	+ Using a modern contraceptive method (e.g., hormonal contraceptives, male or female condoms,

intrauterine contraceptive device, standard days method) [Can consider revising this requirement if and when data on product safety during pregnancy and breastfeeding become available and international guidelines are adapted accordingly.]

* + Able to return to the same health facility or care site during a six-month period

All studies should have the following exclusion criteria for end-user participants:

* + Younger than 18 years [Please see above.]
	+ Currently pregnant or breastfeeding or planning to become pregnant or breastfeed within the next nine to 12 months — The rationale for this criterion is that data for ring safety in pregnancy and during lactation, while reassuring, are relatively sparse. Ongoing studies (DELIVER, B- PROTECTED) are investigating this issue, but these pilot studies will adhere to current ring prescribing guidelines, which stipulate that the ring should not be used by pregnant or lactating women. Women using the ring who become pregnant during the study period should be counselled based on the evidence available at that time and offered the opportunity to switch to oral PrEP. [Please see above.]
	+ Have documented HIV infection, signs or symptoms of acute HIV infection, or suspected HIV exposure in the last 72 hours (i.e., candidate for post-exposure prophylaxis), or have declined HIV testing
	+ Unable or unwilling to be contacted for follow-up appointments

## Healthcare providers

[Please adapt based on current/intended PrEP service site features in your context.]

All studies should have the following inclusion criteria for health care provider participants:

* + Experience with providing oral PrEP services
	+ Currently providing social harm screening and care services at the selected facility/site
	+ Able to provide informed consent
	+ Have participated in the draft provider ring counselling, provision, and management training course
	+ Have recent experience screening for and treating sexually transmitted and other reproductive tract infections
	+ Have recent experience providing HIV counselling and testing

All studies should have the following exclusion criteria for health care providers:

* + Unwilling to provide the ring
	+ No experience providing HIV, PrEP, or sexual and reproductive health services

## Public health sector administrators and key informants

This participant group is optional but recommended for additional insights into feasibility, fidelity, and cost

[

measures.]

Studies may consider inclusion of the following groups for insights into ring feasibility, fidelity of implementation and adaptations, and perceived costs:

* + Provincial/county/district-level health administrators
	+ Government or implementing partner technical advisers for HIV service delivery
	+ Community leaders
	+ Members of HIV advocacy groups

*All studies should record the number of potential participants deemed ineligible, the reason for ineligibility, and, separately, the number who are eligible but declined study participation.*

# Visit schedule and outcome measures and indicators

The MOH [or health authority] asks that all investigator teams include the following required measures/indicators for feasibility and acceptability analyses and safety and also proposes a number of additional indicators for inclusion for each objective. The rationale for this mandate is to ensure comparability across studies and consistent data quality to sufficiently power analyses.

We have mapped a minimum visit schedule, location, and interview type within presumed routine care visits to capture the “real world” nature of implementation studies as well as respect cost and time constraints within study operations (Table 2). This table is illustrative and should be adjusted based on the oral PrEP minimum service package and, where available, draft ring minimum service package schedules unique to each implementing country.

## Table 2. Illustrative study data collection mapped to service engagement points

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| **Service delivery point** | **Participant group; outcome** | **Interview type** |
| Pre-service: Initial service site engagement following provider training | Provider; feasibility | Provider interview with quantitative questions for all; for subsample, qualitative interviews on how to improve in- service training, factors contributing to perceived servicereadiness, and appropriateness |
| Initial patient consultation with HIV testing services (HTS) and HIV prevention counselling (including PrEP) | End-user; feasibility, acceptability (service and method uptake), and fidelity (HIV prevention & PrEP counselling conducted with main points included) | Enrolment visit conducted as exit interview; for subsample, qualitative interview regarding perceived service quality and reasons for PrEP choice/non-use |
| Initial patient consultation with HTS and HIV prevention counselling (including PrEP) | Provider; fidelity | Relevant clinical (e.g., HIV test completed) or validation (e.g., PrEP method selected and dispensed) inputs from chart review and end-user exit interview |
| Phone consultation at one month (or ring visit if reflective of patients preferring provider removal/insertion or service guidelines) | End-user; acceptability | We note that phone follow-up at one month may be limited to study activities but have built in this time point for monitoring use patterns. |
| Phone consultation at one month (or ring visit ifreflective of patients preferring provider removal/insertion or service guidelines) | Provider; fidelity | For ring: to capture provider counselling, pregnancy (asindicated) testing, and offering/teaching self- insertion/removal |
| Quarterly PrEP follow-up visits | End-user; acceptability, fidelity, and clinical measures | Quarterly resupply visits with relevant quantitative acceptability (e.g., continuation, satisfaction, risk perception), fidelity (e.g., received ongoing counselling and adherence support), and clinical outcomes |
| Quarterly PrEP follow-up visits | Provider; fidelity | Quarterly resupply visits with quantitative provider interviewfor fidelity (e.g., services offered with accompanying chart audit) |



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| **Service delivery point** | **Participant group; outcome** | **Interview type** |
| Ad hoc PrEP method issue management, switching, or discontinuation visit | End-user; acceptability, fidelity, and clinical measures | Quantitative interview with acceptability (including reasons for switch/discontinuing), fidelity (e.g., did provider support continuation/ discontinuation decision or counsel on other options), and clinical measures (e.g., serum creatinine for oral PrEP); subsample for qualitative interviews on change inPrEP method use |
| Ad hoc PrEP method issue management, switching, or discontinuation visit | Provider; fidelity | Quantitative interview with chart audit; subsample with qualitative interviews regarding perceived reasons patients change PrEP methods and altered perspectives on how to provide different PrEP methods |

Table 3 includes questions required to achieve the study objectives, along with visit type and application of information. Table 4 provides suggested measures, with some additional entry points listed that correlate with an alternative time point for a required or suggested measure.

