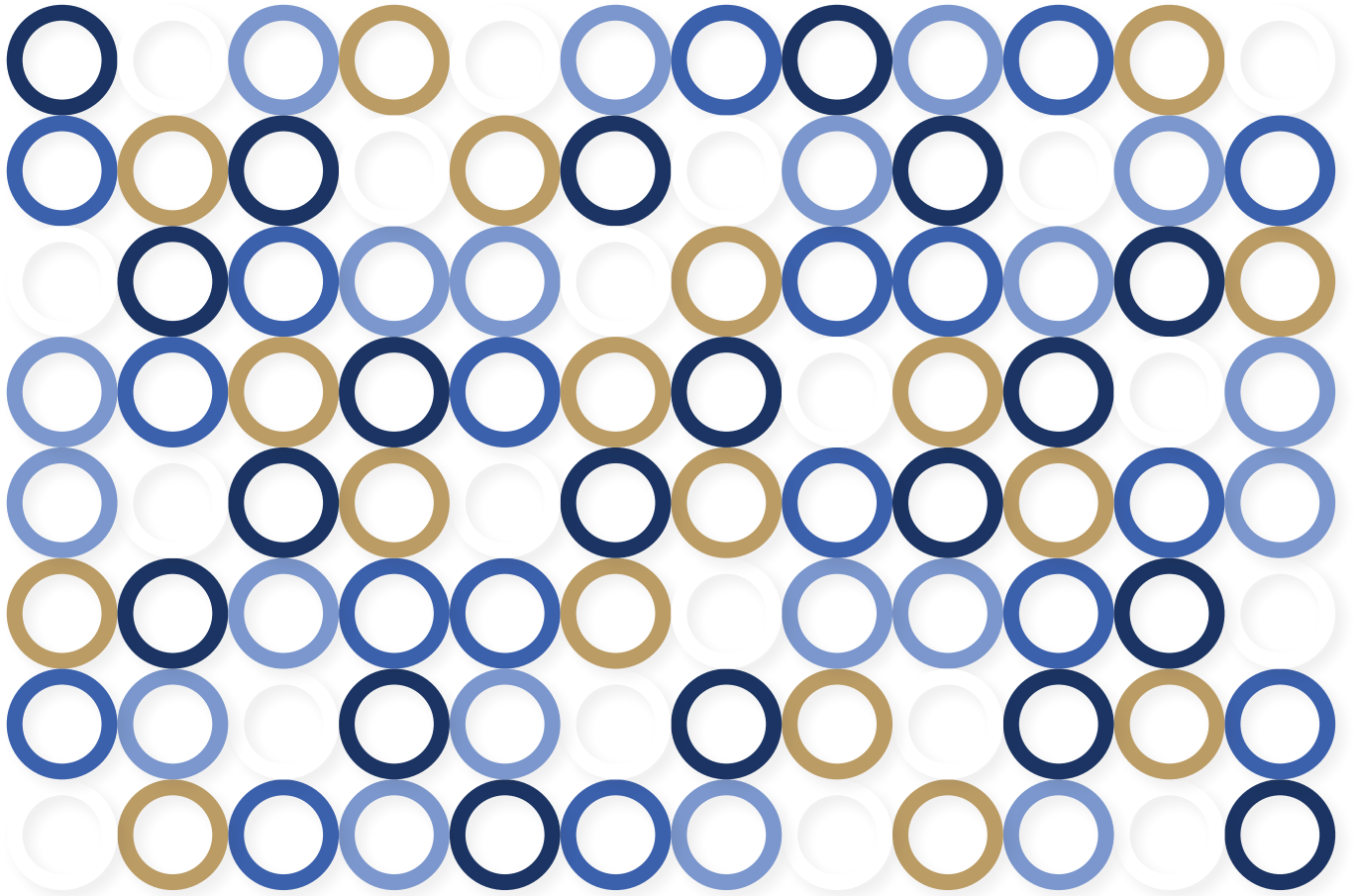


Global Healthcare Provider Training Package

Dapivirine Vaginal Ring



INTERNATIONAL
PARTNERSHIP FOR
MICROBICIDES



Module One

Introducing the Dapivirine Vaginal Ring (DVR)

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About this training manual

This training manual was developed by the International Partnership for Microbicides, as a training resource, that is adaptable to the local country context in which the dapivirine vaginal ring is being implemented.

Each module in the manual is designed to be used either independently or as part of the full pack. Each module has a set of suggested tools which are pull outs at the end of the manual.

Attribution and Citation

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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INTRODUCTION

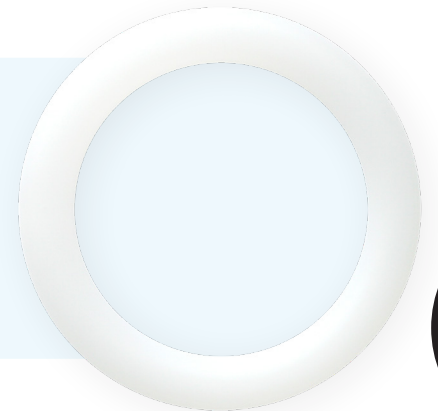
This chapter provides an overview of a new HIV prevention method for women, the long-acting Dapivirine Vaginal Ring (DVR or the Ring).

The development of the Ring was a response to the reality that women remain more likely to acquire HIV than men. HIV is one of the leading causes of death among women ages 15 - 49 worldwide. HIV incidence is particularly high among young women: in the age range 15 - 24 years, they are twice as likely to acquire HIV as men of their age, accounting for nearly 25% of new adult infections in sub-Saharan Africa¹. Biological, economic and sociocultural factors all play a role in increasing women's chances of acquiring HIV and manifest in practices such as early sexual debut, early marriage, intergenerational sex and concurrent partnerships².

Women need new HIV prevention methods – methods that they can choose and they can control. HIV prevention methods currently available, such as condoms, oral pre-exposure prophylaxis (oral PrEP), and treatment as prevention (TaSP) are excellent options, but the high rate of HIV among young women indicates that these methods have not adequately slowed the epidemic in this group.

With 5000 women aged 15 - 24 years acquiring HIV every week³, it is clear that women need multiple prevention options in order to choose those that make sense in their lives, their realities. These options must include discreet products that can be used without male partner consent and the Ring is such a method.

There is a need for discreet products that can be used without male partner consent.



dapivirine
vaginal ring

1 UNAIDS Data 2021

2 Drissa Sia, Yentéma Onadja, Arijit Nandi, Anne Foro, Timothy Brewer, What lies behind gender inequalities in HIV/AIDS in sub-Saharan African countries: evidence from Kenya, Lesotho and Tanzania, Health Policy and Planning, Volume 29, Issue 7, October 2014, Pages 938–949, Ramjee G, Daniels B. Women and HIV in Sub-Saharan Africa. AIDS Res Ther. 2013;10(1):30. Published 2013 Dec 13. doi:10.1186/1742-6405-10-30

3 <https://www.usaid.gov/global-health/health-areas/hiv-and-aids/technical-areas/dreams>

HIV: STILL A MAJOR GLOBAL PROBLEM

UNAIDS 2020 data⁴

- In 2020, more than 37 million people were living with HIV, and 1.5 million people acquired HIV
- 60% of people newly infected with HIV lived in sub-Saharan Africa
- Every week, around 5 000 young women aged 15-24 years became infected with HIV
- Globally, women and girls comprised about 50% of those who acquired HIV in 2020. In sub-Saharan Africa, women and girls accounted for 63% those newly infected

⁴ UNAIDS 2021 data report

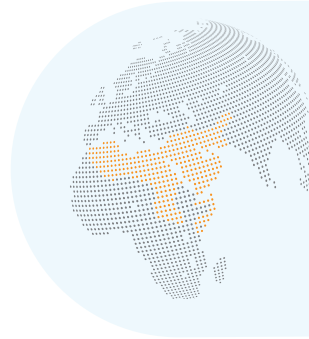
HIV AND AIDS IN WEST AND CENTRAL AFRICA OVERVIEW

- 4.7 m** people living with HIV
- 1.3%** adult HIV prevalence (15-49)
- 150,000** new HIV infections (age >15)
- 55,000** new HIV infections (age 0-14)
- 150,000** AIDS-related deaths
- 73%** of PLWHIV on ART

HIV AND AIDS IN EAST AND SOUTHERN AFRICA OVERVIEW

- 20.6 m** people living with HIV
- 6.5%** adult HIV prevalence (15-49)
- 600,000** new HIV infections (age >15)
- 75,000** new HIV infections (age 0-14)
- 310,000** AIDS-related deaths
- 77%** of PLWHIV on ART

* (UNAIDS 2021 data report - UNAIDS 2020 data)



MIDDLE EAST AND NORTH AFRICA:

230,000 people living with HIV
<0.1% adult HIV prevalence (15-49)
15,000 new HIV infections (age >15)
1,400 new HIV infections (age 0-14)
7,900 AIDS-related deaths
43% of PLWHIV on ART

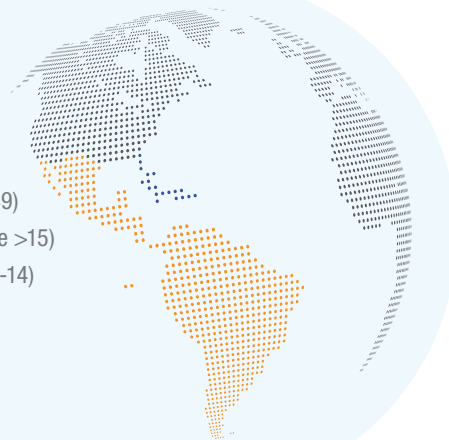


ASIA AND PACIFIC:

5.8 m people living with HIV
0.2% adult HIV prevalence (15-49)
230,000 new HIV infections (age >15)
13,000 new HIV infections (age 0-14)
130,000 AIDS-related deaths
64% of PLWHIV on ART

LATIN AMERICA:

2.1 m people living with HIV
0.4% adult HIV prevalence (15-49)
100,000 new HIV infections (age >15)
2,300 new HIV infections (age 0-14)
31,000 AIDS-related deaths
65% of PLWHIV on ART



CARIBBEAN:

330,000 people living with HIV
1.1% adult HIV prevalence (15-49)
12,000 new HIV infections (age >15)
1,200 new HIV infections (age 0-14)
6,000 AIDS-related deaths
67% of PLWHIV on ART

COMPLEX QUESTIONS DEMAND COMPREHENSIVE ANSWERS

The factors driving high HIV rates among women are complex, and strategies to address the situation need to be multi-faceted.

Treating HIV with antiretroviral therapy (ART) will not, on its own, end the HIV epidemic. UNAIDS has promoted combination HIV prevention as an appropriate strategic approach. This combines:

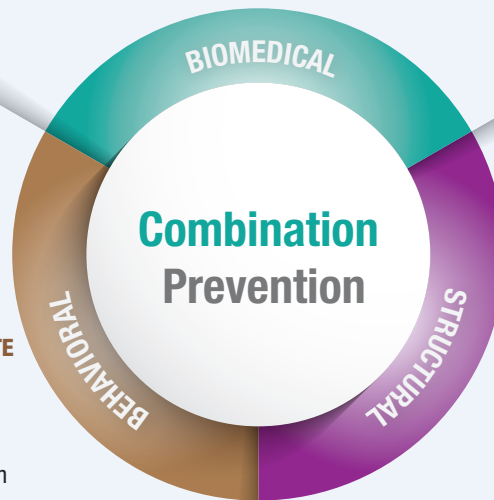
- Biomedical interventions – such as condoms, HIV testing, medical male circumcision, oral PrEP, and TaSP.
- Behavioural interventions – such as sexuality education, peer education and mass media programmes designed to educate and influence relevant behaviours.
- Structural interventions – which include programmes to alleviate poverty, promote sexual and reproductive health, affirm gender equality and combat stigma and discrimination.

Expanding **women's biomedical options** so they can choose the method – or **combination** of methods – that best meets their individual needs is essential to controlling the HIV epidemic. The introduction of the Ring is an important step in this direction. Since the Ring only provides protection during vaginal sex and reduces (rather than eliminates) the risk of HIV infection, it is ideally used in combination with other biomedical options to enhance protection.

It is important to remember that the use of the Ring by women can be reinforced by suitable behavioural programmes and by structural interventions that promote the equality of women and protect women in vulnerable circumstances, such as sex workers.

INTERVENTIONS WITH CLINICAL AND MEDICAL METHODS, FOR EXAMPLE:

- Condoms and lubricants
- HIV testing
- Antiretroviral treatment for all
- Prevention of vertical transmission
- PrEP and PEP
- Voluntary male circumcision
- Needle and syringe programs
- STI management



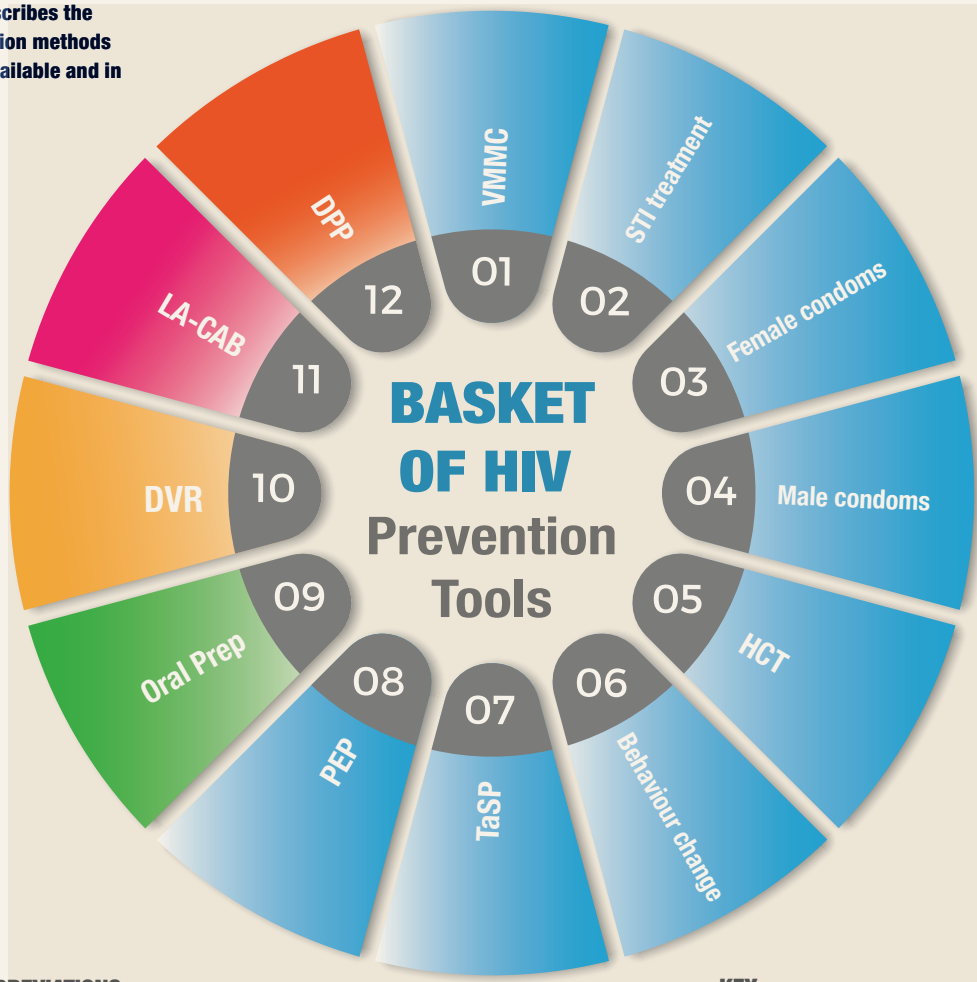
INTERVENTIONS THAT PROMOTE HEALTHY BEHAVIORS, FOR EXAMPLE:

- Counselling on risk reduction
- Comprehensive sex education
- Peer education programs
- Social marketing campaigns (e.g., to promote condom use)
- Abstinence and delayed sexual debut

INTERVENTIONS THAT PROMOTE AN ENABLING ENVIRONMENT, FOR EXAMPLE:

- Decriminalization of transmission and of key populations
- Gender and gender violence approach
- Laws to protect rights
- Interventions to reduce stigma and discrimination

The figure below describes the range of HIV prevention methods that are currently available and in development:



ABBREVIATIONS

- VMMC:** Voluntary medical male circumcision
- HCT:** HIV counselling and testing
- PEP:** Post-exposure prophylaxis
- TaSP:** Treatment as prevention
- Oral PrEP:** Oral pre-exposure prophylaxis
- DVR:** Dapivirine vaginal ring
- LA-CAB:** Long-acting (injectable) cabotegravir
- DPP:** Dual prevention pill

KEY

- Established. Generally available
- Established. Limited availability
- Newest approved product
- Under regulatory review
- In clinical trials

WHAT IS PREP?

Pre-exposure prophylaxis (PrEP) is the use of a biomedical product before being exposed to HIV in order to prevent infection. The pharmaceutical product might be an antiretroviral (ARV) pill, in which case we talk about oral PrEP, or an ARV injection (injectable PrEP), or a device like the Dapivirine Vaginal Ring, which contains an ARV.

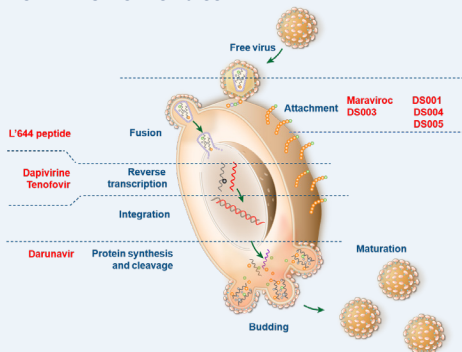
Biomedical HIV prevention includes the use of antiretroviral drugs (ARVs) to reduce the possibility of becoming infected with HIV. These methods include PrEP (see box), TaSP and post-exposure prophylaxis (PEP). Oral PrEP is the only PrEP option currently in general use. But the Ring and long-acting cabotegravir (CAB-LA, an injectable option) are on the horizon as meaningful, woman-centered additions to the PrEP toolbox. Another innovation currently in clinical trials is dual-purpose protection (DPP), which combines oral PrEP and an oral contraceptive.



Comparison of ARV-based HIV prevention options

The Ring	Oral PrEP	CAB-LA
<ul style="list-style-type: none"> • Active ingredients: dapivirine • Monthly vaginal ring • For women only • Approved by WHO 	<ul style="list-style-type: none"> • Active ingredients: emtricitabine and tenofovir (TDF/FTC) • Daily pill • For men and women • Approved by WHO 	<ul style="list-style-type: none"> • Active ingredients: cabotegravir • Two-monthly injectable • For men and women • FDA Approved

How ARVs work on a cell



ARV-based microbicides work by directly targeting HIV and interfering with one of the phases in the HIV life cycle. As illustrated in the graphic above, IPM's pipeline of ARVs work at different stages in the HIV life cycle.

WHAT ARE MICROBICIDES?

A microbicide is a product that is used in the vagina and/or rectum to help prevent HIV infection during sex.

The protective effect of a microbicide is localised to the site of infection – the rectum or vagina – unlike a pill which has a systemic effect, that is, on the whole body. Most microbicides contain ARVs, which are also used in pill form to treat and prevent HIV. Various microbicides act at different stages in the lifecycle of the virus to prevent infection.

Microbicide vaginal Rings

Vaginal rings have been used safely and effectively for women's health needs for 20 years. They provide a steady release of the chosen drug – for example, a contraceptive – to the right place at the right time.

The Ring marks the first time a vaginal ring has been used to deliver an ARV for HIV prevention. This means the Ring is not only a form of PrEP but it also belongs to a category of biomedical products known as microbicides. (See illustration on the left)

The Ring offers women a long-acting tool they can control themselves and use discreetly to reduce their chances of acquiring HIV. Because it is worn continuously and changed once a month, the Ring makes it easier for

women adhere to use of a prevention option. Vaginal rings are simple to use and they are flexible and comfortable. Most women and their male partners report that the Ring cannot be felt during sex and has no impact on their sexual experience.

Other positive aspects of microbicide vaginal rings are convenience, user-friendliness, and the potential to add other drugs to the original ARV – for example, a contraceptive – to produce a dual-purpose product.

How the Dapivirine Vaginal Ring is used

Vaginal rings can be a new option for many women and women may have concerns about how they are used and work. This is often driven by a lack of familiarity with their own anatomy and negative experiences or associations with other sexual and reproductive health (SRH) products, like IUDs. When explained how to use the ring, most women find it easy and comfortable to use.

To use a vaginal ring, a woman simply squeezes the ring and inserts it into her vagina. It is like inserting a tampon. The Ring

stays in the vagina for 1 month and then the woman takes it out, throws it away and inserts a new ring.

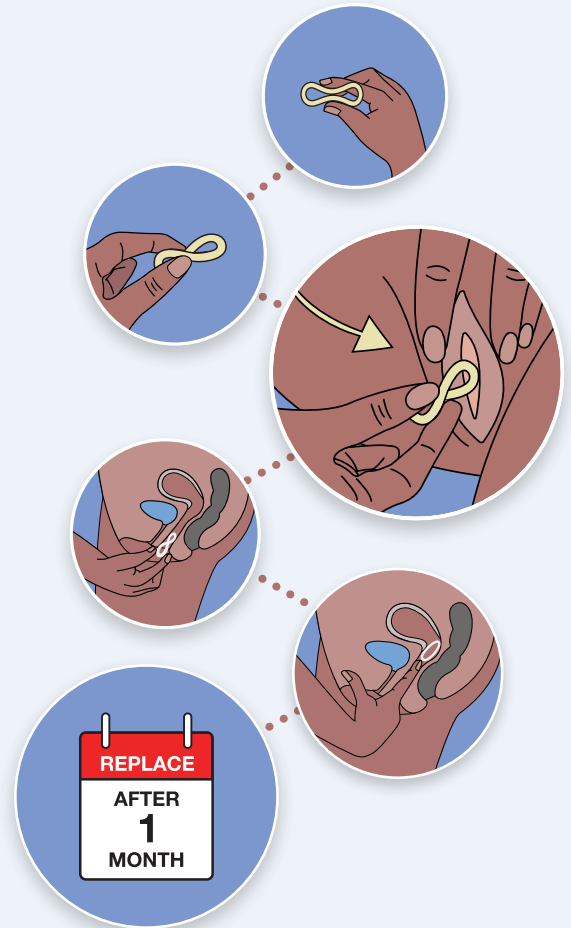
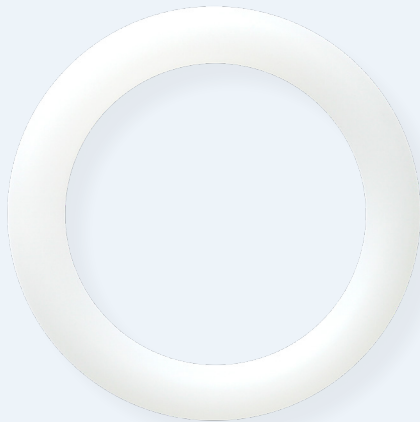
HOW THE DAPIVIRINE VAGINAL RING WORKS

A woman would insert the flexible silicone ring herself and replace it with a new one each month.

The ring sits inside the vagina near the cervix where it slowly releases an antiretroviral drug called dapivirine at the site of potential infection.

Dapivirine works by blocking HIV's ability to make copies of itself inside healthy cells.

It is important that the ring is left in place for the full month to ensure that risk reduction is achieved.



MORE DETAILS ON THE RING

Characteristics

- Flexible silicone vaginal ring, 25mm in diameter and 7.7mm thick
- Contains 25mg of the ARV drug, dapivirine, dispersed uniformly throughout the material
- Slowly releases ARV dapivirine over 1 month into the vagina, at the site of potential infection. Dapivirine prevents HIV from making copies of itself inside healthy cells
- Shelf life of up to 60 months when stored at or below 30°C

Benefits to women

- Woman-controlled
- Reduces but does not eliminate HIV risk
- Easy to store, does not require refrigeration
- Self-inserted into the vagina every 1 month
- Can be used discreetly
- Does not interfere with sex or menses
- Low absorption of dapivirine in the blood, which may minimise side effects and reduce risk of developing HIV resistance

Extent of protection

- Provides partial protection against HIV infection during receptive vaginal sex
 - An average of 30% risk reduction seen in clinical trials
 - Two open label studies found with increased ring use efficacy increased to about 50%
- Does not provide protection:
- Against other STIs
 - Against pregnancy
 - During anal or oral sex

Service delivery benefits

- At most, women need to visit the clinic/ service delivery point once a month for dispensing of the Ring. Multi-month dispensing is possible and visits can be aligned with client's contraception schedule.
- There is no need for the healthcare provider to insert the Ring. Women can insert and remove it themselves.
- The only test needed before initiating the Ring is an HIV test. No blood samples are required.



Points to note:

- The Ring must remain inserted, day and night every day, for 1 month to do its job. This continual use is important. There is no need to remove the ring when bathing or during or after sex.
- The Ring is rarely felt by the partner.
- The Ring must also remain in place during menstruation. It can be used with a tampon but not with a menstrual cup.
- Because the Ring reduces but does not eliminate the risk of acquiring HIV infection and does not prevent STIs or pregnancy, it should be used with a male or female condom wherever possible.
- The Ring is an additional HIV prevention option which has the advantages of being woman-controlled and long-acting. It may be particularly valuable for women who are not able to use highly effective prevention methods such as condoms or oral PrEP, or choose not to do so.
- The Ring can be used with various contraceptive methods – such as condoms, the pill, injectables, IUD and implants – but cannot be used with diaphragms, cervical caps or contraceptive vaginal rings.

The Ring is an additional HIV prevention option which has the advantages of being woman-controlled and long-acting.

Efficacy refers to the ability of a product or treatment to provide a beneficial effect

OVERVIEW OF RESEARCH ON THE RING

There have been many small studies on the Dapivirine Vaginal Ring and two critically important phase 3 trials to establish safety and efficacy, followed by open label extension (OLE) studies.

Findings on efficacy

Efficacy refers to the ability of a product or treatment to provide a beneficial effect. In the case of the Ring, the desired effect was a reduction in acquisition of HIV infection.

Two phase 3 studies – the Ring Study and ASPIRE - evaluated monthly use of the ring in nearly 4 600 women aged 18 – 45 years in Malawi, South Africa, Uganda and Zimbabwe. They found that long-term use of the monthly Ring reduced women’s risk of HIV infection and raised no safety concerns. More specifically:

- The Ring Study, led by International Partnership for Microbicides (IPM), found that the Ring reduced overall risk by 35%.
- The ASPIRE Study, led by the US National Institutes of Health-funded Microbicide Trials Network (MTN), found that the Ring reduced overall risk by 27%.

Two subsequent OLE studies, DREAM and HOPE, showed increased use of the Ring compared to the phase 3 trials, and statistical modelling suggested there was greater risk reduction – of over 50% – across both OLE studies.

What is an open-label study?

An open label extension (OLE) study typically follows a phase 3 study of a new drug, if that study has demonstrated efficacy of the product. At the end of the phase 3 trial participants are invited to enroll in an OLE study.

All OLE participants receive the study product, and both participants and researchers know this.

The primary objective is to gather information about the safety and tolerability of the new drug in long-term, day-to-day use⁵.

5 Taylor, G. J., & Wainwright, P. (2005). Open label extension studies: research or marketing?. *BMJ (Clinical research ed.)*, 331(7516), 572–574. <https://doi.org/10.1136/bmj.331.7516.572>

Dapivirine Ring Trials

Women aged 18 – 45
Malawi, South Africa, Uganda, Zimbabwe

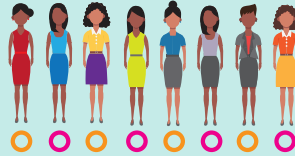
Phase 3



ASPIRE

4500

Women did not know if they're receiving the dapivirine ring or a placebo ring



Placebo

What we saw in Phase 3 trials

HIV risk was lower with dapivirine ring use in the Phase 3 trials

35%
ASPIRE 27%

Adherence was about 80% in Phase 3 trials

80%

No safety concerns were seen with use of the dapivirine ring in the Phase 3 trials

Risk Reduction

Adherence

Safety

Open-Label



Dapivirine



2400

Former Phase III participants

All women know they're receiving the dapivirine ring (there was no placebo group)

HOPE

HIV Open-Label Prevention Extension
Out of ASPIRE, here is HOPE

What we saw in Open-label studies

63%
DREAM 39% HOPE

90%+

The dapivirine ring's safety profile in the open-label studies was similar to the strong profile seen in the Phase 3 trials

Modeling data suggest HIV risk was reduced by about half with ring use across both studies

More than 90% of women used the dapivirine ring at least some of the time

WHAT WE KNOW

01 The Phase 3 trials showed that HIV risk was reduced in women who used the dapivirine ring

02 Open-label study results suggested that the dapivirine ring reduced HIV risk by about half across both studies, an encouraging trend

03 Adherence was higher in the open-label studies

04 The dapivirine ring had a strong safety profile in all the Phase 3 and open-label studies, with no safety concerns

05 The open-label study results suggest that when women are aware that the dapivirine ring reduced HIV risk in large clinical trials, they are more likely to use the product and see greater protection

Findings on safety

There were no safety concerns associated with long-term use of the Ring in the phase 3 and OLE studies. There was no difference in the incidence of adverse events between the trial participants receiving the Ring and those receiving a placebo product. In addition, more than 40 smaller safety studies were conducted on different dapivirine formulations (oral forms used for treatment and vaginal gels, films and rings) and these support the Ring's favourable safety profile.

Findings on acceptability

Nearly all women in two IPM acceptability studies in Africa found the Ring to be acceptable and expressed interest in using it if proven effective.

Many women in the Phase 3 studies reported forgetting the Ring was in place and said that neither they nor their partners could feel it during sex.

Additional research

Although extensive clinical research has been done on the Ring, there are still some research gaps, including information on use of the Ring by young women and its safety and acceptability among pregnant and breastfeeding women.



Additional research¹

More data needed on

REACH Study

Start date: February 2019
Investigating safety and use of the Ring and oral PrEP among 300 young women (16-21 years) in South Africa, Uganda and Zimbabwe

Safety and use by young women (16-25 years)

DELIVER Study

Start date: February 2020
Safety and acceptability of the Ring and oral PrEP among 550 pregnant women in Malawi, South Africa, Uganda and Zimbabwe

Safety and acceptability for pregnant and breastfeeding women

B-PROTECTED Study

Start date: August 2020
Safety and acceptability of the Ring and oral PrEP among 200 breastfeeding women in Malawi, South Africa, Uganda and Zimbabwe

¹ Refer to module 1B for details

MILESTONES FOR THE RING JULY 2020

July 2020

The Ring received a positive scientific opinion from the European Medicines Agency for its use by cisgender women, aged 18 years and older to reduce their HIV risk



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

March 2021

The World Health Organization (WHO) recommends the Ring for women at substantial risk of HIV infection

July 2021

The WHO includes the Ring in the Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring



World Health Organization

IPM is seeking regulatory approval for the Ring in several countries in sub-Saharan Africa.




Key takeaways from this module

- Women are at great risk of HIV infection as a result of a combination of biological, economic, sociocultural factors.
- Young women aged 15-24 years are at highest risk of HIV and account for 25% of new adult infections in sub-Saharan Africa.
- If we are serious about bringing the HIV epidemic under control, we must expand women's HIV prevention options so they can find a method that meets their individual needs.
- Many women need discreet prevention products that can be used without male partner consent.
- The monthly Ring meets the demand for a discreet method that is female-initiated, does not depend on daily use, and offers long-acting convenience.
- Vaginal rings have been used safely and effectively for other health needs of women for 20 years (i.e. the contraceptive ring). They provide a steady release of a drug to the right place at the right time.
- In clinical trials the monthly Ring reduced vaginal acquisition of HIV by 27 - 35% and subsequent open label studies showed a 50% reduction in HIV acquisition.
- In March 2021 WHO recommended the Ring for women who are at substantial HIV risk.

Tools to go with this Module:

THE RING
TOOL 1



A discreet, safe, female controlled, vaginal HIV prevention option.

General Info:


- A discreet, safe, female controlled, vaginal HIV prevention option.
- The Ring provides general protection against HIV – wear the ring 90% use condoms for maximum protection!

Daily activities:

- Wear the Ring for 1 month, take it out, put a new one in!
- There is no need to remove the Ring while menstruating, it can even be used with a tampon.
- You can still use the toilet with the Ring in – it will not fall out.

Sexual activities:

- You can still have vaginal sex while using the Ring – neither you or your partner should feel it.
- The Ring DOES NOT protect against pregnancy.
- The Ring DOES NOT protect against other STIs.



Tool 1

VIDEO ON HOW THE RING WORKS
TOOL 2

Video:
How to use the DVR





<https://vimeo.com/20399112>




Tool 2

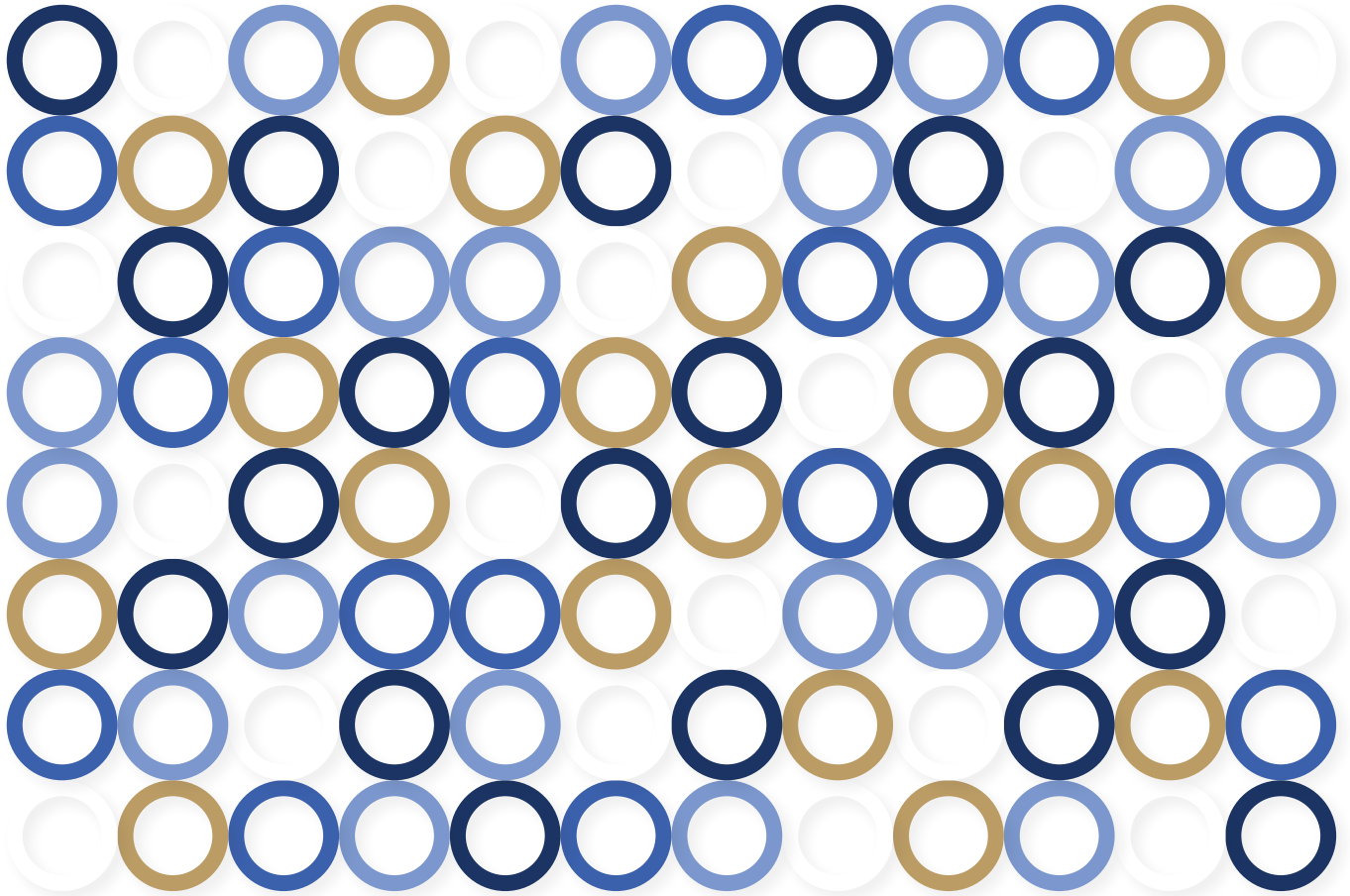
HIV PREVENTION OPTIONS
TOOL 3



	Condoms	Oral PEP	EpiPatch Vaginal Ring
Use	Every time you have sex	Daily	Inserted every 28 days (you do not need to use for 28 days)
Adherence	Effectiveness is dependent on whether a user can remember/remember to use the product during every sex act.	Effectiveness is dependent on daily dosing	Long acting, less user dependent
Discretion	Use needs to be negotiated with the partner. Cannot be used discreetly	Discrete – can be used without partner knowledge	Discrete – can be used without partner knowledge
Effectiveness/Efficacy	91 to 98% effective when used consistently	Over 90% effective, when used consistently	About 20% in clinical trials and over 20% in real world studies that showed greater adherence



Tool 3



Module One B

Evidence of the Ring's Safety and Effectiveness

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Attribution and Citation

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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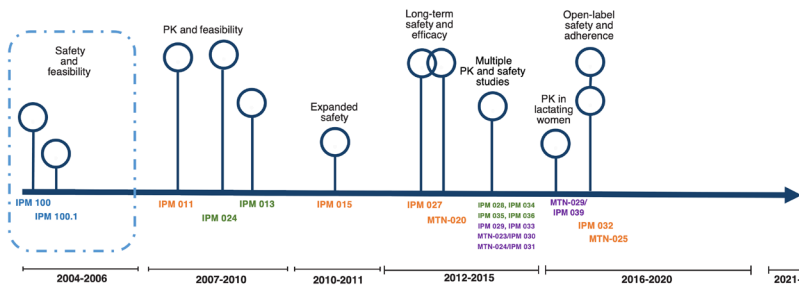
OVERVIEW OF RING STUDIES CONDUCTED

Research on the dapivirine vaginal ring (DVR or the Ring) commenced in 2004 and has spanned multiple phase 1, 2 and 3 clinical trials and subsequent open-label extension (OLE) studies.

