



MTN 034: Next Steps in Understanding HIV Prevention in Young African Women

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On behalf of MTN 034 protocol team

MTN Regional Meeting: 2015

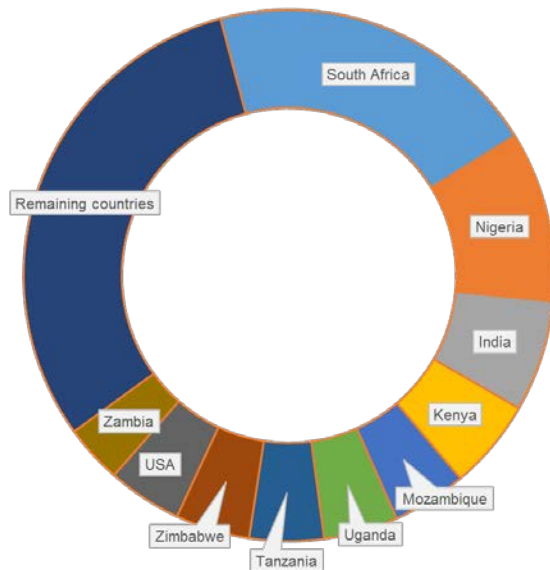
Cape Town

Overview

- Burden of HIV in SSA and characteristics of the epidemic
- Factors that increase the vulnerability of young women to HIV acquisition
- PrEP choices and factors likely to influence uptake
- Next steps to explore safety, acceptability and adherence to dapivirine VR
- MTN 034

