PrEP Ring 101

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MOSAIC
Maximizing Options to Advance Informed Choice for HIV Prevention

1A

PREP RING

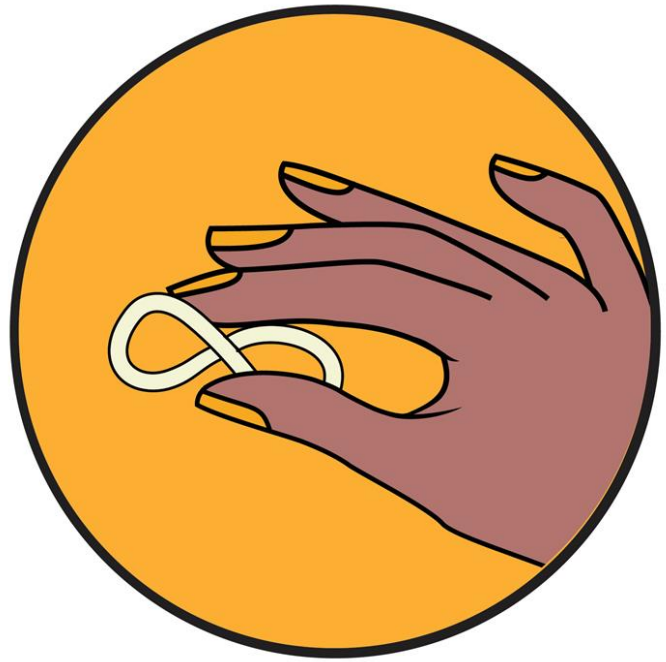
BACKGROUND & CLINICAL DATA

Vaginal rings – an overview

Vaginal rings are small, flexible plastic rings that are inserted into the vagina to release different drugs. Vaginal rings have been used to safely and effectively address reproductive health needs, such as contraception and hormone management, for decades.

Vaginal rings provide the opportunity for:

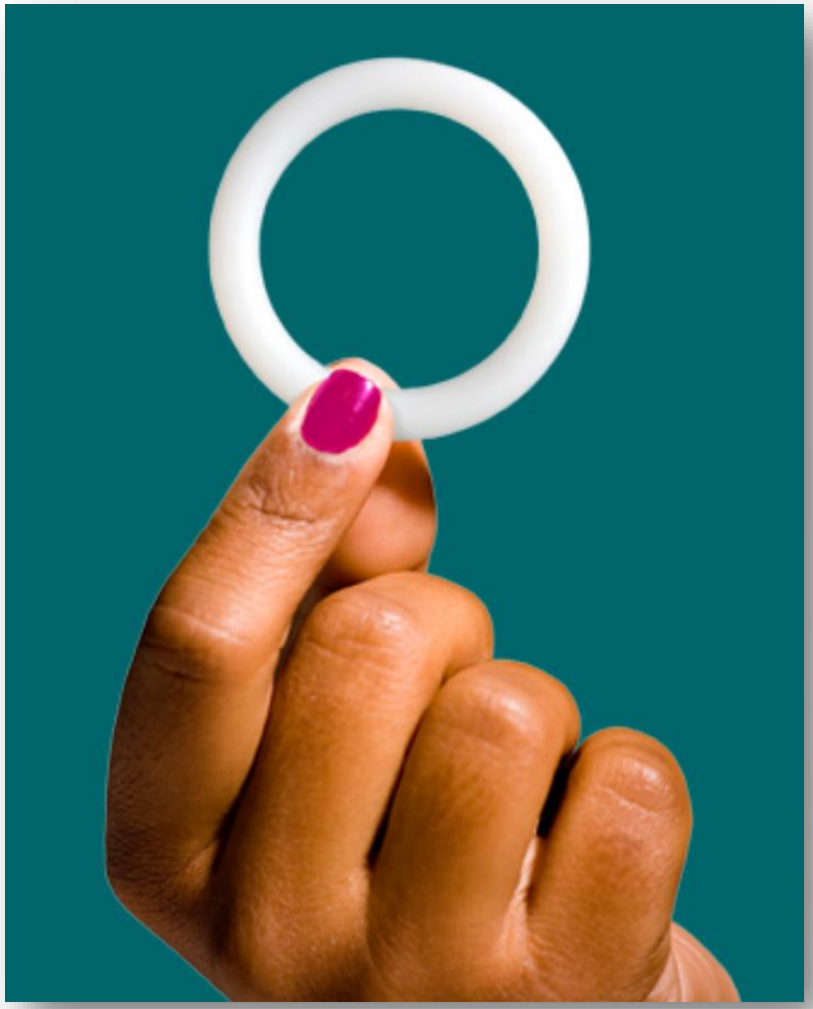
- LOCALIZED, SUSTAINED ACTION
  - Steady drug release
  - Low systemic exposure
- IMPLEMENTATION IN LOW-RESOURCE SETTINGS
  - Relatively low manufacturing cost
  - Stored at room temperature; no cold chain needed
- POSSIBILITY OF MULTIPURPOSE TECHNOLOGIES
  - Rings could be developed to treat or prevent multiple conditions at once (achieve sexual and reproductive health goals, including contraception, hormone management, and HIV prevention)



https://www.contraceptionjournal.org/article/S0010-7824(21)00410-8/fulltext

What is the PrEP ring?

The dapivirine ring (PrEP ring) is a flexible vaginal ring made of silicone that slowly releases an antiretroviral (ARV) drug called dapivirine over the course of one month to reduce the likelihood of acquiring HIV-1.