There are ongoing studies to address unanswered questions on providing the Ring to adolescent girls and young women (AGYW) and to women during pregnancy and breast-feeding. The purpose of the series of studies was to provide scientific evidence on ring safety, pharmacokinetics, dosing, efficacy and tolerability in adult women and special

populations such as adolescents, post-menopausal women, pregnant women and lactating or breast-feeding women. Additionally, after regulatory approval, implementation studies are planned to determine feasible service delivery strategies and real-world consistent product use.

Completed Clinical trials on the Ring in Africa, Europe and the United States

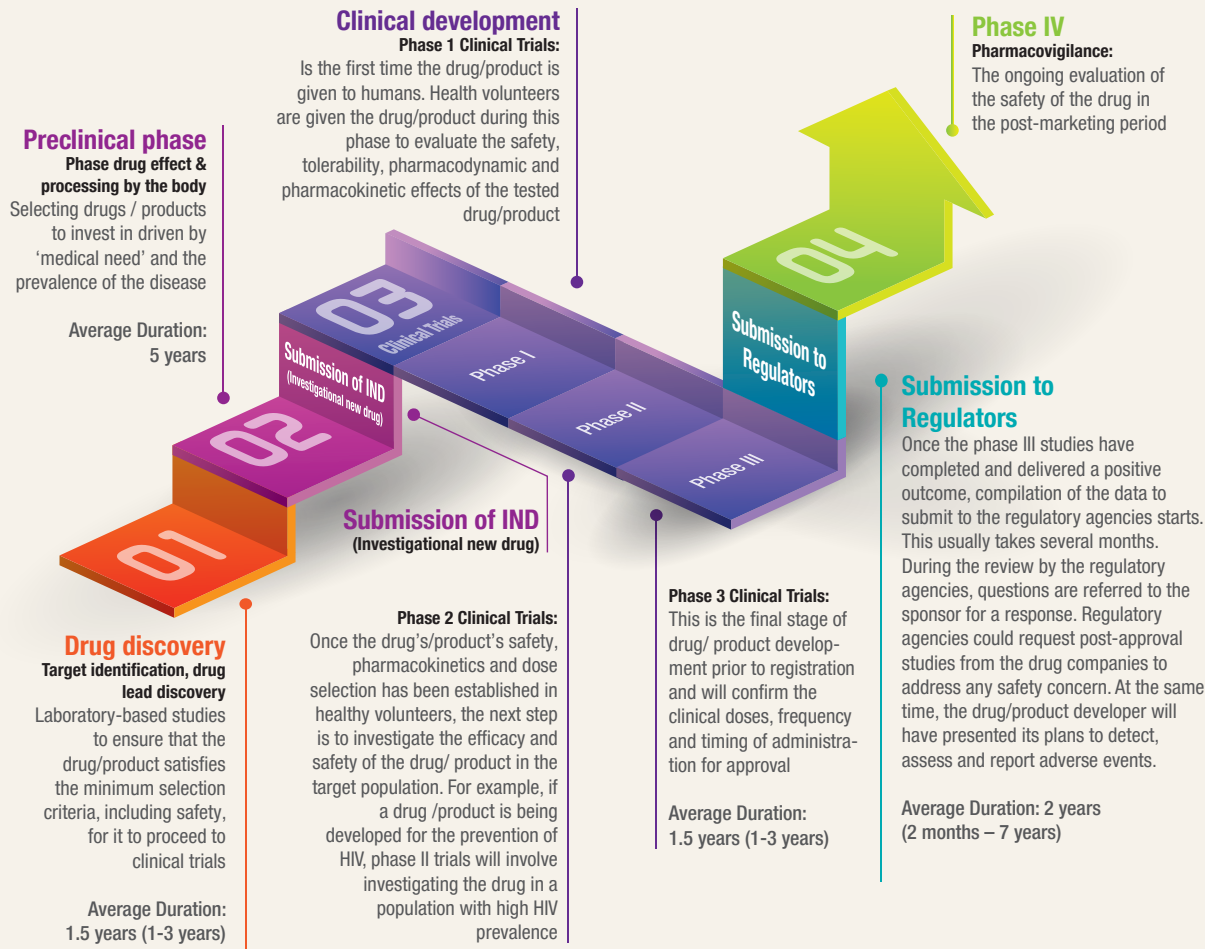


○ Ring Clinical trials in Africa, Europe and United States

- USA
- Belgium
- Africa

*Feasibility studies do not utilise the active pharmaceutical ingredient

General Drug Discovery, Development & Approval Process Overview



Definitions:

Pharmacodynamic effect of a drug/product: the effect of the drug on the body (e.g., effect on heart rate, blood pressure) – *How the drug/product interactions in the body*

Pharmacokinetic effect of a drug/product: effect of the body on the drug (i.e., absorption, distribution, metabolism, and excretion) effects of the tested drug/product) – *How the drug moves in the body*

WHAT IS AN OPEN-LABEL STUDY?

An open label extension (OLE) study typically follows a phase 3 study of a new drug which has demonstrated efficacy of the product.

At the end of the phase 3 trial participants are invited to enroll in an OLE study. All OLE participants receive the study product, and both participants and researchers know this. The primary objective is to gather information about the safety and tolerability of the new drug in long-term, day-to-day use.

Phase 1 and 2 Ring studies

Many phase 1 and 2 studies on the Ring were conducted to investigate matters related to product use, such as: safety related to time of use, interaction with vaginally administered antifungal drugs, effects on menses and tampon use, effects on condom use, and effects on women at different stages of life (adolescence and youth, during lactation and after menopause). The outcomes/findings of these studies are described below.

List of clinical studies on the Ring by study phase



The primary objective is to gather information about the safety and tolerability of the new drug in long-term, day-to-day use.

IPM 013

IPM 013

Safety and pharmacokinetics (PK) of multiple DVR-004 use up to 56/57 days

A total of 48 healthy, HIV-negative, sexually active women were enrolled in this trial in Belgium to assess the safety and delivery of dapivirine from a matrix vaginal ring. Each participant used a vaginal ring for approximately three months. Participants received either a platinum-catalysed vaginal ring containing 25 mg of dapivirine or a placebo vaginal ring for purposes of comparison.

Safety: the Ring was well tolerated in all participants. There was no evidence of any

difference in safety between the Ring and the placebo ring.

Pharmacokinetics: findings indicated a rapid increase in plasma and vaginal fluid concentrations of dapivirine after first ring insertion, resulting in maximum concentrations in plasma by Day 7 and in vaginal fluid between Day 1 and Day 14, after which concentrations decreased steadily over the remainder of the 28-day or 35-day ring use period.

IPM 024

IPM 024

Safety and pharmacokinetics of DVR-004 in sexually abstinent women

A group of 16 healthy, HIV-negative, sexually abstinent women were enrolled in a trial in Belgium to evaluate the delivery of dapivirine from a matrix vaginal ring containing 25 mg of dapivirine and to determine the safety and tolerability of the Ring as compared to a placebo vaginal ring. Each participant used a

vaginal ring for approximately 28 days. The vaginal ring was well tolerated in all participants with no major difference in safety between the Ring and the placebo ring. The platinum-catalysed silicone Ring displayed pharmacokinetic properties indicative of sustained release of dapivirine over 28 days.

IPM 028 and IPM 036**Assessment of drug-drug interactions (miconazole/clotrimazole)**

In IPM 028, participants comprised 36 healthy, HIV-negative women in Belgium. All participants received the Ring only for 28 days, the Ring for 28 days plus a single dose miconazole, and a single-dose of miconazole only, in separate treatment periods and in different treatment sequences. Concomitant use was well tolerated. Dapivirine release from the vaginal ring was similar with or without miconazole, however some differences were noted in the plasma and vaginal fluid concentrations of dapivirine and miconazole when used together*, compared to when either product was used alone. These changes are considered to not be clinically relevant.

** Concomitant use of the dapivirine vaginal ring and a single vaginal dose of miconazole nitrate increased systemic exposure to dapivirine, whereas a lower exposure was observed in vaginal fluid. Exposure to miconazole in both plasma and vaginal fluid was increased after co-administration with the dapivirine ring.*

In IPM 036, participants comprised 36 healthy, HIV-negative women in Belgium. They used the Ring only for 28 days, the Ring for 28 days plus clotrimazole vaginal cream (5g for seven days), or clotrimazole only (5g for seven days) during three separate periods and in three different treatment sequences. Concomitant use was well tolerated. Dapivirine release from the vaginal was similar with or without clotrimazole. Dapivirine exposure and concentrations in vaginal fluid were higher during co-administration with clotrimazole and an increase in systemic exposure of clotrimazole was observed during concurrent Ring use. These changes are not considered clinically relevant.

IPM 034**Assessment of the release profile of the Ring when used continuously over extended periods**

A total of 40 healthy, HIV-negative women in Belgium were enrolled in an open label, parallel group trial. Participants were divided into five groups (Groups A-E) of eight women each and used the Ring continuously for either 1, 2, 4, 8 or 12 weeks.

Dapivirine concentrations in plasma and vaginal fluids decreased linearly with the

duration of ring use for periods of greater than 4 weeks. Nevertheless, the lowest individual dapivirine concentration in vaginal fluids observed after 84 days (12 weeks) of ring use remained substantially high. No clinically significant differences were observed in terms of safety findings between the different ring use periods and the Ring was well tolerated.

**IPM 028/
IPM 036****IPM 034**

IPM 035

IPM 035

Assessment of the effect of menses and tampon use on the pharmacokinetics of the Ring

A total of 16 healthy, HIV-negative women in Belgium were enrolled in an open label, randomized, two sequence, three-period crossover trial. Randomized to two consecutive treatment sequences; each 28-day treatment period separated by 28-day washout period

Dapivirine ring with menses and no tampon use, then ring with menses with tampon use, then ring with no menses

Dapivirine ring with menses with tampon use, then ring with menses and no tampon use, then ring with no menses

Dapivirine vaginal fluid concentrations decreased up to 4-fold during menses but increased again thereafter and achieved concentrations consistent with the group who did not experience menstruation. The use of tampons generally resulted in a further 2-fold decrease of dapivirine in vaginal fluid concentrations during menses.

As the clinical relevance of the reduced vaginal dapivirine levels during menses and tampon use is unclear, the need for additional preventive measures against HIV during menses (e.g. condoms) should be reinforced.

MTN-029 /IPM 039

MTN-029/IPM 039

Safety and pharmacokinetics of the Ring in lactating, but not breastfeeding, women

Participants were 16 healthy lactating women, at least six weeks postpartum. The study was conducted over 14 months at two research centres in the US. The women produced breastmilk but were not breastfeeding during their use of the Ring. The Ring

was safe and well-tolerated. Low levels of detectable dapivirine were found in plasma and breast milk, indicating low infant doses would occur with breastfeeding. The Ring had a favourable safety profile in women.

IPM 011

IPM 011

Safety and acceptability of a placebo vaginal ring used for a 12-week period

Participants were 170 healthy, sexually active women. The trial was an open-label, crossover study conducted at five sites in Kenya, South Africa and Tanzania to assess the safety and acceptability of a silicone elastomer vaginal ring containing no active ingredient. The silicone elastomer vaginal

ring was well tolerated and highly acceptable to trial participants. Based on the incidence of adverse events, abnormal pelvic/colposcopy findings and STI results, there was no evidence of any major difference in safety between the vaginal ring and period when no ring was used.

IPM 029 and IPM 033

Condom functionality (placebo ring used)

IPM 029 investigated male condom functionality with use of a placebo vaginal ring. About 70 healthy, monogamous heterosexual couples in the US were enrolled. The study consisted of two 28-day periods, one with women wearing the ring and men wearing condoms and one with women not wearing the Ring and men wearing condoms. The ring was well tolerated. There was no difference in clinical condom failure with or without ring use.

IPM 033 investigated female condom functionality with use of a vaginal ring. About 80 healthy, monogamous heterosexual couples in the US were enrolled. The study consisted of two 28-day periods, one with women wearing the ring and the female condom and one with women wearing only the female condom. The vaginal ring was well tolerated. There was no difference in the rate of clinical condom failure with or without placebo ring use.

Quick Summary of Phase 1 trial findings

Phase 1 studies, conducted in healthy volunteers, found the following:

- **Safety:** no safety concerns associated with recommended use of the ring. Furthermore, no safety concerns were identified if the ring remained inserted for greater than a month.
- **Pharmacokinetics:** sustained release of dapivirine over 28 days.
- **STI treatment:** the ring can remain in place during STI treatment
- **Menses and Tampons:** the ring can be used during menses and with tampons, however additional prevention measures (such as condoms) are encouraged as dapivirine levels in the vagina may decrease during menses and tampon use but rebound after menses
- **Breastfeeding:** low levels of detectable dapivirine were found in plasma and breast milk, indicating that low infant doses would occur with breastfeeding
- **Acceptability:** the ring was well tolerated and highly acceptable to trial participants
- **Condom Functionality:** the ring does not affect condom functionality

IPM 029/ IPM 033

MTN-029 /IPM 039

MTN-029 /IPM 039

MTN-029 /IPM 039

PHASE 2 RING STUDIES

IPM 015

Safety of the Ring when inserted every 28 days for a 12-week use period

This was a double-blind, randomised, placebo-controlled trial, conducted over 12.5 months at 10 research centres in Kenya, Malawi, Tanzania and South Africa. Participants were 280 healthy, HIV-negative, sexually active women and the purpose was

to assess and compare the safety of 28-day use of the Ring and a placebo vaginal ring. The Ring displayed a favourable safety profile and was well tolerated. It was highly acceptable to participants and adherence to daily use was high.

MTN-023/IPM 030

Safety of the Ring in adolescent girls/young women when inserted once every 28 days for a 24-week use period

A group of 96 healthy, HIV-negative adolescent girls/young women (15-17 years) in the US were enrolled. Each participant inserted either an active or placebo ring once every four weeks. Dapivirine plasma and vaginal fluid concentrations at ring removal remained fairly constant over the 24 weeks of follow-up

and were similar to those observed in adult women of reproductive age. The ring was well-tolerated and showed high adherence, as indicated by drug levels in plasma and used rings. The majority of participants liked the ring, found it easy to use, and reported that it did not interfere with daily activities.

MTN-024/IPM 031

Safety of the Ring in post-menopausal women when inserted once every four weeks for a 12-week use period

Approximately 96 healthy, HIV negative women >45 years in the US were enrolled. Each participant inserted an active or placebo ring once every four weeks. The ring was well-tolerated and dapivirine levels were comparable to those in women of

reproductive age. Safety findings were similar to those observed for women of reproductive age and/or not unanticipated for the enrolled population. There was high acceptability and self-reported adherence.

Quick Summary of Phase 2 trial findings

Phase 2 studies, conducted in HIV negative, sexually active women, found the following:

- **Safety:** the ring showed a favourable safety profile with no safety concerns in adolescents (USA), women of reproductive age (Kenya, Malawi, Tanzania and South Africa) and post-menopausal women (USA)
- **Acceptability:** the ring was highly acceptable to participants and adherence to daily use was high over a 28-day period
- **Use in adolescents in USA:** the ring was well-tolerated, and participants showed high adherence, as indicated by drug levels in plasma and used rings
- **Use in post-menopausal women in USA:** the ring was well-tolerated in women > 45 years and dapivirine levels were comparable to those in women of reproductive age

PHASE 3 CLINICAL TRIALS

Two randomised, double-blind, placebo-controlled trials – the Ring study (IPM 027) and ASPIRE (MTN-020) – were conducted to determine the safety and efficacy of the Dapivirine Vaginal Ring in adult women.

Approximately 4 500 women (aged 18 - 45 years) participated in the two studies and were randomised to receive either the active Ring or placebo ring. The studies found that overall the ring reduced the risk of HIV by 27% (ASPIRE) and 35% (Ring study). Adherence to ring use was about 80% in these studies. The Ring was well tolerated and displayed a favourable safety profile.

Trial terminology

Randomised, controlled trial: a trial where participants are randomly assigned to one of two groups. The experimental group receives the intervention that is being tested. The control group receives an alternative treatment, either a placebo or the conventional treatment available.

Double-blind study: a trial conducted in such a way that neither the participants nor the researchers know which individuals are in the experimental group and which are in the control group.

THE RING STUDY

The Ring study was a randomised, double-blind, placebo-controlled safety and efficacy trial of the Dapivirine Vaginal Ring.

Study participants were healthy, HIV-negative women aged 18 - 45 years (average 26 years), enrolled at six research centres in South Africa and one in Uganda. The women inserted a ring every four weeks over a period of 104 weeks.

A total of 1 959 women were enrolled

- One-third (n = 652) were assigned to the placebo ring group and two-thirds (n=1307) to the Ring group.
- Women self-inserted and removed the Ring at four-weekly visits to research sites and were followed up for two years.
- All received a comprehensive HIV prevention package.

About participants in The Ring Study



Key study findings

HIV seroconversion

During the course of the study 9.1% of the 652 participants who used the placebo ring tested positive for HIV. Among the 1 307 participants who used the Ring, a lower proportion (6.1%) tested HIV-positive. In other words, the risk of HIV seroconversion among those who used the Ring was 35%¹ lower than among those who used the placebo ring.

¹ Based on calculation of follow up time being the on-treatment period only



Percent of participants who tested positive for HIV



Safety and side-effects

- The Ring has a favourable safety profile and was well tolerated when used over 24 months
- The most commonly reported adverse events, not necessarily related to product use, that emerged or worsened during the

study and occurred in at least 10% of participants were: STI infections, metrorrhagia (irregular bleeding), genital infection, upper respiratory tract infection, urinary tract infection, vulvovaginal candidiasis (thrush) and menorrhagia (heavy menstruation).

Resistance

- A low proportion of women in both the Ring and placebo groups had NNRTI resistance associated mutations, identified in samples

taken soon after HIV-1 infection (Ring group: 16/84, 19.0%; placebo ring: 8/58, 13.8%).

Product acceptability

- The vaginal ring was considered acceptable.
- At baseline all participants reported finding it easy to insert the vaginal ring.
- At all assessments > 89% of participants in both the Ring and placebo groups reported not feeling the ring when performing their normal activities and ≥ 94% reported not minding using a vaginal ring every day.

- The proportion of participants who reported that their partner did not feel the ring during vaginal sex increased over time from 77.3% (Ring group) and 74.8% (placebo group) at baselines to 93.3% and 92.5% respectively, at Week 104.
- Concern about the ring falling out reduced from 11.3%/12.1% (Ring /placebo) at baseline to < 2.0% at follow up assessments.



THE ASPIRE STUDY

The ASPIRE study was a randomised, double-blind, placebo-controlled phase 3 safety and effectiveness trial of the Dapivirine Vaginal Ring.

Study participants were healthy, HIV-negative women aged 18 - 45 years (average 27 years). Women would insert the ring every 4 weeks, over a minimum period of 12 months. The study took place in 15 research sites in Malawi, South Africa, Uganda and Zimbabwe.

- 2 969 women were enrolled in ASPIRE.
- Half were randomly assigned to the placebo ring group and half to the Ring group.
- Women self-inserted and remove the ring at 4 weekly visits
- All received a comprehensive HIV prevention package.

About participants in ASPIRE Study



HIV seroconversion

During the course of the study 7.4% of the 1 313 participants who used the placebo ring tested positive for HIV. Among the 1 313 participants who used the Ring, a lower proportion (5.4%) tested HIV-positive. In other words, the risk of HIV seroconversion among those who used the Ring was 27% lower than among those who used the placebo ring.

ASPIRE

Percent of study participants who tested positive for HIV



Safety and side-effects

- The Ring had a favourable safety profile and was well tolerated when used over 24 months.
- The most common side effects emerging or becoming worse during the study were STI infections (chlamydia), metrorrhagia, urinary tract infection and menorrhagia. These occurred in more than 15% of participants.

Resistance

- A low proportion of women in both the Ring and placebo groups had non-nucleoside reverse transcriptase inhibitors (NNRTI) resistance associated mutations, identified in samples taken soon after HIV-1 infection (Ring group: 8/68, 11.8%; placebo ring: 9/96, 9.4%).

Product acceptability

- The vaginal Ring was considered acceptable by participants.
- A total of 79% reported never being aware of the Ring during daily activities
- At three months, approximately 84% of participants in both the placebo and active groups reported they had no difficulty inserting the Ring



Quick summary of the phase 3 trial findings



THE RING STUDY

HIV incidence rates
DVR
4.23 per 100 person years
(95% CI: 3.31 -5.16)

Placebo ring
6.43 per 100 person years
(95% CI: 4.79-8.07)



ASPIRE STUDY

HIV incidence rates
DVR
3.3 per 100 person years
(95% CI: 2.54 -4.08)

Placebo ring
4.6 per 100 person years
(95% CI: 3.64 - 5.45)

Safety and adherence

- Favourable safety profile.
- No clinically important differences between the Ring and placebo groups.
- Proportions of participants with AEs and pregnancies (numbers may differ because denominators differed due to 2:1 randomisation in IPM 027)
- Low potential for selecting resistance associated mutations
- Side effects generally mild to moderate and resolved without interrupting ring use
 - Urinary tract infections,
 - Vaginal discharge,
 - Itching and Pelvic,
 - Lower abdominal pain

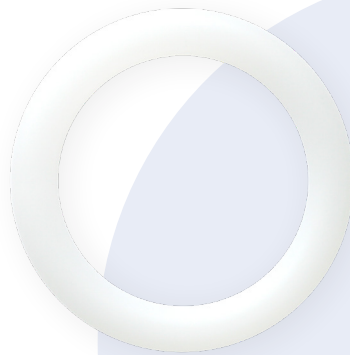


OLE STUDIES ON THE RING

Two OLE studies were conducted with the Dapivirine Vaginal Ring – the DREAM study (IPM-032) and HOPE study (MTN-025) – in order to assess long-term safety and product adherence. The studies enrolled former Ring trial and ASPIRE participants.

About 2 400 women (aged 18 - 45) participated in the two OLE studies. There was no placebo group. The studies found that, based on statistical modelling, the Ring reduced the risk of HIV by 31% (HOPE study) and 62% (DREAM study). There were no new safety concerns in these studies.

Adherence to the ring was higher than the Phase 3 trials, over 90%, suggesting that women who knew they were using an active product were more likely to use it. These OLE results suggested that, with increased adherence, there is potential for higher risk reduction.



OLE results suggested that, with increased adherence, there is potential for higher risk reduction

DREAM STUDY

The DREAM OLE study assessed continued safety of and adherence to the Dapivirine Vaginal Ring in healthy, HIV-negative women.



About participants in DREAM Study



It enrolled 941 former participants in The Ring study at six research sites in South Africa and Uganda and provided all with the Ring. Women were followed up for 12 months.

Key study findings

- Adherence to ring use appeared higher in the DREAM study compared to The Ring study.
- The HIV incidence rate was 62% lower for DREAM study participants compared to that of a simulated placebo group – that is, a rate produced by statistical modelling.
- There were no new safety concerns and the safety profile was similar to that of the Phase 3 trials.

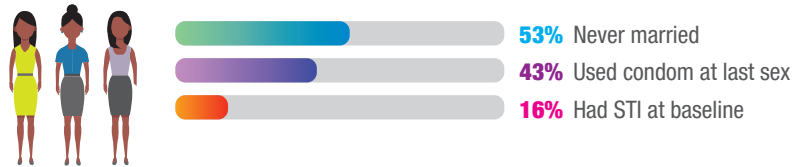


THE HOPE STUDY

The HOPE OLE study assessed the continued safety of and adherence to the Dapivirine Vaginal Ring in healthy, HIV-negative women.

It enrolled 1 456 former participants (average age 32 years) in the ASPIRE study at 15 research sites in South Africa, Uganda, Malawi and Zimbabwe and provided all with the Ring. Women were followed up for 12 months.

About participants in the HOPE study



Key study findings

- Adherence to ring use appeared higher in the HOPE study than in ASPIRE.
- Based on statistical modelling the observed HIV incidence rate was 31% lower than

the estimated incidence in the absence of access to the Ring. There were no new safety concerns in this study and the safety profile was similar to that of phase 3 trials.

OLE study results summary



DREAM

Observed HIV incidence
1.8 per 100 person years
(95% CI: 1.0 - 2.6)

Expected HIV incidence
(Modelled on Ring Study placebo data)
4.7 per 100 person years
(95% CI: 3.4-5.4)



HOPE

Observed HIV incidence
2.7 per 100 person years
(95% CI: 1.9-3.8)

Expected HIV incidence
(Modelled on ASPIRE placebo data)
3.9 per 100 person years
(95% CI: 3.1-4.8)

Safety and adherence

- Favourable safety profile. Similar to phase 3 studies
- Increased adherence. Over 90% in OLEs compared to about 80% in phase 3 studies
- Results suggest women were more likely to use product consistently once they knew it reduced HIV acquisition
- Absence of placebo group in OLEs limits estimation of efficacy. But results show encouraging trend

Additional studies

Despite the extensive clinical research described above, there are still some gaps in information related to use of the Ring. The figure below summarises ongoing research focused on specific categories of women.



THE REACH STUDY

The REACH (Reversing the Epidemic in Africa with Choices in HIV Prevention) study addresses the need for more data on the safety and adherence to use of oral PrEP and Dapivirine Vaginal Ring in young women, aged 16-25 years.

The study is investigating safety and use of the Ring and oral PrEP among 300 young women (16-21 years) in South Africa, Uganda and Zimbabwe.

Start Date: February 2019

Details: Evaluating how adolescent girls and young women use the monthly dapivirine vaginal ring and Truvada® as daily oral PrEP (pre-exposure prophylaxis), and their preferences for either or both approaches or neither, after using each product for six months. In REACH, there are two products: the Ring, which is used for a month at a time, and oral PrEP taken daily. All participants will use each product for six months. Random assignment will determine whether oral PrEP is used for the first six months and then the ring for the following six months, or the ring first and then oral PrEP. After experiencing both approaches, participants will have a choice of using either the ring or oral PrEP – or neither – for an additional six months.

To evaluate the safety of each approach, researchers will conduct medical exams and do laboratory tests of blood, urine and vaginal fluid. To evaluate adherence to and acceptability of oral PrEP and the vaginal ring, participants will answer questions about their use and experience with each product, both on a computer and in face-to-face conversations with site staff.

In-depth interviews and focus group discussions will also help understand what motivates or is challenging about using each product. Objective adherence measures will include detectable drug levels in blood for oral PrEP and residual drug levels in returned rings for the Ring.

The REACH study findings, released in February 2022, showed promising results toward consistent HIV prevention product use in AGYW:

- **Choice:** 67% of participants chose to use the ring and 31% oral PrEP
- **Safety:** No safety concerns were noted for either the ring or oral PrEP
- **Acceptability:** both the ring and oral PrEP were highly acceptable, with ring acceptability at 88.5% and oral PrEP acceptability at 64%
- **Adherence:** the vast majority (97%) of study participants use the ring/oral PrEP some or all of the time. Adherence was higher for both products than had been observed in previous studies.

deliver

A Study of PrEP and the
Dapivirine Ring in Pregnant Women

THE DELIVER STUDY

The DELIVER study addresses the need for more data on the safety and acceptability of oral PrEP and the Dapivirine Vaginal Ring in pregnant women.

Approximately 550 pregnant women are planned to be enrolled in Malawi, South Africa, Uganda and Zimbabwe.

Start Date: February 2020

Details: The study has enrolled women at different times during pregnancy. The women will use either oral PrEP or the Ring until they deliver. Women will be followed up for 6 weeks post-partum and their babies will be followed up for 1 year. The study will measure the effects, if any, this may have on their health.

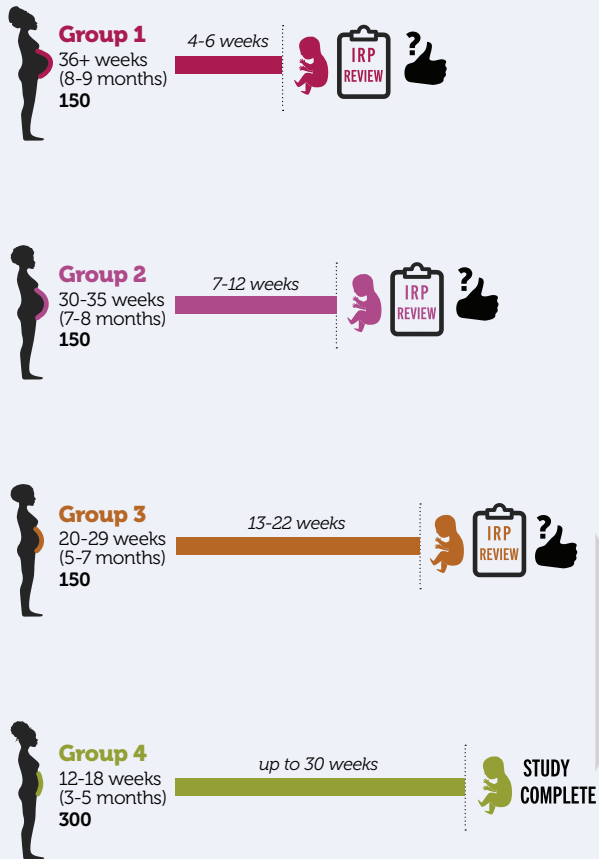
- DELIVER is designed to enroll one group (cohort) of women at a time, beginning with women late in pregnancy (36+ weeks). Cohort two will enroll women from 30 weeks to < 36 weeks gestation and cohort three will enroll women from 12 weeks to < 30 weeks gestation.
- The study will move to the next group only if deemed safe by an independent panel of experts called the Interim Review Panel (IRP), which comprises of experts in paediatrics, obstetrics, gynaecology, nursing, public health, statistics and ethics, from Africa and North America
- Researchers closely monitor participants and note complications during pregnancy, type of delivery and birthweight

The DELIVER study interim findings, released in August 2022, showed promising results toward consistent HIV prevention product use in AGYW:

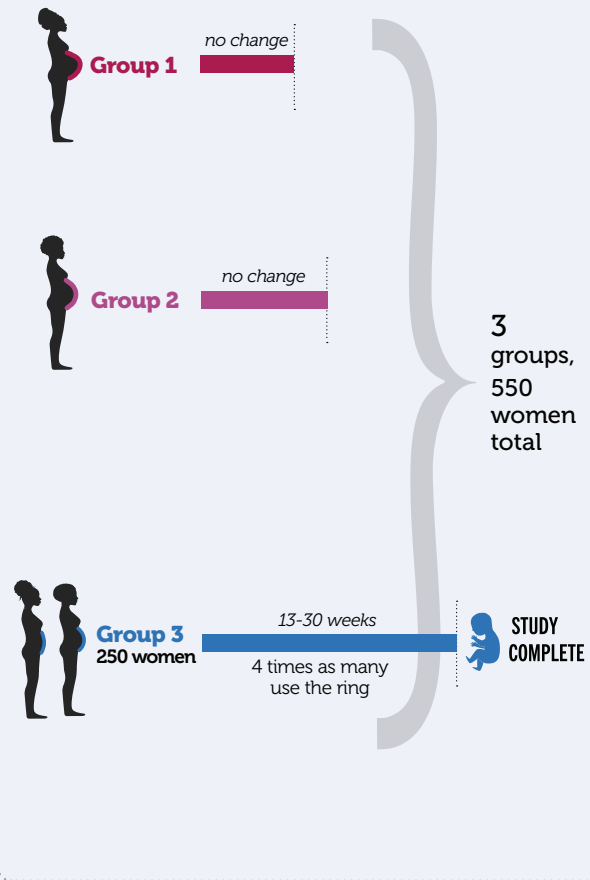
- No safety concerns were found in Cohort 1 = 36+ weeks (8-9 months) pregnant
- The study will now move to Cohort 2 = 30-35+ weeks (7-8 months) pregnant
- Results likely to be available in mid-2022

In July 2021, the study design was modified. The modifications in DELIVER's design would shorten the timeframe for the study's completion and therefore expedite the availability of its final results. Importantly, these changes would not compromise the scientific integrity of the study nor have an impact on the many safety measures already in place

Original Design 4 groups, 750 women total.
In all groups, twice as many use the Ring as oral PrEP.



Modified Design 3 groups, 550 women total.
Twice as many women in groups 1 and 2 use the Ring,
and four times as many women in group 3 use the Ring





THE B-PROTECTED STUDY

The B-Protected study addresses the need for more data on the safety and acceptability of oral PrEP and the Dapivirine Vaginal Ring for breastfeeding women.

The study planned to enroll approximately 200 mother-infant pairs in Malawi, South Africa, Uganda and Zimbabwe.

Start Date: August 2020

Details: The study has enrolled breastfeeding mothers and their 6- to 12-week-old babies. Women will use their assigned product – oral PrEP or the Ring – for three months, with an additional 2 week follow-up. Researchers will assess how much drug from oral PrEP and the Ring passes into breastmilk and how much passes to the baby after breastfeeding, and will measure the effects, if any, this may have on their health.

Interim Findings

First Evaluation of DVR safety during breastfeeding:

- Few SAEs or AEs of Grade 3 or higher occurred among mothers and infants
- Most AEs were mild or moderate, and all infant AEs were unrelated to study product use.

This favorable safety profile and previous data demonstrating low drug transfer to breastmilk support updates of WHO and

national guidelines to include breastfeeding people when recommending the DVR as an HIV prevention choice.

Increased risks of HIV acquisition postnatally and of HIV transmission to infants with incident HIV infection during breastfeeding are ethical and scientific rationales to improve access for breastfeeding people to safe and effective HIV prevention methods such as the DVR



Key takeaways from this module

- The Ring has undergone extensive research in respect of its safety, tolerability to users and efficacy in reducing the risk of HIV infection.
- The Ring has a favourable safety profile and was well tolerated by a great majority of study participants. No laboratory safety monitoring is needed apart from regular HIV testing and pregnancy testing when indicated.
- Studies have shown that the ring is safe to use with STI treatment, condoms, tampons and ring use does not affect menses.
- The efficacy of the Ring was tested in two large randomised, double-blind, placebo-controlled trials involving thousands of women in several African countries. The Ring study and the ASPIRE study both indicated that the Ring reduced the rate of HIV infection among women who used it – but it did not totally eliminate the risk of getting HIV.
- OLE studies following the Ring study and ASPIRE showed a higher rate of use of the Ring among participants and statistical modelling (in the absence of a placebo group for purposes of comparison) suggested that the reduction in HIV infections was greater in the OLE studies than in previous trials.
- There are current ongoing studies to address areas where more data is needed, such as ring use in adolescent girls and young women (REACH study), and pregnant and breastfeeding women (DELIVER/B-PROTECTED Study)
- The Ring reduces the risk of HIV infection only in respect of transmission during vaginal sex. It does not protect against other STIs or prevent pregnancy. Ideally, it should be used in combination with other safer sex practices.
- Research has established that the Ring is easy for women to insert and is seldom felt during sex. It therefore offers a discreet, self-controlled, long-term option for women – particularly those living in areas where HIV is very prevalent.