## Table 3. Required study outcome measures

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| **Required outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Feasibility Measures: End-Users** |
| Interest in ring as a PrEP method | Please see Annex 3. | Enrolment visit with questionnaire following counselling and HIV prevention method selection | Primary feasibility outcome measure for end- users |

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| **Required outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Feasibility Measures: Providers** |
| Perceived readiness tooffer the ring following training session | Please see Annex 3 for quantitative questions.Probe service readiness in qualitative interviews for context. | Post-training interview | To inform pre/post-test as part of provider training package and help refine package |
| Ring knowledge score | Composite score for 5–7 quantitative knowledge questions with answers presented in training materials (questions and answers in Annex 3) | Questions as part of pretest and post-test for ring training package | Primary outcome for feasibility of training package; can add questions on provider’s attitude about time/ability to include ring services within existing duties |
| **Acceptability Measures: End-Users** |
| Uptake: Participants initiating specific PrEP method | # consented eligible participants counselled who receive oral PrEP pills or the ring (placed by provider); enrolment interview questions (Annex 3) verified with clinic or pharmacy record | Enrolment visit (assume done as exit interview) | Primary outcome measure for specific method uptake; denominator for continuation/ acceptability measures |
| Uptake: Reason for method selection | Please see Annex 3 for quantitative questions.In qualitative subsample, ask about why participants selected their specific method or decided not to start PrEP. | Enrolment visit [assume done as exit interview] | To provide context for method uptake and set baseline for determining acceptable features that are sustained over time |
| Continuation: Participants using PrEP method selected at study entry throughcohort period | # participants reporting use of initial PrEP method at follow-up visits with pharmacy record verification/total # initiating that method | All follow-up visits | Primary outcome measure for acceptability; disaggregate by method, target group, prior oral PrEP use, and province |

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| **Required outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Acceptability Measures: End-Users (continued)** |
| Use patterns as part of continuation: Participants modifying PrEP use based on perceived risk oropportunity cost | Please see Annex 3 for quantitative questions.Include qualitative subset to probe reasons for intermittent use. | All follow-up visits | To characterise use patterns as part of acceptability and to inform adherence support; exploratory analyses of barriers to continuation |
| Switching: Participants changing from one PrEP method to another | # participants requesting and changed from PrEP method initiated at enrolment to new method with pharmacy record verification/# total new PrEP usersPlease see Annex 3 for quantitative questions; probe reasons for switching in qualitative subsample. | All scheduled and ad hoc follow-up visits | Acceptability outcome; disaggregate by method, target group, and province |
| Acceptability: Participant perceived acceptability, partner acceptance, and wouldrecommend to friend | Proposed quantitative questions are in Annex 3. Please see Annex 2 for alternative question structure if you anticipate following end-users who decline PrEP use or having highdiscontinuation rates. | All follow-up visits | Mean/median scores; disaggregate by method, age, target group, prior oral PrEP use, and province |
| Acceptability: Discontinuation and reasons for discontinuing PrEP | Please see Annex 3 for quantitative questions.Probe reasons for discontinuation in in-depth interviews among a subsample of those discontinuing PrEP and those switchingmethods. | Visit where discontinuation requested/ reported | Comparison by original method; self-reported length of use; disaggregate by age and target group, prior oral PrEP use, and province; reasons for discontinuing (clinical, use challenges, provider-initiated, partner-related,etc.) |

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| --- | --- | --- | --- |
| **Required outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Acceptability Measures: Providers** |
| Frequency offering oral PrEP and the ring | Quantitative measure in interview [# times counselled/week; see Annex 3]; check facility pharmacy records for # new oral PrEP or ring clients receiving product in designated time period; probe in qualitative interviews to determine provider confidence vs. changes in service readiness (e.g., stock-outs) | Provider questionnaire at end of enrolment period; pharmacy record check at follow-up visits | Overall proportions; disaggregate by cadre and province |
| Acceptability of counselling on the ring/oral PrEP together and offering choice | Please see Annex 3 for quantitative and qualitative questions. | After training | For quality assurance and improvement; observational checklist findings and reported qualitatively in aggregate only |
| **Additional content areas relevant to PrEP effectiveness/safety measurable within pilot studies and for inclusion in minimum service packages** |
| HIV acquisition | HIV testing per national guidelines/minimum service package | 1 month and quarterly/routine follow-up visits | Effectiveness outcome (though note studies are not powered for this outcome); plan aggregate across sites |
| Incident pregnancy\* | Pregnancy testing | 1 month and quarterly/routine follow-up visits | Safety outcome; plan aggregate across sites Ring to be discontinued in event of incident pregnancy. |

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| **Required outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Additional content areas relevant to PrEP effectiveness/safety measurable within pilot studies and for inclusion in minimum service packages** |
| Adverse drug reaction reporting per national guidelines | # of participants reporting adverse drug reactions | All follow-up and ad hoc visits | Safety outcome; relatedness to PrEP method use; plan aggregate across sites |
| Social harms† reported by participant or recorded at study site | # of participants reporting social harms and sub- portion attributed to PrEP use | All follow-up and ad hoc visits | Safety outcome; relatedness to PrEP method use; plan aggregate across sites |

\*Change pending emerging evidence of safety in pregnancy

† Social harms should use the most appropriate national definition. A suggested definition is: “Social harms are events that cause physical, emotional, or financial but nonmedical adverse consequences due to PrEP use.”

