

Dapivirine Ring for HIV PrEP

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September 30, 2021

Last Updated: [September 30, 2021](#)

Disclosures



- I attended Gilead's 2018 U.S. Latinx/Hispanic PrEP Advisory Program.
- Only FTC/TDF and FTC/TAF are approved by the U.S. FDA and only for use as daily PrEP in some but not all populations. This talk will include discussion of other options for PrEP.
- These slides were borrowed and adapted from Dr. Sharon Hillier, PhD.

More options = better choices



Implant



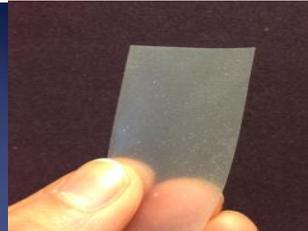
Injection



Pill



Vaginal ring



Vaginal film



Insert



Douche



Lube

Vaginal ring for sustained delivery of ARV drugs

Dapivirine ring



- Flexible, self-inserted silicone ring
- Dapivirine (DPV) = non-nucleoside reverse transcriptase inhibitor
- Dosing interval – 25mg monthly – limited absorption/cross into rectal tissues
- Developed by the International Partnership for Microbicides (IPM) through royalty-free license from Janssen

Status:

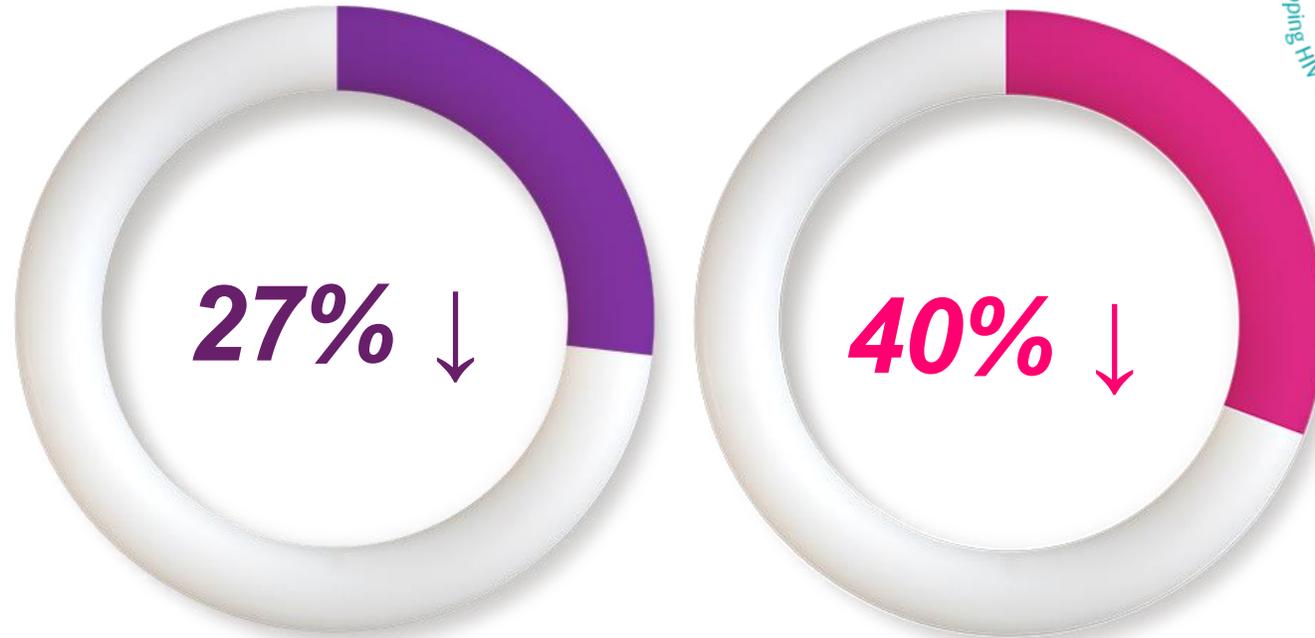
- Open label follow on studies completed
- Recommended by WHO 1/26/2021
- Under review by FDA as of 3/3/2021

Vaginal ring for sustained delivery of ARV drugs

Dapivirine ring



ASPIRE



NEJM 2016; 375: 2121-32 (Baeten et al) and 2133-2143 (Nel et al.)