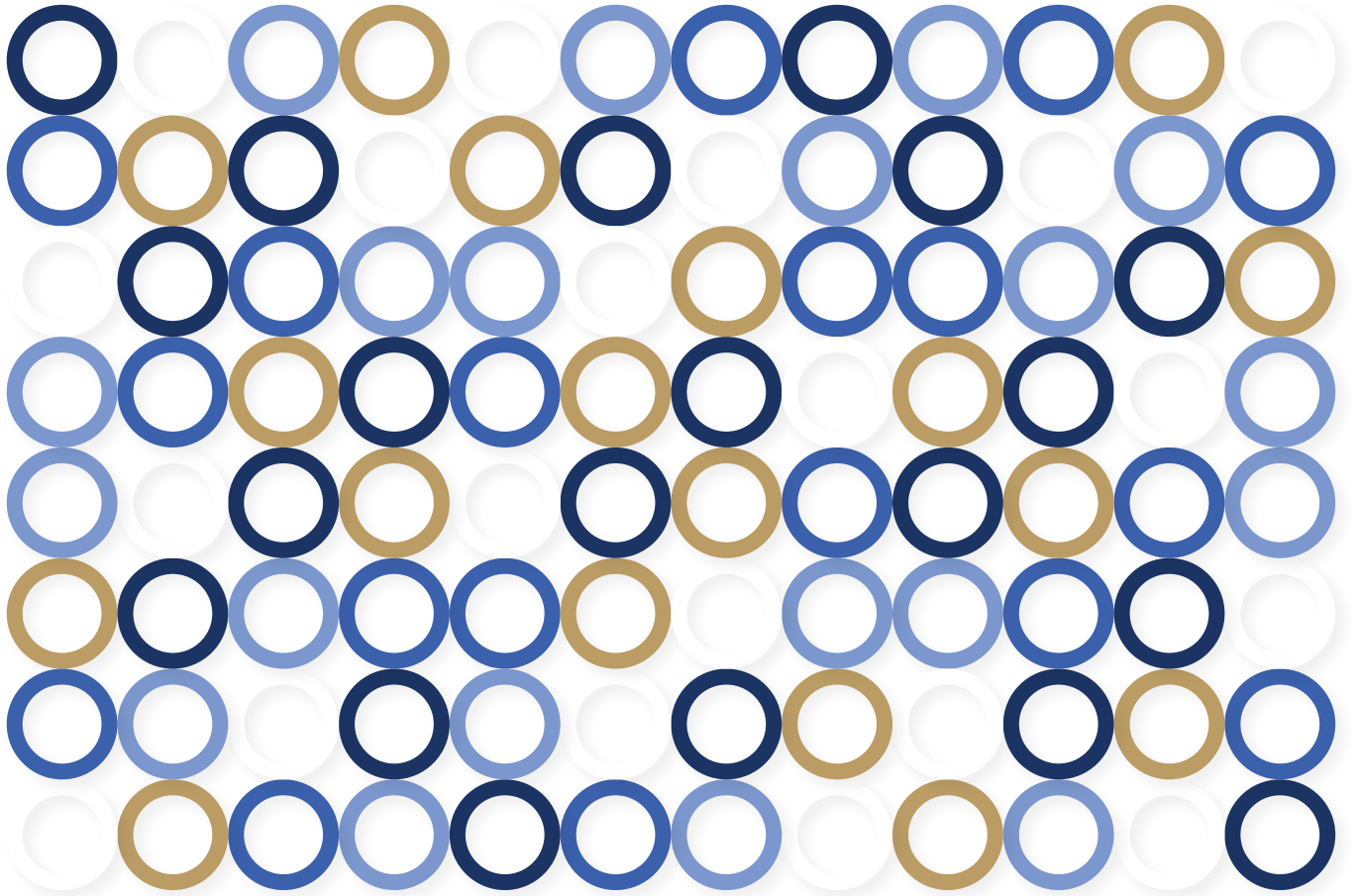
Tools to go with this Module:

RESEARCH ON THE RING TOOL 4

	Phase III	Open-Label	Additional Research	
	ASPIRE	MOSE	MOSAIC	DELIBER
Purpose	Define cost-effectiveness of the DSR in adult women	Long-term safety and effectiveness of the DSR in adult women	Safety and effectiveness in use of ASP and DSR in young women	Safety and acceptability of ASP and DSR in pregnant women
Locations	Mexico, South Africa, Uganda and Dominican Republic	Uganda, Dominican Republic	Mexico, South Africa, Uganda and Dominican Republic	
Sample Size	~4,000 women Group 1B - 60 young pregnant women Group 1C - 60 young pregnant women All women randomized to receive either the active DSR or placebo ring	2,000 women Phase II participants recruited Aug 2011 (no placebo group)	247 young women (ages 16-21) were enrolled	600 women Group 1: 100 were pregnant Group 2: 100 were not pregnant Group 3: 200 were ages 11-30 were pregnant
Risk Reduction	82%	27%	82%	91%
Safety	No safety concerns	No safety concerns	No safety concerns	No safety concerns in Group 1. Study not completed in most group
Adherence	Around 80% of participants used the DSR at most times of the year	Over 80% of participants used the DSR at most times of the year	87% of participants chose to use the ring. 82% of participants from the ring in use consistently. 88% of study participants used the ring most or all of the time. Adherence was higher than that from observed pillbox studies.	On-going study

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 4



Module Two

Providing the Ring – the Basics

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About this training manual

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Each module in the manual is designed to be used either independently or as part of the full pack. Each module has a set of suggested tools which are pull outs at the end of the manual.

Attribution and Citation

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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This guide was supported by the LEADING (Licensure and Ensuring Access to the Dapivirine Ring) Project (Cooperative Agreement Number: AID-OAA-A-17-00013).

INTRODUCTION

Although access to daily oral pre-exposure prophylaxis (oral PrEP) is increasing around the world, a daily pill may not work for everyone. The dapivirine vaginal ring (DVR or the Ring) is the first long-acting, woman-controlled option available for use within a comprehensive HIV prevention approach.

The flexible silicone vaginal ring is discreet and does not interfere with sex. It slowly releases the antiretroviral drug (ARV), dapivirine, directly into the vagina over 1 month and has limited systemic absorption. Efficacy data shows that the ring reduces HIV risk by about 30%.

Systemic absorption:

Systemic drug therapy involves treatment that affects the body as a whole or that acts specifically on systems that involve the entire body, such as the cardiovascular, respiratory, gastrointestinal, or nervous systems. Mental disorders also are treated systemically.

<https://www.britannica.com/science/systemic-drug-therap>

Even a partially effective prevention option – such as the Ring – can have an important protective impact for women and their communities as part of a comprehensive HIV prevention strategy. The Ring could fill an important gap with a long acting prevention method for women who are unable or choose not to use higher-efficacy products like daily oral PrEP.

The Ring has been approved and recommended by the World Health Organization.

WHO IS THE RING INTENDED FOR?

WHO recommends the Dapivirine Vaginal Ring as an additional choice, that is, as an option on a “menu” of preventive products, that should be offered to women who are unable or choose not to use oral PrEP, along with complete information so they can make an informed choice.

The Ring should be considered as part of combination prevention for all cis-gender women, aged 18 years and older, who are HIV-negative and are at significant risk of acquiring HIV infection.

Important points to note:

- Women in situations that elevate HIV risk: The Ring is expected to provide protection from HIV acquired during vaginal sex only. There is no protection offered during anal sex or injecting drug use.
- Adolescent girls and young women (AGYW): The data from phase 3 clinical trials of the Ring were not able to demonstrate efficacy among women younger than 21 years and adherence to Ring use was relatively low in this age group. More data are needed to understand Ring use among younger women¹. Additional counselling should be provided if a young woman chooses the Ring as a prevention option.
- The Ring is a convenient additional HIV-prevention option for sex workers because it places little burden on the user. It is discreet, does not require special storage conditions, and women can insert the Ring themselves without a health care provider’s assistance. Adding the Ring to the prevention options for sex workers could strengthen their self-efficacy and autonomy, and improve their overall engagement with their health.

Contraindications

The Ring should not be provided to women who:

- Are living with HIV or show evidence of possible acute infection (possible symptoms: fever, swollen glands, sore throat, oral ulcers or thrush, weight loss, tiredness, body aches, vomiting, rash).
- Have an STI or other vaginal infection. Genital infections must be treated prior to supplying the Ring.
- Are unwilling or unable to use the Ring continuously for a period of one month.

Caution should be exercised when considering the simultaneous use of the Ring and vaginally administered clotrimazole or miconazole for treatment of vaginal candidiasis. The progression of the candidiasis should be monitored

in case the efficacy of the antifungals is affected. It means that prescriber should be observant for any issues which might arise if used concurrently and consider if there are alternatives available for treatment of candidiasis. Monitor that treatment for candidiasis was effective and reinforce need for condom usage if engaging in sexual activity during concurrent use.

The Ring should be offered only after comprehensive counselling on safer sex practices and a discussion with each woman on the HIV prevention method(s) to enable her to choose the safest and most effective method that she will adhere to and that meets her individual needs.

Side effects

The following side effects were observed during clinical trials: Urinary tract infections, vaginal discharge or itching, pelvic or lower abdominal pain. Side effects were generally mild to moderate and resolved with no interruption in Ring use.



Safer conception, pregnancy, and breastfeeding

The Ring does not have contraceptive properties; it does not prevent pregnancy. If a woman who has opted for the Ring does not wish to become pregnant, she will require counselling on the use of a contraceptive method that works in conjunction with the Ring. This is described in further detail in the section on contraception below.

Safer conception: Pregnancy is associated with higher rates of HIV acquisition. HIV-negative women whose partners are living with HIV are often at risk of acquiring HIV infection when trying to become pregnant. Even if a woman is using the Ring, she should be advised to ensure that her partner is on ART and virally suppressed for a period (ideally six months) before the couple attempts to conceive.

Pregnancy, and breastfeeding: Safe use of the Ring during pregnancy and breastfeeding has not been established. Any woman opting for the Ring must be counselled to inform a

healthcare practitioner immediately in event of pregnancy to discuss continued use of the Ring. The healthcare practitioner should follow country guidelines and use clinical judgment in deciding whether to recommend continued use of the Ring. Factors to be considered include the risk of the woman acquiring HIV during pregnancy and possible transmission to the unborn or breastfed child.

It has been shown that dapivirine is excreted in human breastmilk in low concentrations. Infant exposure is expected to be low – that is, less than 1µg /day.²

Risk discussions and choice

When a client seeks an HIV-prevention service, it is important to have a conversation that explores effective protection in relation to the present risk of HIV. Prevention is user-driven, and the health practitioner can assist each woman to develop a complete understanding of the HIV risk present in her circumstances and the prevention options available. In this discussion it is important to note:



- The Ring alone is not fully effective in protecting against HIV. In phase 3 clinical trials it provided about 30% reduction in the rate of HIV acquisition.
- The Ring is only effective in reducing the risk of HIV acquisition during vaginal intercourse. It is important that women know the Ring does not provide any protection during anal intercourse.
- The Ring should always be used with condoms, if this is possible.

2 Refer to B-Protected Study in Module 1B

Available biomedical HIV prevention options

The following table provides an overview of the characteristics and attributes of both the Ring and oral PrEP to assist a client in making an informed choice.

Neither oral PrEP nor the Ring is a perfect HIV prevention solution. But both products expand our choices and increase the likelihood of suiting individual needs – which should translate to higher use of the selected product.

		
	The Ring	Oral PrEP (TDF/FTC)
Drug	Dapivirine	Tenofovir and emtricitabine
Frequency of use	Monthly vaginal ring	Daily oral pill
Intended user	Specifically for women	For women and men
Degree of efficacy	About 30% reduction in HIV infection (clinical trials)	*90% reduction in HIV infection
Sexual activity protected	Vaginal sex only	Oral, vaginal and anal sex
HIV testing requirement	Every three months	Every three months
Other testing requirements	No	Creatinine clearance tests
Drug distribution	Localized	Systemic
Pregnancy protection	No	No
Other STI protection	No	No
Prevents HIV from injection drug use	No	Yes

* at optimal adherence (daily dosing). Efficacy in clinical trials has been variable, especially in women, and has been linked to adherence. Refer to the following article for more information: O Murchu E, Marshall L, Teijeir C, *et al.* Oral pre-exposure prophylaxis (PrEP) to prevent HIV: a systematic review and meta-analysis of clinical effectiveness, safety, adherence and risk compensation in all populations. *BMJ Open* 2022;12:e048478. doi:10.1136/bmjopen-2020-048478

Effective use of the Ring

Risk reduction is correlated with correct use of the Ring.

This involves:

- Using the Ring continuously over the period of one month.
- Immediately inserting a new Ring at the end of each month.
- Keeping the Ring in before, during and after vaginal intercourse.
- Keeping the Ring in during menstruation.
- The Ring can be used with male or female condoms, and both the Ring and a condom should be used during vaginal sex.

Choosing the Ring

Prior to prescribing the Ring for initial use, the user must have a negative HIV test result, in accordance with local testing guidelines.

The healthcare provider will show the woman how to insert the Ring which only begins to protect against HIV **24 hours** after it is inserted.

The Ring needs to be worn continuously for **1 month**. It should be removed **1 month after the day** it was inserted. A new Ring is inserted **immediately** after the previous

ring is removed. This is to ensure that there is always the **right amount** of dapivirine in the vagina to block HIV.

If the Ring is in for longer than 1 month the level of protection is unknown and if there would be unexpected side effects. The Ring was designed to be used for 1 month.

Additional points to note

- Contact with blood or vaginal fluids may change the colour of the Ring during use. This does not affect the Ring's ability to reduce HIV infection.
- If the user takes the Ring out, she is no longer protected from HIV infection.
- A pap smear is not needed to start using the Ring.

THE RING AND CONTRACEPTION

As already noted, the Dapivirine Vaginal Ring does not protect against pregnancy. It can be used with some forms of contraception but not with others.

The Ring can be used with:

- Male and female condoms
- Oral contraception
- IUD
- Contraceptive implants
- Hormonal injections.

The Ring should not be used with:

- Contraceptive vaginal rings
- Diaphragms.

Disclosure

The Ring is the first woman-controlled, long-acting HIV prevention option that can be used discreetly. The implication of this is that women who use the Ring have no need to disclose this to their partner, if that is their preference.

FREQUENTLY ASKED QUESTIONS

Healthcare providers are likely to receive many questions from women who are interested in the Dapivirine Vaginal Ring. The following list of questions is intended to prepare providers to answer these in simple, direct language.

Is the Ring an option for me?

The Ring could certainly be an option for you if:

- You are HIV-negative
- You are in a situation where you feel you need to protect yourself from HIV
- You have tried oral PrEP but feel oral PrEP is not for you. For example, do you struggle to take a daily pill?

Is the Ring easy to insert and use?

Yes. A woman can insert the Ring easily herself and she can remove and replace it herself each month.

Can women feel the Ring once it's inserted?

In studies that have been done, a large majority of women said the Ring was comfortable and they could not feel it once it had been inserted and left in place.

How safe is the Ring and does it have side-effects?

There have been no safety concerns in any of the studies done on the Ring to date.

There are sometimes side-effects such as urinary tract infection, vaginal discharge and itching. These have been mild to moderate and went away quickly without the affected women having to interrupt their use of the Ring.

How long after insertion is the Ring effective?

The Ring must be in place for at least 24 hours before it will begin to protect against HIV.

Should I worry about drug resistance?

Information from studies on the Ring show no clear evidence that use of the Ring can lead to resistance to dapivirine or other ARVs in the same class as dapivirine, which are used in some HIV treatment regimens.

Does the Ring work for anal sex?

No. The Ring is only effective for vaginal sex.

Can the Ring get lost inside me?

No. The Ring cannot be pushed up too far or get lost in the body.

Will using the Ring affect my sex life?

In studies, the majority of women reported that the Ring does not negatively impact the sexual experience for either partner. Some women reported that the Ring increased sexual pleasure for them and their male partners partly because it reduced their anxiety about HIV.

Should I remove the Ring before sex?

No. It is important to keep the Ring in during sex in order for it to reduce your chances of getting HIV during (male to female) vaginal sex. It is possible that your partner may feel the Ring during sex, although this is infrequently reported. The Ring will not harm you or your partner and is unlikely to affect enjoyment of sex.

Can the Ring get stuck on the penis during sex?

No. The Ring sits high up in the vagina near the cervix (the “neck” joining the vagina and the womb) and cannot become stuck on the penis during sex.

Can I stop using condoms once the Ring is in?

We encourage you to continue using condoms. Remember the Ring offers partial protection from HIV and does not prevent pregnancy or other STIs. It also does not provide protection against HIV during anal sex. Currently, condoms and oral PrEP are the only methods available to prevent HIV transmission during anal sex as well as vaginal sex. Condoms are currently the only product that can prevent HIV, other STIs and pregnancy

Can I use the Ring with contraception/birth control?

Yes. The Ring can be used with most forms of contraception, including male and female condoms, oral contraception, hormonal injections, IUD and implants. It does not have any effect on these forms of contraception. But the Ring should not be used with contraceptive vaginal rings or diaphragms.

Can I use tampons with the Ring?

Yes. Tampons can be used with the Ring. The Ring should be in the vagina before inserting a tampon. Be careful when removing the tampon, in case the Ring is accidentally pulled out. If this occurs, immediately reinsert the Ring.

Should I remove the Ring during my period?

No. It is safe to use the Ring during menstruation. The Ring should remain in the vagina during your period to reduce your chances of getting HIV.

Will the Ring stay in when I go to the toilet?

It's okay to use the toilet when the Ring is inside you. It is uncommon for the Ring to fall out during urination or a bowel movement. To be sure, get into the habit of checking the toilet bowl. If the Ring has fallen into the toilet, insert a new Ring.

Can I use products to cleanse my vagina while using the Ring?

No. Cleaning the inside of the vagina with soap or other products may cause harm and may affect the ability of the Ring to reduce the risk of HIV infection. The vagina is self-cleansing, but if you want to clean it you should only use clean water.

When should I consult my Healthcare Provider if I have problems that could be linked to the Ring?

Contact your clinic/doctor immediately if you experience:

- Pain/severe pain in your lower belly.
- A discharge, with unpleasant smell, from your vagina.
- Pain or bleeding during sex.
- Fever, sometimes with chills.
- Pain or difficulty in emptying your bladder.
- Nausea and vomiting, with an inability to keep food or water down.


Key takeaways from this module:

The Ring:

- Is a new HIV-prevention choice, approved and recommended by the WHO.
 - Is for use by cis-gender women, aged 18 and older, who are HIV-negative.
 - Should be offered only after:
 - Comprehensive counselling on safer sex practices.
 - Discussion on the safest and most effective HIV-prevention option for the individual and the most likely to be used consistently.
 - Provides partial protection against HIV infection.
 - Does not prevent pregnancy.
 - Does not prevent STIs.
 - Is only effective during vaginal intercourse and does not protect during anal intercourse.
 - Can be discreetly used without the knowledge or consent of a sexual partner, if this is preferred.
 - Should always be used with condoms, if possible.
 - Must be in place for at least 24 hours before it will begin to protect against HIV.
 - Must be worn for 1 month and then replaced immediately with a new Ring.
- The Ring fills a critical gap in the HIV-prevention portfolio by expanding women's options with a long-acting product they can choose to use on their own terms:
- Condoms are highly effective but are not feasible for some women.
 - Oral PrEP is highly effective but some persistence and adherence challenges have been seen.
 - The Ring is modestly effective but has the benefit of being a long-acting option with minimal side effects.

Tools to go with this Module

THE RING
TOOL 1



A discreet, safe, female controlled, vaginal HIV prevention option.

General Info:

- A discreet, safe, female controlled, vaginal HIV prevention option.
- The Ring provides up to 90 days of protection against HIV when the ring is used consistently as instructed.

Key features:

- When the Ring is inserted, it is safe, and more one of
- There is no need to remove the Ring after menstruation. It can even be used with a tampon.
- You can still use tampons with the Ring in – it will not fall out.

Key benefits:

- The Ring can be inserted on any day of your cycle – whether you are pregnant or not.
- The Ring does not prevent against other STIs.

INTERNATIONAL PATENT OFFICE FOR MICROBIOIDES

Tool 1

VIDEO ON HOW THE RING WORKS
TOOL 2

Video:
How to use the DVR



vimeo
Microbicides.com/219623

INTERNATIONAL PATENT OFFICE FOR MICROBIOIDES

Tool 2

THE DAPIVRINE VAGINAL RING INSERTION GUIDE
TOOL 5



How the ring works

Depixone vaginal insert (DVI) is a flexible, soft ring that is inserted into the vagina to provide up to 90 days of protection against HIV when used consistently as instructed.

Depixone vaginal insert (DVI) is a flexible, soft ring that is inserted into the vagina to provide up to 90 days of protection against HIV when used consistently as instructed.

It is important that the ring is left in place for the full 90 days to receive the full benefit of protection.

INTERNATIONAL PATENT OFFICE FOR MICROBIOIDES

Tool 5

FAQ SHEET
TOOL 8

1. What is the Dapivirine ring?
The ring is made of flexible silicone with the HIV drug dapivirine dispersed uniformly throughout its matrix. The ring releases the drug slowly, in the vagina over the course of 90 days with two reservoirs embedded in the ring, which helps to maintain both effects and reduce the risk of the development of HIV resistance.

2. How effective is the dapivirine ring?
In early, consistency and correctly, the ring has been shown to provide up to 90% protection from HIV during regular use. It is not a substitute for other HIV prevention methods such as condoms.

3. In the ring easy to insert and use?
Yes, it is easy to insert. The ring is soft and flexible and will not break. It is easy to use.

4. How long do I wear the ring?
The ring needs to be replaced every 90 days and should be replaced with a new ring.

5. How long does the ring need to be in place before it is effective?
The ring needs to be in place for 24 hours before it is effective. It is important to insert the ring before it is effective. It is important to insert the ring before it is effective.

INTERNATIONAL PATENT OFFICE FOR MICROBIOIDES

Tool 8

DAPIVRINE VAGINAL RING END USER GUIDE
TOOL 11

DAPIVRINE VAGINAL RING
Dapivirine Vaginal Ring – A Guide for Users

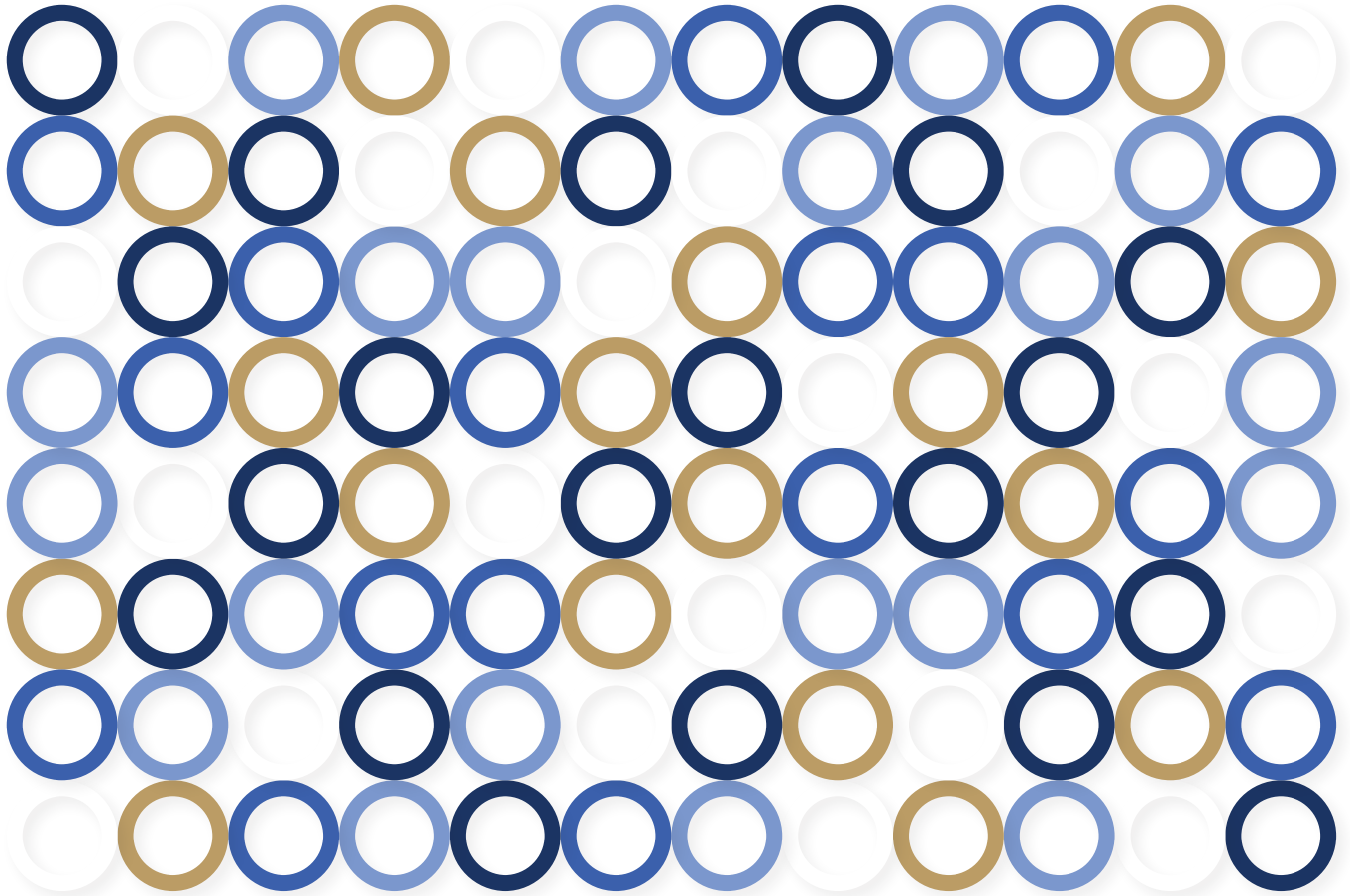
- The ring is for regular use only.
- A new flexible ring should be used every 90 days or when other used to keep in mind.
- The ring reduces the chance of a woman getting a HIV-1 infection during regular use.
- The ring should be used with a condom.
- The ring does not protect a user from getting HIV-1 infection.
- Women must use the ring consistently and replace it each month with a new ring.

INSTRUCTIONS FOR RING INSERTION

1. Wash your hands in clean water and dry them.
2. Check the expiry date on the package label. Do not use the ring if the expiry date has expired.
3. The package is made of plastic. Do not use scissors to open the package. It is a hard plastic. Remove the ring from the package.

INTERNATIONAL PATENT OFFICE FOR MICROBIOIDES

Tool 11



Module Three

Meeting the HIV-Prevention Needs of Diverse User Groups

Contents

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Defining User Groups.....	2
The Ring as an option for key and vulnerable populations	6

About this training manual

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INTRODUCTION

In every country where data are reliably collected and reported, it is evident that at-risk and vulnerable populations have a higher incidence of HIV than the general population. These populations often have lower access to HIV-related services, including prevention interventions.

They usually encounter significant structural and behavioral barriers to exercising their health rights. These barriers include gender inequality in relation to provision of healthcare, limited access to empowering health information, and being subjected to stigma and discrimination, including negative responses among service providers.

Not only do populations at increased risk have an inherent right to healthcare, but a sustainable HIV response will not be achieved without realising this right. In most countries with generalised HIV epidemics, the response has focused almost exclusively on the general population. Even countries that recognise HIV epidemics are concentrated in vulnerable populations often face challenges implementing interventions that reach those most in need.

This module explores how the Ring, as a woman-controlled product, may enhance the prevention options of women whose

circumstances increase their risk of acquiring HIV. These women are quite diverse and include sex workers, adolescent girls and young women (AGYW), women whose partners are living with HIV, women with multiple partners or whose partners have multiple partners, transgender people (who have vaginal sex), pregnant women, and women who are trying to conceive.

The Ring is not restricted to these key populations, it is for anyone who has a self-perceived risk of HIV. That could include women in the general population, post-menopausal women, married women, etc.

Note Module Three adapted from: The Global Fund, Technical Brief: Addressing sex workers, men who have sex with men, transgender people, people who use drugs, and people in prison and other closed settings in the context of the HIV epidemic. January 2017; WHO. Consolidated Guidelines on HIV Prevention, Diagnosis, Treatment, and Care for Key Populations, July 2014.

DEFINING USER GROUPS

Populations with a higher-than-average incidence of HIV are often clustered into two categories:

Key populations are groups that have a high risk and disproportionate burden of HIV in all epidemic settings. They frequently face legal and social challenges that increase their vulnerability to HIV, including barriers to accessing HIV prevention, treatment and other health and social services.

Vulnerable populations are groups of people that are vulnerable to HIV infection in certain situations or contexts. They may also face social and legal barriers to accessing HIV prevention and treatment. These populations are not affected by HIV uniformly in all countries. Vulnerable populations may overlap with key populations.

Each country should define the specific populations that are vulnerable and key to its epidemic and response, based on the epidemiological data and social context.

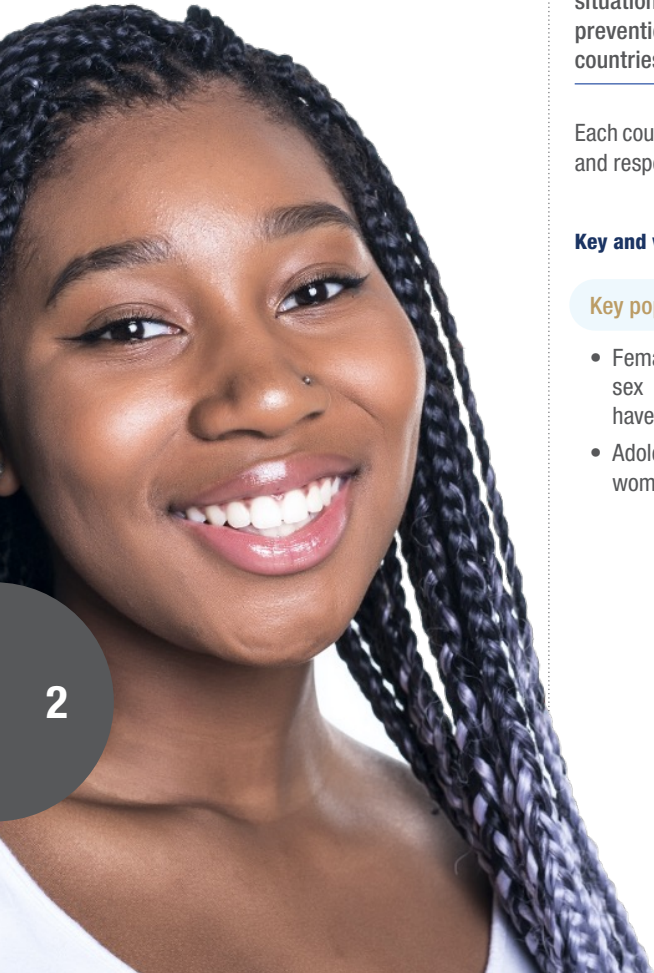
Key and vulnerable populations of women

Key populations

- Female or transgender sex workers (those who have vaginal sex)
- Adolescent girls and young women (AGYW)

Vulnerable populations

- Adolescent girls and young women (AGYW)
- Women in sero-discordant relationships
- Women trying to conceive



Female and Transgender Sex Workers

Globally, sex workers are 13 times more at risk of HIV than the general population and account for 9% of the total number of new HIV infections. Sex workers have significant economic vulnerability and experience marginalisation, criminalisation and high rates of violence.

Most sex workers have high numbers of sexual partners. This does not necessarily increase their likelihood of becoming infected with HIV. The critical risk-factor is whether they are able to use HIV prevention options, i.e. oral PrEP and condoms consistently and correctly. The reality is that many sex workers are powerless to negotiate condom use.

The stigma that sex workers encounter may restrict their access to health, legal and social services. Often they are afraid to seek these

services for fear of discrimination or they are defeated by structural factors associated with the services – such as the location and hours of service.

Sex work is diverse and occurs in various contexts around the world. Some sex workers sell sex through brothels or other venues, while others work independently, soliciting clients directly in public places or online.

WHO IS A SEX WORKER?

- Sex workers are adults – male, female, and transgender – who receive money or goods in exchange for sexual services, either regularly or occasionally.
- Payment for sex with anyone younger than 18 years is considered sexual exploitation.
- Sex workers may or may not “self-disclose” that they are sex workers
- Sex work is consensual and can take many forms. Practices vary among and within countries and communities. (Please note: Non-consensual sex work is considered human trafficking and should be reported to the proper authorities immediately).
- Sex work varies in the degree to which it is organised or formalised and locations for sex work also vary.

In eastern and southern Africa, HIV prevalence among female sex workers is extremely high. In eSwatini, Lesotho, Malawi, South Africa and Zimbabwe more than 50% of sex workers are living with HIV.

(UNAIDS 2018)

UNAIDS DEFINITIONS

ADOLESCENTS:
persons aged
10 - 19 years

YOUTH:
persons aged
15 - 24 years

YOUNG PEOPLE:
persons aged
10 - 24 years

Adolescent girls and young women

AGYW continue to be disproportionately affected by HIV. In sub-Saharan Africa, AGYW comprised 10% of the population but accounted for 63% of new HIV infections in 2020.

Adolescence is a period of complex changes, encompassing rapid physical growth and emotional and psychological growth. This is when sexuality becomes a central concern and young people start experimenting and exploring their independence.

It is important to acknowledge the adolescent is no longer a child, but is not yet an adult. Adolescence is a time of opportunity in terms of establishing healthy behaviours. Healthcare providers need to be non-judgemental, responsive to the needs of AGYW and provide counselling and information in relation to sexual and reproductive health and HIV.

There are sexual and relationship patterns present to varying degrees among AGYW that increase the risk of HIV in this population.

These include:

- Not using condoms consistently and correctly: The most common mode of HIV transmission for AGYW is condomless sex. Condom use in this group is low across much of the world.
- Early sexual debut: In many countries, it is common for young people to become sexually active by early adolescence.
- Older partners: Intergenerational sex (between AGYW and men at least five years older than them) is common in many parts of the world.
- Lack of access to healthcare: In many countries, sexual and reproductive health (SRH) and HIV services are intended primarily for married women with children and do not meet the needs of AGYW.

Women in sero-discordant relationships and women trying to conceive

A woman in a sero-discordant (also known as serodifferent) relationship is HIV-negative while her partner is HIV-positive. The WHO guidelines recommend that the HIV-positive partner be virally suppressed with antiretroviral therapy to prevent their partner from becoming infected with HIV. Focus on the prevention of HIV within these couples remains a critical consideration. Choices for prevention are expanding for serodiscordant couples, but their effectiveness may depend on couples' ability to take coordinated action regarding uptake and adherence.

Both HIV-negative and HIV-positive women should be supported to try to conceive if they want to do so. Health professionals should provide the appropriate guidance for safer conception and pregnancy while maximizing efforts to prevent HIV transmission to partners and infants. For couples who want to conceive while one or both partners have HIV, expert consultation is recommended so that approaches can be tailored to their specific needs.

Transgender populations

The term transgender refers to people whose gender identity and expression are different to social expectations of their biological sex at birth. They may see themselves as male, female, gender non-conformist, or one of a spectrum other genders. Transgender people have diverse sexual orientation and behaviours.

Transgender people are one of the groups most affected by the HIV epidemic and are 49 times more likely to be living with HIV than the general population. Generally, HIV prevalence among transgender women (people who are assigned male at birth but identify as being women) is higher than transgender men (people who are assigned female at birth but identify as being men).

Key populations are groups that have a high risk and disproportionate burden of HIV in all epidemic settings.

Vulnerable populations are groups of people that are vulnerable to HIV infection in certain situations or contexts.

THE RING AS AN OPTION FOR KEY AND VULNERABLE POPULATIONS

Sex workers and the Ring

Global evidence points to community empowerment as a successful approach to HIV-prevention programmes for sex workers. Addressing the underlying social and structural factors that make sex workers vulnerable to HIV and creating an environment where sex workers are able to access HIV services easily, is a major step towards ending the HIV epidemic.

Globally, access to HIV prevention services for sex workers is low despite the exceptionally high incidence of HIV among them.

Combination HIV prevention is central to addressing the high risk of HIV that sex workers face, as is integration of HIV programmes with other essential health services, such as sexual and reproductive healthcare and maternal health services. Condom availability and promotion remains a pillar of prevention for sex workers, yet many sex workers find themselves unable to demand condom use from their clients. Additionally, oral PrEP services are increasing across many countries, yet the effective use of a daily pill has

its challenges and may not be the preferred method of HIV prevention.

HIV prevention programmes for sex workers must take realistic account of the risks they face and the context in which they work.

The Ring is a convenient additional HIV-prevention option for sex workers during vaginal sex because it places little burden on the user. It is discreet, does not require special storage conditions, and women can insert the Ring themselves without a health care provider's assistance. Adding the Ring to the prevention options for sex workers could strengthen their self-efficacy and autonomy, and improve their overall engagement with their health.

AGYW and the Ring

Until now AGYW have relied on condoms, oral pre-exposure prophylaxis (oral PrEP) and post-exposure prophylaxis (PEP) for HIV prevention. These methods have several limitations with regard to access, uptake and consistent use.

