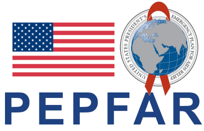
OPTIONS

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.

Source: FSG interviews and analysis

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 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.

Source: FSG interviews and analysis

Questions raised by policymakers

Across the seven countries, several key questions were regularly raised 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

Source: FSG interviews and analysis

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	• Assesses the level of need in the country based on HIV prevalence and incidence • Specifically notes the HIV burden faced by women and girls
HIV prevention program	• Assesses the national HIV prevention program for comprehensiveness, inclusion of biomedical prevention, and dedicated prevention funds
Oral PrEP experience	• 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	• Highlights in-country dapivirine ring trials that could be leveraged for awareness-building and ring introduction
Stakeholder reactions to the ring	• Assesses knowledge, interest, and enthusiasm about the ring from a range of stakeholders including government, civil society, and academia
Product introduction process	• 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
Prevalence rate	13.5%	6.5%	18.8%	4.8%	9.2%	4.7%	3.1%
New infections annually	40,000	52,000	270,000	53,000	36,000	55,000	7,500
Incidence rate	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 *Due to USG ban*	MODERATE OPPORTUNITY	POTENTIAL LIMITATION	STRONG OPPORTUNITY

Sources: (1) UNAIDS Country Factsheets 2016, (2) Prevalence rate calculated among adults. (ages 15-49), (3) Incidence rate calculated per 1000 population (all ages): UNAIDS 2017 Data

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.

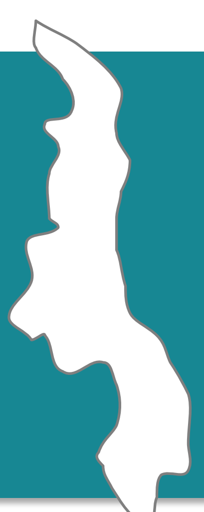
COUNTRY STAKEHOLDERS

- 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

DETAILED COUNTRY FINDINGS

MALAWI



Malawi: Potential for the Ring

SLOWER ADOPTER due to limited resources, gradual adoption of oral PrEP, and policymakers that prefer a robust body of evidence. However, civil society stakeholders are energized, organized, and eager to participate in ring advocacy.

Opportunities

- **Stakeholder interest:** There is **cautious interest** in building out the evidence base to support introduction of the ring in Malawi. Policymakers, implementation partners, and civil society representatives seemed open to discussing a new prevention option.
- **Active and respected civil society:** Civil society plays a strong role in influencing policymakers in Malawi. They are well organized, with structures for communication and coordination, such as MANASO. They are optimistic about ring.
- **Technical advantages of the ring:** In early conversations, stakeholders seemed supportive of the ring since it is a women-owned product. They are particularly interested in additional HIV prevention options for AGYW. Additionally, policymakers seemed open to the ring since it does not carry the same risk of resistance as oral PrEP.

Challenges

- **Robust evidence required:** Policymakers will need to be **engaged carefully** in the process once there is a robust body of evidence. Civil society can be a persuasive voice for policy change.
- **Health system capacity:** Malawi has **resource and health system constraints**, and a low physician and nurse to population ratio. Given these constraints, policymakers emphasize a low burden on the health system and cost-effectiveness as important criteria for new products.
- **Questions about the feasibility for Malawi:** On a recent study tour to South Africa, policymakers from Malawi felt discouraged by progress with oral PrEP, and especially with challenges in adherence. The policymakers felt since **South Africa was facing challenges, it would be impossible for Malawi to succeed** given the difference in resources.