Adapted from Dr. Sharon Hillier's presentation at the Annual Principles of STI/HIV Research Course



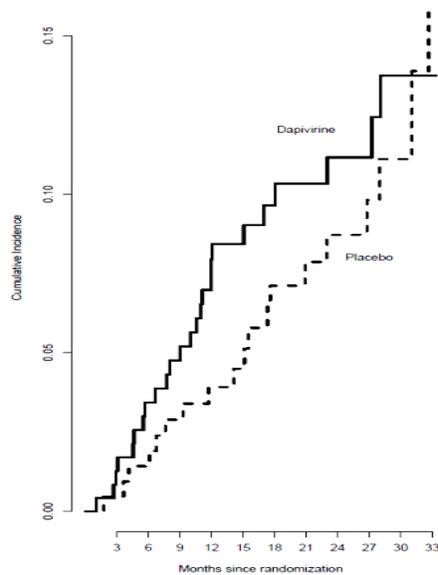
Vaginal ring for sustained delivery of ARV drugs

Dapivirine ring – Efficacy by age

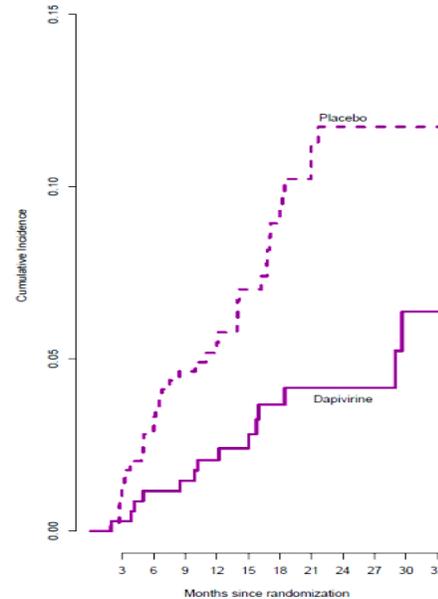


**Among women >21 years of age,
HIV-1 protection effectiveness was 56%
(95% CI 31-71%, p<0.001)**

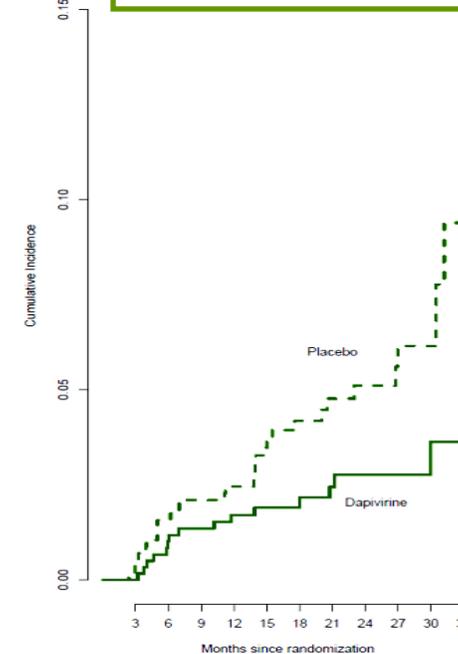
Age 18-21
-27% (-133,31)
placebo incidence 5.4%/yr



Age 22-26
56% (19,76)
placebo incidence 6.1%/yr



Age 27-45
51% (8,74)
placebo incidence 3.0%/yr



Vaginal ring for sustained delivery of ARV drugs

Dapivirine ring – Efficacy and adherence



- With 28 days of continued use, 4mg dapivirine released, <0.9 mg = non-use
- Amount of dapivirine remaining in returned rings was measured in ASPIRE

	Placebo	Non-adherent (<0.9 mg/mo)	Any adherence (>0.9 mg/mo)
Incidence	4.2	4.8	2.3
RRR	-	3.4%	48.0%

Vaginal ring for sustained delivery of ARV drugs

Dapivirine ring - Safety



- Well tolerated with only mild side effects
 - abnormal uterine bleeding
 - pelvic discomfort or pain
 - lower abdominal (suprapubic) pain
 - pain where the ring was located
- NNRTI resistance
 - ASPIRE: 8 (12%) of 68 in DPV group versus 10 (10%) of 96 in placebo
 - The Ring Study: 14 (18%) of 77 in DPV group versus 9 (16%) of 56 in placebo



Open-Label Extension Studies with Dapivirine Vaginal Ring



941 women, median 30 years
South Africa and Uganda

>83% self-report adherence to ring

Observed incidence:

1.8/100py (95% CI: 1.1-2.6)

62% reduction in HIV-incidence c/w expected
incidence based on the Ring study
(4.7 per 100 PY in the placebo arm)