Based on evidence from the rollout of oral PrEP in many countries, AGYW struggle to sustain regular use of a daily pill, and show high drop-off rates in the first few months of use. This may be due to variety of reasons, including side effects, the difficulty of taking a pill every day, and the stigma of relying on an ARV pill for prevention.

For those young women for whom oral PrEP is not a preferred method (by choice or circumstance) of HIV prevention, the Ring is another option to reduce the risk of getting HIV. Logically the Ring would seem to address

many issues that AGYW may have with other methods.

It is discreet, long-acting and has minimal side effects. It is woman-centred and controlled. However, studies have shown low uptake of and adherence to the Ring among women age 18 - 25 years. Providers should take this into consideration when considering the Ring for young women. AGYW are likely to need more adherence support and more frequent contact with healthcare providers in order to achieve effective use and long-term adherence.

Women in sero-discordant relationships and the Ring

A sero-discordant relationship is one where one partner – in this case, the woman – is HIV-negative and the partner is living with HIV. To reduce the risk of HIV transmission, it is important for both partners to take preventive measures.

There are a number of ways to do this: treatment as prevention (TasP), condoms, and PrEP.

A woman may know her partner's HIV status but not know how adherent he is to his

treatment programme. This may leave her feeling anxious and at risk. The Ring provides her with a woman-controlled option for HIV prevention that will reduce her chances of acquiring HIV and give her a greater sense of security.

About TasP

There is clear evidence that HIV-positive individuals on effective antiretroviral treatment (ART) who have an undetectable viral load cannot transmit HIV to others.

Transgender populations and the Ring

Transgender men who have not undergone gender-affirming genital surgery can use the Ring, regardless of whether they are using gender-affirming hormones; however, because there have been no studies of the Ring's use among this population, the product's acceptability and comfort among them are unknown.

There have been no studies of the Ring's use in people with neovaginas (in women who were born men), so its efficacy, safety, side effects, acceptability, and comfort among these populations are unknown. We encourage transgender women with neovaginas to consider oral PrEP if they are able to use it consistently, especially for those who engage in both vaginal and anal sex since oral PrEP covers both routes of HIV transmission.

Pregnancy, breastfeeding, and the Ring

During pregnancy and breastfeeding women are up to four times more likely to acquire HIV. Many women are pregnant or breastfeeding for a significant portion of their reproductive years and therefore this elevated risk of getting HIV is prolonged. Furthermore, during periods when they are trying conceive couples are unable or choose not to use condoms. Women need reliable HIV-prevention methods during the period leading to conception and throughout pregnancy and breastfeeding so that they know they are safe and can protect their babies.

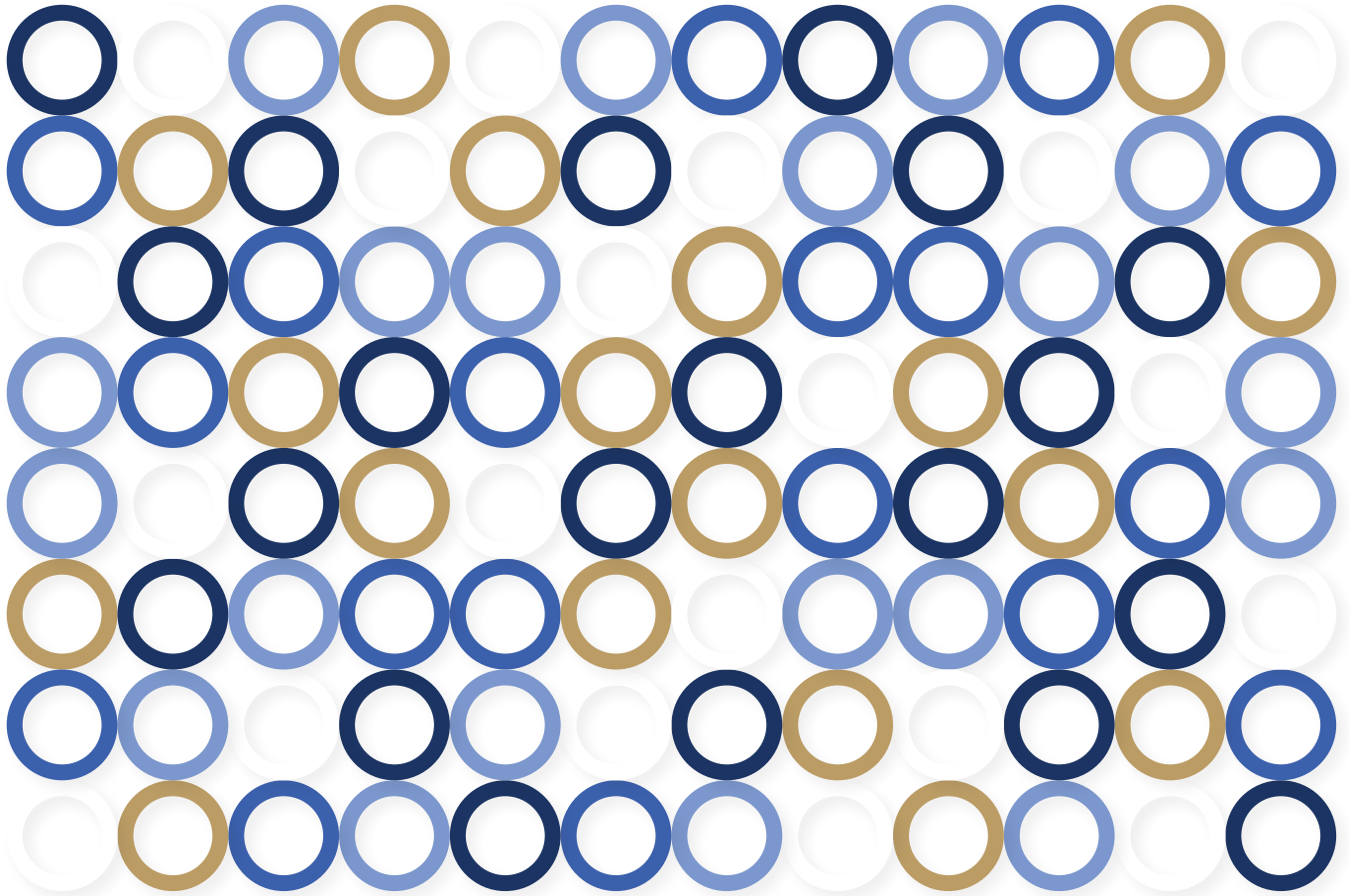
Currently there is insufficient data on the use of the Ring in pregnant and/or breastfeeding women. Although safety has not been established in pregnancy or during breastfeeding, the benefits of the Ring should be considered for pregnant or breastfeeding women at high risk of HIV infection, taking account the subsequent risk of the baby acquiring HIV. Providers should defer to their country guidelines in regards to offering the Ring to pregnant women. For more information on ongoing Ring studies conducted during pregnancy and breastfeeding refer to Module 2

Providing health services to key and vulnerable populations

- Ensure care to all clients is respectful and non-judgemental. Listen to your clients, do not stigmatize their sexual identity, behaviour, or choices.
- Provide a detailed risk discussion while reviewing options for prevention.
- Non-traditional service provision, i.e. outreach, the use of peer educators, flexible hours and locations, will increase the reach to vulnerable populations.
- Integrate HIV prevention services into SRH and maternal health services.
- When providing services to key and vulnerable populations, particularly youth, consider issues relating to access, quality of care and communication. Providing confidential, non-judgmental services is of utmost importance to AGYW.

Key Takeaways from this Module:

- There are identifiable populations that have been shown to be at higher risk of contracting HIV than the general population.
- Female populations with significantly higher HIV incidence include sex workers, AGYW, transgender people, pregnant women, and women in sero-discordant relationships.
- When providing health services to vulnerable populations it is important to be respectful and non-judgmental, and to go the extra mile in terms of outreach and enabling access.
- For vulnerable female populations for whom oral PrEP is not a preferred method of HIV prevention, the Ring is an option.



Module Four

Raising Awareness and Communicating About the Ring

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About this training manual

This training manual was developed by the International Partnership for Microbicides, as a training resource, that is adaptable to the local country context in which the dapivirine vaginal ring is being implemented.

Each module in the manual is designed to be used either independently or as part of the full pack. Each module has a set of suggested tools which are pull outs at the end of the manual.

Attribution and Citation

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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INTRODUCTION

Women account for more than half the number of people living with HIV worldwide. Young women (10-24 years old) are twice as likely to acquire HIV as young men the same age. New women-initiated HIV prevention methods, like the Dapivirine Vaginal Ring (DVR or the Ring) has the potential to shift dynamics and give women more varied options to manage their own sexual health.

For women to select the Ring as an additional option for HIV prevention, there needs to be effective communication and demand generation about the Ring.

This module provides some ideas and approaches on how to inform your clients and the community about the Ring through awareness raising, sensitization, understanding potential clients who might use the Ring and communication strategies along a client's potential Ring use journey.

It is a good idea to engage with a woman at a moment when she is open to new health options that could blend with other life choices she is considering.

CREATING AWARENESS AND SENSITISATION

RAISING AWARENESS MEANS making people conscious of an issue. It is about informing people and providing new bits of information.

SENSITISATION MEANS making people sensitive to an issue. It is at the core of awareness raising and it is what you want to achieve. Not only do people become conscious of the issue but they react to it.

How to raise awareness

Raising awareness requires sustained effort to have a community-wide impact, but there are some practical “rules” to follow when engaging with individuals and/or groups of women.

Be relevant

Women have many competing priorities in their lives and for HIV prevention to receive attention it must feel relevant and be reinforced by sources that the woman relates to and trusts.

Pick the right moment

Women may not proactively seek HIV prevention information due to fear of stigma or discrimination. It is a good idea to engage with a woman at a moment when she is open to new health options that could blend with other life choices she is considering. Try and fit in with her motivations for making these changes. For a young woman, you may want to talk about HIV prevention and the Ring in the context of other important aspects of her life, like her relationships and social life, children and family planning, or study and work aspirations.

Use visual tools and everyday explanations

Vaginal rings are a new product in many countries. Women you encounter will probably be unfamiliar with how the Ring would interact with their bodies and may have concerns about what would happen in their bodies in order to protect them against HIV. Concerns may arise because they are unfamiliar with their anatomy or have had negative experiences with other sexual and reproductive health (SRH) products. You can help by:

- Using resources such as anatomical models (either in physical or virtual form), user guides that contain clear pictures, posters and other digital tools.
- Sticking to simple language and using familiar analogies to explain the product. For example: You can use the strong tea analogy to explain why Ring adherence is important. The more you keep a teabag in water, the stronger the tea becomes. If you use the Ring as indicated – every day for 1 month – you will get maximum protection.
- Use dialogue guides and frequently asked question (FAQ) documents as talking guides.



The more you keep a teabag in water, the stronger the tea becomes.

If you use the Ring as indicated – every day for 1 month – you will get maximum protection.

Points to consider when introducing a new product

Communication is always context specific. Women's concerns and realities may vary from country to country, and also within countries. Factors such as age, literacy, urban-rural location, religion and other aspects of culture all play a role. Be alert to this and respond accordingly. There is no one-size-fits all solution. Visual tools, language and analogies need to be adjusted according to context.

Ways of responding to the diversity of audiences include:

- Identifying communication tools on other health topics that have been successfully used with women of a similar profile and learn from them.
- Developing and collecting a variety of communication tools that might work for different groups of women.
- Testing the explanations that have been developed and the resources that could be used with small groups of women similar to those that will be communicated with.
- When implementing awareness-raising activities, take note of the questions women raise during the discussion. Are there some that keep coming up? Can these topics be included in the explanations?
- Considering appropriate multimedia resources that can be incorporated – short videos to share or audio recordings.



How to approach sensitisation

There are a number of strategies to sensitise your clients and other relevant people to the Ring and its role in HIV prevention. The following approach builds on that recommended by Choice for Youth on their Youth Do It website.

Improve knowledge

Ensure that your clients have correct information, provided in sufficient detail for them to truly understand the product. You want them to think critically about the information you offer, ask questions and actively process information so that they make that information their own.

Change attitudes

Negative attitudes held either by the individual or those in their family and social circle can play a part in limiting uptake of HIV prevention products, like the Ring. Changing attitudes is a long and complex process, but a good place to start is engaging with women who might consider the Ring. It is important to understand and address attitudes that might present barriers to use of the Ring, as well as the beliefs and values that might provide motivation. This, combined with sharing in-depth information on the benefits and impact of the Ring and building woman's self-confidence about her capability to use the Ring, might produce the attitude change required.

Build social support

People you aim to sensitise should know where they can access services and support. It is also possible to mobilise women to provide support to each other. It is often easier to embark on change when there is support from your peers.

SENSITISATION ACTIVITIES

Provide information and interaction opportunities

- Health talks in waiting rooms.
- Educational videos in waiting rooms.

Challenge myths and correct misconceptions

Since the Ring is new, we may not be clear about specific myths surrounding it, but we can draw on experience from ring studies or other insertive vaginal products, such as tampons or the contraceptive ring. The REACH study (MTN-034) highlighted some common myths and misconceptions that have emerged.

Myth	Fact
It causes cancer of reproductive organs	There is no evidence that suggests that the Ring can cause cancer
It causes barrenness (infertility)	The Ring does not contain any materials or drugs that would cause infertility in the short- or long-term.
It widens the vagina	There is no evidence that suggests that the Ring can widen the vagina
It may disappear in the body and go to the lungs	The Ring sits in the vagina near the cervix and cannot enter the fallopian tubes or other organs or travel elsewhere in the body.
It loops the partner's penis	The Ring sits high up in the vagina near the cervix and cannot become stuck on the penis during sex

Present convincing arguments

When communicating, prioritise the positive: introduce the Ring as an additional choice in the HIV prevention toolkit, explain how it may particularly suit a woman's lifestyle and needs, and the general benefits of protection. (However, individual vulnerability to HIV needs to be honestly assessed during one-on-one counselling when considering providing the Ring.)

Introduce skills-building activities

Role-play can be useful to enable staff to convey correct messaging when interacting with clients.

The provision of dialogue guides may also help establish correct messaging.

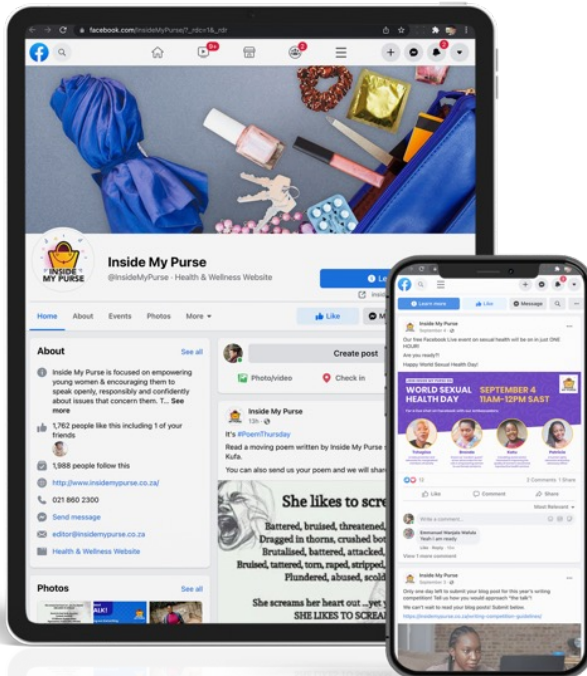
Encourage support networks

You can encourage your clients to link up with social support networks consisting of their peers with similar experiences. The Inside my Purse blog may be a good platform for women to connect and share SRH challenges and solutions.

INSIDE MY PURSE

The purpose of Inside my Purse is to strengthen digital communication on SRH and HIV prevention, including the Dapivirine Vaginal Ring. The name refers to those private, intimate spaces that women control, including the vagina.

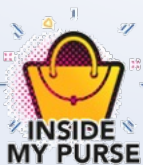
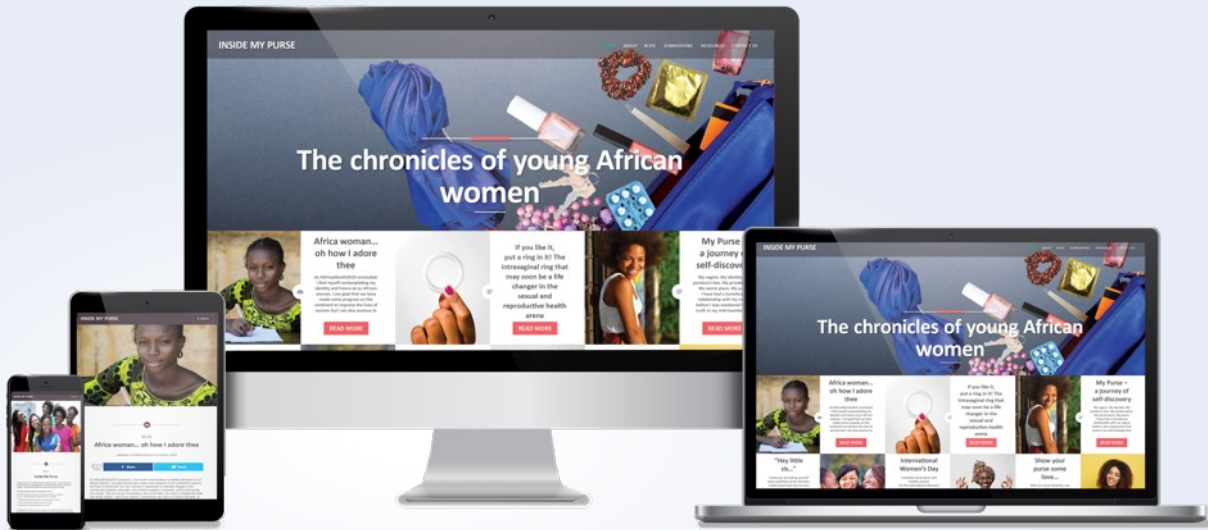
In an era where new tools related to SRH and HIV improve the outlook for women's health, Inside my Purse aims to offer young women a supportive environment, where they can speak openly about their personal stories, experiences and opinions as end-users of these products.



Inside my Purse has two platforms:

A blog (<https://insidemypurse.co.za/>) and Facebook page <https://www.facebook.com/InsideMyPurse/>. In different ways, The platforms enable young women to inspire, engage and educate each other.

You can access the blog and Facebook page using the links above and you can also direct clients to the blog and Facebook page.



Metaphor for a private intimate space that women can control, women's personal "stuff" – including her vagina

UNDERSTANDING USER GROUPS

Overview

Market research on the Ring was conducted in five countries in sub-Saharan Africa (Kenya, Malawi, South Africa, Uganda and Zimbabwe). The study enrolled 1 300 women aged 15 - 29 years. It revealed that common barriers to Ring uptake included concerns about its insertion, perceived side effects and the efficacy of the Ring. These were coupled with widespread perceptions among participants that they were at low risk of acquiring HIV, largely due to the trust they placed in their male sexual partners.



Size of study

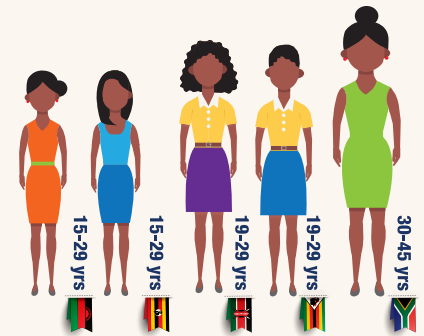
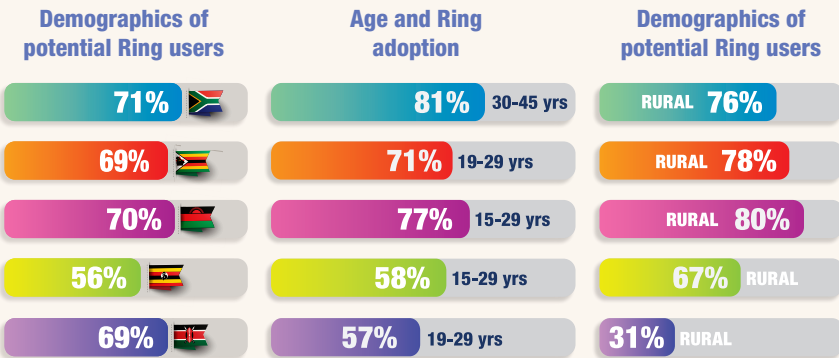
1300

Women across these 5 countries



LIKELIHOOD OF ADOPTING THE RING

Insights on creating demand for the Dapivirine Vaginal Ring by country



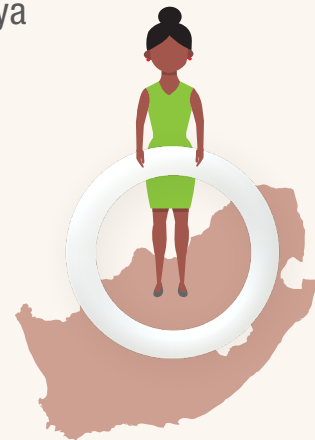
South Africa
Zimbabwe
Malawi
Uganda
Kenya

- Between 56% and 71% of women were interested in using the Ring
- This varied by country, with women in South Africa most enthusiastic (71%) and those in Uganda least keen (56%)

- The age of women intending to adopt the Ring varied by country
- Ring usage was popular in older women (30-45 years) in South Africa, while younger women (15-29 years) favoured it most in Malawi and Zimbabwe

- Women from rural locations were more likely to be interested in using the Ring
- Figures varied by country, ranging from 81% of women in rural South Africa to 31% in rural Kenya

Women from rural locations where more likely to be interested in using the Ring



71%
South Africa women most enthusiastic in using the Ring

INSIGHTS ON CREATING DEMAND FOR THE RING BY COUNTRY



Uganda



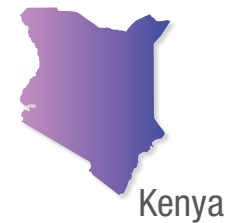
South Africa



Zimbabwe

Opportunities	Barriers	Factors influencing demand
<p>Preference for HIV testing over condom use might favour uptake of the Ring.</p> <p>Trust in the Ring may influence its adoption.</p>	<p>Women are highly averse to inserting anything into the vagina.</p> <p><i>"They told us not to mess with our private parts"</i></p>	Insertion practices
<p>Women were comfortable with inserting items into their vagina.</p> <p><i>"Females bewitch males by putting herbal things in the vagina for stronger relationships"</i></p> <p>There was high familiarity with the functionality of the Ring.</p>	<p>There is relatively low stigma attached to being HIV-positive</p>	
<p>Providing "back-up" to condoms attracts women to the Ring.</p> <p>The moderate efficacy of the Ring is not a barrier</p> <p><i>"People should know that there is nothing that is 100% and it is always better to prevent than to cure"</i></p>	<p>Women often lack sexual autonomy</p> <p><i>"It (the Ring) is my secret. If I tell him, he would use it against me"</i></p>	Lack of autonomy in decision making

Opportunities	Barriers	Factors influencing demand
<p>Low use of condoms for HIV prevention</p> <p>Exposure to traditional practice of “kusasa fumbi” has affected condom use</p> <p>“We are taught by the nankugwis not to have sex with condoms. They would say, ‘You don’t eat sweets while they are wrapped’”</p> <p>Prevalence of Marriage</p> <p>Condoms are only used in certain situations amongst married couples and not as standard practice</p> <p>“Married couples only use condoms as prevention when the lady is not on family planning if one partner is sick”)</p>		<p>Lack of autonomy in decision making</p>
<p>The perception of being at risk of HIV is low among women in Kenya</p> <p>“My risk is low, but you never know what he’s doing out there”</p>	<p>Women’s understanding of efficacy was subjective</p> <p>Ring use might provoke existing stigma around the use of HIV prevention interventions</p>	<p>Perceived risk</p>





Awareness of the Ring



Consideration of the Ring



Obtaining the Ring



First use of Ring



Continued use of the Ring

COMMUNICATION CONSIDERATIONS ALONG A RING USER'S JOURNEY



How might we increase general and improve demand?

- **Agency and empowerment among end-users are motivators for demand**
 - » Encourage agency – the capacity of individuals to act independently and make free choices – around HIV status
 - » Highlight positives of Ring use
- **Users need some level of interaction with the Ring**
 - » Demonstrate Ring insertion/removal either through imagery (for example, a virtual model) or a physical pelvic model used with a dummy Ring
- **Female networks are the optimal point for awareness**
 - » Facilitate female networks, especially those offering peer and a mixed age-group dynamic where older women can speak to younger women
 - » Consider digital platforms like Inside my Purse



How might we reduce perceived stigma around Ring use to encourage consideration of its use?

- Let others similar to the woman lead . . . and she will follow
 - » Influencers and aspirational individuals would work well here
- Social proof can reduce concerns and doubts about using the Ring
 - » Peers who have used the Ring could highlight positive experiences in testimonials or blogs
- Leverage the experience of women close to the individual
 - » Use real stories because they can carry great impact in addressing stigma



How might we strengthen partner support around Ring use?

- Position the Ring as part of shared values and responsibilities
 - » Within a relationship, HIV prevention is the responsibility of both partners
- Create inclusivity in messaging
 - » Direct your messaging to both men and women
- Leverage social norms about the family
 - » Showcase men as valuable to the protection of their families
 - » Where there is shared decision-making, this could increase support for the woman's use of the Ring



How might we increase confidence and comfort in relation to Ring insertion?

- Reaffirm the ease and convenience of the process. The primary concern of women is inserting the Ring and fear that, if inserted incorrectly, it may be dislodged or cause discomfort
 - » The provider may offer to perform the first insertion
 - » The provider could show a simple “how to” video on Ring insertion (link to video)
 - » Display testimonial posters, highlighting the ease and quickness of insertion, and absence of interference with other daily functions
- Offer alternative, convenient channels for women to discuss their concerns
 - » Digital chatbots are a convenient, anonymous channel that can be accessed at any time and repeatedly used, if necessary
- Use simple explanations to aid in understanding the process

MESSAGING AND COMMUNICATION

As a healthcare provider, you will be a significant source of information about the Dapivirine Vaginal Ring. You will be responsible for clarifying misinformation and overcoming stigma.

It is likely you will be communicating in the wider community. Familiarising yourself with key messaging on the Ring is important because:

- Messaging helps to ensure you express yourself clearly and consistently, covering all the intended information in an appropriate manner.
- Messaging has been designed specifically to address women's known concerns about the Ring.
- Messaging emphasises all the attributes of the Ring and presents it positively, while mentioning important limitations of the method.

In other words, messaging is a communication safety device – it keeps you on track and enables you to do a good job even when you are having a day when the words do not come easily.

However, there is some **flexibility in how you deliver messages**. You should feel free to introduce language that connects better with your audience while remaining faithful to the basic content and tone of the key messaging.

Refer to tools [FAQ, dialogues, video] for the key messages to use when communicating about the Ring to a potential user. These key messages focus on messaging that can be used when explaining the ring, how it works, who should use it, its safety, side effects, concerns about drug resistance and impact on a potential users lifestyle.

Key Takeaways from this Module:

Awareness

- Raising awareness requires sustained effort to have a community-wide impact
- When engaging in awareness raising efforts: Be relevant, pick the right moment and make use of visual tools and everyday explanations people can relate to
- There is no one-size-fits all solution. Women's concerns and realities may vary from country to country, and also within countries. Be alert to this and respond accordingly

Sensitization

- Sensitisation means making people sensitive of an issue so that they react to it
- The purpose of sensitization is to improve knowledge, change attitudes and build social support
- Improve: knowledge: supply clients with correct information so that they can an informed decision
- Change attitudes: sharing in-depth information on the benefits and impact of the Ring and building woman's self-confidence about her capability to use the Ring, might produce the attitude change required
- Build social support: people should know where to find services and support and find peer support network.

Understanding user groups

- Market research on the Ring in five countries in sub-Saharan Africa (Kenya, Malawi, South Africa, Uganda and Zimbabwe)¹ revealed that common barriers to Ring uptake included concerns about its insertion, perceived side effects, efficacy of the Ring and autonomy in decision making. These were coupled with widespread perceptions among participants that they were at low risk of acquiring HIV, largely due to the trust they placed in their male sexual partners.
- There are different stages in a clients Ring use journey which include awareness, consideration, obtaining the Ring, first use and continued use.
- Communication considerations need to be taken into account, including: (a) how to improve awareness and knowledge of the Ring, (b) reducing stigma around Ring use, (c) strengthening partner support around Ring use, (d) increasing confidence and comfort around Ring insertion

1 Contact IPM to access country specific reports at hcpsupport@popcouncil.org

Messaging and communicating

- As a healthcare provider, you are a significant source of information about the Ring
- Familiarising yourself with key messaging on the Ring is important: explaining the ring, how it works, who should use it, its safety, side effects, concerns about drug resistance and impact on a potential users lifestyle.
- Make use of available tools to help you along the process

Tools to go with this Module

THE DAPIVRINE VAGINAL RING INSERTION GUIDE
TOOL 5

How the ring works

A doctor would insert the flexible silicone ring herself and replace it with a new one each month.

The ring sits inside the vagina over the cervix where it slowly releases an antimicrobial ring called dapivirine at the site of potential infection.

Dapivirine works by blocking HIV's ability to make copies of itself inside healthy cells.

It is important that the ring is left in place for the full month to ensure that risk reduction is achieved.

1 MONTH

2 MONTHS

3 MONTHS

The ring can also be used with other forms of contraception – but avoid anything that could irritate vaginal tissue, such as douching, vaginal sprays or cervical caps.

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 5

DIALOGUE GUIDES/ TALKING CARDS
TOOL 6

Other advice?

Sure, here are some tips:

- Pick up your timing is important. Try to find a time when he is in a good mood, you're both sober and you have some privacy.
- If you're worried that he may get angry or could be violent, try to find a place where you can reach home or get help if you need to.
- Try practicing what you're going to say. I'm happy to do that with you, or you could use a friend.
- If you have any friends who are using the ring and have had their partners, you could ask them for advice.

I've been told by doctors never to insert anything in my vagina, now you are telling me to insert this ring?

Yes, it is true, you should never insert anything that is not medically approved into the vagina, but this ring has been proven to be safe and effective in preventing HIV.

I've heard that the ring may cause cancer or infertility?

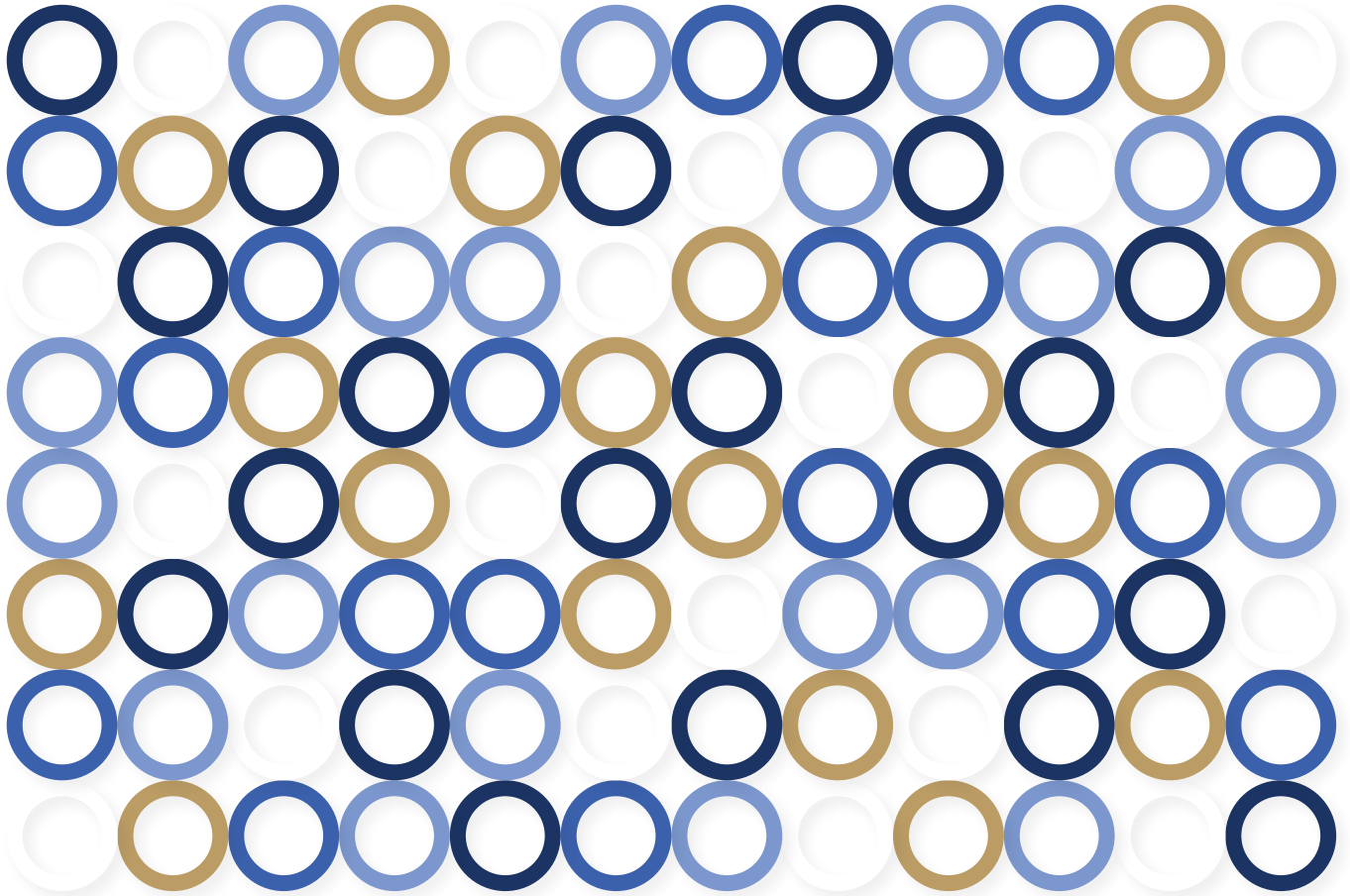
Research has shown that the ring is safe and does not cause cancer or infertility.

The ring may damage my uterus and then I will fail to deliver children?

The ring has been proven very safe and will not do any damage to your uterus or any other part of your reproductive system.

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 6



Module Five

Clinical Management of Clients on the Ring

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About this training manual

This training manual was developed by the International Partnership for Microbicides, as a training resource, that is adaptable to the local country context in which the dapivirine vaginal ring is being implemented.

Each module in the manual is designed to be used either independently or as part of the full pack. Each module has a set of suggested tools which are pull outs at the end of the manual.

Attribution and Citation

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Suggested Citation: IPM Global Health Care Provider Training Manual/Ring Package, 1st edition, International Partnership for Microbicides, South Africa, 2022

Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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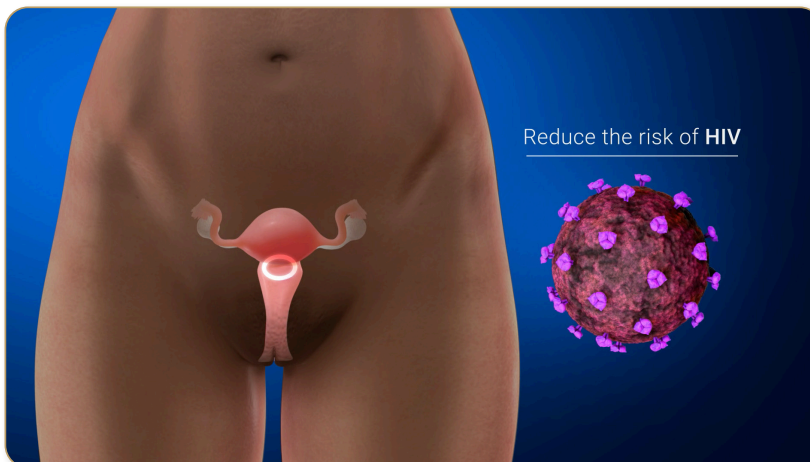
This guide was supported by the LEADING (Licensure and Ensuring Access to the Dapivirine Ring) Project (Cooperative Agreement Number: AID-OAA-A-17-00013).

INTRODUCTION

Our concern as healthcare providers is to enable women to gain access to the most suitable form of HIV prevention by providing appropriate information to allow for informed decision making according to circumstance and need.

This module on clinical management of women using the Ring is designed to enable providers to guide women towards this best-case outcome.

There is strong emphasis on procedures for initiating the Ring as this is a new product and many clients will not have used anything like it before. An important aspect of this module is the role of the healthcare provider in enabling her client to take control and use the Ring with confidence.



ASSESSMENTS PRIOR TO INITIATING THE RING

Ideally the Dapivirine Vaginal Ring should be provided as part of a comprehensive HIV prevention and sexual and reproductive health (SRH) package.

