

Overview of Oral PrEP and the Dapivirine Vaginal Ring

Bonus Makanani, MBBS, FCOG

**Johns Hopkins Research Project
Medical College of Malawi**

**Ensuring Safe HIV Prevention Methods for
Pregnant and Breastfeeding Women**

Blantyre, Malawi – Thursday 21 March 2019



Two HIV prevention methods



- The dapivirine vaginal ring is used every month
 - Well-tolerated and reduced the risk of HIV in two Phase III trials – ASPIRE and The Ring Study
 - Contains an ARV called dapivirine that slowly releases drug into the vagina during the month it is worn
 - Is currently under regulatory review – if approved, it would be the first biomedical HIV prevention method developed specifically for women – and the first long-acting method



- PrEP is daily use of an ARV tablet (Truvada)
 - Is a safe and highly effective method now approved in a number of African countries
 - Each tablet contains two ARVs -- tenofovir and emtricitabine

Both must be used consistently to be effective

The Dapivirine Ring



The Dapivirine Ring



- Made of flexible silicone, making it easy for women to insert and remove themselves
- Intended to be used for a month at a time
 - Women rarely feel it
 - Is discreet – their partners seldom feel during sex
- Slowly releases dapivirine into the vagina – most drug stays in the vagina, the potential site of infection
 - Dapivirine is a new drug only being used for prevention – it is not used in treatment of HIV
- Developed by the International Partnership for Microbicides (IPM) – a nonprofit group – that is seeking its approval

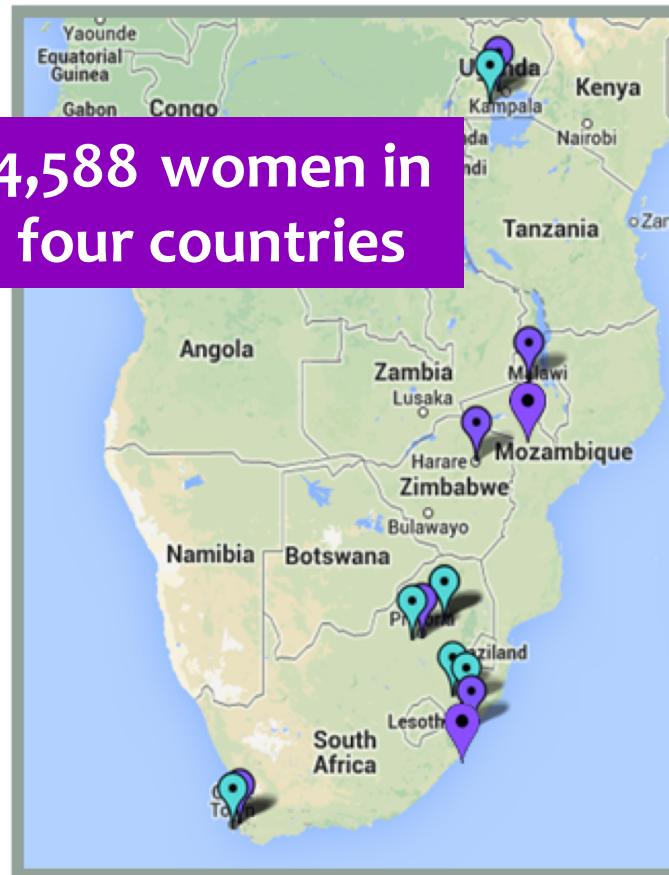
What do we know about the dapivirine ring?

Several studies have been conducted of the ring, including two large Phase III trials – ASPIRE and The Ring Study

ASPIRE

- Conducted by the Microbicide Trials Network (MTN)
- Enrolled **2,629 women age 18-45** at 15 sites in **Malawi, Uganda, South Africa and Zimbabwe**

