



OPTIONS

*Dapivirine Ring
Early Introduction Considerations
Seven Country Analysis*

August 2018



SUMMARY FINDINGS

DETAILED COUNTRY FINDINGS



Executive summary

THE OPPORTUNITY FOR THE RING

- Across countries, there was significant enthusiasm for the ring as a female-controlled technology that could be appropriate for adolescent girls and young women as part of a combination HIV prevention approach.
- The ring also raised questions from country stakeholders including questions on how to improve adherence among 16-24 year olds and how policies should be crafted to build the ring into a comprehensive prevention package.
- Importantly, policymakers and USAID/PEPFAR missions in most countries advised that a demonstration in each country addressing local conditions and concerns is the best way to expedite inclusion of the ring in national policies and plans. However all stakeholders emphasized the importance of linking demonstration projects to implementation – standalone demonstration projects were discouraged. This guidance is based on the experience with the introduction of oral PrEP in many countries.
- While all of the countries included in this analysis were interested in the ring, some are better positioned to be “early adopters.”
- At present, Zimbabwe and Uganda show immediate promise for a demonstration project with the ring due to national stakeholder interest and the anticipated pace of the process. South Africa and Kenya are also promising locations, though in Kenya there are still questions about how to move forward given the constraints of US funding and in South Africa stakeholders are cautious about adding new products and note that demonstrations before regulatory approval would require greater scrutiny.
- To expedite access to the ring, two steps should be pursued simultaneously over the coming year:
 1. A coordinated global effort to prepare demonstration projects in several “early adopter” countries, in close collaboration with key stakeholders and policymakers at the country level
 2. A consistent effort to communicate about the ring at the country level, especially as additional evidence is generated and the regulatory process advances

OVERVIEW OF PROCESS

- The OPTIONS (Optimizing Prevention Technology Introduction on Schedule) Consortium is a five-year, USAID funded effort to expedite and sustain access to new ARV-based HIV prevention products in sub-Saharan Africa with a focus on women and girls.
- In May 2018, seven countries (Rwanda, Uganda, Kenya, Zimbabwe, Malawi, Tanzania, and South Africa) were prioritized for analysis due to the state of the HIV epidemic in each country and experience with ring trials.
- OPTIONS conducted secondary research and interviews with key stakeholders in these countries to understand questions about the ring that could inform demonstration and processes for introducing new biomedical HIV prevention products.
- Interviews comprised a mix of policymakers, civil society representatives, donors, implementing partners, and trial contributors.



Key findings from country consultations

1

Most country stakeholders are intrigued by the ring

Country stakeholders cited female control and limited risk of creating resistance as valuable attributes of the ring. Stakeholders in Zimbabwe expressed a readiness to start a demonstration project on the ring as soon as possible. Stakeholders also had many questions about the ring (*noted on next slide*).

2

Interest in a demonstration to inform implementation

Most country stakeholders indicated a need for a local demonstration on the ring to inform policy-making and implementation planning, noting that evidence generated elsewhere would not provide the contextual detail required. Standalone projects not linked to implementation were strongly discouraged.

3

Need to leverage learnings from oral PrEP and potential to integrate the ring into roll-out in several countries

The recent experience with oral PrEP provides lessons on messaging, processes, and stakeholder engagement for the ring. Existing structures for PrEP, such as Technical Working Groups (TWGs), can also be used for the ring. The ring needs to be assessed as part of a combination prevention approach.

4

Criticality of AGYW populations across countries, and need to better understand adherence

Country stakeholders saw potential for the ring with AGYW populations that have been difficult to serve with other options, though they also requested additional evidence on how to support adherence amongst this population.

5

Thoughtful, sustained engagement process needed to introduce the ring

In many countries there is limited existing knowledge of the ring that will need to be overcome to start planning. The approval process for some countries is straightforward but each product introduction process has idiosyncrasies that need to be managed. Regular stakeholder engagement will be necessary to maintain progress.



Questions raised by policymakers

Across the seven countries, several key questions were regularly raised by policymakers

ASKED BY NEARLY ALL POLICYMAKERS

Key policymakers from five out of six countries analyzed asked the following questions:

- What would be the **impact** of the ring? How many infections would be averted?
- How does the ring **fit into a comprehensive package** of prevention?***
- What is the **effectiveness of the ring in the real-world?**
- What will be the **cost of investing** in the ring?
- What are **adherence to and uptake of** the ring in the real-world?
- Which **populations** are recommended for the ring?
- What are the implications for the **health system and healthcare workers?** What additional demands will the ring place on the health system?