The following comprise a minimum assessment of eligibility for provision of Ring:

- Pre-test counselling
- HIV testing
- Post-test counselling
- Pregnancy testing (as per country guidelines)
- Establishing whether client is planning to become pregnant or currently breastfeeding and or planning to breastfeed (as per country guidelines)
- Regular use of other vaginal products, such as but not limited to contraceptive vaginal rings or diaphragms
- Vaginal cleaning practices, such as, but not limited to, douching

A pelvic exam may be considered at initiation or at any follow-up visit, if clinically indicated

Important points to note

- The Ring is **only** indicated for use in HIV-negative cis gender women (that is, females as assigned at birth).
- Follow country guidelines for use of the Ring during pregnancy and breastfeeding.
- Pap smears are **not** a requirement for initiating Ring use.
- Simultaneous use of the Ring and oral PrEP is currently **not** recommend, as this has not been studied.

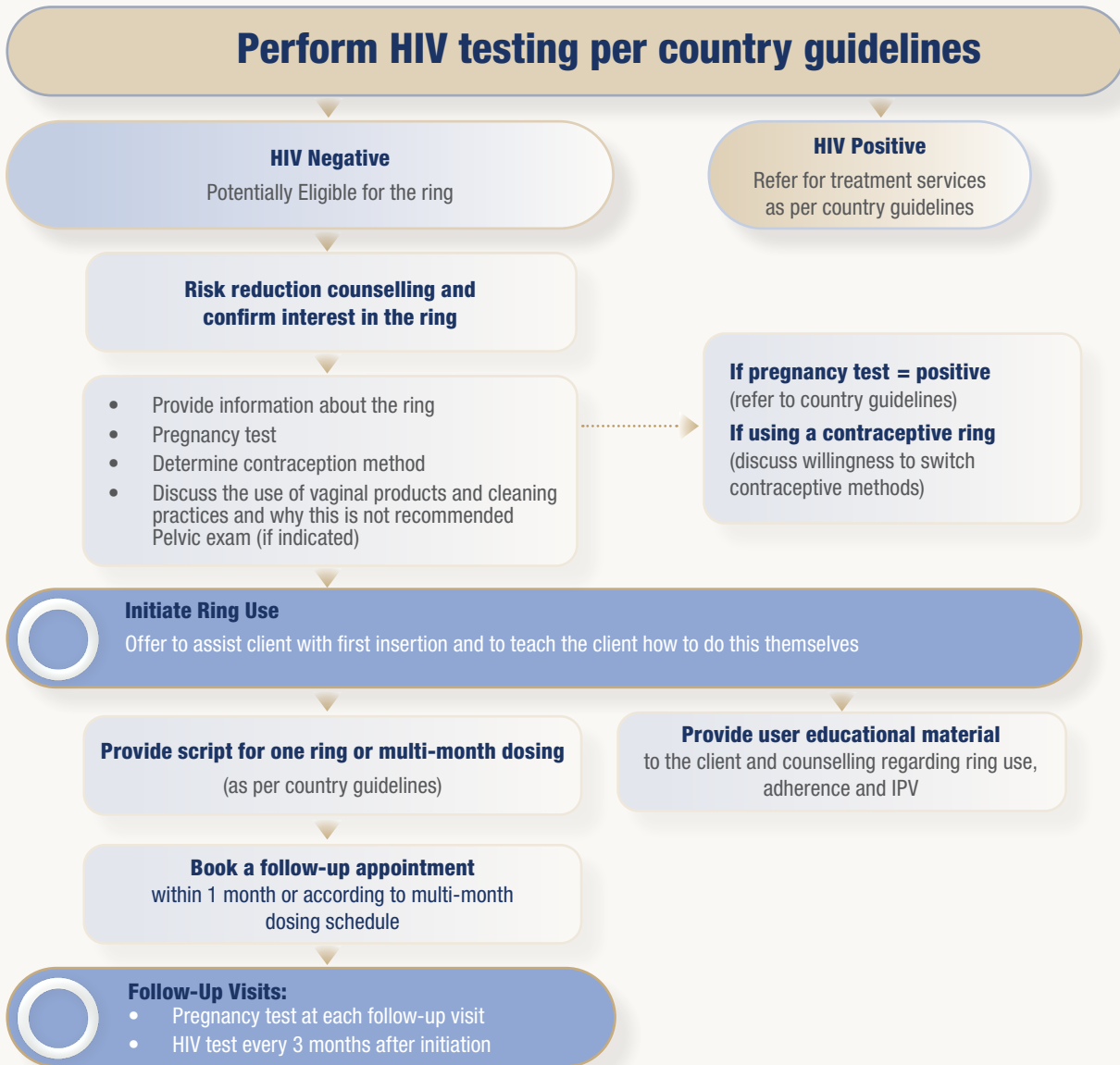
ASSESSMENTS AT FOLLOW-UP VISITS

HIV testing should be provided every three months while using the Dapivirine Vaginal Ring, as part of a comprehensive service.

Visit frequency

This will depend on the policy in your country. Women may come to the facility monthly to receive the Ring or, if there is multi-month dispensing of the Ring, it may be possible to align Ring collection with family planning regimens. For example: if a client is on DMPA (a three-monthly contraceptive injection), she may be able to align her Ring collection with her next injection, which would be convenient for her.

Clinical Algorithm for Ring initiation and follow-up



DISCUSSION ON RING EFFICACY

Overall data from main clinical trials to date suggest the Dapivirine Vaginal Ring's efficacy in reducing the risk of HIV is probably around 30% among all women, which includes women who did not use it consistently. With higher adherence, efficacy seemed to increase to about 50%.

What does efficacy mean?

Efficacy is the ability of a medical product or intervention to produce a beneficial effect on human health in ideal conditions, such as those created in a clinical trial. When analysing the data, it includes all the participants who were planned to use the product whether they used it consistently or not.

Although there are products with higher efficacy, like condoms and daily oral PrEP, not all women can use them or want to use them and some may have challenges using them (i.e. partner consent, daily dosing, etc.). Women in these situations still need a way to reduce their HIV risk and the Ring offers them something that may better suit their circumstance or lifestyle. Getting the HIV epidemic under control will require multiple prevention methods, so every woman can choose an effective product that best meets her needs and life circumstances. Just as with contraception, having more HIV-prevention options to choose from will increase overall use and strengthen population-wide protection. That's the path to epidemic control.

Women should be able to choose the most efficacious product that they can reliably use, as directed. The Ring would be recommended for use when women are unable or choose not to use daily oral PrEP, whether due to side-effects, stigma or other reasons. The Ring ensures they still have an option to reduce their risk of getting HIV.

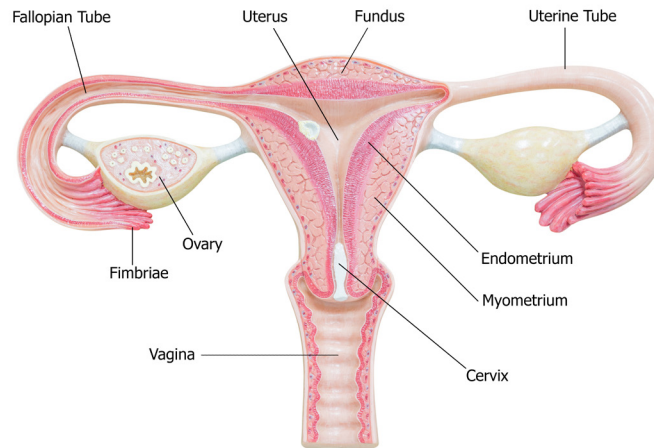
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Video: How to use the DVR



<https://vimeo.com/707699170>

INSERTION AND REMOVAL OF THE RING



- The cervix is a cylinder-shaped neck of tissue that connects the vagina and the uterus or womb
- The Ring sits at the base of the cervix

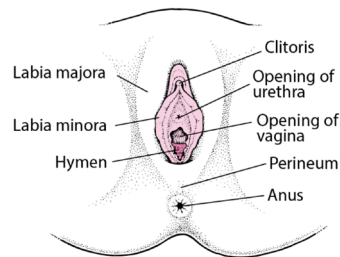
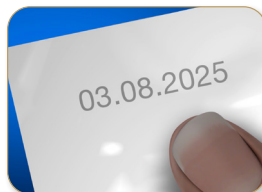


Image Credit – <https://www.msmanuals.com/>

- The vulva is a name for the parts of a woman's vagina that can be seen from the outside, namely: the inner lips (labia minora), outer lips (labia majora) and clitoris

INSERTION AND REMOVAL OF THE RING

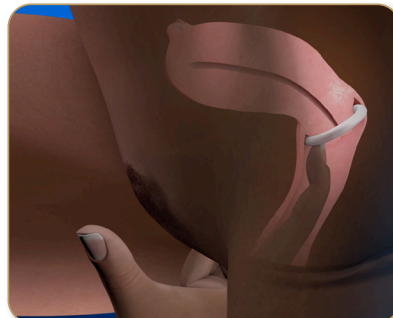
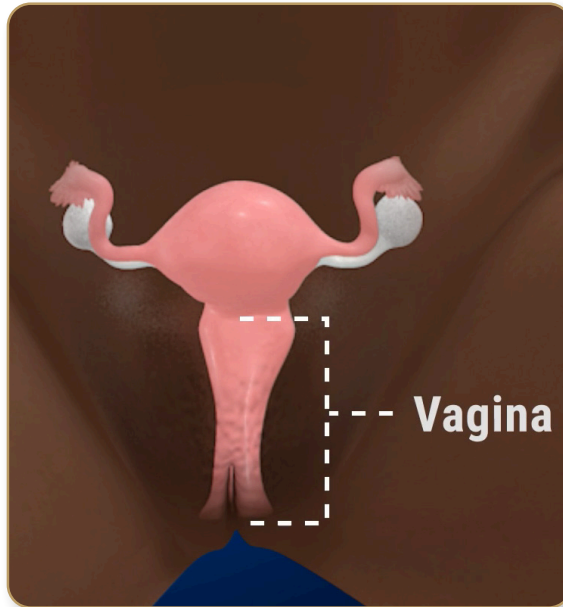
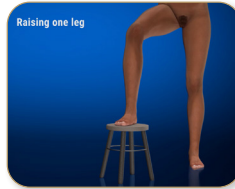


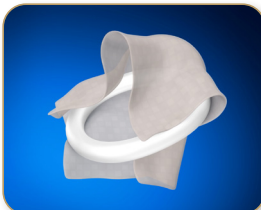
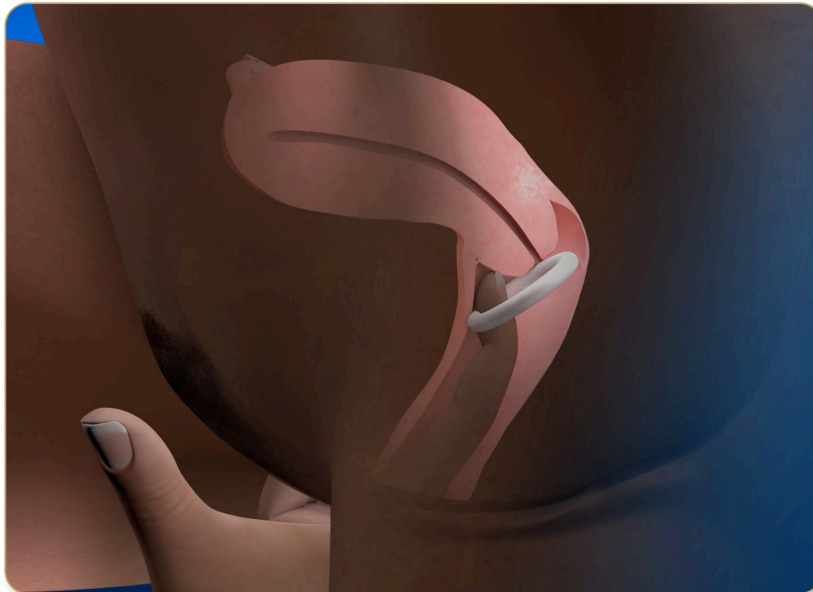
INSTRUCTIONS FOR RING INSERTION

- Wash your hands in clean water and dry them.
- Check the expiry date on the package label.
- DO NOT use if the ring is damaged or expired.
- Tear package to open. DO NOT use scissors to open the package. In a clean place, remove the ring from its package.

POSITION YOURSELF TO INSERT THE RING

- Choose a position that is comfortable for you to insert the ring.
 - For example: raising one leg, squatting or lying down.
1. Twist the ring into the shape of the number 8 or squeeze the sides of the ring together.
 2. Use your other hand and hold open the folds of skin around your vagina. Place the tip of the ring in the vagina opening and then use your index finger to gently push the folded ring in.
 3. Push the ring into your upper vagina as far as you can.
 4. Wash your hands in clean water and dry them.





REPLACING THE RING

1. The ring should be removed **ONE MONTH** from the day it was inserted. Insert a new ring **IMMEDIATELY** after the previous ring is removed.
2. Wash your hands in clean water and dry them.
3. Choose a comfortable position with your legs apart. Use your finger to hook the ring and gently

DISCARD THE USED RING

1. Place the used ring in tissue or in toilet paper.
2. Place it in the rubbish bin out of the reach of children or pets. **DO NOT** throw the ring in the toilet.
3. 2. Wash your hands in clean water and dry them.



Ring should be in place for 24 hours before they rely on it for protection

TIME BETWEEN INSERTION AND EFFECTIVENESS

Advise your clients that the Ring should be in place for 24 hours before they rely on it for protection. The precise period to protection is not known, but data show that concentrations of dapivirine in vaginal fluid are similar 24 hours after insertion to concentrations on day 28 of continuous Ring use.

Levels of dapivirine in the woman's body drop quickly after the Ring is removed. It is estimated that the half-life of dapivirine in vaginal fluid is 20 hours after the Ring is removed. So, it is important that women keep the Ring in place to ensure risk reduction is achieved. For the same reason, when the Ring is removed after one month it must be replaced immediately with a new one.

Half-life: The half-life of a drug is an estimate of the amount of time it takes for the amount of the drug in the body to be reduced by half (50%).

USING THE RING WITH CONTRACEPTION, LUBRICANTS, AND VAGINAL ANTIFUNGALS

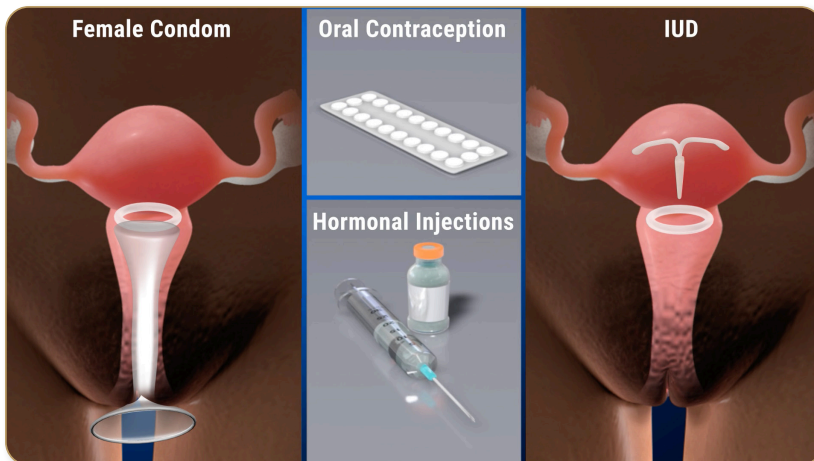
Contraception: The Ring can be used with most forms of contraception including male and female condoms, oral contraception, hormonal injections an IUD, and implants. The Ring should not be used with contraceptive vaginal rings and diaphragms. (Refer to video)

Lubricants: Data from earlier studies suggested that there is no significant impact on the release of dapivirine from the Ring when using water-based lubricants. A higher release of dapivirine from the Ring was associated with silicone-based lubricants, therefore silicon-based lubricants are not recommended for use with the Ring. No data currently exists on the effect of spermicides on the Ring.

Vaginal antifungals: Caution should be exercised when considering the simultaneous use of the Ring and vaginally administered clotrimazole or miconazole for treatment of vaginal candidiasis. The progression of the candidiasis should be monitored in case the efficacy of the antifungals is affected. It means that prescriber should be observant for any issues which might arise if used concurrently and consider if there are alternatives available for treatment of candidiasis. Monitor that the treatment for candidiasis was effective and reinforce the need to use condoms if engaging in sexual activity while using vaginal antifungals.



Caution should be exercised when considering the simultaneous use of the Ring and vaginally administered clotrimazole or miconazole for treatment of vaginal candidiasis.





USING THE RING DURING MENSES

Menses: The Ring should remain in the vagina during menstruation and can be used with tampons. Care should be taken when removing the tampon, not to dislodge the Ring. The Ring should not be used with menstrual cups or cervical caps. (Refer to video)

Clinical trial data has shown that dapivirine in vaginal fluid concentrations decreased up to 4-fold during menses but increased again at the end of menses and achieved concentrations consistent with the no menses.

The use of tampons generally resulted in a 2-fold decrease of dapivirine in vaginal fluid concentrations during menses.

As the clinical relevance of the reduced vaginal dapivirine levels during menses and tampon use is unclear, it is advisable to use additional preventive measures against HIV during menses.

Key Ring counselling messages

- Please contact your clinic or doctor before using any medicines or other products that need to be put in your vagina while using the Ring.
- The Ring should remain in your vagina for one month.
- If you take the Ring out, you are no longer protected from HIV, as the levels of dapivirine in a woman's body drops quickly after removal.
- The Ring starts working 24 hours after insertion.
- The Ring does not prevent other sexually transmitted infections (STIs) or prevent pregnancy or protect against HIV during anal sex or injecting drug use.
- Re-insert a new Ring right away after your used Ring is removed.
- The Ring is intended for use in HIV-negative women only.

Do NOT use with:



Diaphragm



Contraceptive
Vaginal Ring



Cervical cap



Menstrual cup

Refer to Module 6 on Ring Counselling for more detail

RISKS AND SIDE-EFFECTS

In both phase 3 studies on the Ring – The Ring Study and ASPIRE – there were no significant safety issues associated with use of the Ring. There was no clinically important difference in adverse events between participants using the active dapivirine ring and those using the placebo ring. Data from two subsequent open label extension (OLE) studies showed a similarly favourable safety profile, as did 12 smaller safety studies.

Common side-effects

The most commonly reported adverse drug reactions during clinical trials, experienced by at least 5% of participants using the Ring, were:

- Urinary tract infection (15.2%)
- Vaginal discharge (7.1%)
- Vulvovaginal pruritus (itching) (6.5%)
- Vulvovaginitis (inflammation of the vulva and vagina) (6.4%)
- Pelvic pain (6.2%).

Side effects in the phase 3 trials were generally mild to moderate and resolved without any interruption in Ring use. The Ring has not been associated with major side effects in clinical trials to date.

Clinical trials to date have not recorded any allergies due to the Ring or dapivirine.

The International Partnership for Microbicides (IPM) will continue to monitor for any potential side effects.

It is not necessary to clean or remove the Ring during or after menses or sex.

DISCONTINUING USE OF THE RING

Intermittent use of the Ring

Intermittent use of the ring is **not recommended** as it has not been studied and its efficacy is unknown when used intermittently. The Ring is designed to be used continuously for one month and must remain in place to reduce HIV risk. Levels of dapivirine in the vagina drop quickly after the Ring is removed. Therefore, it is important to keep it in place to ensure that the highest levels of risk reduction are achieved. It is not necessary to clean or remove the Ring during or after menses or sex. Furthermore, STIs can be diagnosed and treated without removing the ring.

We have not been able to determine the precise period of “forgiveness” following ring removal – that is, the period during which there is no loss of protection. But we do know that the amount of dapivirine measured in vaginal fluids drops in 20 hours to half the amount present during regular

use of the Ring. If a woman does remove the Ring – for whatever reason – it would take 24 hours after reinsertion for dapivirine vaginal fluid levels to increase to the levels considered high enough to reduce the risk of HIV infection once more. Combination prevention is therefore encouraged.

Stopping Ring use

If at any point, a woman using the Ring no longer feels this is the best option for her, or if she no longer feels she is at risk of contracting HIV, she can discontinue Ring use. Because the level of dapivirine in the vagina drops quickly after Ring removal, it is important that she is prepared to use another reliable method of HIV prevention (such as oral PrEP or condoms) immediately after removing the Ring.

Stopping Ring use due to HIV acquisition

If, at any point after Ring initiation, a woman tests positive for HIV, she must be advised to remove the Ring and be referred for HIV treatment services.

STRATEGIES TO SUPPORT RING USE

There are a number of useful strategies that can be applied at a community and facility level with the aim of influencing client adherence to product use. These are summarized below.

Strengthening staff capacity

Ensure that staff have sufficient training in human-centred counselling approaches (see below) and know how to use adherence support tools effectively.

Using adherence support tools

Tools such as counselling worksheets and checklists may help guide a provider when counselling clients at the point of Ring initiation and during continued use. Other adherence support tools may include interactive blogs, like Inside my Purse ([link](#)), where women can share their experiences and issues regarding sexual and reproductive health.

Adopting human-centred counselling

A human-centred counselling approach will help providers understand the individual client's barriers to adherence and develop personalised strategies to overcome such barriers.

- **Engage:** discuss how satisfied the client is with the product.
- **Frame:** explain the purpose of the discussion.
- **Explore:** explore client's experiences with the product with attention to facilitators of and barriers to use and continuation.
- **Identify needs:** ask what would need to happen for the challenges identified above to improve, be less stressful, be easier to manage.
- **Strategise:** explore new strategies to address identified needs or how to maintain established strategies that have been useful.
- **Goal:** identify strategies that the participant can consider and try.

Enabling adherence meetings

Adherence meetings are formal or informal small group gatherings that take place in person or on a virtual platform. The purpose is to discuss challenges clients are experiencing in adhering to the Ring and share tips and strategies that could possibly work. The group should be peer-led, with support from providers. The frequency of meetings will depend on what the group decides. Members of the group may remain engaged with each other through closed social media groups, such as Whatsapp.

Being accessible for ad-hoc support

Providers can offer ad-hoc support to clients, such as telephonic advice, for any Ring use challenges. They can also offer to undertake home visits, if needed, to offer counselling on the Ring to male partners.



RING USE BY ADOLESCENT GIRLS AND YOUNG WOMEN

Phase 3 clinical trial data for the Dapivirine Vaginal Ring showed overall low or no risk reduction in women under 21, likely due to lower adherence.

However, these trials were not designed to look at HIV risk reduction across different age groups and there is no biological reason identified as to why risk reduction should be lower in younger women. Despite this, the data supported the Ring as a method that reduces HIV risk for women aged 18 and above, with no safety concerns. Ongoing research, in the form of the REACH study, and in-country pilot projects will help us better understand the Ring's effectiveness in this key age group.

Experience in providing oral PrEP services for AGYW suggests that younger women may need more support, especially in the early stages of oral PrEP use, to achieve continued use. This may be similar for the Ring and studies will help us understand implementation requirements and whether adherence challenges can be overcome.



REACH study

on Ring use by adolescent girls and young women (AGYW) Investigated safety and use of the Ring and oral PrEP among 247 young women, aged 16-21 years, in South Africa, Uganda and Zimbabwe. Began in February 2019. Study ended in Sep 2021 and results released in February 2022.¹

¹ reference module 1B for results



BE PROTECTED Study

Start date: August 2020

Safety and acceptability of Ring and oral PrEP among 200 breastfeeding women in Malawi, South Africa, Uganda and Zimbabwe¹



DELIVER Study

Start date: February 2020

Safety and acceptability of Ring and oral PrEP among 550 pregnant women in Malawi, South Africa, Uganda and Zimbabwe

RING USE DURING PREGNANCY AND BREASTFEEDING

Safety in pregnancy and breastfeeding has not been established as there are limited data on the Dapivirine Vaginal Ring's safety during pregnancy and breastfeeding. In the MTN-020/ASPIRE trial, 169 of the 2629 women who were enrolled became pregnant during the study.

Data from this small sub-set of women showed that, dapivirine use in the periconception period does not appear to be associated with adverse effects on pregnancy or infant outcomes (Ref: WHO guidelines). However, additional safety studies are needed of dapivirine vaginal ring use during pregnancy and breastfeeding.

Two important studies are underway to collect more data on the safety and use of the Ring (and daily oral PrEP) among pregnant cisgender women in Africa (MTN-042/DELIVER) and cisgender breastfeeding women (MTN-043/B-PROTECTED). Their results will inform clinical guidelines for the Ring's use among these groups. If these conclude that there are no safety concerns, continuing post-market surveillance activities will be

needed to monitor for adverse pregnancy and fetal outcomes (Ref: WHO guidelines).

Each country that approves the Ring will develop its own clinical guidelines on Ring use during pregnancy and breastfeeding, guided by WHO recommendations. It is possible that individuals who are pregnant or breastfeeding would be advised to consult with their healthcare providers to discuss the potential benefits and risks of using the Ring.

Key Takeaways from this module:

Individualised woman-centred assessment is the key to ensuring that the Ring is provided to women who would achieve their best possible level of protection against HIV by adding the Ring to their personal prevention toolbox. It is not the method of choice for all women. Assessment is most critical immediately before Ring initiation, but it continues throughout the period of use.

In initial assessment of women using the Ring it is important to establish:

- Their current HIV status. Any woman who tests HIV-positive should be referred for treatment.
- If using contraception, whether the method is compatible with Ring use.
- Regular use of other vaginal products or vaginal cleaning practices
- Whether the woman could or would take oral PrEP, which has a higher level of efficacy than the Ring in terms of preventing HIV and should be offered if it suits the individual woman.
- **Counselling, education and building the woman's confidence** in the Ring and her ability to use it successfully constitute a major element of clinical management. It is vital that these be built into the overall clinical experience as they have **make-or-break** significance in terms of the effective use of the Ring.
- The strategies included in this module have been shown to be helpful in **sustaining long-term** adherence to the Ring and those that are best-suited to your practice environment should be pursued as an essential support to clinical management.

Tools to go with this Module

CLINICAL MANAGEMENT QUICK REFERENCE SHEET TOOL 7

Perform HIV testing per country guidelines

All clients: Perform HIV test for the ring

All clients: Refer to HIV testing services at all entry points

Risk reduction counseling and condom use for the ring

- Provide information about the ring
- Counseling on
- Dual-use and regular practice and sharing practices are also the best recommendations (when used if available)

If partners lack a partner: Refer to services to assist (counseling methods)

Inserting the ring: Ring should be inserted into the vagina and be kept in place for 28 days.

Provide support for use ring or mouth-mouth strategy (per country guidance)

Provide user educational material: Refer to the ring user manual regarding ring use, adherence and HIV.

Send a follow-up appointment: When a client is expected to have sexual activity, advise when to return.

Follow-up visits: 1. Determine if client is still using the ring. 2. Determine if client is still using the ring.

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 7

FAQ SHEET TOOL 8

1. What is the dapivirine ring?
The ring is made of a flexible silicone with the HIV drug dapivirine dispersed uniformly throughout its matrix. The ring releases the drug slowly to the vagina over the course of a month with low hormone release in the body, which helps to minimize side effects and reduce the risk of the development of HIV resistance.

2. How effective is the dapivirine ring?
If used consistently and correctly, the ring has been shown to provide up to 95% protection from HIV during regular use for 28 consecutive days. The ring should be used with condoms to reduce the risk of HIV.

3. Is the ring easy to insert and use?
Yes, it is easy to insert the ring. The ring is soft and flexible and can be inserted at any time of the day.

4. How long do I wear the ring?
The ring needs to be in place for 28 days and immediately replaced with a new ring.

5. How long does the ring need to be in place before it is effective?
The ring should be in place for at least 21 hours before the HIV drug begins to help protect against HIV. However, it is best to use condoms until you are sure you are protected. The ring should be used for 28 days and replaced every 28 days.

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 8

STRATEGIES TO SUPPORT ADHERENCE TOOL 9

Step 1: Determine what a client's constraints are to use of adherence support and design interventions.

Step 2: Collect additional context information from the client.

Step 3: If available, encourage client to use a partner or peer buddy to support adherence with appropriate incentives.

Peer Buddy Support

Additional Incentives

Encourage client to set a reminder to wear ring supply appointment!

Provider Support: Encourage client to use a reminder to wear ring supply appointment!

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 9

RING USER JOURNEY TOOL 10

Part 2: Ring Use Journey

1. If you are pregnant, your provider will discuss alternative methods of contraception.

2. If you are not pregnant, your provider will discuss alternative methods of contraception.

Your provider will provide you with a prescription for the ring, an education material, and a follow-up appointment!

3. Insert the ring into your vagina.

4. After six weeks: Monitor continuing ring placement and ensure the ring is still in place. You may have:

- Ring insertion
- Ring removal
- Ring replacement
- Ring insertion

5. All 6 months: HIV test (minimum 25 consecutive days)

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 10

DAPIVRINE VAGINAL RING END USER GUIDE TOOL 11

DAPIVRINE VAGINAL RING

Dapivirine Vaginal Ring – A Guide for Users

- The ring is a flexible silicone ring.
- A ring that has not been used has an off-white color and is easy to bend.
- The ring releases the drug slowly over a month getting HIV-1 infection during regular use.
- The ring should be used with condoms.
- The ring should not be used if you are pregnant or breastfeeding.
- The ring should not be used if you are taking any other HIV medicines.
- The ring should not be used if you are taking any other HIV medicines.
- The ring should not be used if you are taking any other HIV medicines.

INSTRUCTIONS FOR RING INSERTION

1. Wash your hands to clean water and dry them.
2. Check the ring is still in the package (date of expiry) and if the ring is damaged or expired.
3. Tear package to open. DO NOT use scissors to open the package. Use the tear strip to open the ring from the package.

INTERNATIONAL PARTNERSHIP FOR MICROBICIDES

Tool 11

RING HEALTHCARE PROFESSIONALS GUIDE
TOOL 12



DAPIVIRINE VAGINAL RING
Dapivirine Vaginal Ring – A Guide for Healthcare Professionals

This guide summarises key information for use by healthcare professionals to assist with safe and correct use of the Dapivirine Vaginal Ring when counselling and advising potential users.

THE DAPIVIRINE VAGINAL RING FORMS PART OF A COMPREHENSIVE HIV-1 PREVENTION STRATEGY

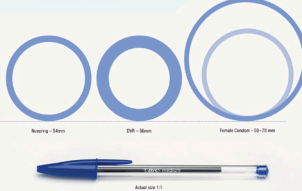
- The Dapivirine Vaginal Ring is indicated for use by women for continuous or on-demand prevention of HIV-1 infection.
- The Dapivirine Vaginal Ring does not protect against other sexually transmitted infections (STIs) including hepatitis B virus (HBV) infection or hepatitis C virus (HCV) infection.
- The Dapivirine Vaginal Ring is only effective in preventing the risk of HIV-1 infection during vaginal intercourse.
- The Dapivirine Vaginal Ring should be used in conjunction with other HIV-1 prevention strategies.
- The Dapivirine Vaginal Ring should be used in conjunction with other HIV-1 prevention strategies.
- The Dapivirine Vaginal Ring should be used in conjunction with other HIV-1 prevention strategies.

INTERNATIONAL PATENTED FOR MACROCODES

Tool 12

PULL OUT SIZE TOOL WITH DVR, NUVARING, FC2
TOOL 13

- Measuring – Shows size placement and shows ring location
- DVR – Shows size placement and 7.7cm size location
- FC2 – Shows size placement and 7.7cm size location
- The inner ring diameter is 6.8cm and 7.7cm, while the inner ring diameter is 6.8cm

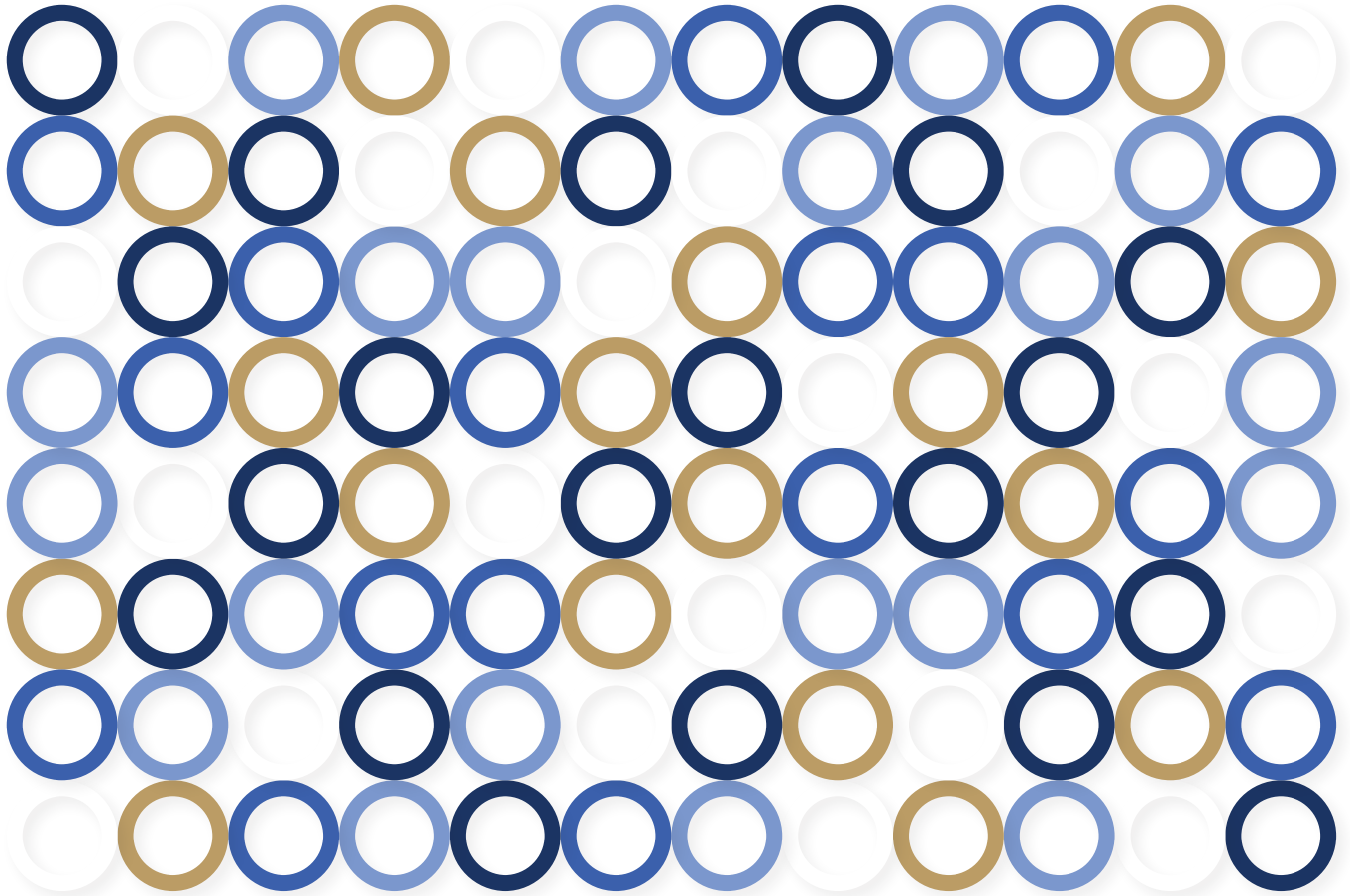


Nuvaring – 56mm DVR – 56mm Female Condom – 58-70mm

Actual size 1:1

INTERNATIONAL PATENTED FOR MACROCODES

Tool 13



Module Six

Counselling and Supporting Effective Ring Use

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About this training manual

This training manual was developed by the International Partnership for Microbicides, as a training resource, that is adaptable to the local country context in which the dapivirine vaginal ring is being implemented.

Each module in the manual is designed to be used either independently or as part of the full pack. Each module has a set of suggested tools which are pull outs at the end of the manual.

Attribution and Citation

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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INTRODUCTION

Findings from the rollout of oral pre-exposure prophylaxis (oral PrEP) programmes in a number of countries have been mixed, with some women reporting difficulty taking daily oral PrEP. This points to the need for additional options for PrEP delivery, including long-acting PrEP products such as the dapivirine vaginal ring (DVR or the Ring).

Like oral PrEP, the Ring can be discreetly used and is woman-controlled but does not rely on daily dosing.

Current evidence suggests that daily oral PrEP, when taken as prescribed, has greater efficacy for HIV prevention than the Ring¹. This does not mean that the Ring should not be offered to women. On the contrary, women should be provided with full information and counselling on all available prevention options and their relative efficacy and safety, and should be counselled to help them to make an informed choice regarding the best option for them².



1 WHO Updated recommendations on HIV prevention, infant diagnosis, antiretroviral initiation and monitoring: March 2021

2 IBID

Draw upon your country's national counselling strategies and guidelines to support your capacity to counsel and guide women to the appropriate HIV-prevention method for them.