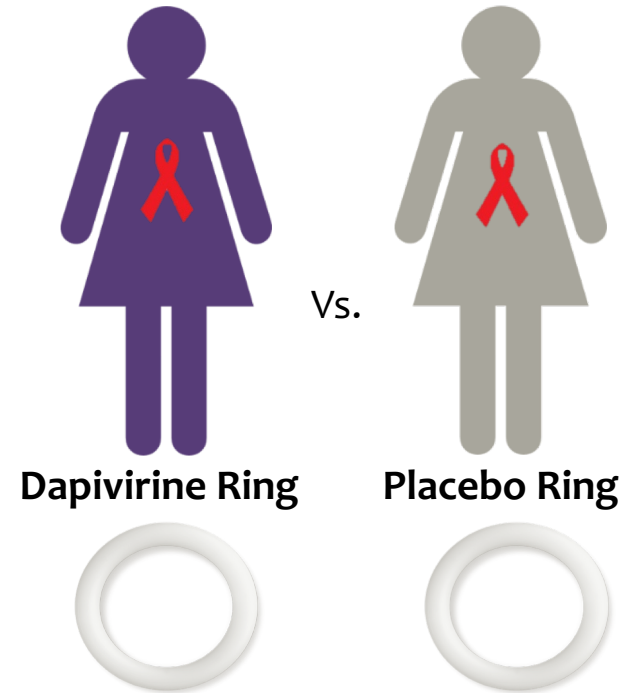
4,588 women in four countries



- Conducted by the International Partnership for Microbicides (IPM)
- Enrolled **1,959 women age 18-45** at 7 sites in **South Africa and Uganda**

How did we learn if the ring was effective?

- ASPIRE and The Ring Study were the kind of trials in which participants were randomized into different groups
 - One group used the dapivirine ring
 - One group used a ring with no active drug – a placebo ring
 - The rings looked the same and no one knew who was in which group
- At the end of each study, researchers looked at how many women in each group acquired HIV
- If effective, we would expect that fewer women in the dapivirine ring group would acquire HIV



All women received HIV counseling and testing, STI treatment and free condoms



What did we learn?

- **The ring is well tolerated – no safety concerns**
- **The ring protects against HIV**
 - Approximately 30% fewer women acquired HIV in the dapivirine ring group than in the placebo group
 - These results include all women – including those who didn't use the ring regularly
- **The ring is more effective when it's used**
 - In ASPIRE, among women older than 21 – who also used the ring more regularly – HIV risk was reduced by more than half (56%)
 - The ring was not effective among 18-21 year-olds – who did not use the ring regularly



Getting used to the ring

- Those who've never used a ring have notions that it will be difficult to use
- ASPIRE participants said they were unsure about it at first ...
- But got more confident in using it over time

When I first saw it, it was like, WOW!

It was easy to use ring and it was comfortable, I couldn't feel the ring. Even during my periods, it was no problem at all. During sex, I didn't have doubts about it.

The dapivirine ring was empowering

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

After ASPIRE and The Ring Study: HOPE and DREAM

- HOPE and DREAM provided former participants of the ASPIRE and The Ring Study the opportunity to use the dapivirine ring for one year
 - There was no placebo ring
- The HOPE and DREAM studies were designed to collect additional information on safety and adherence to inform potential rollout of the ring should it receive regulatory approval
 - One step closer to understanding “real-world” use



HOPE and DREAM Interim Results



- Safety profile similar to ASPIRE and The Ring Study
- Women used the ring more consistently than they did in the Phase III trials
 - Knowing that they were all receiving the active ring and that it has been found to be safe and effective
- Interim results of HOPE and DREAM suggest greater than 50% reduction in HIV risk
- Final results are due later this year

The Dapivirine Ring



Now what?

Next Steps for the Dapivirine Ring

Regulatory Process

IPM is applying for approval through European, African and US regulatory authorities

Additional Research

Safety studies of ring and PrEP among adolescent girls, pregnant and breastfeeding women in Africa

Potential Introduction



It's a big job

- IPM's master dapivirine ring dossier being submitted to regulatory agencies includes:
 - 13 years of data and findings from nearly 250 studies
 - Consists of 260,000 pages
 - When printed could fill a 2X2 meter room!



Truvada as Oral PrEP



What is PrEP?



- PrEP is an HIV prevention method that involves daily use of an ARV tablet - Truvada
- Truvada contains two ARV drugs – tenofovir (TDF) & emtricitabine (FTC)
 - Was already approved for treatment of HIV in combination with other ARVs as part of ART
- Several trials tested Truvada as prevention for HIV
- Was first approved for prevention (PrEP) by the US Food and Drug Administration in 2012
- Now approved in 40 countries
- The World Health Organization (WHO) recommends its use by anyone who is at risk of HIV

What do we know about PrEP?

- Daily oral PrEP is safe
- Because the drug goes everywhere in the body (is systemic), we know that use of tenofovir (one of the ARVs in Truvada) impacts bone density and markers of kidney health, although we do not know whether this is clinically significant
- People using PrEP must be tested for HIV to be sure that they don't start or continue using PrEP if they are infected
 - Although rare, resistance to PrEP drug(s) can arise if the person starts PrEP with undiagnosed HIV and/or if he or she acquires HIV and keeps on taking PrEP afterwards.

What do we know about PrEP?