**Table 4. Suggested outcome measures and questions for investigator consideration**

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| **Outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Suggested Feasibility Measures: End-Users** |
| PrEP method planned to use at time of facility visit (enrolment) | Please see Annex 3 for suggested quantitative questions. | End-user interview following sensitisation session and before provider visit, if feasible | Comparison of client perceptions prior to and following provider counselling |
| Perceived effort to access/use the ring | Please see Annex 3 for suggested quantitative questions. | Interviews following community or waiting room sensitisation sessions | Context-specific client preferences to shape demand creation and service provision |

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| **Outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Suggested Feasibility Measures: End-Users (continued)** |
| Perceived “opportunity costs” associated with ring use | Please see Annex 3 for suggested quantitative questions. | Interviews following community or waiting roomsensitisation sessions | Context-specific client preferences to shape demand creation and serviceprovision |
| Perceived effectiveness of ring compared to oral PrEP or other HIV prevention methods | Please see Annex 3 for suggested quantitative questions. Probe role of perceived effectiveness in decision-makingabout the two methods in qualitative interview subset. | Key informant interviews of representative end-user participants | Context-specific client preferences to shape demand creation and service provision |
| Perceived self-efficacy to use ring as PrEP | Please see Annex 3 for suggested quantitative questions. | Interviews following community or waiting room sensitisation sessions | Context-specific client preferences to shape demand creation and service provision |
| Perceived most reliable source for PrEP information/ recommendation | Please see Annex 3 for suggested quantitative and qualitative questions. | Interviews following community or waiting room sensitisation sessions | Context-specific client preferences to shape demand creation and service provision |
| Preferred site and provider for general PrEP provision andspecifically for the ring | Please see Annex 3 for suggested quantitative questions. | Interviews following community or waiting roomsensitisation sessions | Context-specific client preferences to shape demand creation and serviceprovision |
| Perceived facilitators/barriers to ring access and use | Please see Annex 3 for suggested quantitative and qualitative questions. | Interviews following community or waiting room sensitisation sessions | Context-specific client preferences to shape demand creation and service provision |
| **Suggested Feasibility Measures: Providers** |
| Perceived demand for ring vs. oral PrEP by clients | Please see Annex 3 for suggested quantitative and qualitative questions. | Qualitative semi-structured in- depth interviews of subsample of providers at selected follow- up visit where providers have experience with both PrEPmethods | Provider attitude inventory to determine need and content for values clarification as part of training package |

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Suggested Acceptability Measures: End-Users** |
| Participants reporting ring self- insertion after initiation [ringusers only] | Please see Annex 3 for suggested quantitative questions. | First follow-up visit where self- insertion is reported | Proportions: disaggregate by age and target group, prior oral PrEP use, andsubnational level |
| Participants disclosing PrEP use to at least one person | Please see Annex 3 for suggested quantitative questions. | Enrolment visit [See partner disclosure questions in required questions for follow- up visits] | Proportions: disaggregate by type of person (e.g., male partner, family member), participant age, PrEP method and target group, prior oral PrEP use, and subnational level |
| **Suggested Acceptability Measures: Providers** |
| What is/is not working for providers and how can the tools/job aids/training provided to them be improved upon to better support their role? | Please see Annex 3 for suggested quantitative and qualitative questions. | One month and end line | Overall proportions: disaggregate by cadre and subnational level |

# Costing analyses content

The [MOH or national authority] also requests that the following required and suggested measures be added to permit costing analysis across studies, which will provide essential information to guide ring introduction decisions. Table 5 provides these measures, which will be combined with health system costs in analysis. Should interest and funding be available, willingness-to- pay substudies could be considered in contexts where user fees are part of PrEP service costs.

**Table 5. Required and suggested costing measures**

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome measures** | **How measured?** | **When measured?** | **Role in analysis?** |
| **Required Costing Measures** |
| Patterns of PrEP visits (continuation, cycling) | For each client who initiates PrEP, collect data on dates and PrEP method use (continuation, re-initiation, discontinuation, method switching, non-refill visits for otherreasons) at subsequent visits | Enrolment, scheduled follow-up, and ad hoc visits | Captured above in required acceptability measures, but repeated here because it has implications for costing |
| Incremental PrEP service delivery costs | Please see Annex 3 for costing data inputs needed. |  | Incremental cost of adding ring service delivery to existing services per visit, per client initiated, per person-year, disaggregated by type of site and type ofclient |
| **Suggested Costing Measures** |
| Cost to clients for those seeking ring services | Include wealth quintile measures in demographic data and ask about estimated costs borne by clients to access PrEP services. Please see Annex3. | Conducted at the pilot testing phase or during early stages of scale-up | Clarifies the cost to clients of seeking ring services and assesses the extent to which these costs represent barriers |
| Ratio of numbers of rings dispensed to used | Data relating numbers of rings dispensed to patterns of use (please see Annex 3). | Track ring insertion and removal via reported use across follow-up visits | Estimating costs of service delivery per person-year of protection |

# Study efficiency review

The MOH [or health authority] requests that each investigator group list specific subnational sites, type(s) of service sites, and end-user groups planned for each study prior to submission to the institutional review boards (IRBs). These selections will be reviewed to ensure coordination across investigator groups and to suggest alterations or expansion in target groups or service sites to ensure multiple data sources for key measures. A matrix will be provided to facilitate this process (Annex 1). Each investigator team should include a plan for sustained ring provision for women who participate and wish to continue ring use after the study period.

# Ring implementation pilot Advisory Committee

The MOH [or health authority] will convene an advisory committee to provide ongoing guidance and input during protocol development (upon request of the MOH or the investigator team), implementation, initial results presentation (feasibility and uptake data), and final results presentation. We recommend that investigator teams avail themselves of the expertise within the Advisory Committee for the wording of the consents and questionnaires as well as selection of study facilities and engagement with local community-based organisations.

The committee will comprise MOH [or health authority] and stakeholder representatives, including representatives from end-user groups, who are not investigators on the pilot implementation studies (number to be determined by health authority). The committee will also include representation from advocacy groups for sexual and reproductive health and HIV prevention in [country name] and civil society organisations comprised of specific ring end-user groups. Advisory Committee members will be nominated by the MOH, NAC, [or health authorities] and selected members of the PrEP task force [or relevant technical working group] not affiliated with pilot implementation studies. At least one Advisory Committee member will be selected from the provincial health team and one from the health teams of each district where the pilot studies will be conducted.