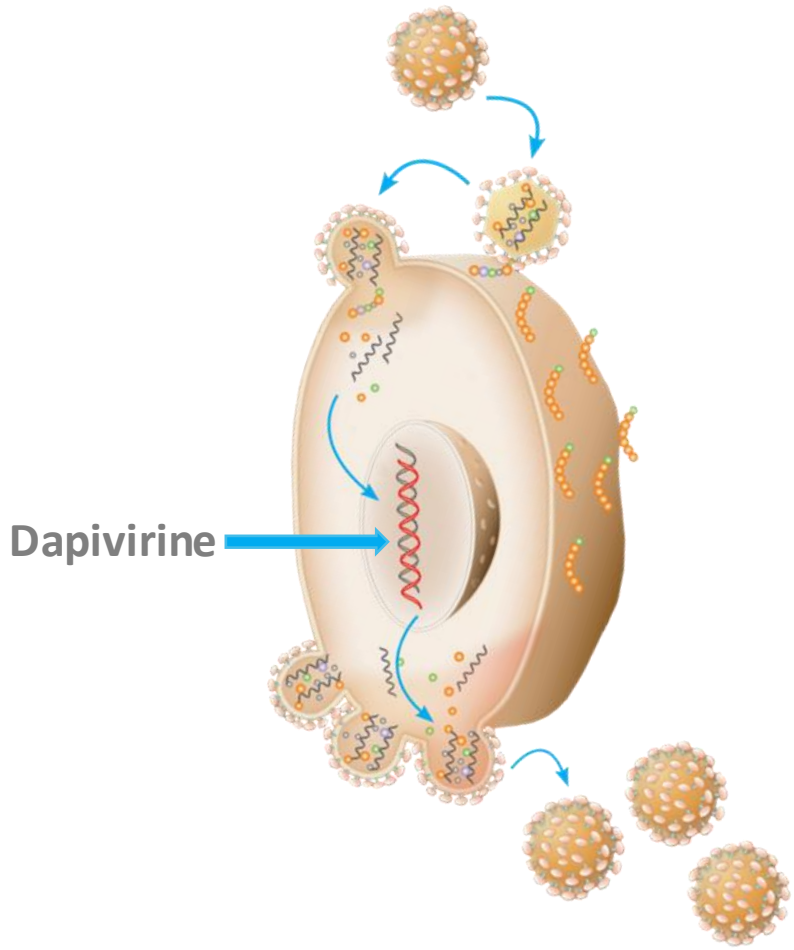
- Developed by the nonprofit International Partnership for Microbicides (IPM). IPM was acquired by Population Council in 2022, and Population Council is moving ring access forward.
- Recommended by WHO:
  - "[A]s an additional prevention choice for women* at substantial risk of HIV infection as part of combination prevention approaches"

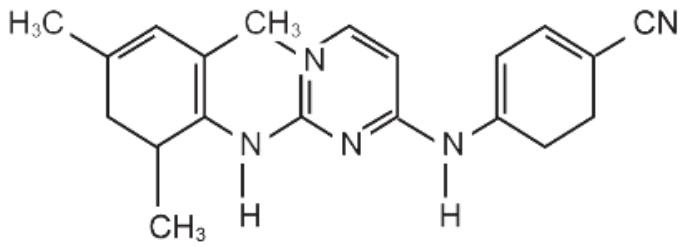
*Assigned female at birth https://www.who.int/publications/i/item/9789240031593

What is dapivirine?

Dapivirine is a highly potent ARV that acts inside cells to block the ability of HIV to multiply.

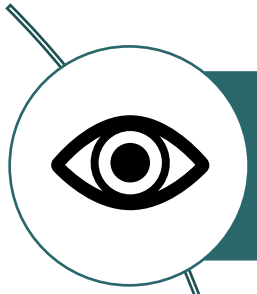
- A non-nucleoside reverse transcriptase inhibitor (NNRTI)
- Developed by Janssen and licensed to IPM in 2004
- Dapivirine had a favorable safety profile in all clinical trials to date—oral and topical.
- Each PrEP ring contains about 25mg of dapivirine upon manufacturing, and about 4mg of the drug is released during one month of use.





Dapivirine molecular structure

Why the PrEP ring?



Privacy

Can be stored, inserted, and removed in private

Safety

No safety concerns noted from clinical trials

Efficacy

Shown to reduce HIV risk in clinical trials

Easy to use and a **long-acting** PrEP method

PrEP ring Phase 3 trials: Safety results

The PrEP ring was shown to have a strong safety profile with no safety concerns.

- No difference between dapivirine and placebo groups in:
  - Number of side effects/health problems
  - Number of pregnancies
  - Number of sexually transmitted infections (STIs)
- No ring-related HIV-1 drug resistance
- Side effects generally mild to moderate and resolved with no interruption in ring use
  - Common side effects included urinary tract infections, vaginal discharge, itching, and pelvic and lower abdominal pain

PrEP ring: Efficacy and safety summary

Open-label studies and adherence analyses suggest that the PrEP ring reduces the chance of acquiring HIV by 50% or more with consistent use.

The PrEP ring was shown to have a strong safety profile with no safety concerns:

No difference between dapivirine and placebo groups in numbers of STIs, pregnancies, side effects

Side effects generally mild to moderate and resolved with no interruption in ring use

No statistically significant HIV-1 drug resistance

https://www.ema.europa.eu/en/opinion-medicine-use-outside-EU/human/dapivirine-vaginal-ring-25-mg
https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30304-0/fulltext
https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(20)30300-3/fulltext

Further details on PrEP ring trials can be found in the annex.

PrEP ring: Use during pregnancy & breastfeeding

For most people who live in places where HIV is common, there are more known benefits than risks of using an HIV prevention method during pregnancy and the postnatal period.