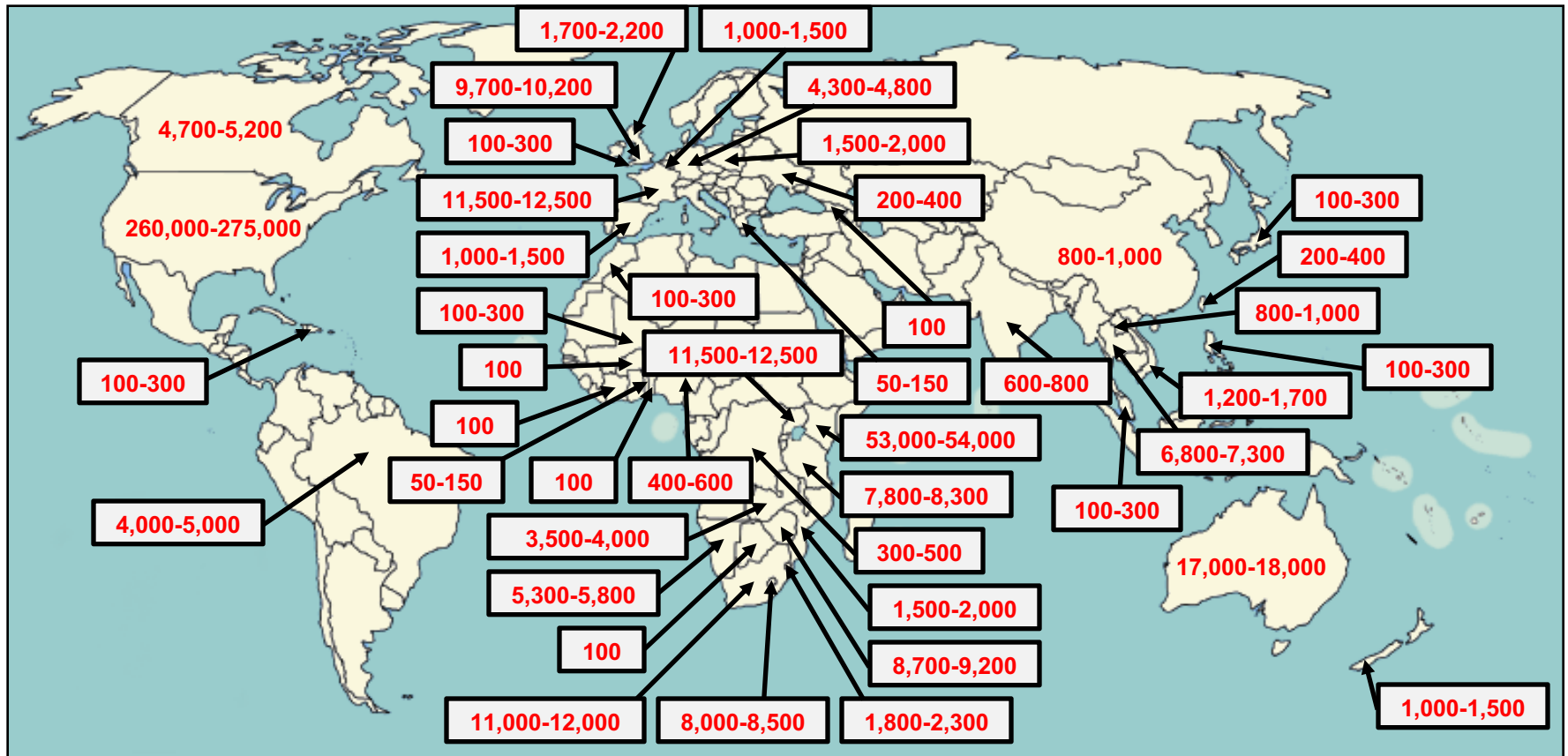
- PrEP is highly effective against HIV, but for it to be protective, adherence is essential
- Daily pill taking can be a challenge for some people
- Some people have expressed concern about the stigma associated with taking a drug that is also used for HIV treatment

Where are we now?