The Advisory Committee will be available to review study instruments and protocols to provide contextual insights as well as suggest improvements in phrasing or supplemental questions to better achieve the study outcomes.

Committee members will also assist investigator teams and the MOH in designing dissemination plans and will provide direct support, as possible, for community updates on study progress and findings, aligned with study and national community sensitisation efforts.

To ensure alignment with MOH [or health authority] guidance, investigator teams should submit the protocols, instruments, and consent documents for MOH [or health authority] review and concurrence prior to IRB submission. The MOH [or health authority] will consult the committee as needed to confirm guideline adherence. The committee will also ensure that study efficiency review (e.g., geographic and end-user representation) has been completed prior to implementation.

**The Advisory Committee will meet quarterly to monitor study progress and input from sites and communities in the study areas. The committee may convene ad hoc meetings in the event of reported safety or social harms and ensure mitigation measures proposed by the investigators are sufficient to address the issue, potentially in collaboration with the local IRB. At study end, the investigator team will present the main results to the committee for input on synthesis and interpretation, and the committee will report to the MOH [or health authority] regarding study alignment with MOH [or health authority] guidance and lessons learned to inform product introduction decisions and planning.**

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# Annex 1. Proposed study subnational site and focus population matrix

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Investigator Team** | **[Province or other sub- national level]** | **[District or other sub- national level]** | **Site (facility or civil society organisation community or DREAMS centre name)** | **Focus group** | **Sample size** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

**Annex 2. Domain considerations for acceptability questions**

## Streamlined approach to assess end-user ring feasibility measures for implementation studies

[Assuming questions are asked after initial visit with an HIV prevention counsellor or after a PrEP method has been selected]:

## Which method would you prefer to use for HIV prevention?

* 1. Dapivirine ring
	2. Oral PrEP
	3. Male condom
	4. Other: [describe]
	5. None of the above
1. **[If PrEP method selected as preferred method]:** What influenced your decision about your preferred method for HIV prevention? (*Select all that apply using statements in Column A.*)

**[If non-PrEP method selected as preferred method, or no method selected at all]:** What influenced your decision about why you prefer not to use the ring or oral PrEP? *(Select all that apply using statements in Column B.)*

|  |  |  |
| --- | --- | --- |
| ***Relevant domain*** | **COLUMN A** | **COLUMN B** |
| **Reasons for preferring PrEP method (ring or oral PrEP)** | **Reasons for not selecting either PrEP method for HIV prevention****(or selecting no prevention method at all)** |
| *Cost* | It is affordable (or free). | The PrEP methods are too expensive. |
| *Access* | It is available in my community. | The PrEP methods are not currently available in my community. |
| *Ability to access* | It is available and will be easy for me to get (*e.g., reasonable clinic wait times, no transportation issues*). | The PrEP methods might be available, but they would not be easy to get (*e.g., long clinic wait times, transportation issues*). |
| *Ease of use* | It will be easy for me to use. | I do not believe the PrEP methods will be easy to use. |
| *Side effects* | I will not worry about the side effects. | I think the PrEP methods will cause side effects. |
| *Emotional comfort/discomfort* | It will cause me to feel pleasant feelings like happiness or reassurance. | Either PrEP method would cause me to feel unpleasant feelings like sadness or anger. |
| *Physical comfort/ discomfort* | It will not cause my body discomfort to use. | Either PrEP method would cause my body discomfort. |
| *Social comfort/ discomfort* | It will not cause me worry related to the reactions of people around me. | Either PrEP method would cause me worry related to the reactions of people around me. |
| *Effects on health and**well-being more generally* | It will be good for my well-being. | Either PrEP method would not be good for my well-being. |
| *Perceived effectiveness* | It will be effective for me in preventing HIV if I use it well. | Either PrEP method would not be effective for me in preventing HIV. |
| *Support/disclosure* | I will have support from someone close to me to use it well. | I will not have support for using either PrEP method from someone close to me. |
| *Self-efficacy* | I can use it correctly and consistently. | I would not be able to use either PrEP method correctly and/or consistently. |
| *Risk perception (only relevant for those who chose no prevention**method)* |  | I am not at risk for getting HIV right now. |

*[For each option selected, one could go on to ask a more specific question about that particular response similar to or the same as items we have already pulled out from the existing surveys.]*

## What most influenced your decision?

Response option 1: Repeat options from the questions above but have participants rank their top three reasons.

Response option 2: Think about what things are most important to you now in choosing a product that would provide HIV prevention. What is the most important to you? What is the second most important? (Have participant free list and record responses verbatim below:)

* 1. (Most important):
	2. (Second most important):

Annex 3. Illustrative questions for ring pilot implementation studies

|  |  |  |  |
| --- | --- | --- | --- |
| **Domain** | **Question** | **Responses** | **Skip pattern** |
| **Required measures: These questions correspond to Table 3 in the guide** |
| **Feasibility Measures: End-Users** | Which method do you prefer to use for HIV prevention? | 1. Dapivirine ring
2. Oral PrEP
3. Male condom
4. Other: [describe]
5. None of the above
 | Add for questions that follow regarding reason(s) for preference prior to actual use. |
| **Feasibility Measures: Providers** | How well did your training prepare you to counsel and offer the dapivirine ring to clients? | 1. Very well prepared
2. Adequately prepared
3. Not very well prepared
4. Not prepared at all
 |  |
| How comfortable do you feel about counselling clients on use of the dapivirine ring? | 1. Very comfortable
2. Somewhat comfortable
3. Somewhat uncomfortable
4. Uncomfortable