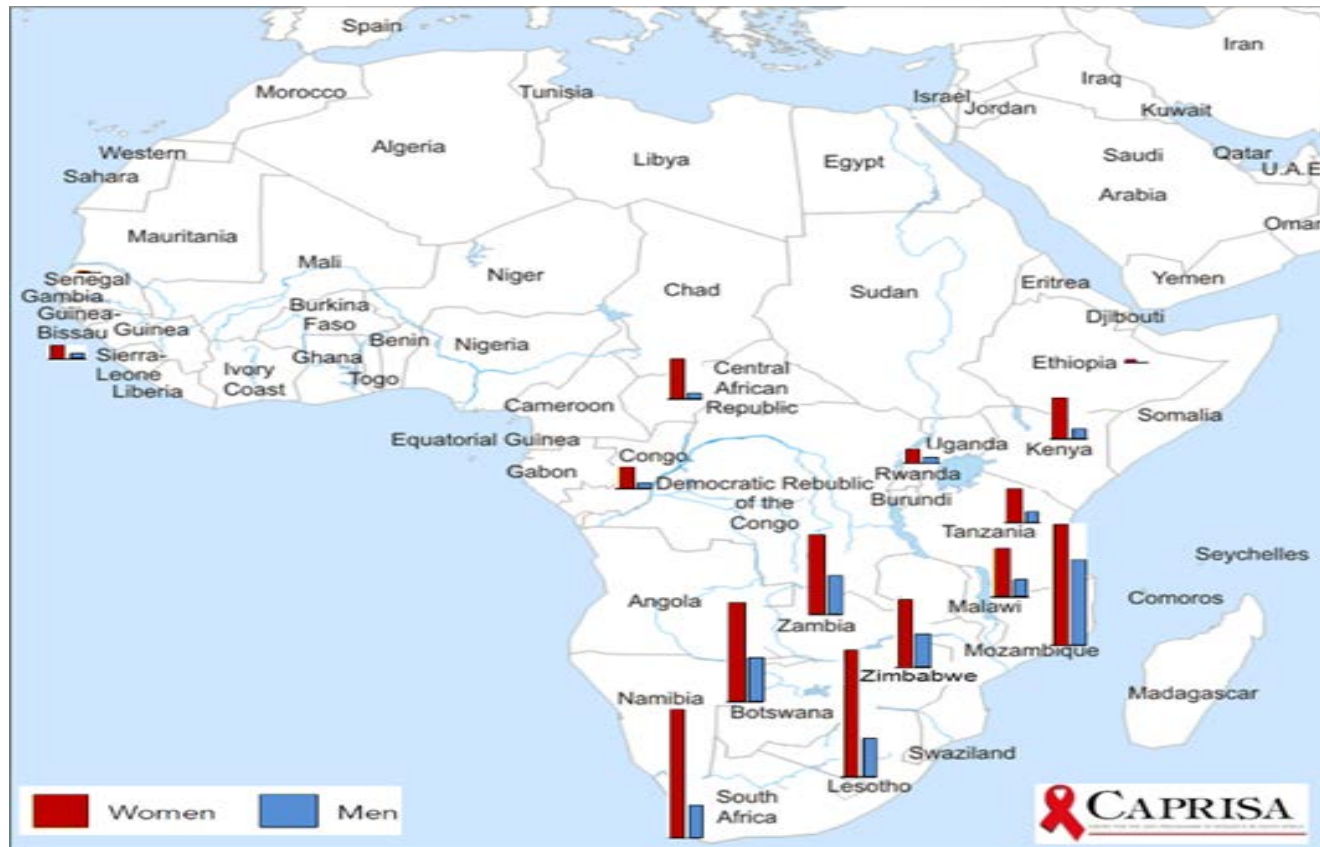
Burden of HIV in SSA

- Southern Africa: 40% of global burden of HIV infection
- Generalized epidemic (>10% population incidence) with significant heterogeneity



Rank	Country	% of people with HIV in the world
1	South Africa	18%
2	Nigeria	9%
3	India	6%
4	Kenya	5%
5	Mozambique	4%
6	Uganda	4%
7	Tanzania	4%
8	Zimbabwe	4%
9	USA	4%
10	Malawi	3%
	Remaining countries	39%

Disproportionate burden of HIV in Women

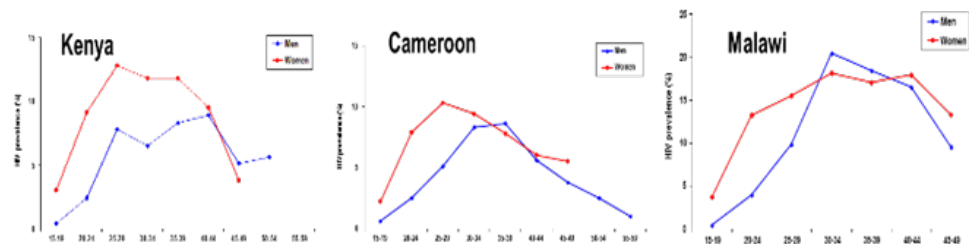
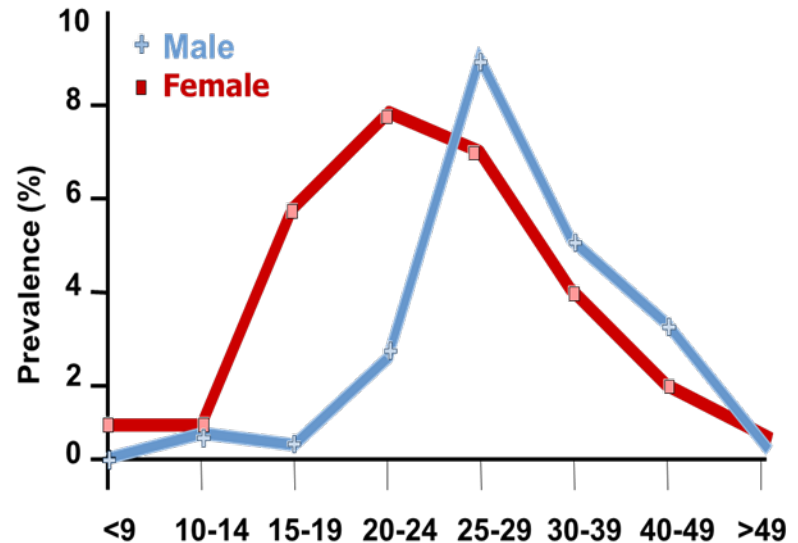


- 30% of new infections occurs in women in 15-24 year age group
- 4 fold greater increase in HIV Incidence in young women vs men

Source: Dellar R, et al. Journal of International AIDS Society 2015

Age-Sex Disparity in HIV acquisition

- Young women acquire HIV infection 5-7 years earlier than male peers
- Mechanism for sustained intergenerational transmission
- Vital to address this key population



Definition: “Young Women”

- Standard definition: 15-24 years of age
- Different vulnerabilities at different time points within this age range
- Differences between >18 years and <18 years
 - Neurobiological development; desire for risk and experimentation; limited access to healthcare; legal and ethical challenges
- Exclusion <18 year olds has implications for PrEP access during rollout

Source: Dellar R, et al. *Journal of International AIDS Society* 2015

Why are young women so vulnerable to HIV infection?