COUNSELLING

When counselling a woman about her HIV-prevention options, it is important to create a supportive environment where she can discuss her needs and experiences, and to recognise that product use is ultimately the woman's choice. Your role is to encourage product use but not to expect or demand it.

Key points relating to counselling:

- Recognise that changing sexual or risk behaviours is equally (if not more) complicated as changing behaviours associated with non-communicable diseases.
- Correct, evidence-based information should be provided to women and it should include other prevention strategies
- Discussing risk with women is highly contextualised and personal, but it can easily be integrated into current practices by lay counsellors, nurses and clinicians

Draw upon your country's national counselling strategies and guidelines to support your capacity to counsel and guide women to the appropriate HIV-prevention method for them.

PRINCIPLES OF GOOD COUNSELLING

The following principles of good counselling practice have been adapted from the counselling guide used in the ASPIRE safety and efficacy study on the Dapivirine Vaginal Ring. You should be striving to ensure the counselling you provide is:

Client-centred: The woman is the expert on her life and behaviours.

Comprehensive (or multi-targeted): Providing accurate information is necessary but insufficient to produce behaviour change or promote engagement in discussions about product use. Motivation – which is both personal and vested in the woman’s social networks – and skills are also critical to help produce change.

Counsellor-guided: Guide the discussion through questioning and do not do most of the talking. The woman should have the majority of “talk time” in any session.

Context-driven: Counselling explores the context in which one negotiates product use. It is not focused on events when the product was removed or, specifically, on barriers. The focus is on the aspects of product use that facilitate or challenge the ease with which one experiences product use (or non-use) in their daily life.

Genuine: Maintain a genuine interest in the woman and reflect that interest through exploration of her experiences. Remain engaged and authentic (real, honest, present and attentive) throughout the conversation.

Individualised: Counselling for product use is individually tailored to the levels of engagement and product-use behaviours of a specific woman at a given point in time.

Neutral: Maintain a supportive, non-judgmental, and neutral stance to convey acceptance of both the woman and her disclosures of positive and negative aspects of product use.

Aware of limited role: Recognise that your impact is in the immediate session and that you cannot “make” women do anything. You can, however, ensure that a safe environment is consistently provided for the women to openly discuss product use.

Maintain a genuine interest in the woman and reflect that interest through exploration of her experiences. Remain engaged and authentic

EFFECTIVE USE AND ADHERENCE

When discussing the effective (or correct) use of the Dapivirine Vaginal Ring, it is important to address the topic in a neutral manner in order to enable the woman to feel comfortable and free to discuss instances of non-adherence.

Encourage your client to ask questions and raise issues or problems at any time. Suggest that she should pay attention to her experiences in using the Ring between the current visit and the next, and share these with you when you meet.

Supporting the use of a biomedical HIV prevention option in women should be honest, direct and non-judgmental. The key to encouraging the effective and correct use of the Ring is by having an open relationship with the client.



YOUNG WOMEN AND EFFECTIVE USE

Young women are exceptionally vulnerable to HIV due to a complex web of cultural and economic factors that inhibit their sexual and health agency.

Countries differ in terms of the way these factors combine to impact on the lives of young women – so it is important that you bring your understanding of your society to bear on your engagements with young clients.

When offering the Ring to young women, it is important to prepare for caey questions intended to support their uptake and use of HIV prevention products:

- What delivery models will work best for young women?
- How do we support young women to understand their risk?
- How can we help improve the ability of young women to negotiate the use of Ring and other HIV-prevention methods with their partners?
- How can we mitigate any potential harms, such as gender-based violence?

Young women require social support that, ideally, not only addresses immediate adherence challenges but also empowers them with tools for greater self-efficacy in a gender inequitable society³.

The REACH study⁴ demonstrated that young women can adhere to monthly use of the Ring with appropriate support. They need a tailored package of consistent adherence support. This does not need to be one-on-one or face-to-face. It can utilise digital and social media platforms, such as WhatsApp groups and other telephonic contact, and peer clubs.

3 Baron, D., Scorgie, F., Ramskin, L. et al. "You talk about problems until you feel free": South African adolescent girls' and young women's narratives on the value of HIV prevention peer support clubs. *BMC Public Health* 20, 1016 (2020). <https://doi.org/10.1186/s12889-020-09115-4>

4 <https://www.mtnstopshiv.org/news/study-finds-adolescent-girls-and-young-women-africa-will-use-hiv-prevention-products>

INTEGRATING THE RING INTO STANDARD RISK-REDUCTION PRACTICES

It is important to highlight to women that the Dapivirine Vaginal Ring is new and can be used with other HIV prevention methods, such as condoms.

It is also important to highlight that a larger variety of HIV prevention options, specifically those that are women-controlled, may better support achievable risk reduction, particularly where more traditional prevention strategies have not been used effectively (i.e. condoms, abstinence, etc.).





GOAL: Using active listening skills and an individualised approach, create a comfortable environment to talk about client experiences.

METHOD: Exploration of context (experiences, thoughts, beliefs, feelings, skills) to identify what would need to happen or continue happening for the behavior to be most manageable or "easy."

CLIMATE: Supportive, nonjudgmental, neutral, reinforcing of open discussion/efforts, avoidance of "fixing," recognition of limited role, and emphasis on client as a whole person.

IMPLICIT ASSUMPTION: Clients choose whether or not to do something based on feeling well informed, motivated and skilled. We cannot make a client adopt a behavior, but we can provide and promote opportunities to develop information, motivation, and skills relevant to her in her life.

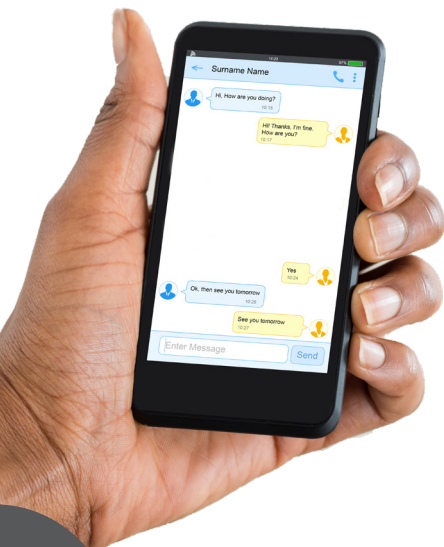
BUILDING A STRONG FOUNDATION FOR EFFECTIVE RING USE

When initiating a woman in use of the Dapivirine Vaginal Ring or supporting a long-term user, you must:

- Ensure that proper education has been provided regarding: Ring use, required lead in times, length of use, and required use for protective levels.
- Ensure that your patient leaves with a plan in place to support herself in her HIV-prevention journey, has identified at least one potential barrier and developed a solution for that barrier.

Other ways to support use of the Ring

- Use alternative channels of communication to send reminders about follow-up appointments: SMS, WhatsApp, social networks, mobile applications.
- Integrate mobile health services and outreach programmes into existing HIV-prevention services.
- Combine HIV services with complementary services such as family planning and psycho-social care.
- Enhance peer support strategies, for example, by introducing or expanding clubs.
- Provide alternative clinic hours, if possible. This is particularly important for adolescent- and youth-friendly services.
- Collect additional contact information for each patient so you can follow-up and check on the client and provide additional support if needed.
- In event of a clients migrating, provide her with additional product (or a script) to see her through the move and with a referral letter to a service provider at the destination.
- Help your client, and particularly AGYW, figure out the best way to disclose (to her partner) that she is on Ring, if she so chooses.



KEY INFORMATION TO PROMOTE EFFECTIVE USE

Explain to the client that the Ring provides a consistent release of dapivirine locally in the vagina, which is the potential area of HIV infection.

- Ensure that the client knows there is minimal systemic absorption, so side effects are minimized.
- Emphasise that this localised drug delivery also means the Ring only protects during vaginal sex – not during anal sex.

Discuss the need for continuous use of the Ring for maximum effectiveness.

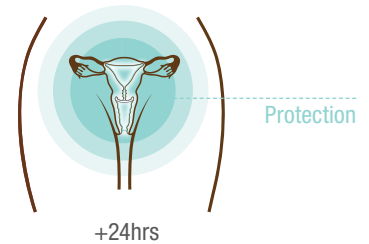
- Continuous use – meaning inserting the Ring and keeping it in place for one month.
- The Ring does not prevent other STIs or unintended pregnancy, so it should be used with either a male or female condom.

Discuss the necessary time required after insertion for the Ring to become effective.

- It takes 24 hours after insertion for the Ring to release enough dapivirine to provide protection.
- Advise your client that if she has sex before the 24 hours have passed, she should make every effort to use a condom.

Discuss the need for the Ring to stay inserted to do its job.

- Inform your client that she can go about her daily activities as usual. There is no need to remove the Ring during menstruation, and the Ring can be used with a tampon.
- There is also no need to remove the Ring during sex, and it is rarely felt by either partner during sex.



When the ring is in the vagina, the medication dapivirine is slowly released.



Rinse the ring in clean water.



Place the dirty ring in a tissue or toilet paper and throw it in a rubbish bin

Explain what to do if the Ring falls out or gets damaged

- Indicate that the Ring falls out very infrequently, but it can occur. Provide advice on how to deal with this. (See box)
- If a Ring is damaged or broken, it should not be inserted or re-inserted. The client should report the incident to their health-care provider.
- Some women are concerned that the Ring can become dislodged and “get lost” inside their bodies. It is important to explain that this is not possible, because it sits firmly against the base of the cervix. (Use a visual resource to demonstrate this.) [link to video]

If the ring comes out

In a CLEAN place (for example in your bed or your clothes):

1. Rinse the ring in clean water.
2. Do not clean the ring with soap or other cleaning products.
3. Immediately reinsert it into your vagina.

In a DIRTY place (for example in the toilet, on the floor):

1. DO NOT put it back in your vagina.
2. Place the dirty ring in a tissue or toilet paper and throw it in a rubbish bin.
3. Immediately insert a new ring.

Explain that the Ring can be used with most forms of contraception.

- Ensure you discuss that the Ring should not be used with contraceptive vaginal rings, menstrual cups or cervical caps.

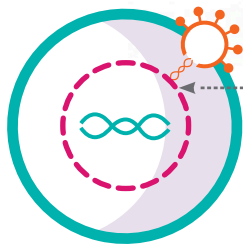
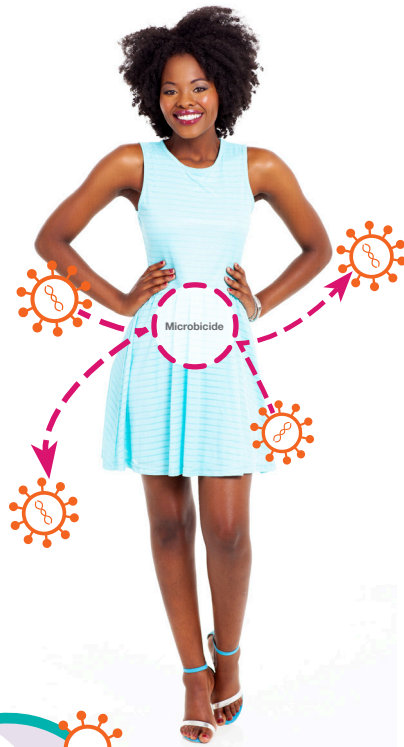
Inform women not to share their Ring.

- Insert only the Ring provided to you and do not share your Ring with other women.
- The Ring will only work for you if you use it the way it is meant to be used.

Women whose partners are living with HIV

- Emphasise the importance of her HIV-positive partner continuing his antiretroviral treatment (ART), as prescribed, or initiating ART if he has not done so.

Dapivirine works by preventing HIV from making copies of itself, so if a woman is exposed to HIV when the dapivirine ring is in place, the virus is more likely to die before spreading in her body.

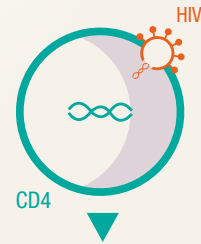


CD4

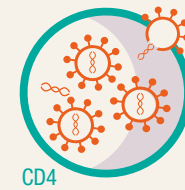
A **microbicide** which contains dapivirine (ARV) stops the virus from infecting its host by preventing it using the CD4 cell to make copies of itself – interrupting the HIV cycle. No virus copies mean no infection.

How HIV infects the human body

The virus breaks into the CD4 cell and inserts its own genes. It then uses the CD4 cell to make copies of itself. HIV cannot copy itself and needs a CD4 cell to reproduce.



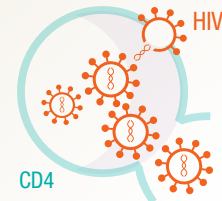
CD4



CD4

HIV Infection occurs when HIV enters the body, finds a CD4 cell and uses it to make copies which spread and infect other cells.

The new copies of the HIV breakout of the CD4, killing the cell. These many copies then find other healthy CD4 cells in which to repeat this process.



CD4



ENCOURAGING PARTNER INVOLVEMENT

Women's perceptions of her partner's potential support for Dapivirine Vaginal Ring use may be based on past experience or on her fears and subjective interpretations. However, it has been demonstrated that male partner involvement can increase the effective use of the Dapivirine Vaginal Ring⁵.

Male partner involvement usually begins with disclosure. Supporting women to disclose Ring use to their partners is valuable and may minimize the risk of any violence in the response of their partners. Some women may elect to bring their partners to the clinic

to facilitate disclosure. Disclosure and clinic attendance may work independently or together to move partners along the continuum from opposition towards active support for Ring use.

5 Montgomery ET, Roberts ST, Reddy K, Tolley EE, Hartmann M, Mathebula F, Wagner LD, Lanham M, Wilcher R, Browne EN, Baeten JM, Palanee-Phillips T. The CHARISMA randomized controlled trial: a relationship-focused counseling intervention integrated within oral PrEP delivery for HIV prevention among women in Johannesburg, South Africa. *J Acquir Immune Defic Syndr*. 2022 Apr 13. doi: 10.1097/QAI.0000000000002991. Epub ahead of print. PMID: 35416797.

If a client brings her partner to the clinic, encourage male engagement to enhance Ring use

- Facilitate dialogue on men's sexual health and HIV prevention.
- Educate on female sexual and reproductive health.

Other sources of potential support

- Engage older women who have influence in young women's daily lives and decisions.
- Collaborate with higher education institutions with a view to supporting female students.
- Identify potential new partners working on women's issues in the broader health environment.

Intimate partner violence

While partner support for a woman's choice to use the Ring is likely to improve prevention outcomes, it is not achievable for all women. Intimate partner violence (IPV) is common in

many countries and some women who opt for the Ring will do so precisely because it can be used discreetly, without the partner's approval.

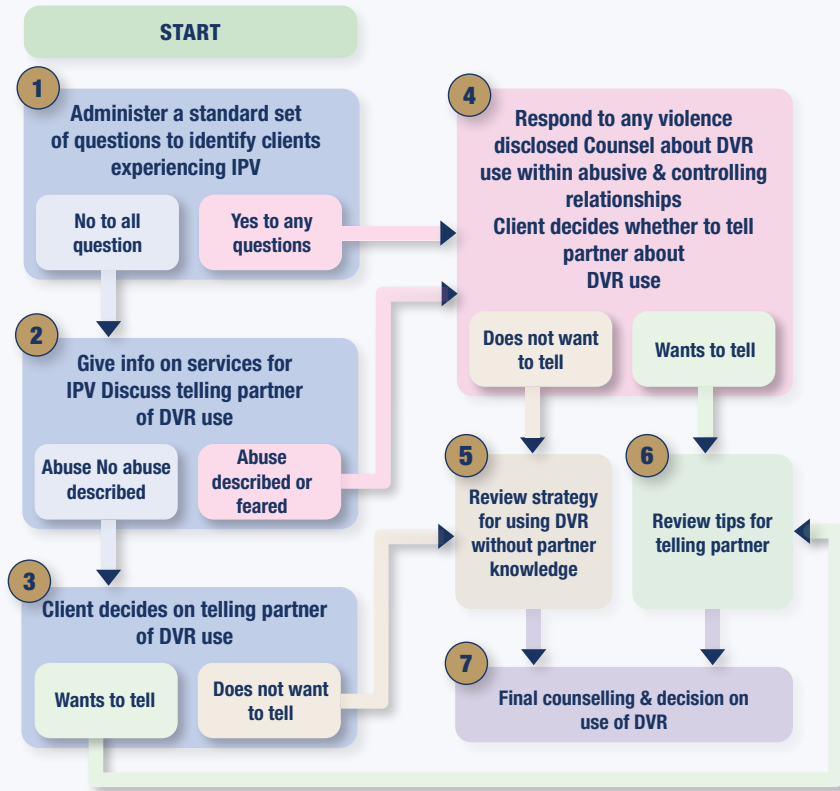
All your clients should be assessed for the presence of IPV in their lives at every visit:

- The presence or absence of IPV will inform their decisions on whether to disclose Ring use.
- It will affect the nature of support you need to offer.

The following chart and accompanying table outline a process for assessing every client and then adopting different approaches for those who disclose the presence of partner violence and those who do not. It further indicates how to respond to the different needs of women who wish to tell their partners they are using the Ring and those who do not want their partners to know.

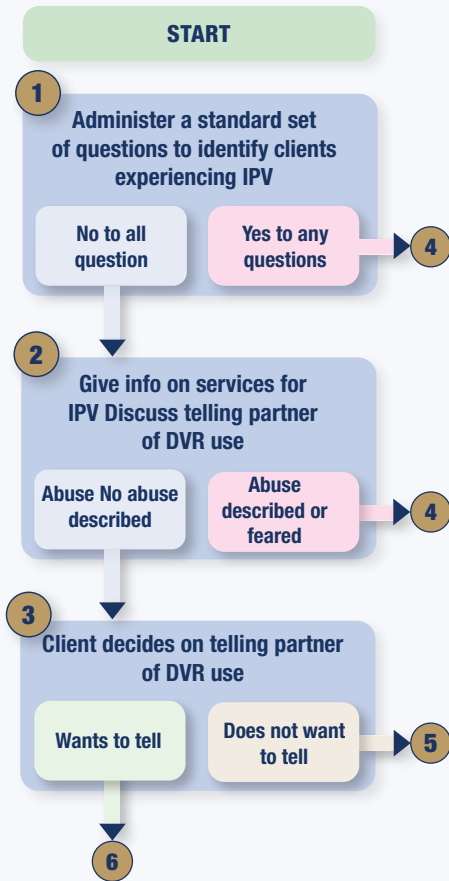


Managing decisions on Ring disclosure in light of possible partner violence



Source: Adapted from the CHARISMA study on use of oral PrEP.

Summary of steps for discussing partner relationships and ring use



1. Explain: Partner abuse is common. Can affect ability to use the Ring, so all clients are routinely asked about it. (If there are limits to confidentiality, also explain these)

Ask if partner has:

- Ever made client feel afraid, bullied or insulted or tried to control her
- Ever hit, kicked, slapped or physically hurt her
- Ever forced her into sex or any sexual contact she did not want

Never force a client to disclose violence even if you believe it is occurring

2. Advise client if she ever wants to share anything or issues arise, you are there to support her. Supply a list of resources providing support in situations of IPV.

Discuss whether she wants to tell partner she is using the Ring.

Indicate

1. It is her decision
2. Some women tell their partners to secure their support
3. Others with privacy, safety and other concerns prefer partner not to know.
4. Many women use the Ring successfully without their partner knowing.

Tell her you want to hear her wishes on whether to tell her partner. Ask her how she thinks he would respond – explore what she means

3. Ask client: “Would you like to talk to your partner about the Ring?”

4. Respond to disclosure of violence by offering support:

- **Listen:** closely and with compassion
- **Inquire:** assess needs and respond to them
- **Validate:** show your belief in the client
- **Enhance safety:** discuss plan to protect from further harm, including HIV protection
- **Support:** offer to connect client with additional services and support

Counsel about Ring use in abusive/controlling relationships.

Acknowledge client’s possible vulnerability to HIV and possible difficulty of knowing partner’s status and negotiating condom use

Brainstorm specific challenges that might arise in relation to using the Ring

Help client decide whether to tell partner about using the Ring or not.

If client does not want to tell partner, advise her it may be challenging but many women have successfully used the Ring without telling their partner

If client wants to tell their partner, offer to discuss ways to do this more safely and advise someone at clinic would be available to talk to partner

5. Strategy for using the Ring without partner's knowledge should include plan for safe storage of new Rings and "explaining" regular clinic visits to partner. It should also include response if he finds out and is angry, including where client will get support if she needs to leave home.

6. Tips for telling partner should cover:
- How to tell: simple language, calm manner, ready to answer questions
 - When to tell: allow enough time for discussion
 - Where to tell: maybe choose place where help is close by in event of angry response

Perhaps start with general discussion on the Ring & move slowly over time to disclosing intention

7. If the client wants to start (or continue) using the Ring:

- Help her identify her main reason for using the Ring and remind her of her own strength
- Prompt her to think of someone who could support her in this decision and ask what support she needs from provider.
- Discuss other options for HIV prevention in event it becomes impossible to continue using the Ring





PRIORITISING COMMUNITY ENGAGEMENT

- Community engagement involves raising awareness of the Ring in the broader community which exercises an influence on our clients.

Every community is complex and has multiple layers and groups and it may be helpful to categorise these in terms of proximity to a client's life.

- **Immediate environment:** this comprises the people closest to your client, such as her sexual partner, family, and friends. community, healthcare providers, and other community groups.
- **Intermediate distance:** this layer of influence may include people the client interacts with directly, such as religious leaders or congregation, elders in the
- **Furthest removed:** these may include people that the client does not interact with but who have an influence on her life – political figures, public health officials and influencers.

Strategies aimed at increasing understanding of the Ring across these layers can have an impact on community support. Activities within these strategies to raise awareness could include radio discussions and campaigns, health talks in clinics, and participation in community forums.



Key takeaways from this Module

- Counselling should be supportive and based on a woman's needs, resources and preferences. It is never prescriptive.
- The key to encouraging effective and correct use of the Ring is having an open and honest relationship with the client.
- Recognise that behaviour change is not easy and human beings are not perfect
- Focus on the identification of “small wins” and more achievable “next steps” in reducing risk and/or making the use of new methods of HIV prevention easier.
- Supporting effective use of the Ring among women presents new opportunities to address HIV in an effective, efficient and achievable way.

Tools to go with this Module

COUNSELLING QUICK REFERENCE SHEET
TOOL 14

- 1. WELCOME AND TRAIN**
Outline purpose of discussion. Seek consent to continue discussion.
- 2. IDENTIFY NEEDS**
Ask what the client needs for Ring use to be most likely to be used by them or their partner.
- 3. EXPLORE**
Explore experiences with Ring (including) challenges to having Ring inserted or to remembering it, if applicable.
- 4. GOAL**
Identify a realistic discussion for the client to try, confirm or consider using between now and the next visit.
- 5. STRATEGISE**
Explore how needs can be addressed or how strategies/factors that currently for Rings use can be implemented.
- 6. CLOSE**
Reinforce and summarise client's wish to use (or not use) Ring use and what they will do in between visits.

ESSE: Using active listening skills and an observational approach, create a supportive environment to talk about client experience.

EMPOWER: Supportive, non-judgmental, active involvement of non-consultant, primary, consistent or "they" responses, if available, and evidence of client as a ring person.

INTERVIEW ASSUMPTIONS: Clients choose whether or not to use condoms based on their own decision, but also the social norms and personal opportunities to access, integrate, maintain and skills related to be in sex.

ESSE: Supportive, non-judgmental, active involvement of non-consultant, primary, consistent or "they" responses, if available, and evidence of client as a ring person.

INTERVIEW ASSUMPTIONS: Clients choose whether or not to use condoms based on their own decision, but also the social norms and personal opportunities to access, integrate, maintain and skills related to be in sex.

INTERNATIONAL PATENTIONS FOR MICROBIOCIDES

Tool 14

IPV RESOURCE
TOOL 15

RING JOB AID FOR DISCUSSING PARTNER RELATIONSHIPS

Summary of steps for discussing partner relationships and ring use

START

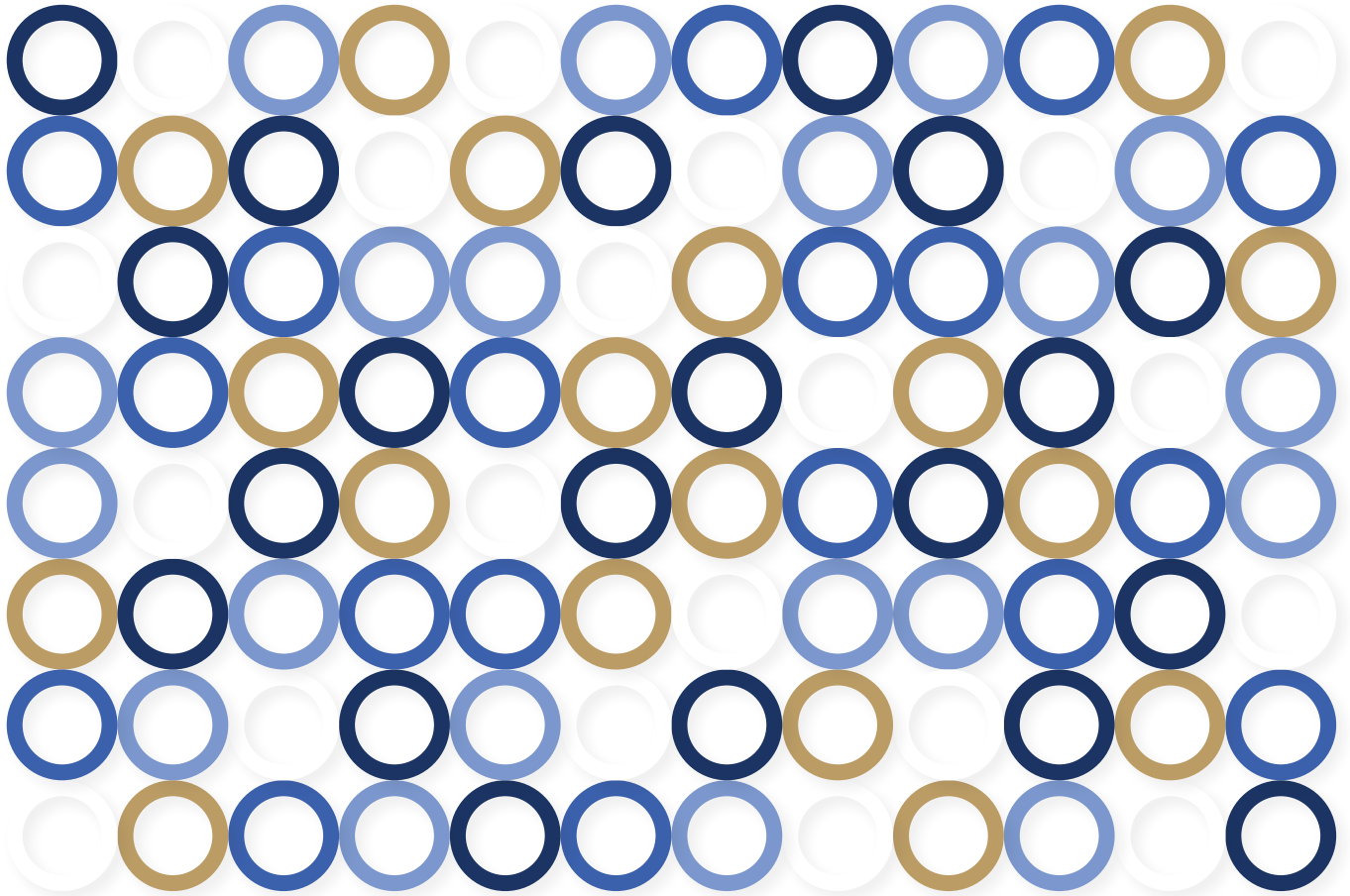
- 1. Administer a standard set of questions to identify clients experiencing IPV**
No to all questions → 2. Give info on services for IPV Discussing partner of DTR use
Yes to any questions → 3. Respond to any evidence disclosed. Counsel about DTR use with/without & controlling relationships. Client decides whether to talk partner about DTR use.
- 2. Give info on services for IPV Discussing partner of DTR use**
About No above described → 3. Respond to any evidence disclosed. Counsel about DTR use with/without & controlling relationships. Client decides whether to talk partner about DTR use.
About Yes above described → 3. Respond to any evidence disclosed. Counsel about DTR use with/without & controlling relationships. Client decides whether to talk partner about DTR use.
- 3. Respond to any evidence disclosed. Counsel about DTR use with/without & controlling relationships. Client decides whether to talk partner about DTR use.**
Does not want to talk → 4. Review strategy for using DTR without partner knowledge.
Wants to talk → 5. Review tips for talking partner.
- 4. Review strategy for using DTR without partner knowledge.**
Does not want to talk → 7. Final counselling & decision on use of DTR.
Wants to talk → 5. Review tips for talking partner.
- 5. Review tips for talking partner.**
Client decides on talking partner of DTR use → 6. Client decides on talking partner of DTR use.
Does not want to talk → 7. Final counselling & decision on use of DTR.
- 6. Client decides on talking partner of DTR use.**
Wants to talk → 7. Final counselling & decision on use of DTR.
Does not want to talk → 7. Final counselling & decision on use of DTR.
- 7. Final counselling & decision on use of DTR.**

Instructions for Use
Design of the screen labeled "Start" or other the summary or detailed version of the job aid, depending on your profession.

- Complete each step indicated by the flowchart before moving on to the next step.
- When decisions are required, follow the original screen according to the client's wishes or responses.
- Text in italics on the detailed flow chart is a support script.

INTERNATIONAL PATENTIONS FOR MICROBIOCIDES

Tool 15



Module Seven

Case Studies

Contents

Case Study 1A:	1
Difficulty inserting or removing the Ring due to being overweight	
Case Study 1B:	2
Difficulty removing the Ring due to being overweight	
Case Study 2:	3
Partner concerns/discomfort with use of the Ring	
Case Study 3:	5
Misconceptions about STI's when using the Ring	

About this training manual

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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CASE STUDY 1A:

Difficulty inserting or removing the Dapivirine Vaginal Ring due to being overweight

Introduction:

This case shows the importance of DVR user training, especially in those patients who have an increased BMI, considered as overweight

Case presentation:

A 20-year-old female client presents to the clinic stating that she wants to stop using the Ring because she struggled with insertion and removal due to her being overweight and not being able to physically get her fingers to her vaginal introitus to insert the Ring.

She would often ask the clinical team to rather insert/remove the Ring and developed a fear of doing it herself due to this dependence. She was committed to using the Ring and was motivated to continue on the Ring should she be able to overcome this challenge.

Management and Outcome:

The client underwent extensive counselling in a non-pressured and judgement free space. Time was set aside by the clinician/nurse, and she was able to practice removal and insertion with the clinical team.

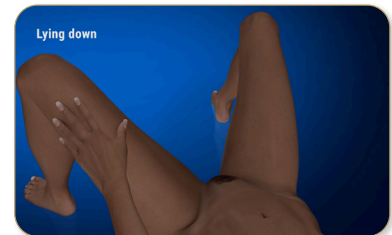
Simply modifying her technique by instructing her to squat or lie in a lithotomy position showed her that she was indeed able to reach her vaginal introitus and insert the ring with ease. The next barrier was her concern over positioning of the Ring. The clinic (as with

condom use models) has a dummy model with a transparent vaginal wall which shows where the ring should sit within the vaginal canal. This re-assured the client that when she inserts it, it is in the correct place, and she was able to practice with the model as well.

Once these issues were resolved she was asked to do it on her own and was encouraged to practice with positive re-enforcement offered by the clinic team.

Discussion:

We noted during the clinical trials that women with a higher BMI tended to struggle with self-insertion and removal of the Ring. This led to them becoming hesitant to use the Ring as they were concerned that they may not insert it correctly or be able to remove it at home. By discussing and practicing different insertion/removal positions in an unrushed space, while addressing concerns over correction insertion using a pelvic model helped to overcome this challenge.



Simply modifying her technique by instructing her to squat or lie in a lithotomy position showed her that she was indeed able to reach her vaginal introitus and insert the ring with ease.



CASE STUDY 1B:

Difficulty removing the Dapivirine Vaginal Ring due to being overweight

Introduction:

This case highlights challenges with removal of the Ring for clients with increased BMI, and partners can form part of the strategy to support consistent and continued Ring use.

Case presentation:

An obese client in her twenties, initiated ring use at the clinic and was able to insert and remove the ring with ease. However, at her next clinic visit she failed to remove the ring whether she tried a squatting position, semi-sitting position (lithotomy), side lying position with one leg elevated (flexed) or one leg elevated on a chair, and therefore was assisted by a nurse. She managed to insert the new ring easily. She was again advised to

contact site staff if she has any issues. She left the clinic comfortable knowing that she has our support.

At her next visit she failed to remove the ring again as well as insert the new ring although she tried all positions mentioned above again. Several failed attempts continued throughout the follow-up visits, but she was assisted by the study nurses.

Management and Outcome:

In addition to assisting the client to insert and remove the Ring at the clinic, the client was offered an additional ring, in order to attempt removal and insertion in the comfort of her home. On her return to the clinic, she reported

during the counselling session that given the challenges she had with self-insertion, she taught her partner how to remove the old ring and insert the new one as he was aware of and supported her ring use.

Discussion:

In this case partner disclosure was important to maintain consistent ring use and support

CASE STUDY 2:

Partner concerns/discomfort with use of the Dapivirine Vaginal Ring

Introduction:

This case focuses on partner concerns with the use of the Ring. The case highlights the importance of ongoing, open and non-judgemental communication about Ring use challenges and how to navigate partner concerns.

Case presentation:

An 18-year-old female client presents to the clinic stating that she wants to stop using the Ring because her partner reports it to be uncomfortable during sexual intercourse. She reports that he is her only partner but isn't sure if he has more than one sexual partner.

She understands the benefit of being on some form of pre-exposure prophylaxis (PrEP) but isn't sure how to navigate the difficulties of this situation without losing her sexual partner. She asks for advice or alternatives to using the Ring.

Management and Outcome:

The client underwent extensive counselling prior to commencing the Ring so that she understood its benefits and to speak to a healthcare provider to make an informed decision prior to discontinuation in order to seek alternative options or optimise her care. Establishing a good relationship with the client facilitated her willingness to disclose the partner issues and discuss these with a healthcare provider rather than simply discontinuing it because of her partner concerns.

The client was offered partner counselling to discuss these challenges. She consented

to the partner presenting for counselling and to explain the importance of the Ring. Upon counselling the partner, he stated that he understood the importance of the Ring and didn't mind her being on the Ring. He expressed concern about having penetrative vaginal sex whilst she was using the Ring because he was worried it would affect her sexual and reproductive health. The client stated "it was just a shock to him to have felt it during sex". It is important to note that the ring can remain in during sexual intercourse, does not affect the clients health and will not have an effect on the penis.



CASE STUDY 2:

Partner concerns/discomfort with use of the Ring

Discussion:

This case highlights the importance of not only pre-commencement counselling, but ongoing counselling to users of the Ring. It is imperative to build a good relationship with clients to ensure that counselling and communication remains open, honest, and non-judgemental.

It is important to inform clients that sexual health is not be impaired by use of the Ring and providing re-assurance that speaks to this. In cases where partner disclosure is possible, it important that partners have correct information about the Ring.

CASE STUDY 3:

Misconceptions about STI's when using the Dapivirine Vaginal Ring

Introduction:

This case shows the importance of pre-commencement counselling and continued counselling to prevent misconceptions about the Ring that could discourage Ring use.

Case presentation:

A 19-year-old female client contacts the clinic after using the ring for 2 months as she now has a yellowish malodorous discharge that started 5 days prior to contacting the clinic. She had penetrative vaginal sex with a new partner 2 weeks ago without using a condom. She reports no other symptoms but is highly

concerned that she has contracted a sexually transmitted infection (STI) from using the Ring. She is also upset because she thought the Ring would have provided her with some protection from STI's and wants to know why this wasn't the case.

Management and Outcome:

This client was seen in the clinic as soon as possible after she had made telephonic contact (<1 day) to provide not only a medical assessment and treatment, but also to provide further counselling and correct her misconceptions around the Ring and STI's. She was counselled on STI/HIV transmission and preventative measures.

It was clarified to her that the Ring is only for HIV prevention, but does not guarantee that she will not contract HIV through unprotected sexual contact, only that it will reduce her risk of contracting HIV. She was reminded that other STI's (Chlamydia, Gonorrhoea etc) and pregnancy are not prevented with the Ring.

She understood, after counseling, how STI's spread and that condoms should always be used in conjunction with the Ring to prevent the spread of STI's.

Further counselling was done to explain to her that the Ring contains no bacterial components or components that would increase her risk of contracting STI's and it was likely that unprotected sex with a new partner was most likely responsible for the STI. A clinical examination was conducted to rule out pelvic inflammatory disease and she was treated for the STI based on her symptoms. She was also counselled on partner tracing and treatment and a partner letter was issued.