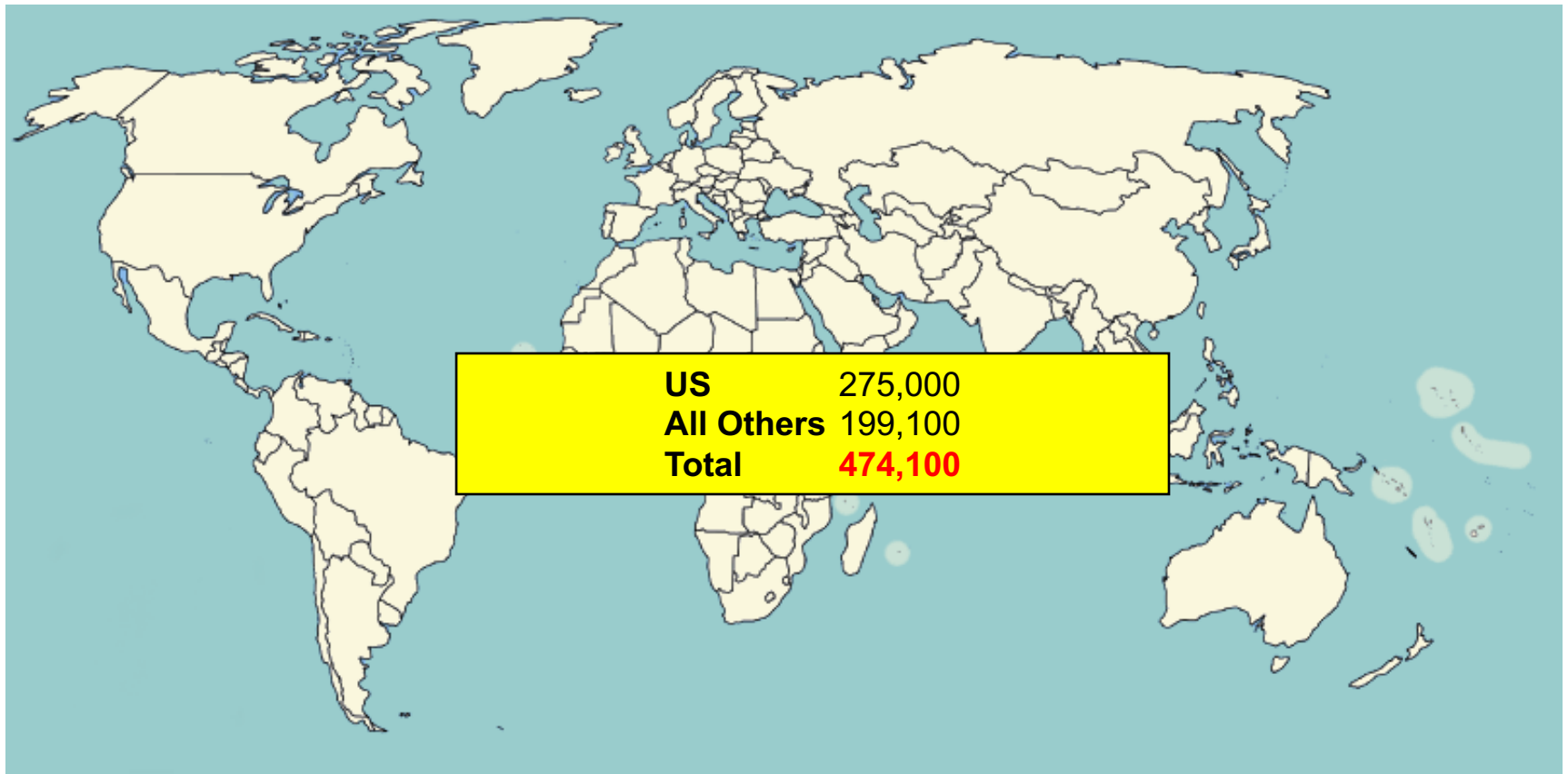
- Several countries have approved Truvada as PrEP, and implementing in different populations.
 - People with ability to pay can access PrEP in the private sector
- Several ongoing or planned demonstration projects are geared for different high-risk populations.



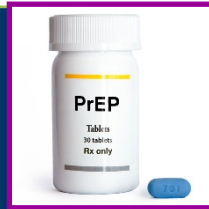
Global Oral PrEP Use by Country Feb 2019



Global Oral PrEP Use by Country Feb 2019



We've had longer to learn more about PrEP



**Truvada as
daily PrEP**



**Monthly
Dapivirine**

Phase III Trials	6	2
Open-Label Studies (with no placebo)	20+	2
How effective with consistent use?	Very (more than 90%)	Don't know yet (at least 50% or more)
Where drug goes	Drug goes throughout body – must monitor potential effects	Drug delivered into vagina - little goes elsewhere
Challenges	Daily pill-taking can be difficult; stigma of HIV meds	Vaginal rings unfamiliar; takes time to get used to
Approval Status	Approved in many countries for non pregnant or breastfeeding women	Approval Pending – for non pregnant or breastfeeding women 18 and older

People need choices

- Neither PrEP nor the ring is perfect
- People's preferences are different
- The more choices in HIV prevention products the more likely that one will be used



Acknowledgements



Thank You!

The Microbicide Trials Network is funded by the National Institute of Allergy and Infectious Diseases (UM1AI068633, UM1AI068615, UM1AI106707), with co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Mental Health, all components of the U.S. National Institutes of Health.

What is happening with PrEP in Malawi?