- Results from trials of PrEP ring use during pregnancy and breastfeeding indicate that PrEP ring use was well tolerated for pregnant and breastfeeding people and their infants.
- In clinical trials, pregnancy outcomes among ring users were similar to outcomes in the general population.
- Results from a final cohort of participants 12–29 weeks pregnant, in an ongoing ring study, are anticipated in 2024.
- Dapivirine can pass into breast milk, but at very low levels. There were no safety issues for breastfeeding people or their infants.

PrEP ring use by pregnant and breastfeeding people will be determined by national guidelines.

1 - MTN-042/DELIVER Results Cohorts 1 and 2
2 - MTN-043/B-Protected Results
3 - MTN-016/EMBRACE Results

PrEP ring: Use by trans and nonbinary people

The PrEP ring has been studied only among people assigned female at birth.

- Participants in ring trials were not asked their gender identity.
- All participants in ring clinical trials underwent pelvic exams during participation.
- People assigned male at birth or people with neovaginas were not included as ring users during ring clinical trials.
- Although data were collected on medications taken by ring users during the trials, there was insufficient evidence around gender-affirming hormone use.

It is likely that the PrEP ring can be used by people assigned female at birth who would like to prevent HIV during receptive vaginal sex, regardless of their gender identity or use of gender-affirming hormones.

PrEP ring: Use by adolescent girls and young women

- In Phase III trials, PrEP ring efficacy was lower among participants ages 18-21, likely due to lower adherence to the ring.[1]
- Two studies have explored PrEP ring use by people younger than 18.[2, 3]
  - The safety profile of the PrEP ring among people younger than 18 was similar to the strong safety profile seen in adults.
  - PrEP ring acceptability was high among people under 18.
- MTN-034/REACH, a safety and acceptability study of the PrEP ring among people ages 15-21 in Africa, highlighted no safety concerns and showed that the ring is an important option for many members of this population.[3]

PrEP ring use by people younger than 18 will be determined by national guidelines.

1 - MTN-020/ASPIRE Results
2 - MTN-023 Results
3 - MTN-034/REACH Results

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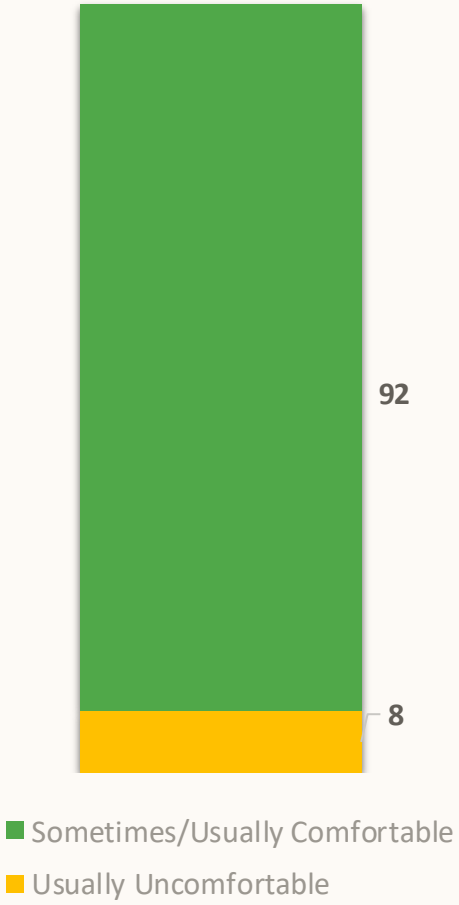
ACCEPTABILITY AND WILLINGNESS DATA FOR PREP RING

End-user perspectives on the PrEP ring: Acceptability

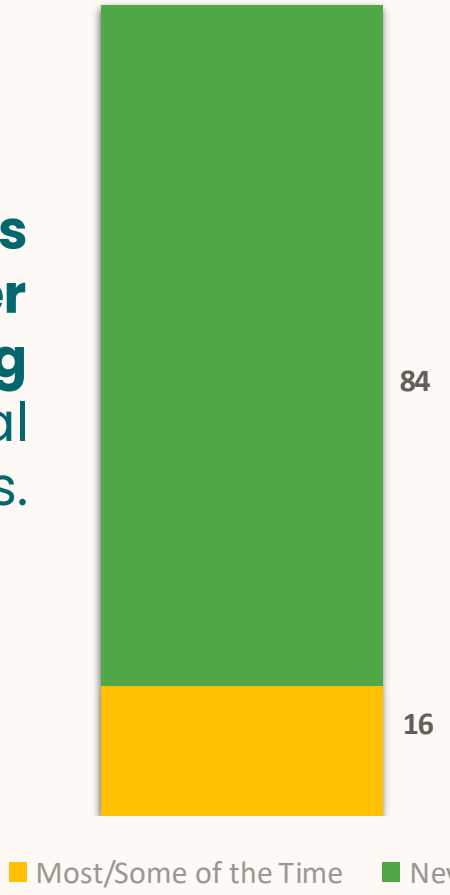
Among more than 2,000 participants who completed the ASPIRE study in Malawi, South Africa, Uganda, and Zimbabwe, **92% said the ring was usually comfortable with daily use**.

How did it feel to have the ring inside you every day?



84% of participants said they were never aware of the ring during their normal daily activities.

Were you aware of the ring during normal daily activities?