8. No response |  |
| How confident are you that you can teach a client how to insert and remove the dapivirine ring herself? | 1. Very confident
2. Mostly confident
3. Somewhat confident
4. Not confident

8. No response |  |
| If the ring is available at your facility, how likely are you to recommend the ring to your future clients? | 1. Very likely
2. Somewhat likely
3. Neither likely nor unlikely
4. Somewhat unlikely
5. Very unlikely
 | Probe service readiness in qualitative interviews for context. |
| **Ring Knowledge Score [Composite score for the following 5–7 quantitative knowledge questions with answers presented in bold, italicized font.] Circle all that apply.** |
|  | The dapivirine ring (“the ring”) is used: | 1. To prevent mother-to-child transmission of HIV
2. To prevent HIV infection after potential exposure to HIV
3. ***By HIV-negative persons to prevent HIV acquisition***
4. To treat HIV infection
 | Primary outcome for feasibility of training package; can add questions on provider’sattitude about time/ability to include ring serviceswithin existing duties |

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | 5. Only by key populations |  |
| The ring is: | 1. Often felt by partners during sex
2. ***For use in combination with safer sex practices when oral PrEP is not/cannot be used or is not available***
3. For people at substantial risk of HIV infection who want to prevent HIV acquisition during receptive anal sex
4. ***For people at substantial risk of HIV infection who want to prevent HIV acquisition during receptive vaginal***

***sex*** |  |
| The ring is replaced: | 1. At the same time each day
2. ***Once a month***
3. Every 3 months
4. Once per year
5. After every sexual encounter
 |  |
| Contraindications to the ring include: | 1. HIV-negative status
2. ***HIV-positive status***
3. Concurrent treatment with vaginal miconazole
4. ***Allergy to any medicine in the ring***
5. Estimated creatinine clearance <60 cc/min
 |  |
| The ring should be discontinued if a client: | 1. ***Has a positive HIV test***
2. Develops renal disease (creatinine clearance <60ml/Min) \*
3. Reports headaches and stomach upset
4. ***Requests to discontinue***
5. ***Is no longer at substantial risk and wishes to discontinue***
 |  |
| Which of the following statements is/are true regarding the ring? | 1. ***Adherence to drug(s) means that an individual is taking prescribed medications correctly and consistently.***
2. Effectiveness of the ring does not depend on adherence.
3. The ring also provides protection against other STIs.
4. The ring should be used for life.
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | 1. ***There are no food or alcohol restrictions when using the ring.***
2. ***The only diagnostic required before ring initiation is an HIV test. (Note: This will be true only if studies in pregnant women document ring***

***safety in pregnancy)*** |  |
| The ring should be removed during menses. | 1. True
2. ***False***
 | Indicate whether the following statementsabout the ring are true or false. |
| The ring is most effective after it has been in place for 24 hours. | 1. ***True***
2. False
 |  |
| The ring should not be disposed in a flush toilet. | 1. ***True***
2. False
 |  |
| The ring can be used with male condoms. | 1. ***True***
2. False
 |  |
| The most commonly reported adversereaction to the ring is urinary tract infection. | 1. ***True***
2. False
 |  |
| The ring can be inserted only by a trained medical professional to ensure proper fit. | 1. True
2. ***False***
 |  |
| **Acceptability Measures: End-Users** | Were you counselled on HIV prevention methods today? | 1. Yes
2. No
 | If NO, end interview. |
| **Uptake/Feasibility** | Which HIV prevention methods were you counselled about? | 1. Oral PrEP
2. Dapivirine ring
3. Male condoms
4. Female condoms
5. Limiting number of partners
6. STI screening and treatment
7. Other (specify):
 |  |
| Of these methods, which method(s)have you chosen to use? [Circle all that are stated] | 1. Oral PrEP
2. Dapivirine ring
3. Male condoms
4. Female condoms
5. Limiting number of partners
6. STI screening and treatment
7. Other (specify):
 | If 1 or 2 is selected, verifyin clinic notes and proceed with interview. |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Would you say you chose this method mainly because you liked the methodyou chose, or because you disliked the other method? | 1. Liked this method
2. Disliked the other method
 |  |
| What do you like most about the PrEP method you selected? | [Open response or populate with most frequent reasons detected during pretesting.] |  |
| What do you dislike most about the other PrEP method? | [Open response or populate with most frequent reasons detected during pretesting.] |  |
| **End-Users: Follow-up Acceptability** | What HIV prevention method(s) are you currently using? | 1. Oral PrEP
2. Dapivirine ring
3. Male condoms
4. Female condoms
5. Limiting number of partners
6. STI screening and treatment
7. Other (specify):
 | If 1 or 2 is NOT included in response, confirm with prompt and, if confirmed, skip to discontinuation questions. |
| Did you temporarily stop using yourPrEP method at any time since the last appointment? | 1. Yes
2. No
 |  |
| For how long did you stop using the method? | # days  |  |
| Why did you stop using the method? | 1. Menses
2. Broke up with partner
3. Removed before sex
4. Forgot to take pills for a day or more
5. Discussed with partner and agreed that we do not need PrEP
6. Other (specify)]
 |  |
| Did you resume using your PrEP method? | 1. Yes
2. No
 | If No, skip to questions below for discontinuation/ switching. If Yes, see below, # days. |
| How long ago did you start using the method again? | # days  |  |
| Why did you resume using the method? | 1. Menses finished
2. New partner
3. Feel personal risk for HIV has increased
4. Partner encouraged PrEP use
5. Other (specify)
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
| **Switching: Participants changing from one PrEP method to another** | Did you change your PrEP method today? | 1. Yes
2. No
 | If NO, go to method- specific acceptability questions. |
| If yes, what method have you selected? | 1. Oral PrEP
2. Dapivirine ring
3. Other (specify):
 |  |
| Why did you switch PrEP methods? | 1. Side effects
2. Not convenient to use
3. Difficult to keep private
4. Partner did not agree
5. Clinic stock-out of first method
6. Other (specify)
 |  |
| **Acceptability: Participant perceived acceptability, partner acceptance, and would recommend to friend** | Since your last visit, overall, how much do you like using the dapivirine ring/oral PrEP every day? | 1. Like very much
2. Like
3. Neither like nor dislike
4. Dislike
5. Dislike very much
 |  |
| Since your last visit, overall, how satisfied have you been with this method for preventing HIV? | 1. Very satisfied
2. Somewhat satisfied
3. Neutral
4. Somewhat dissatisfied
5. Very dissatisfied
 | Add skip pattern based on current PrEP method; ring questions here, immediately followed byoral PrEP questions |
| **Ring Users** | How easy or difficult is it for you to insert the ring? | 1. Very easy
2. Somewhat easy
3. Neither easy nor difficult
4. Somewhat difficult
5. Very difficult
 |  |
| How easy or difficult is it for you to remove the ring? | 1. Very easy
2. Somewhat easy
3. Neither easy nor difficult
4. Somewhat difficult
5. Very difficult
 |  |
| **Oral PrEP Users** | How easy or difficult is it for you to remember the pill every day? | 1. Very easy
2. Somewhat easy
3. Neither easy nor difficult
4. Somewhat difficult
5. Very difficult
 |  |
| How easy or difficult is it for you to swallow the pill? | 1. Very easy
2. Somewhat easy
3. Neither easy nor difficult
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | 1. Somewhat difficult
2. Very difficult
 |  |
| **All Participants** | Is your primary partner: | 1. Supportive
2. Not supportive
3. Does not know about PrEP use
4. Not applicable
 |  |
| Would you use this method in the future? | 1. Yes
2. No