Source: FSG interviews and analysis

Malawi: Assessment overview

	High-level assessment for the ring
HIV epidemic characteristics	**SIGNIFICANT NEED:** There is a particularly high prevalence rate, at 9.2%. Estimates also suggest that an additional 36,000 people are infected annually, and that AGYW are highly vulnerable.
HIV prevention program	**MODERATE OPPORTUNITY:** Malawi is growing its investments in HIV prevention. In particular, policymakers are seeking additional HIV prevention options for AGYW.
Oral PrEP experience	**POTENTIAL LIMITATION:** Malawi has moved slowly to introduce oral PrEP and is still in the demonstration project phase, as of August 2018.
Ring trial experience to-date	**MODERATE OPPORTUNITY:** Malawi has been the site of several ring studies, but many stakeholders were not familiar with the ring.
Stakeholder reactions to the ring	**MODERATE OPPORTUNITY:** Policymakers seemed cautiously interested in the ring, and saw benefits over oral PrEP in their context. Civil society advocates were eager to be engaged further.
Product introduction process	**MODERATE OPPORTUNITY:** There is a clear process for product introduction in Malawi, although the perceptions of a few key decision-makers that have not yet been engaged will be critical.

Additional details on following slides

Source: FSG interviews and analysis

Malawi has an estimated

1.0 million

people living with HIV, which accounts for

9.2% of the adult population

and

36,000 new infections

occur annually [1]

Women are disproportionately affected [2]

Prevalence among adult women (aged 15-64) is **12.8%, compared to 8.2%** among Malawian adult men

The gender disparity is largest among young adults [2]

HIV prevalence among 25- to 29-year-olds is **three times higher among females** (14.1 percent) than males (4.8 percent).

The health system is deeply burdened [3]

Malawi has one of the **most severe health workforce crises** in Africa, with a low physician-to-population ratio at 2:100,000 and a nurse to population ratio at 28:100,000.

Sources: (1) UNAIDS Data 2017, (2) Malawi Population-based HIV Impact Assessment MPHIA 2015–2016: Summary Sheet Link, (3) Avert: HIV and AIDS in Malawi: Link

Malawi: HIV prevention context

Context

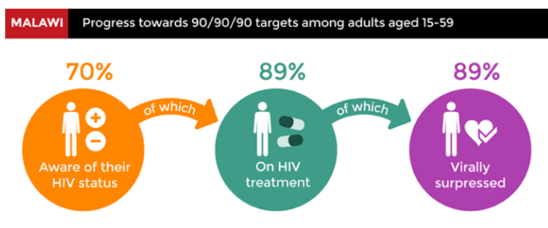
- ***Political landscape:*** Policymakers in Malawi are **cautious** about committing to another intervention without robust evidence. This caution has slowed oral PrEP adoption in Malawi. Additionally, in 2019 there will be a presidential election, and stakeholders shared that it is **politically unpopular** to provide access to technology that could be perceived to increase promiscuity.
- ***Recent progress with prevention and treatment:*** Through significant investment from donors and the government, a focus on education, and a combination prevention strategy, Malawi has made significant progress towards the 90-90-90- goals. Incidence has declined from **98,000 new infections in 2005, to 36,000 new infections in 2016**. [1]

National Policies and Strategies for HIV Prevention

- The recent National Strategic Plan focuses on advancing **condom** availability and use, **HIV education** / behaviour change, **PMTCT**, and **VMMC**. Oral PrEP is referenced as under **research to inform policy**.
- Malawi has been very successful and a **leader regionally with PMTCT**, and was the first country to implement the Option B+ approach. [2]
- Target populations in the Prevention Strategy include **MSM, FSW, AGYW (10-24), and serodiscordant couples.**
- In 2016, Malawi received 86% of funding for its HIV response from donors and 14% from domestic funding. [3] The majority of funding (47%) is spent on treatment and care, 5% on PMTCT and **23% on prevention interventions**. [4]
- The NSP for HIV and AIDS and the National HIV Prevention Strategy are **developed by NAC** in coordination with partners every 5 years. Both were last written for the years 2015-2020, and are revised every 2.5 years, with a full review in 2020.