ASKED BY HALF OF POLICYMAKERS

Key policymakers from three out of six countries analyzed asked the following questions:

- Will the ring be **affordable** for end users?
- Has the ring been proved to be **safe?***
- To what extent does the **effectiveness of the ring differ** among various populations? Is the ring **effective among AGYW?*****
- What does behavioral data demonstrate about the impact of the ring on **condom use and other reproductive health practices?**

* Questions that have been adequately demonstrated through past clinical trials







*** Questions that are partially studied in the upcoming REACH study

Note: Policymakers in Kenya were not surveyed due to US government restrictions



Country readiness assessment framework

A preliminary assessment for each country is included based on six dimensions. More dimensions may be added (e.g., availability of implementing partners) as discussions progress

High-level assessment for the ring	
 HIV epidemic characteristics	<ul style="list-style-type: none">Assesses the level of need in the country based on HIV prevalence and incidenceSpecifically notes the HIV burden faced by women and girls
 HIV prevention program	<ul style="list-style-type: none">Assesses the national HIV prevention program for comprehensiveness, inclusion of biomedical prevention, and dedicated prevention funds
 Oral PrEP experience	<ul style="list-style-type: none">Assesses speed and ease of previous oral PrEP research, demonstration, and implementation, including inclusion in national guidelines and strategic plans
 Ring trial experience to-date	<ul style="list-style-type: none">Highlights in-country dapivirine ring trials that could be leveraged for awareness-building and ring introduction
 Stakeholder reactions to the ring	<ul style="list-style-type: none">Assesses knowledge, interest, and enthusiasm about the ring from a range of stakeholders including government, civil society, and academia
 Product introduction process	<ul style="list-style-type: none">Assesses clarity and speed of typical product introduction process



Cross-country assessment for ring potential

	ZIMBABWE	UGANDA	SOUTH AFRICA	KENYA	MALAWI	TANZANIA	RWANDA
HIV epidemic characteristics	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	SIGNIFICANT NEED	MODERATE NEED
<i>Prevalence rate</i>	13.5%	6.5%	18.8%	4.8%	9.2%	4.7%	3.1%
<i>New infections annually</i>	40,000	52,000	270,000	53,000	36,000	55,000	7,500
<i>Incidence rate</i>	3.03	1.50	5.46	1.21	2.29	1.19	0.70
HIV prevention program	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
Oral PrEP experience	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	POTENTIAL LIMITATION	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
Ring trial experience to-date	STRONG OPPORTUNITY	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	POTENTIAL LIMITATION
Stakeholder reactions to the ring	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY
Product introduction process	STRONG OPPORTUNITY	STRONG OPPORTUNITY	MODERATE OPPORTUNITY	MODERATE OPPORTUNITY <i>Due to USG ban</i>	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	STRONG OPPORTUNITY



Implications of findings for ring planning



GLOBAL STAKEHOLDERS

- Country stakeholder interest and questions about the ring should **be shared with global stakeholders to inform planning and prioritization.**
- Feedback from country stakeholders underscores **the need for demonstration projects** as part of the global rollout and **the importance of coordinated demonstration planning** amongst global actors.
- Supporting awareness-building about the ring and its potential within **USAID, WHO, Global Fund and their relevant missions** is a fundamental step in the introduction process as planning, financing and approval of rollout in most countries hinges on their involvement.



COUNTRY STAKEHOLDERS

- Introducing the ring through demonstration projects will require resources and may mean that the **first phase of rollout should take place in a subset of “early adopter” countries.**
- Identifying **strong implementing partners in each priority country** to steward the stakeholder engagement and planning process will be a critical first step.
- The limited existing knowledge of the ring, coupled with country stakeholders’ eagerness to engage on demonstration planning, suggests a need for thoughtful, **consistent communications and engagement of priority stakeholders** in country between now, the EMA opinion and thereafter.
- A **customized engagement approach for different types of stakeholder groups** in each country could support introduction. For example, civil society members across countries were supportive of the new option, though they have varying levels of influence on policy-making. They can be engaged to generate demand for the ring through formal or informal channels.