1456 women, median 31 years
Malawi, South Africa, Uganda, Zimbabwe

Ring acceptance > 79% at each visit

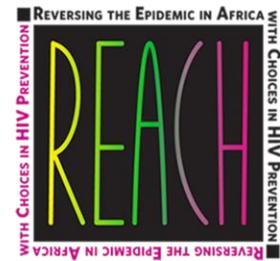
Observed incidence:

2.7/100py (95% CI: 1.9-3.8)

39% reduction in HIV-incidence c/w expected
incidence based on Aspire
(4.4 per 100 PY in the placebo arm)

REACH (MTN-034) at a Glance

Reversing the **E**pidemic in **A**frica with **C**hoices in **H**IV Prevention



- **Randomized, open-label crossover study** of the dapivirine vaginal ring (the ring) and oral PrEP (FTC/TDF)
- **Eligibility Criteria:**
 - 16-21 yr
 - HIV negative
 - Not pregnant and on reliable contraception for at least 70 days
- **Anticipated follow-up completion:**
October 2021

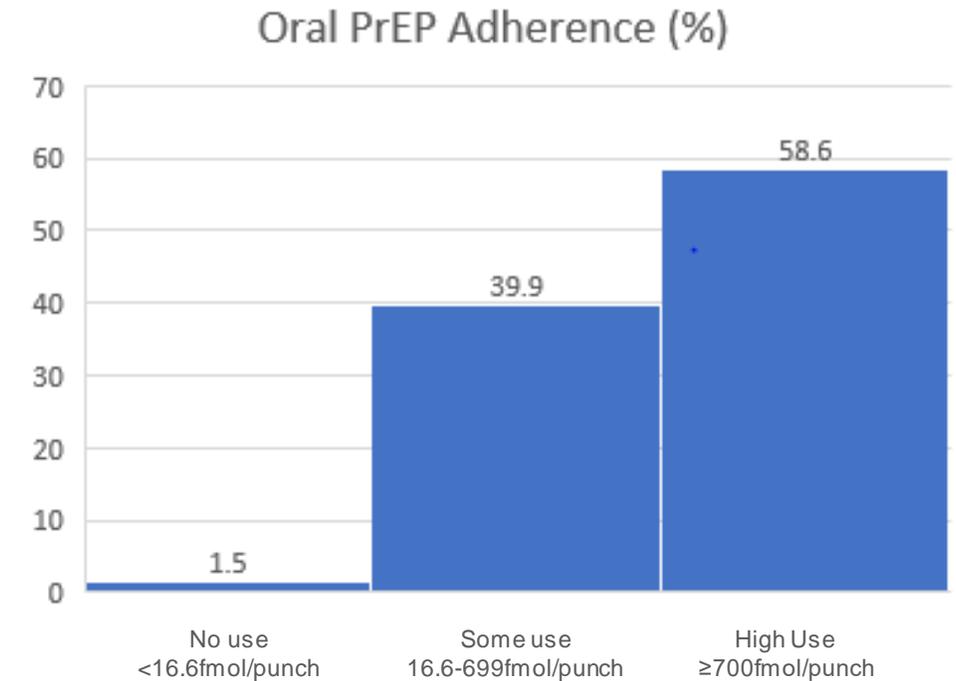
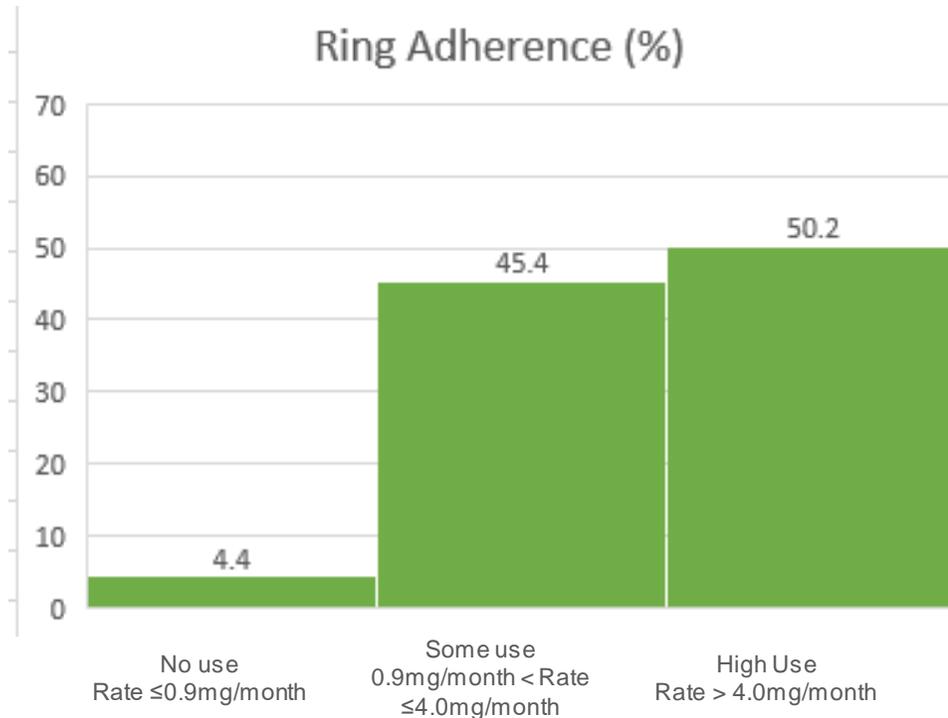
Crossover Study Design