Remaining Challenges with HIV Prevention

- **Protecting AGYW:** Two-thirds of the population in Malawi is under 25. Policymakers are seeking additional approaches to cover AGYW, as they are very vulnerable. [2]
- **Human resources for health:** In Malawi there are 3.5 healthcare staff per 1,000 ART patients, relative to the WHO recommendation of 7/1000. Fewer than 2,000 FTE are currently actively providing ART for half a million patients. [5]
- **Socio-cultural practices:** Recognized to increase risk for young women, socio-cultural barriers include the lower socio-economic status of women, gender based violence, and initiation ceremonies for young women, all of which remain a challenge for HIV prevention. [2]



Sources: (1)) Avert: HIV and AIDS in Malawi: Link, (2) 2015-2020 HIV Prevention Strategy : National AIDS Commission (3) 2017 PEPFAR Country Operational Plan: Link , (4)2015 Malawi AIDS Response Progress Report: Link, (5) 2015-2020 National Strategic Plan for HIV and AIDS

Malawi: Status of oral PrEP rollout

Oral PrEP Rollout

- Oral PrEP is currently **under demonstration in Malawi**. Policymakers wanted to see evidence that was generated within the country, so it is currently written into the national guidelines as oral PrEP demonstration and research to "**generate evidence to inform policymaking.**" Current demonstration projects include:
  - **LINKAGES Malawi**, sponsored by PEPFAR and USAID and among KPs and target populations, expected to roll out in late 2018
  - Also sponsored by PEPFAR, **Lighthouse through CDC** will roll out a demonstration project focused on AGYW in late 2018
  - **PrEP Operational Research Project**, sponsored by Médecins Sans Frontieres and among MSM and FSW
  - A planned **observational study sponsored by IMPAACT Network** to assess the acceptability of oral PrEP among pregnant and breastfeeding AGYW
- Malawi has been the site of both **clinical trials and demonstration projects**. For these projects, Gilead's Truvada (TDF/FTC) has been registered and approved for prevention, and registration of generic versions of TDF/FTC for prevention is planned.
- Oral PrEP is **not currently included in the current Global Fund grant.** One stakeholder shared that the Global Fund did advocate for including oral PrEP, but policymakers did not include oral PrEP in the grant request.
- The two biggest concerns that policymakers in Malawi have about oral PrEP are the **potential to build resistance** and **difficulty in ensuring adherence** among oral PrEP users.
- On a recent study tour, an implementing partner took the Deputy Director of the Department of HIV / AIDS to learn from oral PrEP progress in South Africa. Ultimately, Malawian policymakers were **discouraged by South Africa's continued challenges with adherence**. With fewer resources, policymakers felt Malawi be unable to succeed with oral PrEP rollout. This concern has led to minimal enthusiasm for oral PrEP from policymakers, and has slowed down the demonstration and implementation of oral PrEP.

Sources: (1) PrEP Watch: Malawi: Link ,(2) FSG interviews

Malawi: Ring trials activity

Malawi has been involved in the **phase III trial ASPIRE**, and the associated **open-label extension HOPE**.

Study	Phase	Results	Partners
ASPIRE (ages 18-45) MTN-020	III	The ring reduced risk of HIV-1 infection by **~27%** overall compared to a placebo. HIV risk was cut by **56%** in women older than 21, who appeared to use the ring most consistently	• Led by: Microbicide Trials Network (MTN) • Funding: US NIH, US NIMH, US National Institute of Allergy and Infectious Disease (IND Sponsor: IPM)
HOPE (ages 18-45) MTN-025	IIIb OLE	(Preliminary) Risk reduced by **~54%**	• Led by: MTN • Funding: US NIH, US NIMH, US National Institute of Allergy and Infectious Disease (IND Sponsor: IPM)

- Malawi **accounted for 10%** of the women enrolled in the ASPIRE and HOPE studies.
- **Blantyre and Lilongwe** were the two sites for the studies.
- The **key contacts** at the ASPIRE and HOPE study sites in Malawi are: Bonus Makanani and Linly Seyama (Blantyre) and Lameck Chinula and Tchangani Tembo (Lilongwe).