SUMMARY FINDINGS

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KENYA





Kenya: Potential for the ring

STANDARD ADOPTER due to past successes with prevention and enthusiasm from stakeholders. However, health system constraints and political challenges may slow the demonstration process.

Opportunities

- **Past success with prevention:** Kenya is considered a prevention success story – annual new HIV infections are less than 1/3 what they were at the peak of the epidemic in 1993 and new infections have continued to decline.¹ Moreover, Kenya has invested in combination prevention, so the ring could be a natural addition to the menu of prevention options.
- **Addresses a challenge that oral PrEP faces:** Interviewees noted that people who have trouble with adherence to a daily pill may find it easier to use a ring.
- **Current revision of national plans:** The National Strategic Plan for HIV/AIDS expires next year, and the country is in the process of revising it, which presents an opportunity to incorporate mention of the ring.
- **Provider Capacity:** Kenya has invested in developing health care provider capacity to deliver oral PrEP, which may also provide a foundation for the ring.

Challenges

- **Concerns about integration with oral PrEP rollout:** Stakeholders raised concerns that introducing the ring while Kenya is still rolling-out oral PrEP may cause confusion, especially for healthcare providers. As the ring will not be available until late 2019, this concern will likely be alleviated.
- **USG suspension on working with the Kenya MoH:** Currently, USAID funds cannot be used for work with the national Ministry of Health. How the ring could be introduced without strong MoH collaboration is a big question. Currently, engagement at the county level is not affected, but counties can only act following a national launch. Other activities could proceed such as: examining willingness to pay through public and private sector, scenario planning about distribution locations, and segmentation considerations about who would use the ring vs. oral PrEP or condoms.



Kenya: Assessment overview

High-level assessment for the ring	
A blue icon showing a bar chart and a pie chart, representing data analysis or epidemic characteristics.	HIV epidemic characteristics SIGNIFICANT NEED: Kenya has a high HIV prevalence rate (5.4%), with 62,000 new infections per year. Young women are most at-risk, accounting for 33% of new HIV infections.
A blue icon showing a building with a cross and a pill bottle, representing a healthcare or prevention program.	HIV prevention program SIGNIFICANT OPPORTUNITY: Kenya has invested significantly in HIV prevention and has had success with introduction of VMMC, PMTCT and, most recently, oral PrEP. Kenya also has a significant focus on youth (who account for 51% of new infections), which may be a good fit for the ring.
A blue icon showing a pill bottle with a cross, representing oral PrEP.	Oral PrEP experience SIGNIFICANT OPPORTUNITY: Kenya was one of the first countries to approve oral PrEP and implement it at scale; a PrEP technical working group (TWG) has already been established and could be leveraged for ring introduction.
A blue icon showing a circle with a gap, representing a ring or trial.	Ring trial experience to-date MODERATE OPPORTUNITY: No Phase III trials or OLEs for the ring were conducted in Kenya, but Kenya will have sites in the REACH study.
A blue icon showing two speech bubbles, representing communication or stakeholder reactions.	Stakeholder reactions to the ring SIGNIFICANT OPPORTUNITY: Most stakeholders have little knowledge about the ring, but expressed enthusiasm about the product once they learned more.
A blue icon showing a clipboard with a checklist, representing a process or introduction.	Product introduction process MODERATE OPPORTUNITY: Kenya has a clearly defined product introduction process that worked well for oral PrEP; however, there may be complications to working with the Kenyan MoH due to the USAID ban.

Additional details on following slides



Kenya: HIV context

Kenya has an estimated

1.6 million

people living with HIV,
which accounts for

5.4% of the population

and an estimated

55,000 new infections

occur annually^{1,4}

Kenya has the joint **fourth-largest** epidemic in the world.¹ However, it is also considered a prevention “success” story and new infections have fallen in recent years. Kenya was one of the **first countries to approve the use of oral PrEP**. They are also leading in VMMC provision, having surpassed the VMMC target of 80% in 2014 and reached 92.6% of men in 2016.²