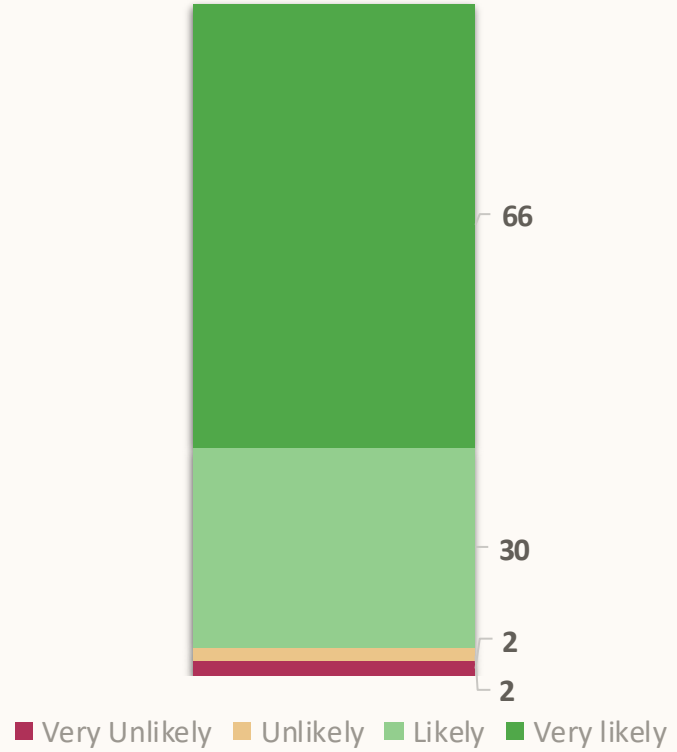
*Based on use in the past 3 months at their last product use visit

Mayo AJ et al. Acceptability of the dapivirine vaginal ring for HIV-1 prevention and association with adherence in a Phase III trial.

End-user perspectives on the PrEP ring:
Willingness to use

Among ASPIRE participants, **96% said they were either "likely" or "very likely" to use the PrEP ring**—or one like it—in the future.

If a future vaginal ring was available that provided some protection against HIV and it was similar to the one you used in this study, how likely would you be to keep it inserted in your vagina every day?



*Based on use in the past 3 months at the last product use visit

Mayo AJ et al. Acceptability of the dapivirine vaginal ring for HIV-1 prevention and association with adherence in a Phase III trial.

What did women have to say about the PrEP ring?

"It wasn't difficult, I got enough education before using it because I was really scared when I first saw it… But during education I learned that the ring was soft, I thought the ring was hard and painful. They showed that to insert the ring you need to twist it like 8 and when I tried it, it was easy and doable."[1]

"I like that the ring stays inside you and nobody can see it…. you don't have to disclose ring use to others if you want. My family doesn't know that I am using the ring. … And the partner can't feel it as well."[1]

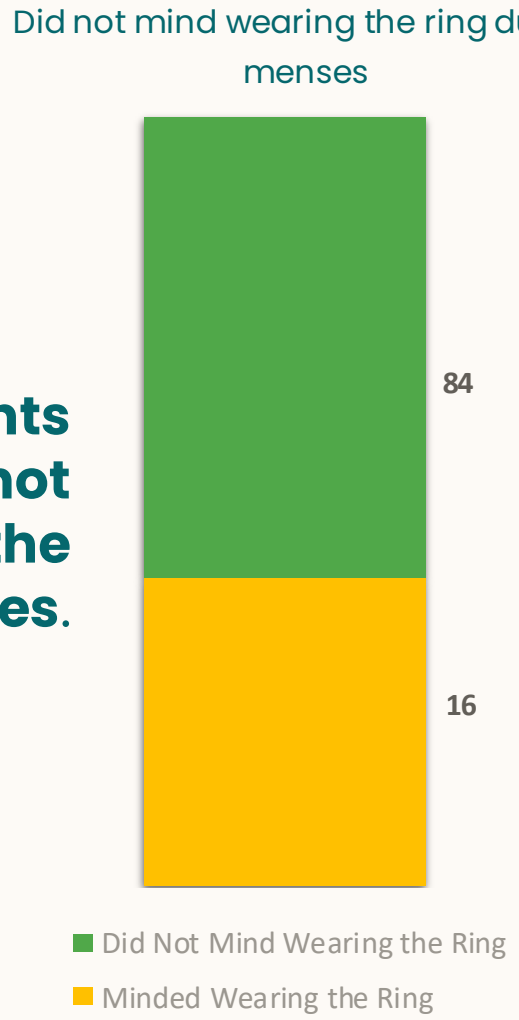
"I don't feel the ring when it is inside me, I only feel it during insertion. I don't feel it though when I'm seated or walking. The ring has never fallen; it's not painful… the ring is not felt when you are walking or sleeping; it doesn't even move."[2]

(1) Montgomery et al. Acceptability and use of a dapivirine vaginal ring in a phase III trial
(2) MTN-020 Qualitative IPM Report, April 2017.

End-user perspectives on the PrEP ring:
Ring use and menses

Among ASPIRE participants, **91% said that they kept the ring in place during menses.**

60% of participants said they did not mind wearing the ring during menses.



*Based on use in the past 3 months at the last product use visit

Duby Z et al. Hygiene, blood blow, and vaginal overload: Why women removed an HIV prevention vaginal ring during menstruation in Malawi, South Africa, and Uganda.

End-user perspectives on the PrEP ring:
Ring use and menses

Although most ASPIRE participants (60%) said that they did not mind wearing the ring during menses, **some participants reported removing the ring during menses**.

The ring can be left in place, without cleaning during menses and does not affect menses or the menstrual cycle or block blood flow. However, trial participants reported a variety of responses to ring use during menses.

"You do not feel anything even if you have the ring inserted during menses. You remain comfortable. It does not bring any changes; you remain as you would be if you did not have it."

"There was little blood coming out, so I got worried thinking maybe the vaginal ring had blocked the passage..."

"During menses, this is the time a woman needs to bathe thoroughly... blood may get trapped on the ring, will I not smell?"

"This ring felt heavy... so whenever I was having menses, I was removing it... I felt more comfortable when I cleaned it and reinserted it."