- Low sexual frequency but high risk sex
- Partners are recently infected men 5-10 years older
- Low condom use
- Biological vulnerability of the genital tract, potentially including:
 - Ectopy: larger surface area of vulnerable cells exposed?
 - Increased HIV co receptors in cervical cells?
 - Recent HSV-2 infection?
 - Hormonal contraception?
 - Vaginal cleansing or drying practices?
 - Trauma during sex?

Does PrEP work in young women?

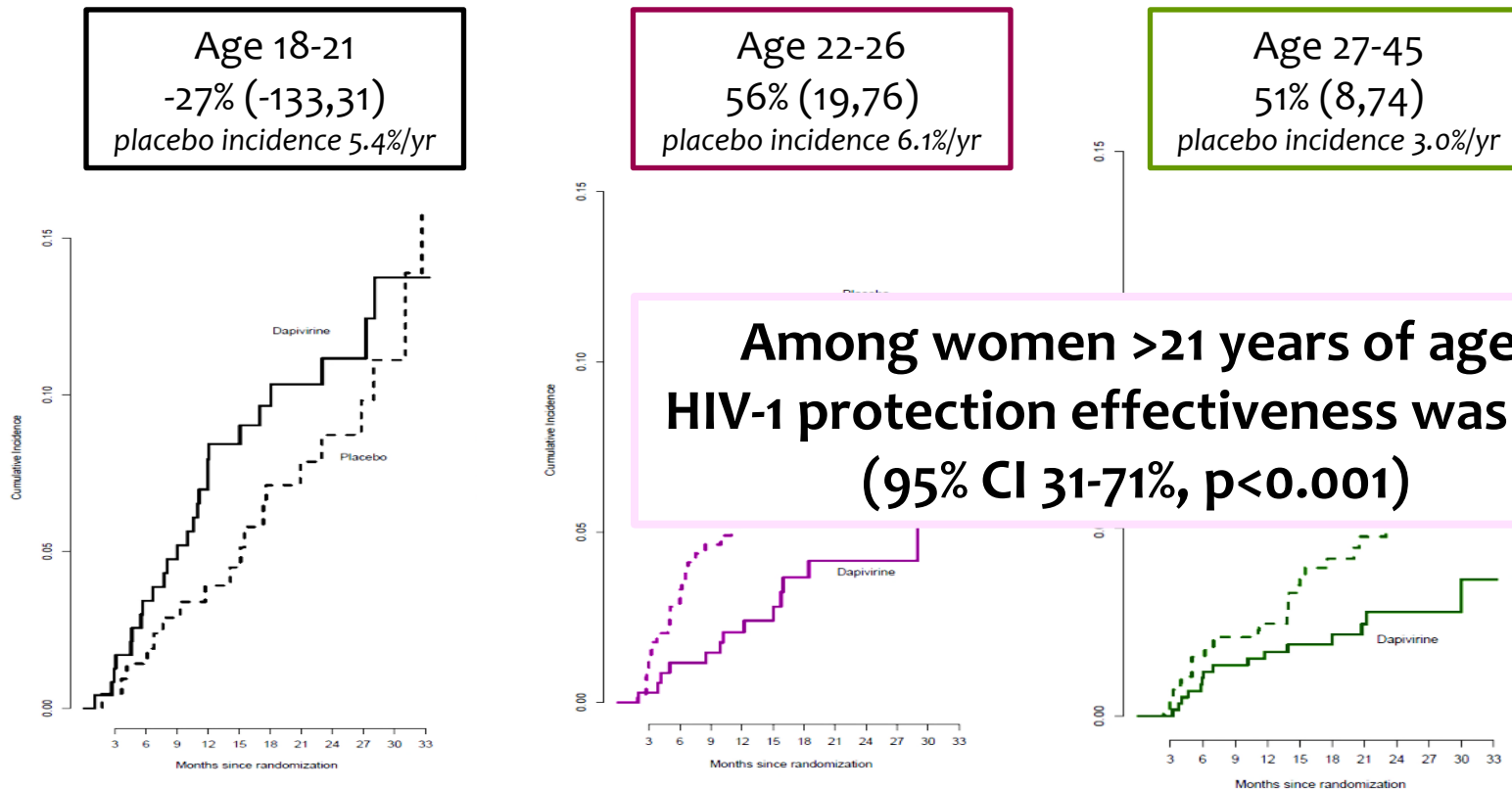
- Yes, if taken; PrEP efficacy $\approx 70\%$ in all subgroups of women in Partners PrEP
 - Age <30 , high risk, high plasma viral load in partner
 - Adherence $\approx 80\%$ based on drug levels (Murnane, et al, *AIDS* 2013)
- No efficacy with low uptake in VOICE & FEM-PrEP
 - $<30\%$ with drug detected
 - Disconnect between low perceived risk and high STI incidence in FEM-PrEP (Van Damme NEJM 2012)
 - Low uptake due to low risk perception, low motivation for prevention, need for social support and/or challenges with daily pill-taking (remembering, product storage)?