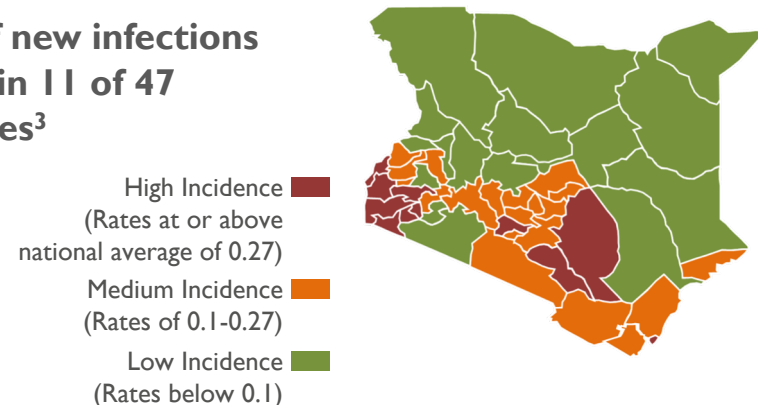
Young people, especially young women, are disproportionately affected by HIV¹

In 2015, **over half** (51%) of new infections are were among young people ages 15-24.¹ Young women were almost **twice as likely** to contract HIV as their male counterparts. Young women accounted for **33%** of new infections, while young men accounted for 16%¹

MSM, FSW and PWID are heavily impacted¹

30% of new infections happen among key populations.¹ **Sex workers** have the highest HIV prevalence (29.3%) along with MSM (18.2%), and PWID (18.3%)¹

65% of new infections occur in 11 of 47 counties³





Kenya: HIV prevention context

Context

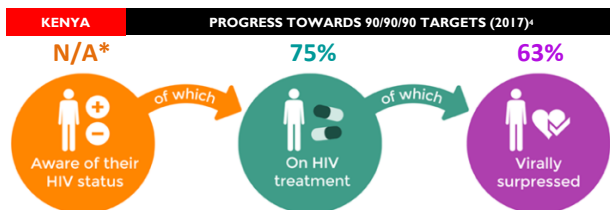
- **Political landscape:** The current administration is largely supportive of HIV prevention. However, due to alleged corruption in the MOH, projects with USAID funding can no longer solicit national input or collaboration from the MOH. County level engagement is not affected. This situation will likely impact the near-term prospects for funding from US-based donors.
- **Recent progress with prevention and treatment:** Kenya has made considerable progress to address the HIV epidemic through investments in combination prevention such as condoms, PMTCT, VMMC, and education and awareness. Kenya has decreased annual new infections from 77,000 in 2010 to 55,000 in 2016 and 90% of HIV.

National Policies and Strategies for Prevention

- **Goal:** The prevention goal is to **reduce new infections by 75%** using biomedical, behavioral, and structural interventions.
- **Targeted intervention among youth:** Given that 51% of new HIV infections in 2015 occurred among **youth ages 15-24**, the Kenyan government is investing in targeted interventions among youth.³
- **Target geographies:** The large cities of **Nairobi and Mombasa** saw a 50% increase in new HIV infections between 2013 to 2015, which has lead to a greater emphasis of reducing rates in large cities.³ The HIV burden in Kenya is geographically concentrated, so interventions are focused at the **county level**.

Remaining Challenges with Prevention

- **Financial limitations:** Despite growing investment, Kenya **struggles with financial sustainability** for HIV treatment and prevention. Like peer countries, the government is heavily reliant on donor funding to support HIV prevention and treatment programs.⁴
- **Health system constraints:** The current **health service system** faces challenges in **planning, coordination, and inadequate investment** in infrastructure leading to capacity constraints in HIV-AIDS clinics.⁴
- **Stigma:** **PLHIV** continue to face **high levels of stigma and discrimination** throughout the country.¹
- **Low risk perception:** Risk perception is **low** among certain target populations, making prevention uptake a challenge.⁴
- **Young adults:** Half of new infections among adults occur among **15 and 24 year olds**.⁴ Young women in this group represented a **third of all new infections** in 2015.⁴



* Recent data does not include the first of the three 90's. The most recent data, from [KAIS 2012](#) recorded **47% aware of their status**.