"I would prefer using the ring while in menses... the ring doesn't affect menses... (and) if I remove it, the medication in the ring will not work as it was supposed to..."

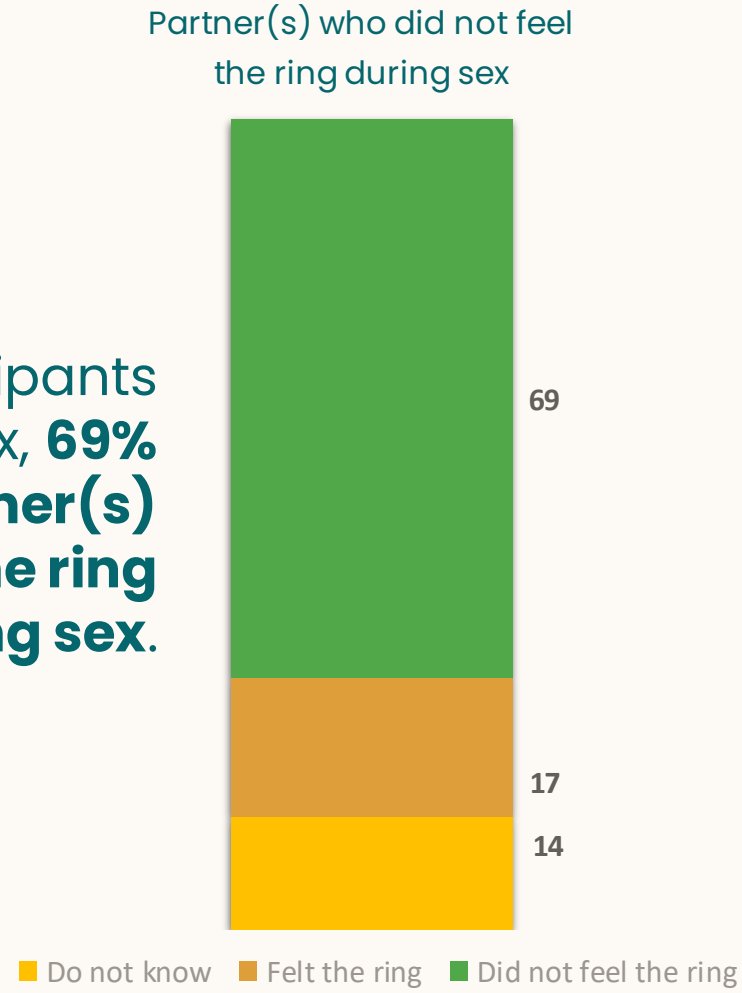
*Based on use in the past 3 months at the last product use visit

Duby Z et al. Hygiene, blood flow, and vaginal overload: Why women removed an HIV prevention vaginal ring during menstruation in Malawi, South Africa, and Uganda.

End-user perspectives on the PrEP ring:
Ring use and sex

Among ASPIRE participants who had sex in the 3 months prior to being asked, **76% said they never felt the ring during sex**.

Among participants who had had sex, **69% said their partner(s) did not feel the ring during sex**.



*Based on use in the past 3 months

Mayo AJ et al. Acceptability of the dapivirine vaginal ring for HIV-1 prevention and association with adherence in a Phase III trial.

End-user perspectives on the PrEP ring:
Ring use and sex

Although most ASPIRE participants (69%) said that their partner did not feel the ring during sex, **participants had a variety of experiences with the ring and sex**, including increased or decreased sexual pleasure or wetness. Some participants reported removing the ring during sex.

The ring should be kept in place during sex for maximum HIV prevention.

"He doesn't feel the ring. He was feeling it before; I am clever now. He felt it because I was incorrectly using it before. Everything now is sorted and it doesn't affect my sexual life."

"I think it increased a lot of fluids… I have really liked the vaginal ring a lot."

"I noticed a difference before I had the ring and after… I enjoy (sex) now, and my partner enjoys it."

"We argued and he would say that I must remove it when we were having sex… I would end up removing it because I was scared of losing him."

"He said 'Your thing is big now'… He was feeling like it has been stretched."

"When I started using the ring my husband told me that my vagina was tight as opposed in the past… so he was appreciating that the ring was good."

"Yes, it is good because there won't be fluids during sex… there shouldn't be lots of fluid."

Laborde ND et al. Impact of the dapivirine vaginal ring on sexual experiences and intimate partnerships of women in an HIV prevention clinical trial: managing ring detection and hot sex.

End-user perspectives on the PrEP ring: Male partner opinions

To better understand men's experiences with the ring, researchers invited **male partners of former ring open-label trial participants to participate in focus groups and one interview** in Malawi, South Africa, Uganda, and Zimbabwe.

Montgomery ET et al. Men's sexual experiences with the dapivirine vaginal ring in Malawi, South Africa, Uganda and Zimbabwe.

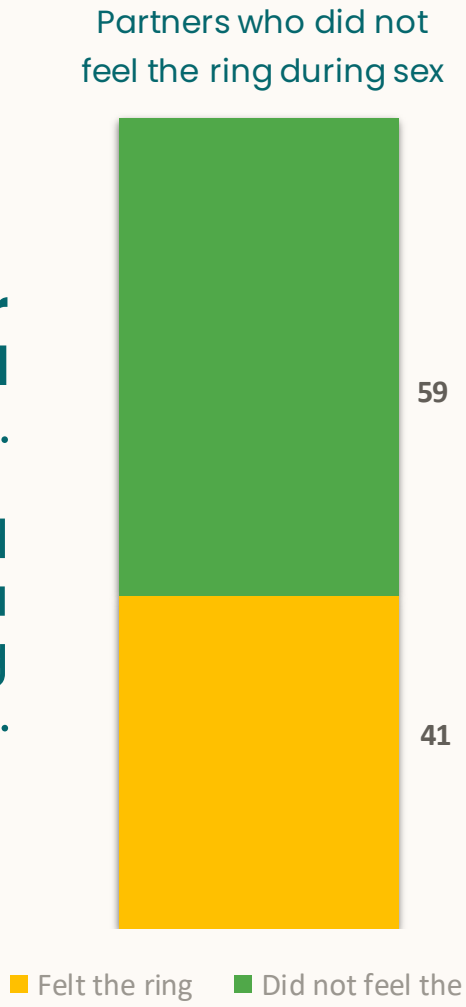
End-user perspectives on the PrEP ring:
Male partner opinions

Among male partners who did feel the ring, **most reported minimal or no changes to their sex life**.