Acceptability & adherence to oral PrEP among Young South African Women

- ADAPT HPTN 067 Study:
 - 179 women randomized to one of 3 arms in Cape Town (daily; twice weekly + post sex; event-driven)
 - Daily dosing resulted in better coverage of sex acts, and adherence: 79% detectable tenofovir at 30 wks
 - Adherence consistent at 10 and 30 weeks
 - Young women equally as adherent as older women
 - PrEP likely to be used when counseled about efficacy

ASPIRE: Age and HIV-1 Protection

- HIV-1 protection effectiveness was explored in additional age-stratified categories, and lack of HIV-1 protection was limited to those ≤ 21 years of age:



Rationale for evaluating PrEP & vaginal rings in young African women

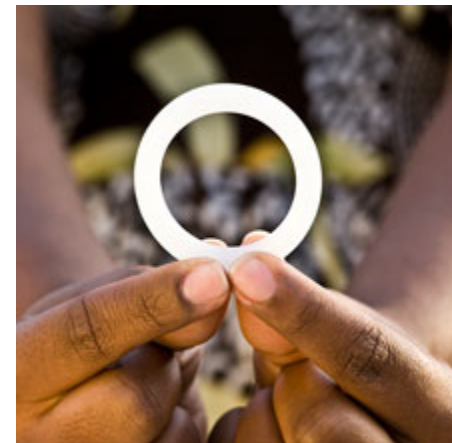


- Oral PrEP and dapivirine VR ring have efficacy & adherence predicts efficacy
- Given lower adherence & efficacy with FTC/TDF & dapivirine ring among young women in clinical trials
 - Need to assess biological factors that may influence safety & efficacy of products in adolescents & young women
 - Need to understand acceptability and adherence to oral PrEP & vaginal rings
 - Need safety data in <18 year old women for regulatory approvals

MTN 034

Safety and Adherence Study of the DPV (25 mg) VR and TDF/FTC Tablet in a Young African Female Population