[Open response: Why or why not?] |  |
| Would you recommend this method to a friend? | 1. Yes
2. No

[Open response: Why or why not?] |  |
| **Acceptability: Discontinuation and reasons for discontinuing PrEP** | Did you stop using your PrEP method at any time since the last appointment without resuming use? | 1. Yes
2. No
 |  |
| Why did you stop using oral PrEP/the ring? [***Multiple responses allowed, probe until all are elicited.***] | 1. Side effects
2. Not at risk/not sexually active
3. Partner objected
4. Now HIV positive
5. Fear of side effects
6. Fear of inadvertent partner discovery
7. Discomfort with use
8. Interferes with daily activities
9. Cannot remember daily use/monthly use
10. Product not available
11. Provider said not to use it
12. Other (specify)
 |  |
| What is the most important reason you stopped using oral PrEP/the ring? [***Select single best answer.***] | 1. Side effects
2. Not at risk/not sexually active
3. Partner objected
4. Now HIV positive
5. Fear of side effects
6. Fear of inadvertent partner discovery
7. Discomfort with use
8. Interferes with daily activities
9. Cannot remember daily use/monthly use
10. Product not available
11. Provider said not to use it
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | 12. Other (specify) |  |
| When did you stop using oral PrEP/the ring? | # days ago  |  |
| With whom did you discuss stopping using the ring/oral PrEP? | 1. No one
2. Regular partner
3. Parent
4. Friend/neighbour
5. Provider at health facility
6. Community health worker
7. Other (specify)
 |  |
| What have you been using to preventHIV since stopping? | 1. Nothing, not at risk/sexually active
2. Nothing, partner will not use condoms
3. Male condoms
4. Female condoms
5. Voluntary medical male circumcision
6. Oral PrEP
7. Ring
8. Other
 |  |
| Are you still using this/these methods today? | 1. Yes
2. No
 |  |
| Did your partner/husband know you were using PrEP? | 1. Yes
2. No
 | If NO, skip next question. |
| If yes, does your partner/husband know you stopped using PrEP? | 1. Yes
2. No
 |  |
| Was the decision to stop using PrEP made mainly by you, mainly by your partner, or did you make the decision together? | 1. Mainly your decision
2. Mainly partner’s decision
3. Joint decision
4. Partner was not aware of PrEP use
 |  |
| **Acceptability Measures: Provider** | About how many clients have you counselled this week about PrEP method use? | # clients  | Check facility pharmacy record for new PrEP starts during the relevanttime interval. |
| About how much time does it take to counsel clients on PrEP methods, | # minutes  |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | including discussion of side effects and need for follow-up? |  |  |
| About how much additional time does it take to counsel clients on the ring, including discussion of side effects andinsertion/removal? | # minutes  |  |
| How important is it for a provider to insert the ring for the first time? [Readoptions and select option provider agrees with.] | 1. Essential
2. Prudent but not necessary
3. Unnecessary but clients like it
4. Not important
 |  |
| Qualitative questions: | How does offering the ring affect service delivery? (Probe for negative and positive effects.) |  |
| How does offering the ring affect your workload? |  |
| How do you determine whether or not to discuss oral PrEP with a client? What about the ring? |  |
| These questions should be a short response in a quantitative tool as well as probed in qualitative interviews. | Who needs to be counselled on all PrEP methods? (What are some client characteristics?) |  |
| Who needs to be counselled on using oral PrEP? (What are some client characteristics?) |  |
| Who needs to be counselled on using the ring? (What are some client characteristics? |  |
| **PrEP Safety, Fidelity, & Effectiveness Measures** *[These measures should be abstracted from the end- user record and reviewed with the provider following end- user follow-up interview]* | Did the client receive HIV counselling and testing at this visit? | 1. Yes
2. No
 | Enrolment & follow-up visits per Minimum Service Packageschedule |
| What was the result of the HIV test? | 1. Reactive (Positive)
2. Non-reactive (Negative)
3. HIV test not performed [Query provider after client interview completed on stated reason: ]
 | Go to next question if the test was reactive. If non- reactive, skip to pregnancy testing question for ring users; skip to adverse drug reaction question for oral PrEP users. If the testwas not performed, query and add stated reason. |
| For clients with a reactive HIV test, was the client referred and seen for | 1. Yes
2. No
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | rapid counselling on and start of antiretroviral therapy (ART)? |  |  |
| **Ring Users only** | Did the client receive a urine pregnancy test? | 1. Yes
2. No
 | Enrolment & follow-up visits per Minimum Service Packageschedule |
| What was the result of the pregnancy test? | 1. Reactive (Positive)
2. Non-reactive (Negative)
3. Pregnancy test not performed [Query provider after client interview completed on stated reason: ]
 |  |
| **Ring and PrEP Users**[Chart and provider query] | Was a side effect or adverse reaction reported and attributed to PrEP use? | 1. Yes
2. No
 | If no, skip to social harms questions. |
| If yes, please describe. | [Short answer] |  |
| [Chart and provider query] | Did the client report any social harms related to PrEP use? | 1. Yes
2. No
 | If NO, skip to next series of questions, perinvestigator team preferences. |
| If yes, what type of issue was reported? | 1. Negative reaction to inadvertent PrEP use disclosure/discovery
2. Intimate partner violence
3. Family shunning/disapproval
4. Community shunning/disapproval
5. Other (specify):
 |  |
| What type of services or referral was provided? | [Short answer] |  |
| **Required Costing Measures** |
| Incremental PrEP service delivery costs [calculate for each PrEP method] | Record aggregate data during the study period at each involved facility for the following:* Additional staff time per PrEP visit by different types of visits and staff cadre [use MOH human resources for health scale for salaries & benefits]
* Numbers of different types of visits by site/population served (annually