Reported changes often went away with time or were fixed by changing positions or reinserting the ring. Some male partners reported that the ring increased sexual pleasure for themselves and/or their partners.

59% of male partner participants reported never feeling the ring.

Those who reported feeling the ring noted a scratching or prodding sensation.



Montgomery ET et al. Men's sexual experiences with the dapivirine vaginal ring in Malawi, South Africa, Uganda and Zimbabwe.

What did male partners have to say about the PrEP ring?

"I did not see any difference between the time she was wearing the ring and when she was not wearing the ring. I tried all the ways I could as a man, all the ways a man can possibly have sex with his wife, but I never felt the ring. I knew that she was wearing the ring, but that did not concern me. I still did things as I always did."[1]

"I also experienced the same problem like my colleagues have said; when you enter into the vagina, you hit the ring but when the vaginal fluids start coming, then you stop feeling the ring. It also depends on the force you use during sex because if you have sex slowly, fluids come, and you enter the vagina well."[1]

"I also agree that when she inserts it properly, I would not feel it. No matter how blessed you are naturally [even if you have a big penis], you cannot reach up to the cervix of the woman. But, if the ring is not inserted well, then I would tell her to say, 'you did not insert the ring properly' and she would fix it."[1]

Montgomery ET et al. Men's sexual experiences with the dapivirine vaginal ring in Malawi, South Africa, Uganda and Zimbabwe.

The PrEP ring and gender-based violence

Reports of social harms* related to intimate partner violence during PrEP ring trials were low and included:

- Male partner destruction of the ring
- Increases in an existing pattern of physical violence
- Increases or changes in existing patterns of control

Younger women were more likely to experience a social harm.

In PrEP ring studies and studies of other HIV prevention products, experiences of male-partner-related social harms were associated with lower adherence to the product.

*nonmedical consequences of PrEP ring use or trial participation more broadly

Social harms and the PrEP ring: The ASPIRE experience

Among 2,629 women who participated in MTN-020/ASPIRE, 3.2% (n=85) reported 87 partner-related social harms during approximately 1.5 years of study participation.

Of these 87 instances of partner-related social harms, 44.8% (n=39) were related to the ring.

Common triggers of social harm included:

- Partner discovery of the PrEP ring during foreplay or sex
- Notifying the partner of an STI
- Partners suspecting that the ring was associated with ill health, "promiscuity," or "witchcraft"

- Experiences of social harm were associated with short-term decreased product adherence.
- Younger women (18–26 years) were more than twice as likely to experience social harm as older women were.

Palanee-Phillips T et al. Impact of partner-related social harms on women's adherence to the dapivirine vaginal ring during a Phase III trial.

The PrEP ring and gender-based violence

! It is imperative to provide clients with gender-based violence (GBV) screening and individualized counseling that emphasizes their relationship experience. Clients must be supported to choose products that best fit within their lifestyles without exacerbating risk.

! GBV is driven by gender norms, power, and control. No HIV prevention method causes GBV. Rather, a violent individual may seek power in a relationship by controlling the sexual and reproductive health choices of their partner.

There are many available trainings and tools related to identification and response of GBV and other forms of gender-based violence, including the **WHO LIVES** training. First-line support, such as that outlined in the LIVES response, with an offer of warm referrals, are required as part of standard PrEP services in PEPFAR programming. Other resources are available to help plan for screening and responding to GBV as part of PrEP services.

ACKNOWLEDGMENTS

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ANNEX

PREP RING CLINICAL TRIALS

OVERVIEW

PrEP Ring Research Conducted in East & Southern Africa:
Early safety trials

Study	Description	Study location(s)	Participant sample	Status
IPM-007	An observational, long-term follow-up study for participants who acquired HIV during IPM 027 and IPM 032. The study assessed the impact of exposure to an antiretroviral microbicide at the time of HIV acquisition.	7 sites in South Africa and Uganda	**Total sample: 151** South Africa: 139 (6 sites) Uganda: 12	Completed August 2019. Results presented at SA AIDS 2019.
IPM-007 key takeaway: No notable difference in HIV-1 disease progression was observed in participants who seroconverted while using the ring, as compared to the placebo group.				
IPM-011	An open-label crossover study designed to assess the safety and acceptability of a placebo vaginal ring (containing no drug) when inserted for a 12-week period in healthy, sexually active women.	4 sites in South Africa and Tanzania	**Total sample: 170** South Africa (3 sites): 120 Tanzania: 50	Closed to follow-up March 2010. Primary safety manuscript and primary acceptability manuscript completed.
IPM-011 key takeaways: No safety concerns were identified for any safety variables assessed during the trial. The ring appeared to be highly acceptable for women and men.				
IPM-015	A Phase 1/2 trial designed to assess and compare the safety of a dapivirine vaginal ring against a placebo vaginal ring when inserted once every 28 days over a 12-week period.	10 sites in Kenya, Malawi, South Africa, Tanzania	**Total sample: 280** Kenya: 20 Malawi: 16 South Africa (7 sites): 235 Tanzania: 9	Closed to follow-up May 2011. Primary manuscript completed.
IPM-015 key takeaways: No safety concerns or clinically relevant differences were observed between the dapivirine ring and placebo groups. At trial end, 96% of participants reported that the ring was usually comfortable.				