Sources: (1) https://mtnstopshiv.org/news/studies/mtn020/factsheet (2) https://mtnstopshiv.org/news/womens-use-vaginal-ring-higher-open-label-study-level-hiv-protection

Malawi: Impressions of the ring

Opportunities

*"We've been trying to find ways to protect AGYW since they are vulnerable. I see this as **an opportunity for AGYW**."*
– Policymaker

*"This is the first mention of the ring, but I think it might be promising. With the progress we are making with the three 90's **we are looking toward prevention** soon. Since the ring is topical, I think we will favor that."*
– Policymaker

*"For communities that do know about the ring, **there is high acceptability**, because it is a longer-lasting option compared to condoms or oral PrEP. There is high acceptability among young women."*
– Civil society representative

*"I'm excited about the ring because of the potential for AGYW. Women are vulnerable. **We need more options to empower choice**."*
– Civil society representative

Challenges

*"If we invest in the ring it is **at the expense of another HIV prevention intervention**. We need to be certain how many infections the ring will prevent over other interventions and in what populations."* – Policymaker

*"To what extent should civil society get involved with ring advocacy now? We still have not completed PrEP, and **we need to choose our battles wisely.**"*
– Civil society representative

*"There has been **sensitivity around PrEP, which could easily extend to the ring.** The challenge has been getting the government onboard; they want to see evidence generated in Malawi."* – Donor

*"I'm excited for the ring, but there have not been discussions about the ring. **People do not know about the ring.** Also, we need to make sure that adherence for AGYW goes up."*
– Civil society representative

Source: FSG interviews and analysis

Malawi: Key questions about the ring

1. To what extent do **young women adhere** in a real-world setting? How can **adherence be promoted**?
2. How do you identify the **right population** that has risk high enough? How do you **reach** this population?
3. How does the ring's **cost-effectiveness compare** to other prevention methods (e.g., condoms, oral PrEP, VMMC)? What is the **distinct impact** of the ring over other prevention intervention options?
4. Is there "**risk compensation**" on the ring? What does behavioral data demonstrate about the impact of the ring on **condom use** and other **reproductive health practices**?
5. What are the **implications on the health system**? What additional demands will the ring place on the health system? Can the health system meet those demands?

Technical questions

- Is the ring efficacious? Is it safe?
- Is there a risk of drug resistance with the ring?

Source: FSG interviews and analysis

Malawi: Interviews

Policymakers

1. Dr. Andrina Mwansambo, National AIDS Commission, Head of Policy Support and Development
2. Chimwemwe Mablekisi, National AIDS Commission, Director of Programs
3. Joel Suzi, National AIDS Commission, Head of Behaviour Change Communication
4. Shawn Aldridge, National AIDS Commission, Senior Technical Advisor
5. Michael Odo, Department of HIV/AIDS, Technical Advisor

Civil Society

6. Abigail Dzimadzi Suka, MANASO
7. Maureen Luba, COMPASS and AVAC
8. David Kamkwamba, JONEHA
9. Dingaan Mithi, JournAIDS
10. Grace Kumwenda, Pakachere Institute
11. Foster Mapiala, Youth Hub
12. Linly Dymuka, SAT
13. Mwendo Phiri, Youth champion
14. Dennis Mseu, MATERELAT
15. Sammie Mac Jessie, Bry Foundation
16. Brian Dauzos, Médecins Sans Frontières
17. Ulanda Mtamba, AVAC Fellow / AGE Africa
18. Antonio Yon, MANASO
19. Cait Orwig, MANASO
20. Tiferanyi Vizyalowe, CEDEP
21. Vincent J Ngosi, MANASO
22. Edward Phiri, Oridoc
23. Mercy Chikadza, MANASO

International Donors / Implementing Partners

24. Aayush Solanki, CHAI / PMM, Program Manager
25. Rachel Goldstein, USAID, Health Officer
26. Stephanie Weber, PEPFAR
27. Nicole Buono, CDC, Health Services Branch chief
28. Andrew Auld, CDC, Country Director
29. Jill Peterson, FHI360