and by month) |  |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | * Numbers of rings or monthly supply of oral PrEP dispensed (total dispensed per visit during study implementation)
* Numbers and prices of additional lab tests and HIV tests conducted for PrEP users (including rates of confirmatory and tiebreaker HIV tests, annually and by month)
* Numbers of clients tested for HIV who choose to initiate the ring
* Numbers and prices of additional commodities used for the ring (gloves, test tubes, stationery, etc.) [Use MOH commodity unit cost data.]

Estimate other PrEP method-specific costs, e.g., equipment, disposal, training, ring-specific demand creation, mass media, and community outreach costs. |  |  |
| **Suggested Measures: These questions correspond to Table 4 in the guide** |
| **Suggested Feasibility Measures: End-Users** | Which method do you intend to use for HIV prevention? | 1. Oral PrEP
2. Ring
3. Condoms
4. Other (specify)
5. Have not decided
 |  |
| Would you be willing to use oral PrEP for HIV prevention? | 1. Yes
2. No
 |  |
| Would you be willing to use the ring for HIV prevention? | 1. Yes
2. No
 |  |
| Perceived effort to access/use the ring | If you were interested in using the ring to prevent getting HIV and it was available for free at local clinics, please rate how likely you would be to use theproduct on a scale of 1–5. | 1. Definitely would NOT use it
2. Probably would NOT use it
3. Not sure
4. Maybe would use it
5. Definitely would use it
 |  |
| Perceived opportunity costs related to PrEP use [***Divide into two*** | In general, how worried are you about the effect of the ring/oral PrEP on your own health? | 1. Very worried
2. A little worried
3. Not worried at all
 | Proceed with skip pattern based on selected PrEP method. |

|  |  |  |  |
| --- | --- | --- | --- |
| ***questions each by specific PrEP method***] | Do you think using the ring/oral PrEP would cause emotional discomfort? By this we mean the product causes you to feel unpleasant feelings likesadness or anger. | 1. A little bit
2. A lot
3. Not at all
 |  |
| Do you think using the ring/oral PrEP would cause physical discomfort? By this we mean the PrEP method makesyour body feel uncomfortable. | 1. A little bit
2. A lot
3. Not at all
 |  |
| Do you think the ring/oral PrEP would cause sexual discomfort? | 1. A little bit
2. A lot
3. Not at all
 |  |
| Do you think the ring/oral PrEP would cause social discomfort? By this we mean discomfort or worry related to the reactions of people around you. | 1. A little bit
2. A lot
3. Not at all
 |  |
| Some women may have worries about the effect of ring on their own health or wellbeing. Are you worried the ring could…?:1. Cause infections or cancer
2. Make you gain weight
3. Affect your future fertility?
4. Result in people thinking you are HIV positive
5. Anything else related to the ring? (specify)
6. Anything else related to oral PrEP? (specify)
 | a – d:1. Yes
2. No

e. [Open response]f. [Open response] |  |
| Would you mind wearing the dapivirine ring…?:1. During sex
2. When not sexually active
3. During menses
4. During daily activities
 | 1. Yes
2. No
3. Not applicable