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.

PrEP Ring Research Conducted in East & Southern Africa:
Observational studies of HIV drug resistance and pregnancy/breastfeeding

Study	Description	Study location(s)	Participant sample	Status
MTN-015	Prospective, observational cohort study of participants who acquired HIV-1 in microbicide trials, including the ASPIRE and HOPE studies. The study provides data on HIV disease progression, virologic responses following initiation of ART, and HIV-drug resistance.	PrEP ring cohort: 15 sites in Zimbabwe, South Africa, Uganda, Malawi	**Total cohort: 158 across the 15 sites**	Closed to follow-up June 2019. Manuscript on ASPIRE cohort completed.
MTN-015 key takeaways: The acquisition of HIV-1 during dapivirine or placebo ring use in ASPIRE did not lead to differences in HIV-1 disease progression. NNRTI-based ART regimens remained effective among those who acquired HIV-1 while using the ring.				
MTN-016/ EMBRACE	Prospective, observational cohort study of participants who became pregnant in microbicide trials, including the ASPIRE and HOPE studies. The protocol monitored for adverse pregnancy outcomes and monitored babies for their first year of life.	PrEP ring cohort: 15 sites in Zimbabwe, South Africa, Uganda, Malawi	**Total cohort: 143 adults, 133 infants** South Africa (9 sites): 65 adults, 63 infants Uganda: 19 adults, 18 infants Zimbabwe (3 sites): 47 adults, 40 infants Malawi (2 sites): 12 adults, 10 infants	Closed to follow-up May 2020. Manuscript on ASPIRE cohort completed.
MTN-016 key takeaway: Dapivirine ring use during early pregnancy was not associated with adverse effects on pregnancy or infant outcomes.				

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.

PrEP Ring Research Conducted in East & Southern Africa:
Phase 3 Trials

Study	Description	Study location(s)	Participant sample	Status
MTN-020/ ASPIRE	Phase 3, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the safety and efficacy of the PrEP ring.	15 sites in Zimbabwe, South Africa, Uganda, Malawi	**Total sample: 2,629** Zimbabwe (3 sites): 678 South Africa (9 sites): 1,426 Uganda: 253 Malawi (2 sites): 272	Closed to follow-up June 2015. Primary manuscript completed. Further manuscripts addressing adherence and effectiveness, and acceptability and adherence are also available.
MTN-020 key takeaways: The ring was associated with 27% HIV-1 risk reduction, with increased efficacy in subgroups with evidence of increased adherence. No safety concerns were identified. At trial exit, 66% of participants reported being "very likely" to use the ring in the future. Participants who minded wearing the ring during sex or menses, or reported a negative change in the vaginal environment, were more likely to have periods of nonadherence.				
IPM-027/ The Ring Study	Phase 3, randomized, double-blind, placebo-controlled clinical trial designed to evaluate the safety and efficacy of the PrEP ring.	7 sites in South Africa and Uganda	**Total sample: 1,959** Uganda: 197 South Africa (6 sites): 1,762	Closed to follow-up December 2016. Primary manuscript completed.
IPM-027 key takeaways: The ring was associated with 35% HIV-1 risk reduction. No safety concerns were identified.				

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.

PrEP Ring Research Conducted in East & Southern Africa:
Open-label extensions

Study	Description	Study location(s)	Participant sample	Status
MTN-025/ HOPE	Phase 3B, open-label, randomized, trial open to participants previously enrolled in MTN-020/ASPIRE. HOPE participants could choose to use the ring – or not – for 1 year of participation. The study gained more information on the safety of and adherence to the PrEP ring.	14 sites in Zimbabwe, South Africa, Uganda, and Malawi	**Total sample: 1,456** Zimbabwe (3 sites): 420 South Africa (8 sites): 707 Uganda: 172 Malawi (2 sites): 157	Closed to follow-up October 2018. Primary manuscript completed.
MTN-025 key takeaways: ***More than 73% of participants chose to accept the ring at all study visits, with 89.3% of returned rings showing some use, reflecting an overall increase in adherence over the ASPIRE trial. Modeling data suggests HIV-1 risk reduction of approximately 39%. No safety concerns were identified.***				
IPM-032/ DREAM	Open-label follow-on trial to IPM-027 to collect additional safety data and establish adherence to ring use of the PrEP ring monthly for 12 months.	6 sites in Uganda and South Africa	**Total sample: 941** Uganda: 121 South Africa (5 sites): 820	Closed to follow-up December 2018. Primary manuscript completed.
IPM-032 key takeaways: ***Residual dapivirine levels in returned rings were 0.25mg lower, on average, than in DREAM, reflecting an overall increase in adherence. Modeling data suggests HIV-1 risk reduction of approximately 63%. No safety concerns were identified.***				

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.