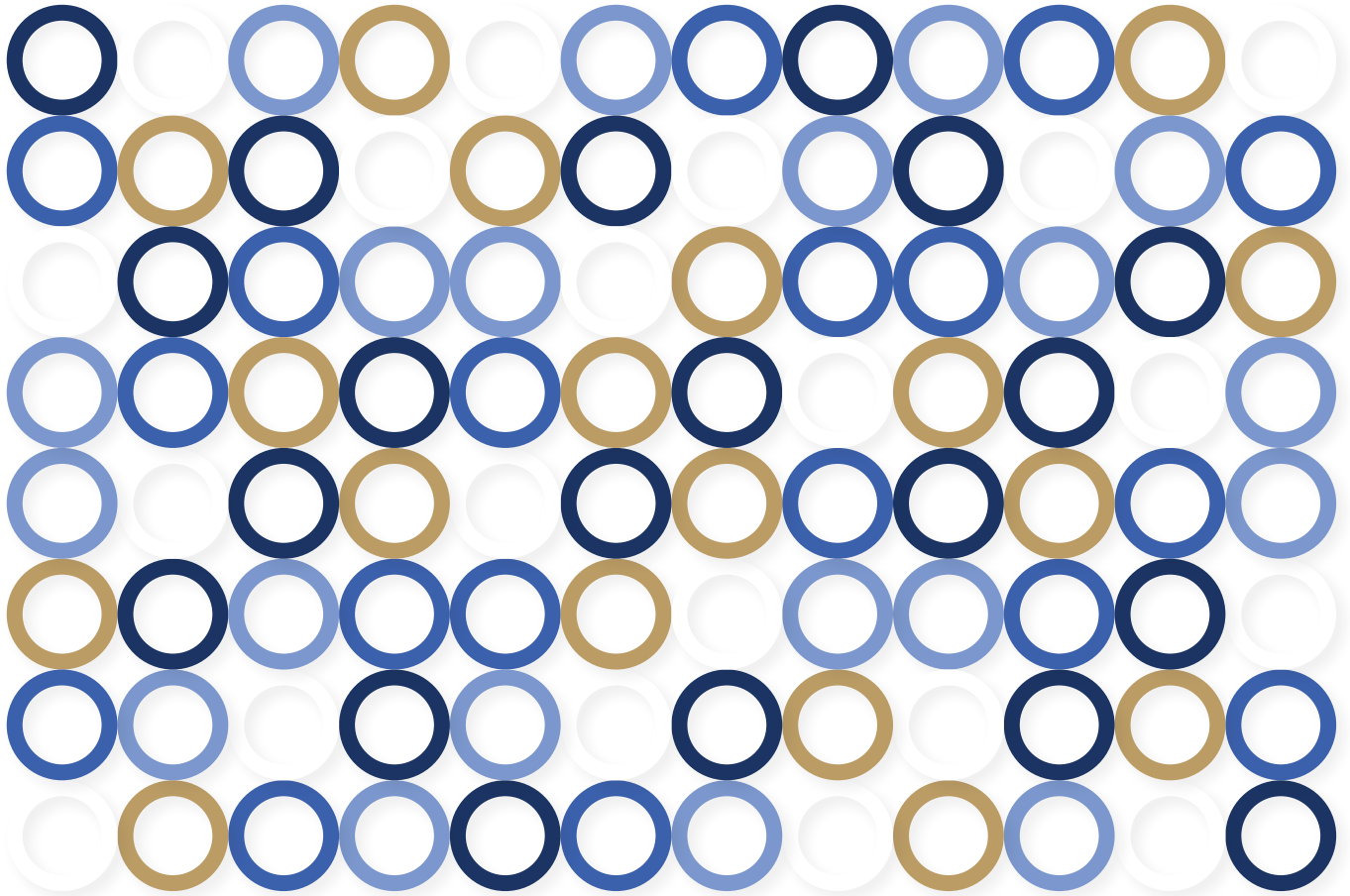
CASE STUDY 3:

Misconceptions about STI's when using the Dapivirine Vaginal Ring

Discussion:

This case speaks to resolving misconceptions surrounding DVR use. Sexual health education should form part of a team-based approach through community outreach, counsellors and clinicians who should re-enforce important topics to prevent misinformation which could discourage Ring use.

It also highlights the importance of ongoing counselling in clients who may forget information offered to them at the initiation of the Ring. It should be discussed with the client that they have an increase in normal physiological vaginal discharge or slight itching upon initial use of the Ring, but if it becomes malodourous or discoloured, they should seek assistance from the clinic.



Module Eight

Tools

About this training manual

This training manual was developed by the International Partnership for Microbicides, as a training resource, that is adaptable to the local country context in which the dapivirine vaginal ring is being implemented.

Each module in the in the manual is designed to be used either independently or as part of the full pack. Each module has a set of suggested tools which are pull outs at the end of the manual.

Attribution and Citation

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Comments & Feedback: Please direct any comments and feedback related to this manual to Diantha Pillay, at hcpsupport@popcouncil.org

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Global Healthcare Provider Training Package

Dapivirine Vaginal Ring

Modules

Module One

Introducing the Dapivirine Vaginal Ring (DVR)

Module One B

Evidence of the Ring's Safety and Effectiveness

Module Two

Providing the Ring – the Basics

Module Three

Meeting the HIV-Prevention Needs of Diverse User Groups

Module Four

Raising Awareness and Communicating About the Ring

Module Five

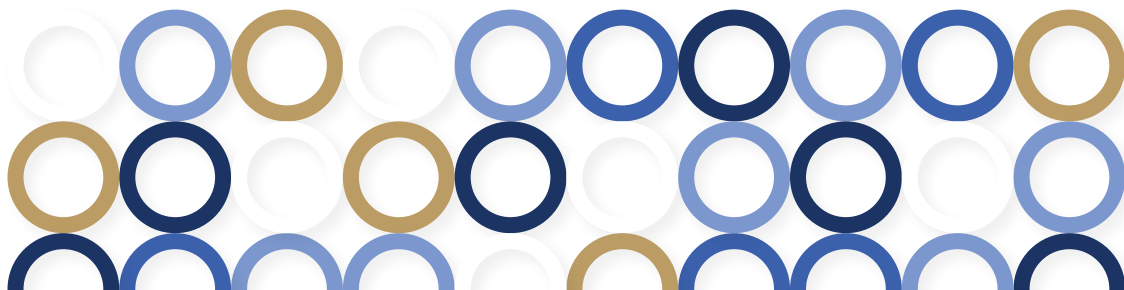
Clinical Management of Clients on the Ring

Module Six

Counselling and Supporting Effective Ring Use

Module Seven

Case Studies



Global Healthcare Provider Training Package

Dapivirine Vaginal Ring

Tools

Tool 1

The Ring

Tool 2

Video on how the Ring works

Tool 3

HIV prevention options

Tool 4

Research on the Ring

Tool 5

Ring Insertion Guide

Tool 6

Dialogue Guides/Talking Cards

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Clinical Management Quick Reference Sheet

Tool 8

FAQ Sheet

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Strategies to support adherence

Tool 10

Ring User Journey

Tool 11

Ring End user Guide

Tool 12

Ring Healthcare Professionals Guide

Tool 13

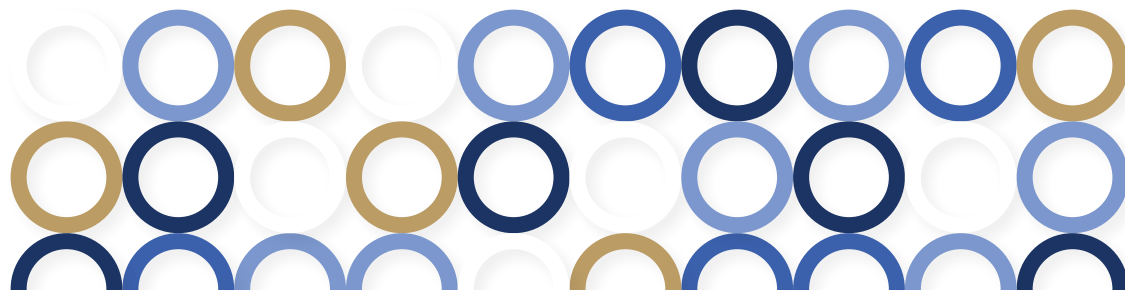
Pull out size tool with DVR, Nuvaring, FC2

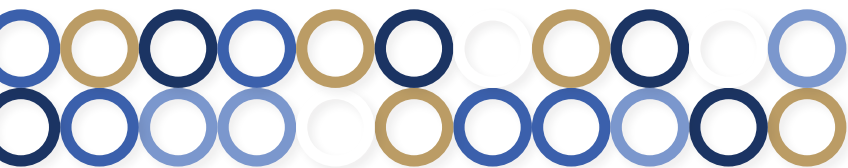
Tool 14

Counselling Quick Reference Sheet

Tool 15

IPV Resource





THE DAPIVIRINE VAGINAL RING

TOOL 1



**A discreet, safe, female controlled,
vaginal HIV prevention option.**

General Info:

- A discreet, safe, female controlled, vaginal HIV prevention option.
- The Ring provides partial protection against HIV – wear the ring AND use condoms for maximum protection!

Daily activities:

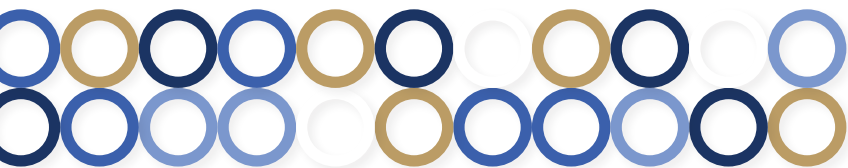
- Wear the Ring for 1 month, take it out, put a new one in!
- There is no need to remove the Ring while menstruating, it can even be used with a tampon.
- You can still use the toilet with the Ring in – it will not fall out.

Sexual activities:

- You can still have vaginal sex while using the Ring – neither you or your partner should feel it.
- The Ring DOES NOT protect against pregnancy
- The Ring DOES NOT protect against other STIs



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VIDEO ON HOW THE DAPIVIRINE VAGINAL RING WORKS

TOOL 2

Video:
How to use the DVR



vimeo

<https://vimeo.com/707699170>

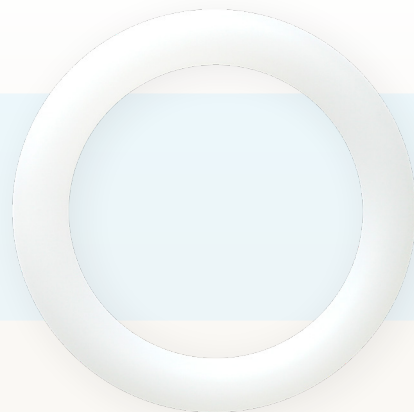


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HIV PREVENTION OPTIONS

TOOL 3



Condoms

Oral PrEP

Dapivirine Vaginal Ring





	Condoms	Oral PrEP	Dapivirine Vaginal Ring
Use	Every time you have sex	Daily	Inserted every 28 days (ring to remain in place for 28 days)
Adherence	Effectiveness is dependent on whether a user can remember/negotiate to use the product during every sex act	Effectiveness is dependent on daily dosing	Long acting, less user dependent
Discretion	Use needs to be negotiated with the partner. Cannot be used discretely	Discrete – can be used without partner knowledge	Discrete – can be used without partner knowledge
Effectiveness/ Efficacy	90 to 95% effective when used consistently	Over 90% effective, when used consistently	About 30% in clinical trials and over 50% in open label studies (that showed greater adherence)





RESEARCH ON THE DAPIVIRINE VAGINAL RING

TOOL 4

	Phase 3		Open-Label		Additional Research		
	 The Ring Study	 ASPIRE	 DREAM	 HOPE	 REACH	 DELIVER	 B-Protected
Purpose	Safety and efficacy of the DVR in adult women		Long-term safety and adherence to the DVR in adult women		Safety and adherence to use of oral PrEP and DVR in young women	Safety and acceptability of oral PrEP and DVR in pregnant women	Safety and acceptability of oral PrEP and DVR for breastfeeding women.
Locations	Malawi, South Africa, Uganda and Zimbabwe.			Uganda, Zimbabwe, South Africa	Malawi, South Africa, Uganda and Zimbabwe.		
Sample Size	4 500 women (aged 18 - 45 years) participated in both studies and were randomised to receive either the active DVR or placebo ring.		2400 former Phase 3 participants received the DVR (no placebo group)		247 young women (aged 16-21) were enrolled	550 women Group 1: 150 who are 36+ weeks pregnant Group 2: 150 who are 30-15 weeks pregnant Group 3: 250 who are 13-30 weeks pregnant	200 mother-infant pairs
Outcome							
Risk Reduction	35%	27%	62%	31%			
Safety	No safety concerns		No safety concerns		No safety concerns	No safety concerns in Group 1. Awaiting results for group 2 and 3	Favourable safety profile in interim analysis
Adherence	About 80% of participants used the DVR at least some of the time		Over 90% of participants used the DVR at least some of the time		67% of participants chose to use the ring. 88.5% of participants found the ring to be acceptable. The vast majority (97%) of study participants used the ring some or all of the time. Adherence was higher than had been observed in previous studies.	On-going study	On-going study





THE DAPIVIRINE VAGINAL RING INSERTION GUIDE

TOOL 5

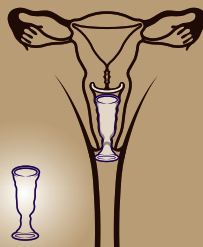
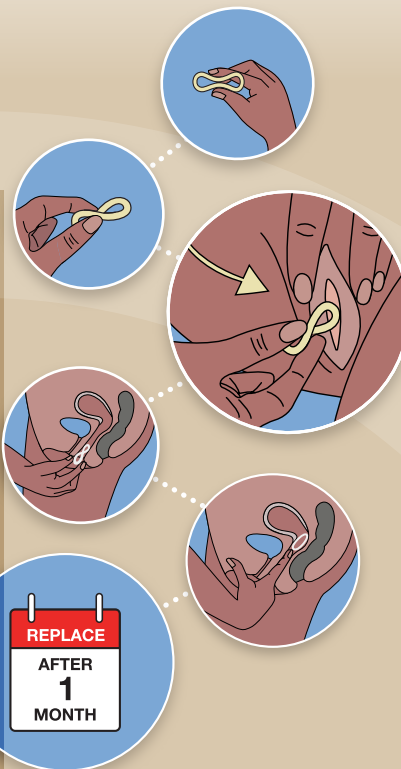
How the ring works

A woman would insert the flexible silicone ring herself and replace it with a new one each month.

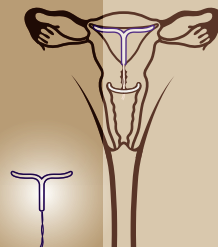
The ring sits inside the vagina near the cervix where it slowly releases an antiretroviral drug called dapivirine at the site of potential infection.

Dapivirine works by blocking HIV's ability to make copies of itself inside healthy cells.

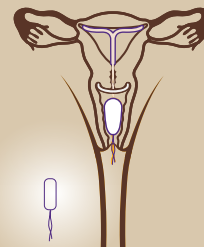
It is important that the ring is left in place for the full month to ensure that risk reduction is achieved.



Position of the female condom in relation to the vaginal ring



Position of an intrauterine contraceptive device (IUCD) relative to vaginal ring



Position of a tampon, IUCD and vaginal ring

The ring can also be used with other forms of contraception, but should not be used with contraceptive vaginal rings, diaphragms, menstrual cups or cervical caps.



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DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

Client initiating:

What is the ring?

It's a flexible silicone ring with an ARV drug dapivirine that slowly releases directly into the vagina over the course of 28 days. It provides partial protection against HIV infection during vaginal sex.

How effective is it?

Phase 3 clinical studies found that the ring reduced women's HIV risk by about 30% overall. HIV risk reduction is higher among those who use the ring more regularly. Open-label studies found increased ring use with greater risk reduction - up to 50%.

How long do I need to wear it?

The ring should stay in the vagina for 28 days, then immediately be replaced.

How long until it is effective?

The ring must be in place for 24 hours before it will begin to protect against HIV.

Will the ring protect me from other STIs and pregnancy?

No! The ring will not prevent other STIs or pregnancy. It's best to use condoms and contraception with the ring.

Are there side effects?

Side effects are very mild but can include urinary tract infections, vaginal discharge or itching, pelvic or lower abdominal pain.





DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

Client initiating:

Should I remove the ring before sex?

No. The ring reduces the chances of HIV infection during vaginal sex. Although most people say their do not feel the ring, if your partner does feel it, it will not harm him, and it won't affect his enjoyment.

Can I use the ring with contraception/birth control?

Yes, you can use the ring with condoms and all other forms of contraception that do not need to be inserted into the vagina (i.e. pills, implants, injectables, IUDs).

Should I remove the ring during my period?

No. The ring should remain in your vagina during your period. You can also use tampons with the ring. The ring should be in the vagina before inserting a tampon. Be careful when removing the tampon, in case the ring is accidentally pulled out. If this occurs, immediately reinsert the ring.

Can I use products to cleanse my vagina while using the ring?

No. Cleaning the inside of the vagina with soap or other products may cause harm and may affect the ability of the ring to reduce the risk of HIV infection.

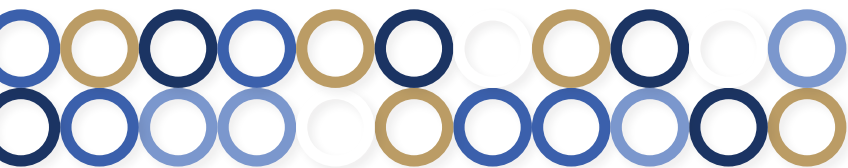
Do I have to tell my partner if I want to use the ring?

You don't have to tell anyone. Your body belongs to you, and you have the right to make your own decisions about your health.

Some women use the ring without their partner knowing – it is very discrete and should not be felt by either you or your partner during sex – and some choose to tell their partner. It might be helpful to think about the reasons you would like to tell him and the reasons you don't want to.



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DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

How to talk to a partner about the Ring:

Do you have advice on how to tell my partner?

I'm glad to hear you're interested in talking to your partner. Many women say it's helpful to have their partner's support. Your partner is most likely to be supportive if he has accurate information about the ring. Without it, he may believe some of the myths, which might make him less supportive.

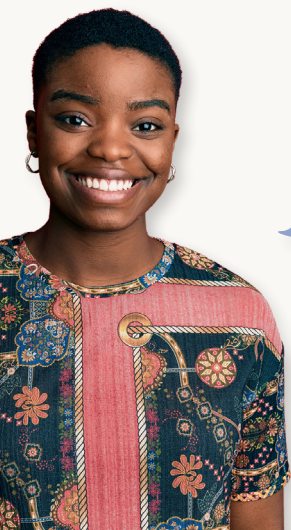
It might be helpful to talk to your partner about the ring before you tell him you're using it. Try mentioning it casually a few times to start a conversation so you can provide him with accurate information. These conversations might also help you understand what he thinks about the ring.

You can think about saying:

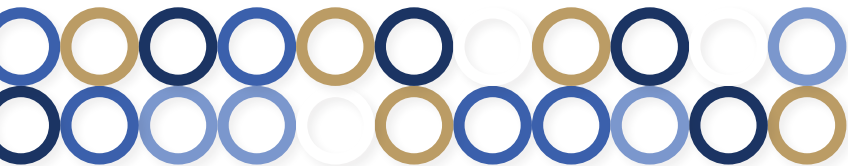
- Using the ring is just like using any other medication that protects your health – it's not a big deal.
- Many girls/ women my age are getting HIV, and I want to be able to protect myself.
- I've heard a lot about it. It's completely safe and won't have any impact on you.
- It was recommended to me by a health care provider. It's about my health and it won't have any impact on you.
- I would really like your support.
- These are just some options. You know your partner best, so it's important that you decide what you want to say. Don't forget, using the ring is your right. You are making a responsible decision to protect your health.

What if he thinks this means we don't need to use condoms?

Explain that the ring will only protect you from HIV. It won't protect him. It also won't protect either of you from STIs. Condoms are always the best method because they protect against HIV, STIs, and unplanned pregnancy.



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DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

How to talk to a partner about the Ring:

Other advise?

Sure, here are some tips:

- Picking your timing is important. Try to find a time when he's in a good mood, you're both sober and you have some privacy.
- If you're worried that he may get angry or could be violent, try to find a place where you can easily leave or get help if you need to.
- Try practicing what you're going to say. I'm happy to do that with you, or you could ask a friend.
- If you have any friends who are using the ring and have told their partners, you could ask them for advice.

I've been told by doctors never to insert anything in my vagina, now you are telling me to insert this ring?

Yes, it is true, you should never insert anything that is not medically approved into your vagina, but this ring has been proven to be safe and effective in preventing HIV.

I've heard that the ring may cause cancer or infertility?

Research has shown that the ring is safe and does not cause cancer or infertility.

The ring may damage my uterus and then I will fail to deliver children?

The ring has been proven very safe and will not do any damage to your uterus or any other part of your reproductive system.



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DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

Client
Follow-Up:

What if it gets lost in my body?

The ring will not get lost in your body. It sits at the top of the vaginal canal against the cervix, it cannot go any further. (Show the client the graphics of female reproductive anatomy and/or the video of the ring).

Some people have said that inserting things in the vagina is witchcraft to control our male partners?

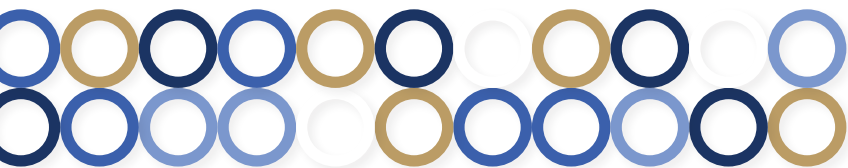
The ring is a biomedical device proven to help prevent HIV, it is not witchcraft.

Questions to ask the client:

- How has it been for you with the use of the ring?
- Have you had any side effects?
- Last time you were here, you were going to try to talk to your partner about the ring. How did that go?
- Have you experienced any challenges?
- Do you have any concerns about the ring?
- Has using the ring changed what else you do to protect yourself from getting HIV and STIs (i.e. using condoms, discussing HIV and STI status and/or testing with partners)?
- In addition to using the ring, what are your plans to stay HIV negative?



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DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

Talking to a male partner

Where there is mystery, there is room for myth—especially with men. Male perceptions of SRH choices can act as a barrier for women in personal relationships

My partner has told me that she wants to use the ring to protect against HIV, I am worried that the ring will affect our sex life.

The majority of women in clinical trials on the ring reported that one of the ring's most favorable characteristics is that it does not negatively impact the sexual experience for either partner. Some women reported that the ring increased sexual pleasure for them and their male partners partly due to reduced anxiety about their HIV risk.

Can the ring get stuck on my penis during sex?

No. The ring sits high up in the vagina near the cervix and cannot become stuck on the penis during sex.

Can the ring cause pain or harm to my penis?

No. Studies have shown that dapivirine causes no harm to a man's penis.

Can I stop using condoms?

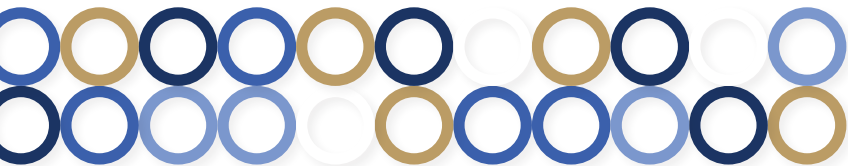
We do not encourage stopping condom use as the condoms are currently the only product that can prevent HIV as well as other STIs.

Can men use the ring?

Men cannot use the ring because the ring is designed to release the ARVs locally inside the vagina.



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DIALOGUE GUIDES/ TALKING CARDS

TOOL 6

Talking to a community member

HCP - Will introduce the concept of the ring during a health talk. Thank you for taking the time to listen, does anyone have any questions.

Won't use of the ring encourage women to be promiscuous?.

No, the dapivirine ring does not encourage sexual activity beyond what is already taking place in people's lives — but if approved, it would provide women with a discreet and self-initiated prevention tool

Why do we need the ring if we already have highly effective products like oral PrEP, the promise of injectable CAB soon?

Condoms and daily oral PrEP are all great options, but not all women can or want to use them. That's why getting the epidemic under control will require multiple types of prevention methods, so a woman can choose the most effective product that best meets her needs and life circumstances. We are thrilled that a bimonthly injectable may help expand women's options. We hope women have as many choices as possible. But no product is perfect, so offering all products is important to ensure every woman has a way to protect herself. Just as with contraception, having more options to choose from will increase their overall use. That's the path to controlling this virus.

We have been told that inserting products into your vagina can lead to cancer, is this the case for the ring?

To date there is no evidence that the ring can cause cancer.

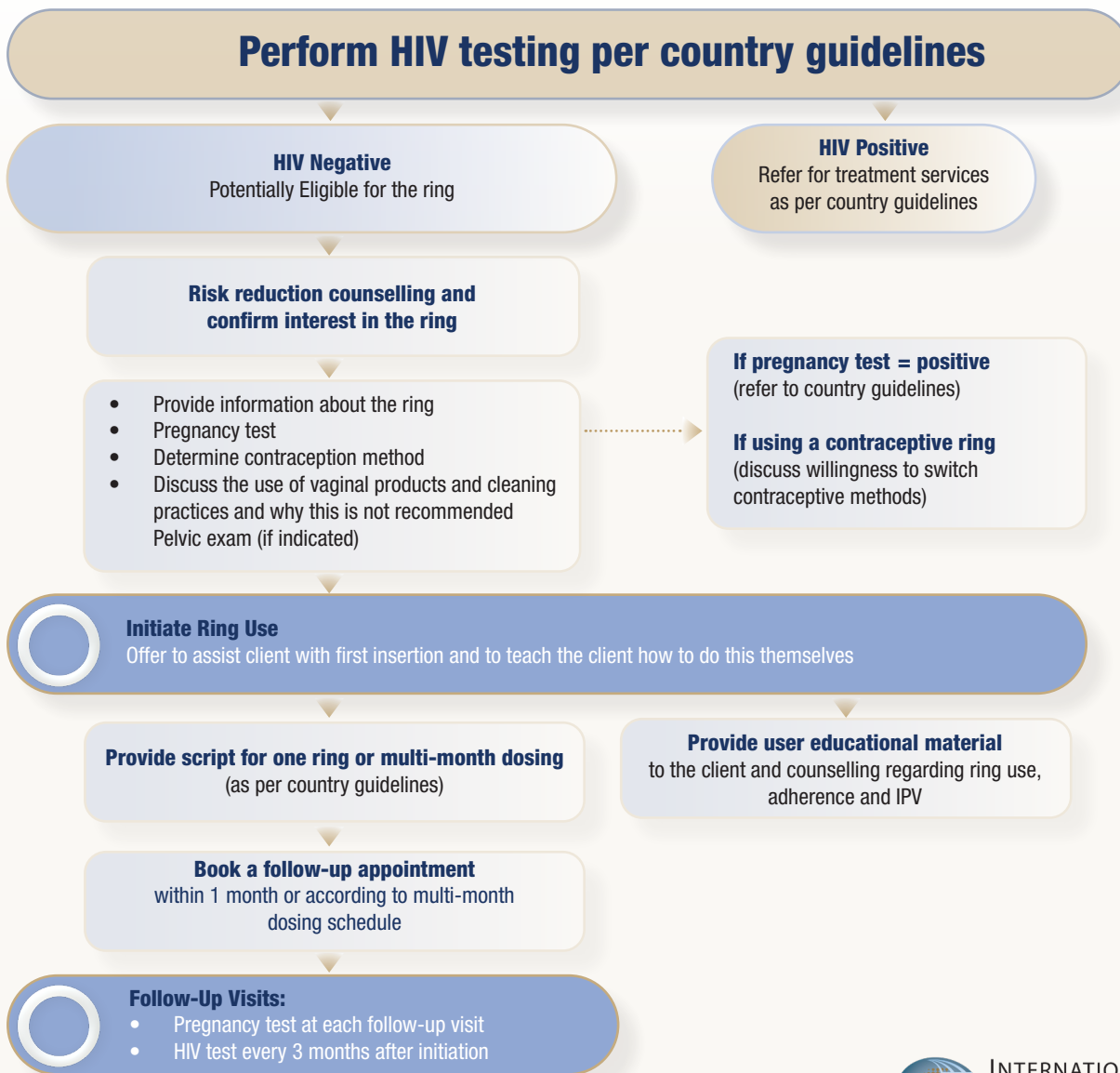


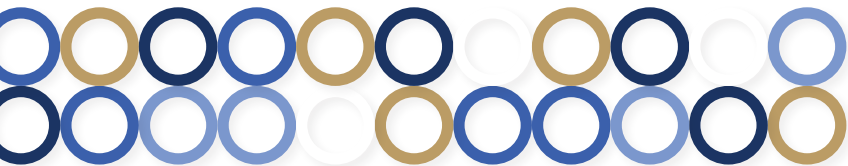
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CLINICAL MANAGEMENT QUICK REFERENCE SHEET

TOOL 7





FAQ SHEET

TOOL 8



What is the dapivirine ring?

The ring is made of a flexible silicone with the ARV drug dapivirine dispersed uniformly throughout its matrix. The ring releases the drug directly in the vagina over the course of a month with low exposure elsewhere in the body, which helps to minimize side effects and reduce the risk of the development of HIV resistance.



How effective is the dapivirine ring?

If used consistently and correctly, the ring has been shown to provide up to 50% protection from HIV during vaginal sex. For full protection the ring should be used with male or female condoms.



Is the ring easy to insert and use?

Yes. A woman can insert the ring easily herself and would replace it each month.
(Offer to insert the ring for the client for the first time).



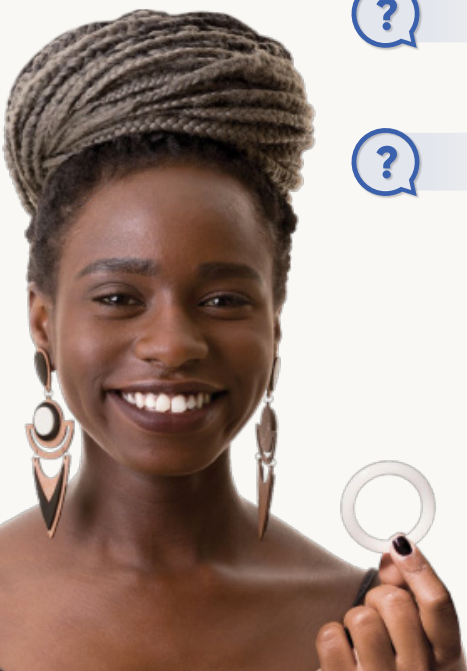
How long do I wear the ring?

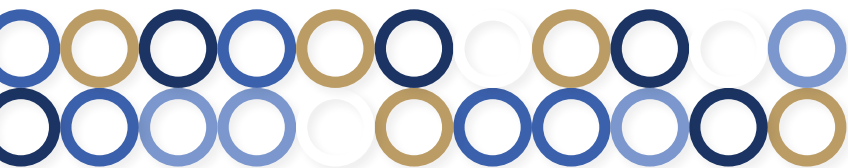
The ring needs to be kept in place for 28 days and immediately replaced with a new ring.



How long does the ring need to be in place before it is effective?

The ring must be in place for at least 24 hours before the ARV can begin to help protect against HIV. However, it is the level of sustained-release over the course of a month that helps reduce risk, which is why it is so important that the ring be work for 28 days and replaced monthly.





If a woman takes the ring out to clean it, how long does the HIV protection last? After she reinserts the ring, does she need to wait another 24 hours for the ring to provide protection again?

The precise period of 'forgiveness' cannot be determined. For this reason, it is recommended that the ring be kept in place continuously for 28 days until it is replaced with a new ring. It is not necessary to remove the ring for cleaning or during menses.



Can women feel the ring once it's inserted?

Most women have reported that the ring is comfortable and they cannot feel it once it is inserted and left in place.



How safe is the ring?

There are no safety concerns with long-term use of the ring.



Does the ring have side effects? What are they?

Side effects are generally mild and include urinary tract infections, vaginal discharge or itching, and pelvic or lower abdominal pain, that in most cases resolved without interrupting ring use.



Can the ring get lost inside me?

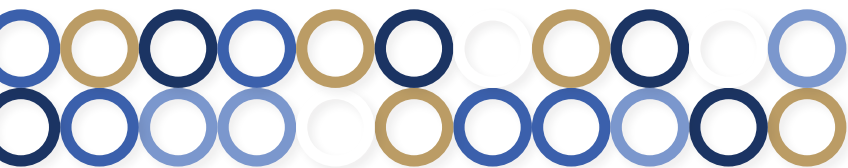
No. The ring cannot be pushed up too far or get lost in the body.



Should I remove the ring before sex?

No. The ring should not be removed during sex. Keeping the ring in place for the full 28 days reduces the chances of HIV transmission during vaginal sex.





FAQ SHEET

TOOL 8

Could the ring be used simultaneously with other HIV prevention products?

The ring should be used in combination with safer sex practices such as male or female condoms. However, simultaneous use of the ring and oral PrEP, is not currently recommended as this has not been studied.

Does the ring protect against HIV during anal sex?

No. The monthly ring only protects during vaginal sex. Currently, condoms and oral PrEP are the only methods available to effectively prevent HIV transmission during anal sex as well as vaginal sex.

Does the ring prevent STIs other than HIV?

No. Condoms are currently the only product that can prevent HIV as well as other STIs.

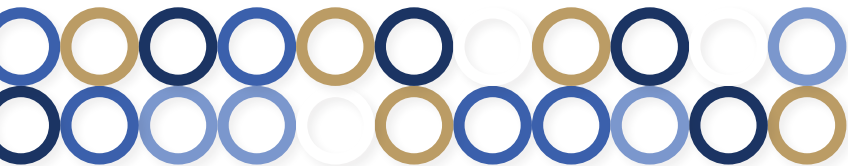
Does the ring prevent pregnancy?

No, the monthly dapivirine ring does not act as a contraceptive in any way.

Can I use the ring with contraception/birth control?

The ring can be used with some forms of contraception, including male or female condoms, IUDs, oral contraception, hormonal injections, and implants. The ring should not be used with other contraceptive vaginal rings or diaphragms.





FAQ SHEET

TOOL 8



Can I use tampons with the ring?

Yes. Tampons can be used with the ring. The ring should be in the vagina before inserting a tampon. Be careful when removing the tampon, in case the ring is accidentally pulled out. If this occurs, immediately reinsert the ring.



Should I remove the ring during my period?

No. It is safe to use during your period (menstruation). The ring should remain in the vagina during your period to reduce the chances of HIV.



Will the ring fall out?

This is not common, but may happen. If the ring falls out, it should be rinsed in clean water and reinserted immediately if possible.



Can I use products to cleanse my vagina while using the ring?

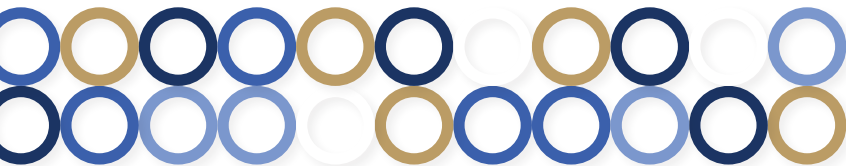
No. Cleaning the inside of the vagina with soap or other products may cause harm and may affect the ability of the ring to reduce the risk of HIV infection.



Contact your clinic/doctor immediately if you experience:

- Pain/severe pain in your lower belly.
- A discharge, with unpleasant smell, from your vagina.
- Pain or bleeding during sex.
- Fever, sometimes with chills.
- Pain or difficulty in emptying your bladder.
- Nausea and vomiting, with an inability to keep food or water down.