[Response series for each component a–d of this question.] |  |
| Perceived effectiveness of ring compared to oralPrEP or other HIV prevention methods | How effective do you think the ring is at preventing HIV? | 1. Not at all effective
2. Somewhat effective
3. Very effective
4. Do not know
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | How effective do you think oral PrEP is at preventing HIV? | 1. Not at all effective
2. Somewhat effective
3. Very effective
4. Do not know
 |  |
| Which method do you think would be most effective at preventing HIV for you? | 1. Dapivirine ring
2. Oral PrEP
3. Neither
4. Do not know
 |  |
| The ring is about 50% effective at preventing HIV if used correctly and consistently. Would you use the ring if you think you could use it well? | 1. Yes, the ring provides enough protection to make me want to use it.
2. Yes, I think I can use the ring better than I can take oral PrEP.
3. No, the ring is not effective enough. I prefer oral PrEP.
 |  |
| Perceived self-efficacy to use ring as PrEP | How comfortable do you think you will be wearing the dapivirine ring every day? | 1. Usually/mostly comfortable
2. Sometimes uncomfortable
3. Usually/mostly uncomfortable
 |  |
| Perceived most reliable source for PrEP information/ recommendation | To whom do you look to help guide your decision making about PrEP use? | 1. Your primary partner
2. Your mother
3. Another family member (specify)
4. A friend
5. Your doctor or clinician
6. Traditional healer [*insert local term*]
7. A religious leader [*insert local term*]
8. Other (specify)
 |  |
| Qualitative question: | Where would you go and who would you talk to for answers to questions you might have about oral PrEP? What about for the ring? |  |
| Preferred site and visit frequency | How acceptable would it be to get PrEP methods like oral PrEP or the ring from…?:1. An STI clinic
2. Family planning clinic
3. ART clinic
4. Pharmacy
5. Drop-in centre
 | 1. Very unacceptable
2. Somewhat unacceptable
3. No opinion
4. Somewhat acceptable
5. Very acceptable
 |  |
| How acceptable would it be to you if you had to go to the clinic every # months to get new rings and be tested for HIV?a. Every month | 1. Very unacceptable
2. Somewhat unacceptable
3. No opinion
4. Somewhat acceptable
5. Very acceptable
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | 1. Every 3 months
2. Every 6 months
 |  |  |
| Perceived facilitators/barriers to ring access and use | Indicate which barriers/challenges you have to ring use or access. Mark all that apply or "None could be identified.” | 1. Barriers to return to clinic for resupply (e.g., money or time)
2. Disruption in routine (for example, travel away from home)
3. Forgetting/no dose available
4. Job commitments
5. Lack of privacy
6. Medication side effects
7. Negative reactions (family, friends, partner)
8. Partying/drugs/alcohol
9. School commitments (classes or exams)
10. Side effects
11. Stigma/fear of stigma
12. Other (specify: \_ )
13. None could be identified
 |  |
| Did you require any help from the clinician to insert the ring? | 1. Yes
2. No
 |  |
| Qualitative questions: | What are some things that can make it easier to use the ring throughout the month? |  |
| Is there anyone who supports/helps you use your ring throughout the month? |  |
| Some people have problems with using a monthly ring. Tell me about a specific time when you had a challenge with the ring. |  |
| **Suggested Feasibility Measures: Providers** Perceived demand for the ring vs. oral PrEP by clients | What do you see as the benefits of the ring?” [Select all that are named spontaneously.] | 1. User-controlled method
2. Easy to use
3. No problems remembering to use
4. Protects against HIV
5. Helps clients who cannot use oral PrEP
6. Other (specify):
 |  |
| What about the ring makes it hard for clients to consider using it? | 1. Ideas that it promotes promiscuity
2. Fears that the ring causes cancer or other illness
3. Not enough research
4. Less effective for HIV prevention
5. Need to replace every month
6. Other (specify):
 |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | What about the ring makes it hard for women to continue using it after they start? | 1. Partner disagreement
2. Fears that the partner will feel it during sex or find it
3. Side effects like itching
4. Less effective for HIV prevention
5. Concerns about supply stock-outs
6. Need to replace every month
7. Other (specify):
 |  |
| Qualitative questions: | In your experience, which clients prefer the ring to oral PrEP? |  |
| What are some of the concerns clients might have about the ring? What do you do to address these concerns? |  |
| In your experience, what concerns do you have about providing oral PrEP to clients? What about the ring? | Probe effectiveness, safety, correct use, sustained supply. |
| **Suggested Acceptability Measures: End-Users** |
| **Ring users only:** | Right after being trained to insert the ring, how did you feel about inserting the ring yourself for the first time (at the health facility)? Would you say youwere…? | 1. Very at ease
2. At ease
3. Somewhat nervous
4. Very nervous

8. No response |  |
| How confident were you about inserting the ring that very first time? Would you say you were…? | 1. Very confident,
2. Somewhat confident
3. Not very confident

8. No response |  |
| **Participants disclosing PrEP use to at least one person** [All types of PrEP] | Do you plan to tell your husband or main partner about your PrEP use? | 1. No, I do not plan to tell him.
2. Yes, I plan to tell him.
3. Do not know

8. No response |  |
| Do you plan to tell any other adult you live with about your PrEP use? | 1. No, I do not plan to tell them.
2. Yes, I plan to tell them.
3. Do not know

8. No response |  |
| **Suggested acceptability measures: Providers** | On a scale of 1 to 10, where 1 is not at all prepared and 10 is very well prepared, how well did the ring training prepare you to counsel and provide thering? |  (scale number) |  |

|  |  |  |  |
| --- | --- | --- | --- |
|  | Are you aware of the [insert name of job aid]? | 1. Yes
2. No
3. Do not know
 | If No or Do not Know, skip to next section. |
| On a scale of 1 to 10, where 1 is not at all useful and 10 is very useful, howuseful is this job aid? |  (scale number) |  |
| Were you trained on the use of this job aid? | 1. Yes
2. No
3. Do not remember

8. No response |  |
| Qualitative questions | What about the ring provider training worked well? |  |
| What would you like to change or improve about this training package? |  |
| How do you feel about the level of training you received on [specific name] job aid? |  |
| **Suggested Cost Measures: These questions correspond to Table 5 in the guide** |
| Cost to clients for those seeking ring services | Qualitative interviews with current or potential PrEP clients to assess the impact of transport, opportunity, and other costs to clients by wealth quintile. ***Include wealth quintile measures in demographic data*** and ask about estimated costs borne by clients to access PrEP services. |  |
| Ratio of numbers of rings or monthly oral PrEP supply dispensedto used | Aggregate data relating numbers of rings or oral PrEP used to supply dispensed. | Quantify patterns of use (obtained from required end-user acceptability measures) and compare to quantity dispensed. |  |