Sources: (1) Kenya Aids Strategic Framework 2014/15-2018/19, Ministry of Health, 2014; (2) Kenya Prevention Revolution Roadmap, Ministry of Health, 2014; (3) Kenya AIDS Response Progress Report, National Aids Control Council, 2016 (4) https://www.prepwatch.org/wp-content/uploads/2017/05/Kenya_PrEP_Implementation_Framework.pdf; (5) <https://www.avert.org/professionals/hiv-around-world/sub-saharan-africa/kenya> (6) Graphic from AVERT (modified by FSG); Data: UNAIDS Special Analysis, 2018



Kenya: Status of oral PrEP rollout

Status of oral PrEP Rollout

- Oral PrEP is included in Kenya's strategic HIV/AIDS documents including the **Kenya AIDS Strategic Framework (2014-2019)** and the **HIV Prevention Revolution Roadmap (2014)**.
- In 2016, Kenya became the **second** country in sub-Saharan Africa to issue **full regulatory approval of oral pre-exposure prophylaxis (PrEP)**.¹ Rollout began in 19 high and medium incidence counties in 2017, and by 2018, rollout touched almost every county.⁶
- Kenya is currently **conducting research into the uptake and impact of oral PrEP**, specifically with young women and girls in high-incidence areas.¹
- Kenya has a **mature HIV care and treatment program**, so there is existing infrastructure at both the facility and community level for rolling out oral PrEP.³
- As of February 2018, there were 30,000 people enrolled with **20,000 people active on oral PrEP**, representing clients across the country from over 800 facilities.^{2,6} The government aims to reach 500,000 people facing substantial ongoing risk with oral PrEP by 2022.³ People who face such ongoing risk include sex workers, MSM, PWID, and SDC in high and medium incidence counties.³ SDC are the most frequent users, while AGYW are the lowest users.⁶ Oral PrEP is **available for free for all populations at substantial ongoing risk**, and anyone else willing to pay can access it from pharmacies and private hospitals.⁶
- At LVCT Health demonstration sites in Kenya, there were several challenges for women accessing oral PrEP, including the fact that women find it **difficult to visit clinics** for oral PrEP services (often due to stigma). Women also noted challenges with taking oral PrEP, including **side effects** and the **daily pill burden**.⁵
- Providers and staff at these demonstration sites shared solutions they used to overcome barriers to access for women including **testing in the community** rather than a health clinic, reaching women where they access **family planning** or other services, and **peer-to-peer** encouragement.⁵ These strategies are now being used all around the country.



Kenya: Ring trials activity

Kenya has **not been the site for any phase III trials or open-label extensions**, but will be a site for the **REACH study for young women** which is expected to provide safety, adherence and acceptability data on the ring for girls and young women ages 16 to 21.

Study	Phase	Results	Partners
REACH (ages 16-21) MTN-034	II a	(Pending) Will collect safety and adherence data over the course of study product use for young women. Will also examine the acceptability of the study products. (6 month ring, 6 month oral PrEP, then choose between the ring, oral PrEP, or neither for 6 month)	<ul style="list-style-type: none">• Led by: MTN• Funding: US NIH, US NIMH, US NIAID. US NICHD• Sponsors: IPM, Gilead Sciences, Inc.• Key Site: KISUMU CRS Clinical Research Center



Kenya: Key questions raised about the ring

The following questions were raised in consultations with key stakeholders.

Strategic questions

- 1 What is the acceptability of the ring for Kenyan women and men? How comfortable are women with using the ring? Can male partners feel the ring during sexual intercourse?
- 2 How much will the ring cost? If it will not be given for free, what would be a sustainable price? Will the funding for the ring take away from oral PrEP?
- 3 What supports can we put in place for adherence? How do we ensure that people attend appointments at health facilities at the right time?
- 4 How will women be identified to participate in a demonstration study? Would women already using oral PrEP who have an issue with “pill burden” be an appropriate target group? If so, what is the best way to transition a woman from oral PrEP to the ring? Will the ring result in a decrease in oral PrEP use?

Technical questions

- What is the disposal process for the ring?
- When will the ring contain contraception in addition to HIV prevention?
- What are the side effects of using the ring? Are they similar to the side effects of using oral PrEP?



Kenya: Interviews

Civil Society

1. Winnie Wadera, Alice Visionary Foundation Project
2. Jeff Mwaisagu, International Centre for Reproductive Health (ICRH)
3. Jane Thiomi, LVCT Health

International Donors / Partners

4. Vincent Ojiambo, USAID

Researchers / Academia

5. Dr. Nelly Mugo, KEMRI
6. Jordan Kyongo, LVCT Health

Informal conversations at the International AIDS Society (IAS) International AIDS Conference 2018 also informed this analysis.