PrEP Ring Research Conducted in East & Southern Africa:
Qualitative studies about male partners and community attitudes on PrEP ring use during pregnancy/breastfeeding

Study	Description	Study location(s)	Participant sample	Status
MTN-032/AHA	Qualitative sub-study of the ASPIRE and HOPE trials that examined socio-contextual and trial-specific issues impacting participant adherence to the PrEP ring, and male partner attitudes about the ring.	7 sites in Zimbabwe, Malawi, South Africa, and Uganda	**Total sample: 227 former ASPIRE and HOPE participants (FPs), 54 male partners (MPs)** Zimbabwe (2 sites): 41 FPs, 13 MPs Malawi: 44 FPs, 11 MPs South Africa (3 sites): 103 FPs, 22 MPs Uganda: 39 FPs, 8 MPs	Data collection completed in October 2016. ASPIRE cohort manuscript, HOPE cohort manuscript, and male partner manuscript completed.
MTN-032 key takeaways: ***Former ASPIRE and HOPE participants reported multiple reasons for ring removal, including fear of male partner reactions or ring interference with sex, or dislike of wearing the ring during menses. More than half (59%) of male partners reported never feeling the ring. Among those who did feel it, few reported sexual problems or changes as a result.***				
MTN-041/MAMMA	Qualitative acceptability study to explore attitudes of community members and key informants from the community about the use of the PrEP ring or oral PrEP during pregnancy and breastfeeding.	4 sites in Malawi, South Africa, Uganda, Zimbabwe,	**Total sample: 232 pregnant or breastfeeding people (PBFP) aged 18-40, male partners (MPs) of current or recent PBFP, key informants (KIs), and mothers/mothers-in-law of current or recent PBFP (grandmothers/GMs)** Malawi: 51 (15 PBFP, 16 MPs, 10 GMs, 10 KIs) South Africa: 53 (15 PBFP, 12 MPs, 20 GMs, 6 KIs) Uganda: 68 (18 PBFP, 19 MPs, 21 GMs, 10 KIs) Zimbabwe: 60 (17 PBFP, 16 MPs, 17 GMs, 10 KIs)	Closed to follow-up November 2018. Results presented at IAS 2019. Primary manuscript on willingness to use PrEP during pregnancy and breastfeeding completed. Results informed development of MTN-042/DELIVER and MTN-043/B-PROTECTED.
MTN-041 key takeaways: ***Participants agreed that PBFP have an increased need for HIV prevention options, and new choices were welcomed for this population. Participants agreed that endorsement by healthcare providers and confirmation of safety for infants were key to product acceptance.***				

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.

PrEP Ring Research Conducted in East & Southern Africa:
Studies in additional populations

Study	Description	Study location(s)	Participant sample	Status
MTN-034/ REACH	Phase 2a, randomized, open-label, crossover study. Participants use the PrEP ring monthly for 6 months, oral PrEP (Truvada) for 6 months, and then choose the ring, Truvada, or neither for final 6 months. The study will evaluate safety, adherence, and acceptability of the ring and oral PrEP in users aged 16-21.	4 sites in Zimbabwe, Uganda, South Africa	**Total sample: 247 adolescent and young women aged 16-21 (inclusive)** Zimbabwe: 60 (28 age 16-17) Uganda: 60 (20 age 16-17) South Africa (2 sites): 127 (37 age 16-17)	Data collection completed in September 2021. Interim results presented at IAS 2021. Final results presented at CROI 2022 and final manuscript published in 2023.
MTN-034 key takeaways: Most (88% and 64%) of participants reported that the ring and oral PrEP were acceptable, respectively. More than 50% of participants had high adherence levels to both products. About 2/3 of participants chose the ring in the choice period, with those who had high adherence to oral PrEP in the randomization period more likely to select oral PrEP in the choice period.				
MTN-043/ B-PROTECTED	Phase 3b, open-label, randomized study designed to assess the safety and PK of the PrEP ring and oral PrEP when used during breastfeeding. The study is the first to be conducted of the ring during breastfeeding.	4 sites in Zimbabwe, Uganda, Malawi, South Africa	**Total Sample: 197 breastfeeding parent/infant pairs** Malawi: 39 South Africa: 36 Uganda: 55 Zengeza: 67	Closed to follow-up November 2021. Interim results presented at AIDS 2002 and final results presented at CROI 2023 and FIGO 2023.
MTN-043 key takeaway: ***Both PrEP ring and oral PrEP have a favorable safety profile among breastfeeding parent-infant pairs. Drug levels in breast milk and infant samples were very low. Acceptability and adherence were generally high.***				

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.

PrEP Ring Research Conducted in East & Southern Africa:
Multi-cohort trial among pregnant participants & their infants

Study	Description	Study location(s)	Participant sample	Status
MTN-042/ DELIVER	Phase 3b, open label, randomized study designed to assess the safety and pharmacokinetics (PK) of the PrEP ring and oral PrEP when used during pregnancy. Participants will enroll at different times during pregnancy and will use either the monthly ring or Truvada as daily PrEP until the time they deliver. The study is the first to be conducted of the ring during pregnancy.	4 sites in Zimbabwe, Uganda, Malawi, South Africa	**Total sample: 550 pregnant individuals** **Cohort 1 (36-37 weeks pregnant):** 150 Malawi: 27 South Africa: 42 Uganda: 44 Zimbabwe: 37 **Cohort 2 (30-35 weeks pregnant):** 157 Malawi: 40 South Africa: 28 Uganda: 42 Zimbabwe: 47 **Cohort 3 (12-29 weeks pregnant):** 251 Malawi: 66 South Africa: 44 Uganda: 68 Zimbabwe: 73	Accrual took place from February 2020 to January 2023. Interim results from Cohort 1 presented at IAS 2021, and Cohort 2 presented at CROI 2023. Safety paper from Cohorts 1 and 2 published in JAIDS. Note: Background rates of pregnancy outcomes and complications described in MTN-042B.

***MTN-042 key takeaway:** Adverse pregnancy outcomes and complications were uncommon among ring and oral PrEP users and were generally similar to rates observed in study communities.*

*participants in PrEP ring trials were assumed to be assigned female at birth and were not asked their gender identities. All participants underwent pelvic exams as part of enrollment procedures.