Presenting interim results from the first 2 study periods (Feb 2019-Apr 2021)

REACH

Product Adherence

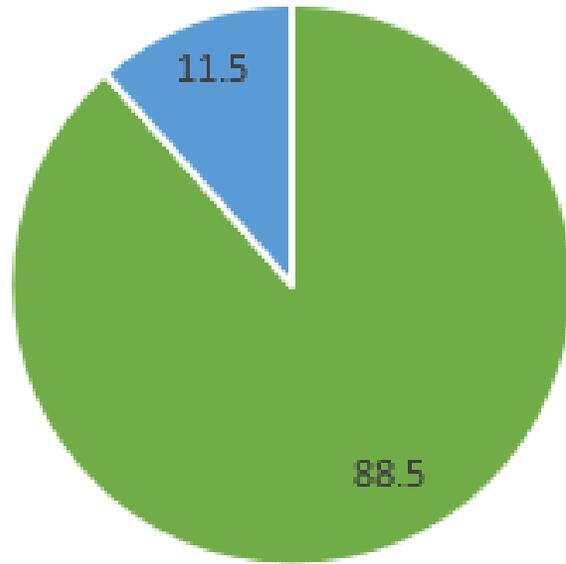


97% used some study product in first year
54% were highly adherent

REACH

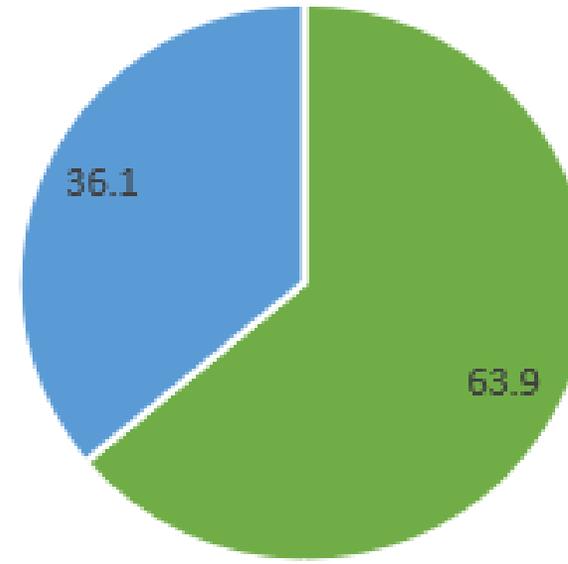
Product Acceptability

Ring Acceptability (%)



■ Acceptable ■ Not acceptable

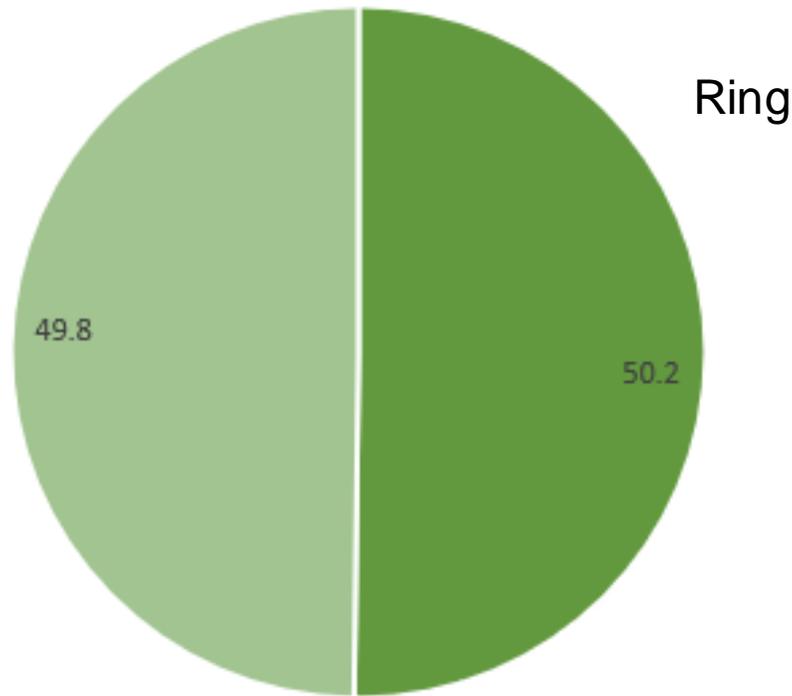
Oral PrEP Acceptability (%)