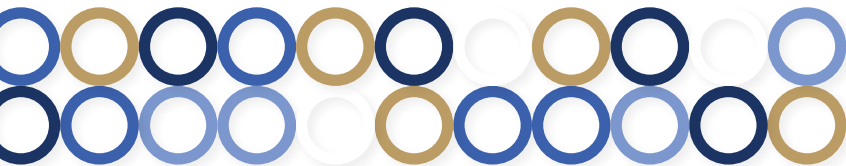
STRATEGIES TO SUPPORT ADHERENCE

TOOL 9

- Step 1:** Determine what a client is comfortable with in terms of adherence support (see diagram below)
- Step 2:** Collect additional contact information from the client
- Step 3:** If applicable, encourage client to keep a diary of questions to discuss with a provider or peer buddy or with a support group



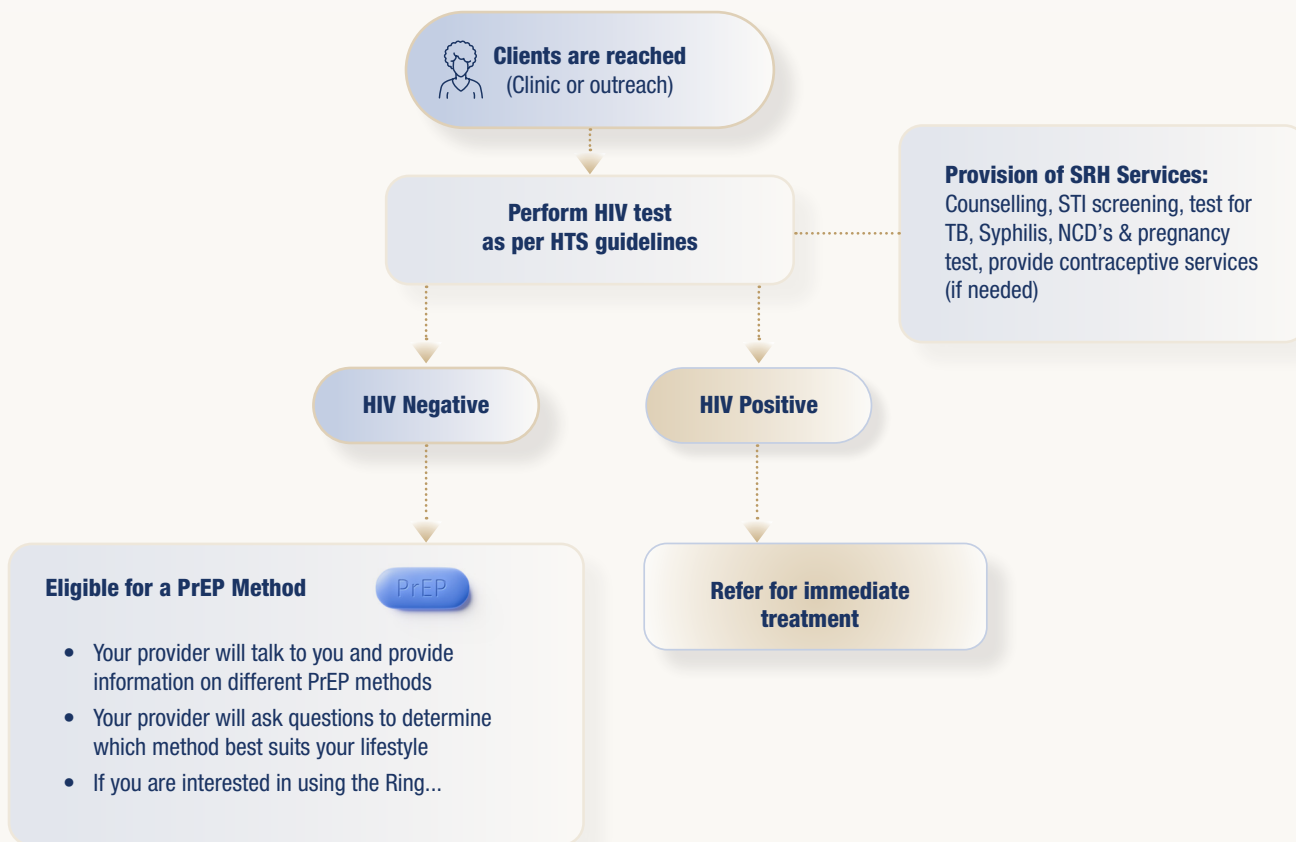
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DAPIVIRINE VAGINAL RING USER JOURNEY

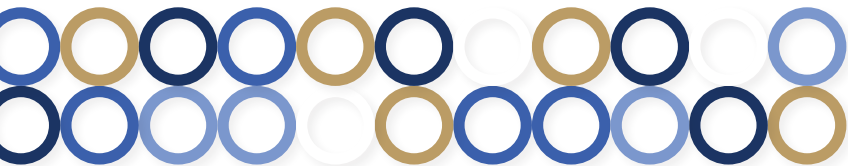
TOOL 10

Part 1: Deciding to use an HIV prevention method



Continue Part 2






RING USER JOURNEY


TOOL 10

Part 2: Ring Use Journey

 If you **are pregnant**; your provider will discuss the risks and benefits of using the ring


If you are **not pregnant**, your provider will discuss what contraceptive methods are suitable for use with the ring

Your provider will provide you with a prescription for the ring, user education material, and a follow-up appointment

 1 monthly ring provision

After one month:
Remove current ring, your provider will provide you with the next ring and address any concerns you might have

At 3 months:
HIV test required STI screening
Counselling

 Multi-month ring provision (usually every 3 months)

Every 3 months:
Next script for ring provision
HIV test required STI screening
Counselling



DAPIVIRINE VAGINAL RING END USER GUIDE

TOOL 11

DAPIVIRINE VAGINAL RING

Dapivirine Vaginal Ring – A Guide for Users

- The ring is for vaginal use only.
- A ring that has not been used has an off-white colour and is easy to bend.
- The ring reduces the chance of a woman getting a HIV-1 infection during vaginal sex.
- The ring should be used with a condom.
- The ring does not protect a man from getting HIV-1 infected.
- Women must use the ring continuously and replace it each month with a new ring.

INSTRUCTIONS FOR RING INSERTION



1. Wash your hands in clean water and dry them.



2. Check the expiry date on the package label DO NOT use if the ring is damaged or expired.



3. Tear package to open. DO NOT use scissors to open the package. In a clean place, remove the ring from its package.



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If the ring is uncomfortable or causes pain the ring might not be in far enough, try pushing it in further, or removing and re-inserting it. If it still feels uncomfortable or causes pain, contact your clinic/doctor.

POSITION YOURSELF TO INSERT THE RING



Choose a position that is comfortable for you to insert the ring. For example: raising one leg, squatting or lying down.

INSERT THE RING



1. Twist the ring into the shape of the number 8 or squeeze the sides of the ring together.



2. Use your other hand and hold open the folds of skin around your vagina. Place the tip of the ring in the vagina opening and then use your index finger to gently push the folded ring in.



3. Push the ring into your upper vagina as far as you can.



4. Wash your hands in clean water and dry them.

REPLACING THE RING



1. The ring should be removed **ONE MONTH** from the day it was inserted. Insert a new ring **IMMEDIATELY** after the previous ring is removed.



2. Wash your hands in clean water and dry them.



3. Choose a comfortable position with your legs apart. Use your finger to hook the ring and gently pull the ring out.

IF THE RING COMES OUT



In a **CLEAN** place (for example in your bed or your clothes):

- Rinse the ring in clean water.
- Do not clean the ring with soap or other cleaning products.
- Immediately reinsert it into your vagina.

In a **DIRTY** place (for example in the toilet, on the floor):

- **DO NOT** put it back in your vagina.
- Place the dirty ring in a tissue or toilet paper and throw it in a rubbish bin.
- Immediately insert a new ring.

DO NOT USE THE RING IF:

It is broken, damaged, or looks a different colour to what you would expect when you first open the packaging (remember that the colour of an unused ring is off-white).



Report this to your clinic/doctor immediately.

- You are HIV-infected.
- You are breastfeeding.
- You are using another type of vaginal ring.

DISCARD THE USED RING



1. Place the used ring in the empty package of the replacement ring, in tissue or in toilet paper. Place it in the rubbish bin out of the reach of children or pets. **DO NOT** throw the ring in the toilet.



2. Wash your hands in clean water and dry them.

IMPORTANT INFORMATION

- Please contact your clinic/doctor before using any medicines or other products that need to be put in your vagina while using the ring.
- The ring should remain in your vagina for one month.
- Re-insert a new ring right away after your ring is removed.
- Contact with blood or vaginal fluids may change the colour of the ring during use. This does not affect the way in which the ring protects you against HIV-1 infection during vaginal sex.
- If you take the ring out, you are no longer protected from HIV-1 infection.
- The ring does not prevent other sexually transmitted infections (STIs) or protect from HIV-1 infection during anal sex or other ways of getting HIV, such as sharing of needles with a HIV infected person.
- You must have tests which show you are HIV negative before you start using the ring. You must also get tested for HIV regularly (for example at least every 3 months) while using the ring to make sure you do not use the ring if already HIV infected.



The ring should always be used with a male or female condom to have better protection against HIV-1 infection.



Tell your clinic/doctor about any flu-like illness – either in the month before starting to use the ring, or at any time while using it, especially if you think you may have been exposed to HIV.

WHAT TO DO IF YOU THINK YOU MAY BE HIV INFECTED

- If you think you were exposed to HIV, tell your clinic/doctor straight away. They may want to do more tests to make sure you are still HIV negative.
- If you continue to use the ring while being HIV-1 infected, the HIV-1 virus may undergo changes which may make it more difficult to treat with available anti-HIV treatments.
- Basic HIV tests may miss an infection in the early stages. Signs and symptoms of early HIV infection are similar to a flu-like illness.

These may be signs of HIV infection:



Tiredness



Enlarged glands in the neck or groin



Fever



Rash



Joint or muscle aches



Night sweats



Headache



Vomiting or diarrhea

VAGINAL INFECTION

What to do if you think you may have a vaginal infection or sexually transmitted infection

- The ring does not protect against sexually transmitted infections other than HIV-1 infection.
- If you suspect you may have a vaginal infection or sexually transmitted infection, visit your clinic/doctor for treatment. If left untreated, these infections make it easier for the HIV to infect you. Early treatment of these infections may also prevent the spread of infection to other female organs higher up in your abdomen.
- Symptoms that may indicate an infection include itching in your vagina, discomfort or pain and a discharge from your vagina, and possibly pain or discomfort during sex.
- Pelvic inflammatory disease (PID) is an infection of the female organs in your abdomen. It usually occurs when sexually transmitted bacteria spread from your vagina to your other female organs higher up in your abdomen.

CONTACT A CLINIC/DOCTOR IF YOU ARE USING THE RING AND YOU:



- Miss a period (menstruation).
- Think you might be pregnant or plan to fall pregnant.
- Have questions or concerns about ring use.



- Have pain or discomfort after inserting the ring.
- Think you may have been exposed to HIV.



Contact your clinic/doctor immediately if you experience:

- Pain/severe pain in your lower belly.
 - A discharge, with unpleasant smell, from your vagina.
 - Pain or bleeding during sex.
 - Fever, sometimes with chills.
 - Pain or difficulty in emptying your bladder.
 - Nausea and vomiting, with an inability to keep food or water down.
-

FREQUENTLY ASKED QUESTIONS

How does the ring work?

The ring contains a medication called dapivirine that reduces the chance of HIV-1 infection during vaginal sex. The medicine is released from the ring slowly over one month.

Should I remove the ring before sex?

No. The ring reduces the chances of HIV-1 infection during male to female vaginal sex. It is possible that your partner may feel the ring during sex; the ring will not harm you or your partner.

Can I use products to cleanse my vagina while using the ring?

No. Cleaning the inside of the vagina with soap or other products may cause harm and may affect the ability of the ring to reduce the risk of HIV-1 infection.

Should I remove the ring during my period?

No. It is safe to use during your period (menstruation). The ring should remain in the vagina during your period to reduce the chances of HIV-1 infection.

Can I use tampons with the ring?

Yes. Tampons can be used with the ring. The ring should be in the vagina before inserting a tampon. Be careful when removing the tampon, in case the ring is accidentally pulled out. If this occurs, immediately reinsert the ring following the instruction on previous page.

Does the ring protect me from getting pregnant?

No. The ring only reduces the chances of HIV-1 infection during vaginal sex. It will NOT prevent you from getting pregnant.

What to do if I suspect that I am pregnant?

Remove the ring and contact your clinic/doctor immediately for advice. Discuss other HIV prevention methods with your doctor.

Can I use the ring with contraception/birth control?

You should use the ring with male or female condoms and all other forms of contraception that do not need to be inserted into the vagina

DO NOT use the ring with other vaginal rings or diaphragms. If you are unsure, contact your clinic/doctor

Can the ring get lost inside me?

No. The ring cannot be pushed up too far or get lost in the body.

Sex – it's okay to have vaginal sex while wearing the ring. You or your partner may or may not feel the ring and if you do feel it, it's not likely to affect your or your partner's enjoyment of sex.

Menstruation – it's okay to keep the ring in during your period/menstruation. If you do clean the ring, immediately re-insert the ring after cleaning.

Toilet – it's okay to use the toilet when the ring is inside you. It is uncommon that the ring falls out during urination or a bowel movement. To be sure get in the habit of checking the toilet. If the ring has fallen in the toilet insert a new ring following the instructions on the previous page.

Washing – it's not necessary to clean inside the vagina.



Sex



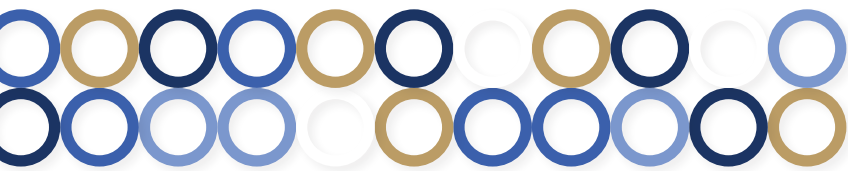
Menstruation



Toilet



Washing



DAPIVIRINE VAGINAL RING HEALTHCARE PROFESSIONALS GUIDE

TOOL 12



DAPIVIRINE VAGINAL RING

Dapivirine Vaginal Ring – A Guide for Healthcare Professionals

This guide summarises key information for use by healthcare professionals to assist with safe and correct use of the **Dapivirine Vaginal Ring** when counselling and advising potential users.

1. THE DAPIVIRINE VAGINAL RING FORMS PART OF A COMPREHENSIVE HIV-1 PREVENTION STRATEGY

- The **Dapivirine Vaginal Ring** is indicated for use in adult women.
- The **Dapivirine Vaginal Ring** alone is not fully effective in reducing the risk of HIV-1 infection. An approximately 30% reduction in the risk of HIV-1 infection was shown in the clinical Phase 3 program.
- The **Dapivirine Vaginal Ring** is only effective in reducing the risk of HIV-1 infection during vaginal intercourse.
- The **Dapivirine Vaginal Ring** should be offered only after comprehensive counseling on safer sex practices and a discussion on the most effective and safe option of HIV prevention tools suitable for the women to consistently adhere to using it.
- The **Dapivirine Vaginal Ring** should always be used



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2. ADHERENCE TO THE CORRECT USE OF THE DAPIVIRINE VAGINAL RING

Risk reduction of HIV-1 infection is correlated with adherence to the correct use of the Dapivirine Vaginal Ring.

Advise user on the following:

- To continuously use the **Dapivirine Vaginal Ring** over the period of one month, and follow with immediate insertion of a new ring.
- The **Dapivirine Vaginal Ring** must remain in situ during vaginal intercourse.
- The **Dapivirine Vaginal Ring** should not be removed at the time of menses. Tampons may be used, however the user should be cautioned to not accidentally remove the ring when removing the tampon.
- In the event of accidental expulsion or removal in a clean environment, the **Dapivirine Vaginal Ring** may be rinsed in clean water and immediately re-inserted.
- If expulsion or removal occurred in an unhygienic area, the **Dapivirine Vaginal Ring** should be disposed of in a refuse bin. A new ring should be inserted immediately.
- If the **Dapivirine Vaginal Ring** is damaged or broken, it should not be inserted or re-inserted. The incident should be reported to the healthcare professional.
- To report any problems associated with ring insertion such as discomfort or pain to the healthcare professional if these symptoms do not resolve after re-positioning of the **Dapivirine Vaginal Ring**.

3. RISK OF HIV RESISTANCE

Use of the **Dapivirine Vaginal Ring** in the presence of HIV-1 infection could potentially lead to the selection of HIV-1 mutations associated with non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance and may limit the future options for HIV treatment.

To reduce the risk of **Dapivirine Vaginal Ring** being used in the presence of HIV-1 infection, the following steps are advised:

- Prior to prescribing the **Dapivirine Vaginal Ring** for initial use, the user must have a negative HIV test(s) per local testing guidelines.
- If doubt exists about whether the potential **Dapivirine Vaginal Ring** user could be HIV-infected despite a negative serological test for HIV, consideration should be given to delay introduction of the **Dapivirine Vaginal Ring** for one month until such time as repeat HIV testing can be done.

- Use clinical judgment to evaluate the potential risk of not detecting an early HIV infection versus the benefit of providing the **Dapivirine Vaginal Ring** for HIV prevention.
- Perform HIV tests at frequent intervals (e.g. at least every three months) while using the **Dapivirine Vaginal Ring**.
- Counsel the user to report any clinical symptoms consistent with acute HIV infection, especially for recent exposure (<1 month). If HIV infection is suspected while women are using the **Dapivirine Vaginal Ring**:
 - Discontinue use of the **Dapivirine Vaginal Ring** and recall the user after one month to perform HIV tests per local guidelines.
 - Reinforce counseling messages on safer sex practices while the **Dapivirine Vaginal Ring** is not being used.
 - The **Dapivirine Vaginal Ring** may be reintroduced if the user has negative HIV tests after one month.
 - Counsel the user to immediately report to a healthcare practitioner if she has a positive HIV test result and to stop use of the **Dapivirine Vaginal Ring**.

4. PRESENCE OF GENITAL INFECTIONS

The **Dapivirine Vaginal Ring** does not protect against sexually transmitted infections (STIs), other than HIV-1 infection. In addition, the presence of an STI and/or other genital infections is associated with an increased risk of acquiring HIV infection, and if not treated appropriately, these infections may result in an ascending or complicated genital tract infection.

Prior to initiating treatment with the **Dapivirine Vaginal Ring**, identify and treat any genital infection as per local guidelines.

- Counsel the user on the signs and symptoms that may be associated with genital infections such as:
 - Provide counselling on safer sex practices per local guidelines.
- STIs, vulvovaginal infections (non-STI related) and pelvic inflammatory disease in order to ensure early identification and treatment of these conditions.

5. VAGINAL PRACTICES AND VAGINAL MEDICATIONS

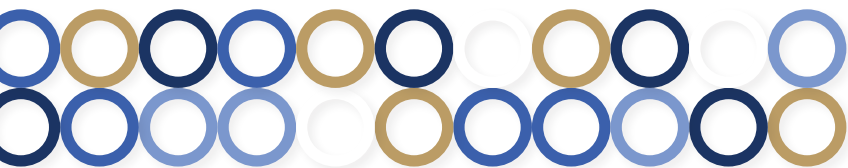
No data are available that describe the effect of vaginal practices on the safety and efficacy of the **Dapivirine Vaginal Ring**.

- Prior to prescribing the **Dapivirine Vaginal Ring** enquire about past or current use of vaginal products and/or vaginal practices. The concomitant use of the **Dapivirine Vaginal Ring** and vaginally administered clotrimazole or miconazole used to treat vaginal candidiasis should be considered with caution.
- Advise that dry sex practices or douching may potentially interfere with the efficacy and safety of the **Dapivirine Vaginal Ring**. No data on the use of other vaginal medications, such as metronidazole and clindamycin are available.
- These vaginal practices, in particular douching, may alter the vaginal/genital microflora and could potentially increase the risk of acquiring genital infections/STIs (including HIV).

6. PREGNANCY AND BREASTFEEDING

Safe use of the **Dapivirine Vaginal Ring** during pregnancy and breastfeeding has not been established.

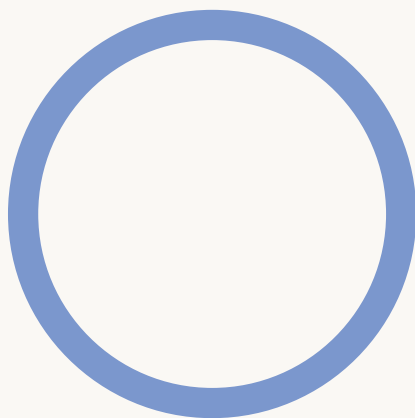
- The **Dapivirine Vaginal Ring** does not have contraceptive properties and therefore does not prevent pregnancy. Use clinical judgment in deciding whether to recommend continued use of the **Dapivirine Vaginal Ring** in pregnancy after considering the risk of HIV-1 infection during pregnancy and the risk of possible transmission to the unborn or nursing child.
- If the user does not wish to fall pregnant, counsel on the use of an appropriate contraceptive method.
- The user must be counseled to immediately inform a healthcare practitioner to discuss continued use of the **Dapivirine Vaginal Ring** in the event of pregnancy. Dapivirine has been shown to be excreted in human breastmilk in low concentrations. Infant exposure is expected to be low (less than 1µg /day).



PULL OUT SIZE TOOL WITH DVR, NUVARING, FC2

TOOL 13

- Nuvaring – 54mm outer diameter and 4mm cross section
- DVR – 56mm outer diameter and 7.7mm cross section
- Female Condom - outer-ring diameters of both are 7.1/7.2 mm, whilst the inner-ring diameters are both 58 mm



Nuvaring – 54mm



DVR – 56mm



Female Condom - 58~78 mm



Actual size 1:1



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COUNSELLING QUICK REFERENCE SHEET

TOOL 14



GOAL: Using active listening skills and an individualised approach, create a comfortable environment to talk about client experiences.

METHOD: Exploration of context (experiences, thoughts, beliefs, feelings, skills) to identify what would need to happen or continue happening for the behavior to be most manageable or "easy."

CLIMATE: Supportive, nonjudgmental, neutral, reinforcing of open discussion/efforts, avoidance of "fixing," recognition of limited role, and emphasis on client as a whole person.

IMPLICIT ASSUMPTION: Clients choose whether or not to do something based on feeling well informed, motivated and skilled. We cannot make a client adopt a behavior, but we can provide and promote opportunities to develop information, motivation, and skills relevant to her in her life.



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Welcome and Frame

Provider: Hi there, how are you feeling today?

Woman: I'm good, thanks.

Provider: Have you ever used any kind of birth control or protection during sex before?

Woman: Yeah, I use condoms sometimes.

Provider: Great. I wanted to talk to you about a new method of HIV prevention called the dapivirine vaginal ring. Have you heard of it before?

Woman: I don't think so.

Provider: Okay, let me explain. The ring is a small, flexible silicone ring that's inserted into the vagina, where it releases a low dose of a drug called dapivirine, which is an ARV, over the course of a month. This can help protect you from getting HIV during vaginal sex. It's discreet and easy to use, and you can put it in and take it out yourself. It's been shown to reduce the risk of HIV infection by about 50% overall in some studies among women who used it consistently. It lasts for a month at a time and is easy to use.

Identify Needs

Provider: Would you be interested in using the Ring?

Woman: Yes.

Provider: Great, first I would like to understand a bit more about your lifestyle and needs. How old are you? Do you have a partner? Are you using any form of contraception? Can you explain what is your motivation for wanting to use the Ring?

Woman: I'm 25 and I have two sexual partners, I think they don't have other partners but I am not certain. That is why I'm thinking of using the Ring. I'm on injectable contraception because I don't like taking pills and I don't have time to come to the clinic every month.

Provider: Thank you for that information, yes, the Ring does sound like it would be a good fit for you.

Explore

Provider: Do you have any questions about using the Ring?

Woman: I'm not sure. I've heard that some methods can have side effects, is this the same for the Ring?

Provider: That's a good point. Like any medication, the Ring can have some potential side effects, like irritation or discharge. But for most women, these are mild and go away on their own. If you do experience any side effects, we can talk about ways to manage them.

Woman: Will the Ring affect the contraceptive I use?

Provider: No, the Ring can be used with your injectable contraception but cannot be used with other methods like contraceptive vaginal rings or a diaphragm.

Woman: I don't want my partner to know I'm using the Ring, is there a chance he will feel it?

Provider: It is very discrete and should not be felt by either you or your partner during sex.

Provider: Would you like to try out the Ring? I can show you how to insert and remove it.

Woman: Yes, that would be good.

Provider [Shows the client the Ring video and performs a demonstration using the demo Ring on the anatomical model.]

Goal

Woman: This doesn't look so bad, I'm willing to give it a try.

Provider: Ok, so great our goal is to help you get the Ring today and support you to use it continuously to keep you protected.

Woman: Yes, I think I can keep the Ring in continuously, but I cannot come in every month to pick up a new Ring.

Strategise

Provider: As you said you are unable to come to the clinic every month, we can provide you with three Rings for three months and schedule your follow up visit to coincide with your next injectable contraceptive appointment.

Woman: That would be very convenient and helpful.

Provider: Will you be able to come to the clinic to have an HIV test and collect new Rings every three months?

Woman: I will try.

Close

[After inserting or showing how to insert the Ring]

Provider: Thank you for coming in. Please feel free to contact me if there is anything we can do to make it easier to attend appointments or if you are having any questions or concerns about your use of the Ring.



IPV RESOURCE

TOOL 15

RING JOB AID FOR DISCUSSING PARTNER RELATIONSHIPS

Overview

Providers initiating a client on the ring or helping a client who is struggling to use the ring as prescribed can use this job aid to ask about a client's relationships with their partner(s).

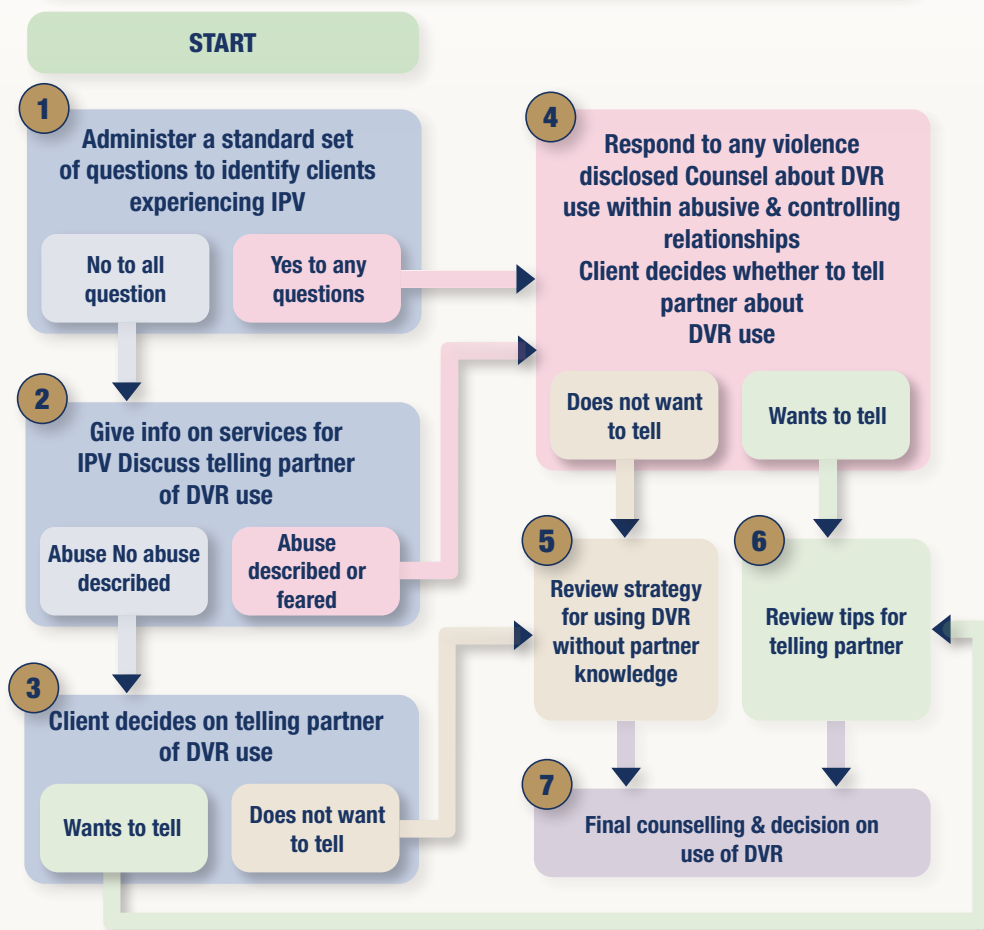
This includes asking about intimate partner violence (IPV), responding to IPV (as needed), and counseling on how to use the ring with or without a partner's knowledge.

Instructions for Use

Begin at the arrow labeled "Start" on either the summary or detailed version of the job aid, depending on your preference.

- Complete each step indicated by the tick boxes before moving on to the next step.
- When decisions are required, follow the relevant arrow according to the client's wishes or responses.
- Text in italics on the detailed flow chart is a suggested script.

Summary of steps for discussing partner relationships and ring use



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Detailed steps for discussing partner relationships and ring use

START

No to all question

Administer a standard set of questions to identify clients experiencing IPV

- Explain: Partner abuse is common and can make it harder to use the ring
- Explain: Questions about partner abuse are asked of everyone to support ring use and general well-being.
- Explain: Any limitations to confidentiality (as relevant).
- Ask (about all current “primary” partners):
 1. *Has your partner ever made you feel afraid, bullied or insulted you, threatened to hurt you, or tried to control you (for example, controlling your movements or limiting your ability to access money when you need it)?*
 2. *Has your partner ever hit, kicked, slapped, or physically hurt you?*
 3. *Has your partner ever forced you into sex or forced any sexual contact you did not want?*

Never attempt to force a client to disclose violence, even if you believe it is occurring.

Yes to any questions

Inform client about violence response resources available

- Say: If you remember anything else you'd like to share OR if issues arise in relationship(s), I will be available to provide support as needed.
 - Share: A *list of services* for individuals experiencing violence (if *the list of services* is provided as a printed document, remind the client that it may not be safe for partners to find this information).
- Discuss whether to tell partner(s) about ring use
- Say: You decide whether to tell your partner about the ring. Ring users may want their partner to know so they can be supportive. Other users, with privacy, safety, or other concerns, do not want partners to know. Many people can successfully use the ring without their partner's knowledge. I would like to hear from you about whether you want to discuss your ring use with your partner(s).
 - Ask: How would your partner(s) respond if they knew you were using the ring? Are you afraid that your partner(s) would have a negative or violent reaction if they knew you were using the ring?
 - If the client is afraid of a negative response, ask why. Probe for client concerns about abusive behavior by the partner.

Client describes abuse or fear of abuse

No abuse described

Decide whether to tell partner(s) about ring use

- Ask: Would you like to talk with your partner about the ring?

Does not want to tell partner

Wants to tell partner



Recent (<72 hours) sexual violence may require immediate access to post-exposure prophylaxis (PEP) and emergency contraception

Respond to the violence disclosed

Provide first-line support (LIVES):

- Listen:** Closely, with empathy, and without judging
- Inquire:** Assess/respond to needs/concerns—emotional, physical, social, practical
- Validate:** Show understanding and believe client; assure client—they are not to blame for IPV
- Enhance safety:** Discuss a plan to protect from further harm
- Support:** offer to connect to additional information, services, and social support
- If referrals are accepted, offer active referral OR accompaniment to any desired services

Counsel about ring use within abusive and controlling relationships

- Say:
 - *People in abusive and controlling relationships are often more vulnerable to HIV. It may be difficult to negotiate condom use and to know your partner's status. This can make ring use even more important.*
 - *Let's brainstorm specific challenges that you may face and strategies to overcome these challenges.*

Document disclosed violence, services provided, and referrals made on <insert form title>

Decide whether to tell partner(s) about ring use

Does not want to tell partner

If you do not want to tell your partner, it may be challenging, but many people successfully use the ring without telling their partners.

If you want to tell your partner, I can help you brainstorm ways to do so more safely, including having your partner speak to a healthcare worker here

Wants to tell partner

Review strategies for using the ring without partner's knowledge

- Storing rings: if you receive one ring at every visit, storage is not a concern as it will be immediately inserted. If you are on a multi-month dosing regimen and have an extended ring supply, store rings in places partner will not look (handbag, with pads and tampons).
- Think of a reason for regular clinic visits.

Remind the client that using the ring as prescribed is important, but it is not as important as their safety.

Brainstorm what to do if partner discovers ring use and becomes angry

- Discuss who can provide support if the client needs to leave home quickly; consider creating a complete safety plan per step "E" of LIVES.
- Ask the client what kind of support the clinic could provide.

Review tips for telling a partner

- How to tell a partner (simple language, maintain eye contact, remain calm, prepare answers)
- Where to tell a partner (location with easy exit to reach help quickly if afraid for your safety)
- When to tell a partner (time to fully explain and answer all partner questions)

Additional tips:

- Talk about the ring generally to see what partner says before telling partner you are using it.
- Give a little information at a time.
- Only tell your partner what they need to know.
- If they are resistant at first, bring it up over time to gain support.

Schedule an appointment for the client and partner if the client wants the provider's help telling partner about ring use

Document that provider asked about IPV as part of ring counseling in

Final counseling and decision regarding ring use

- If the client wants to start or continue using the ring, prescribe the ring. Help the client identify their main reason for using the ring and remind the client of their strength and power.
- If the client will use the ring, ask who else can support the client's ring use and what kind of support the client needs from the clinic.
- If, due to violence or other obstacle, the client is not able to use the ring as prescribed, or anticipates they will not be able to use the ring as prescribed, discuss other options for reducing vulnerability to HIV.

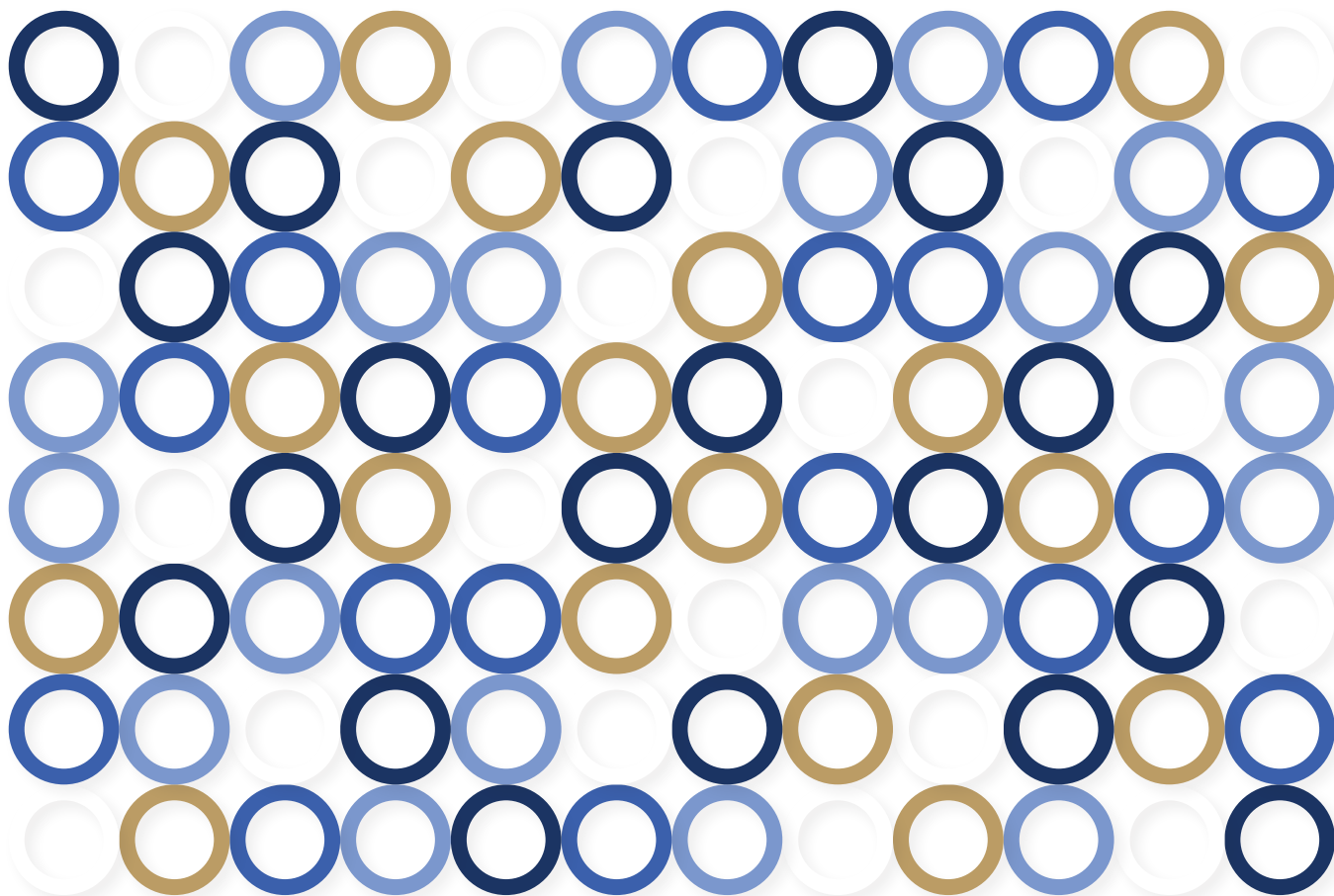


IPV
RESOURCE

TOOL 15



INTERNATIONAL
PARTNERSHIP FOR
MICROBICIDES



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