■ Acceptable ■ Not acceptable

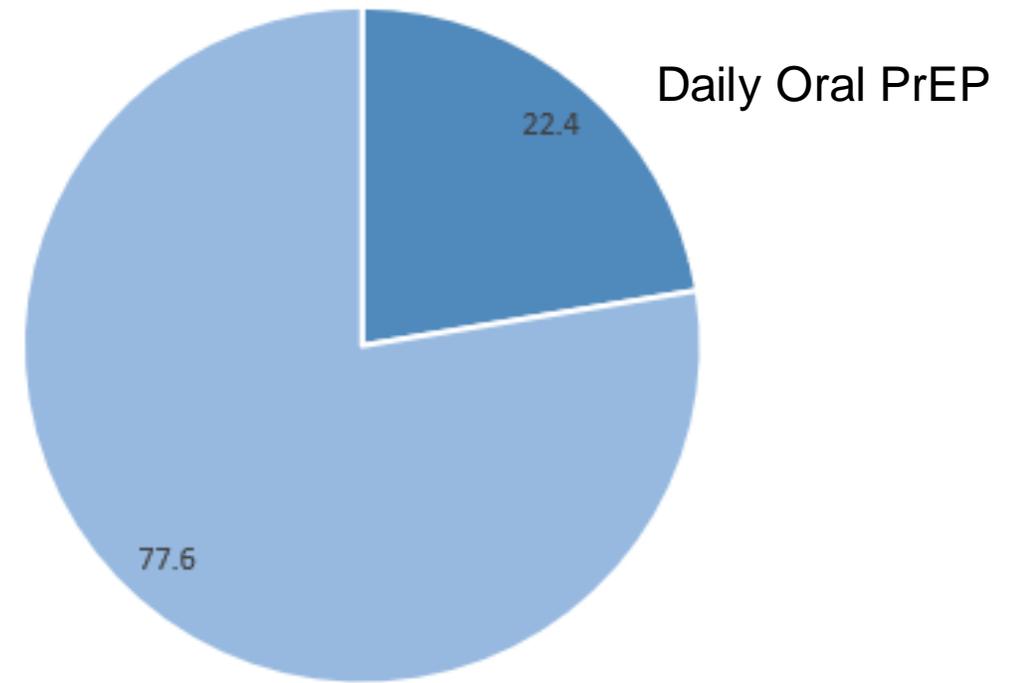
REACH Full Compliance to Study Product

More participants were fully compliant to the ring (i.e. leaving the ring inserted for a full month) compared to oral PrEP (i.e. 6+ doses per week)



■ Fully compliant use
Rate > 4.0mg/month

■ Below full compliance
Rate ≤ 4.0mg/month



■ Fully compliant use
≥1200fmol/punch

■ Below full compliance
<1200fmol/punch

Vaginal ring for sustained delivery of ARV drugs

Future products

- Longer duration vaginal rings
- Multipurpose rings (PrEP + ...)
 - Contraception
 - Dapivirine 200mg Levonorgestrel 320mg
 - Tenofovir + Levonorgestrel
 - STI prevention

Vaginal ring for sustained delivery of ARV drugs

Conclusions

- The dapivirine vaginal ring is currently at FDA for possible approval as PrEP.
- Like with oral PrEP, efficacy is dependent on adherence.
- Efficacy at current dose may not be as high as with high adherence to oral PrEP.

Not attributable to receptive anal intercourse (Peebles JAIDS 2020)

- Persistence may be better.
- More options = better choices!

Questions?



Acknowledgment

The Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling \$2,886,754 with 0% financed with non-governmental sources.

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