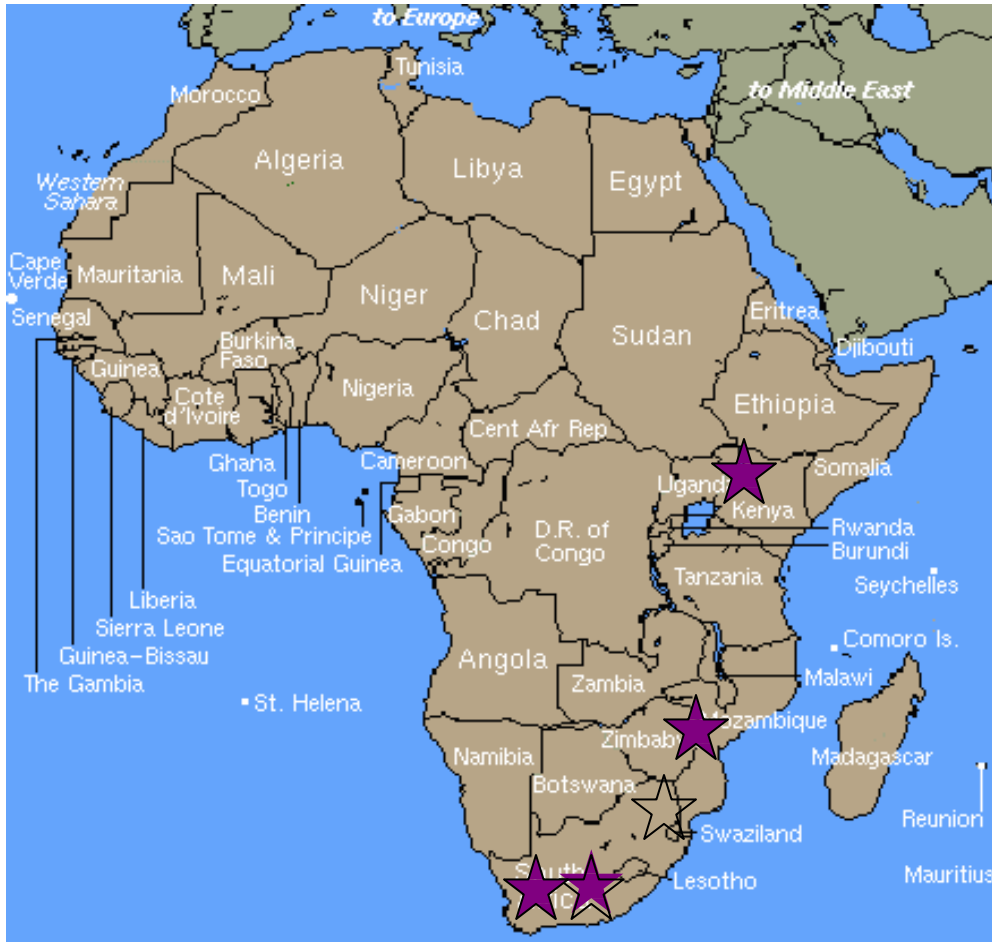
- VR safety data will be provided by MTN 020, MTN 023 and other studies
- MTN 034: safety and tolerability amongst African adolescent women



Participants

- **Sample Size:** Approximately 450 participants
- **Study Population:** Healthy, HIV-uninfected, adolescent females (15 - 17 years old) and young women (18-21 years old) on effective contraception
- **Study Duration:** 73 weeks of follow-up per participant with a projected accrual period of approximately 12 months at each site .

4 Sites across 3 countries



Uganda

Zimbabwe

South Africa

Proposed Modified Study Design

March 2016

- Protocol first reviewed by PSRC Dec 1, 2015, N = 300 adolescents ages 15-17
- Proposed changes based on ASPIRE results:
 - Add 150 additional participants aged 18-21
 - Add a third period during which young women will be allowed to select their preferred product

	Assigned Study Product Period 1 (24 Weeks)	Assigned Study Product Period 2 (24 Weeks)	Choice of product period 3 (24 Weeks)
Sequence A	Dapivirine VR	Oral FTC/ TDF	Oral FTC/TDF or ring
Sequence B	Oral FTC/ TDF	Dapivirine VR	

Rationale for Study Design

- Cross over design to evaluate two HIV prevention technologies in young women
 - Allows smaller sample size; each woman serves as her own control for behavioral and biologic data
 - Provides direct comparison of user acceptability, product safety, adherence, and product preferences
 - Contributes data for licensure of VR & safety data of oral PrEP for young women

Study objectives

- Primary objectives
 - Safety of oral Truvada and Dapivirine VR
 - Compare adherence to TDF/FTC and the dapivirine VR by drug concentrations in blood, vaginal fluid & ring
- Exploratory objectives
 - Characterize the vaginal microenvironment during product use
 - Microbiome
 - Biomarkers for safety and efficacy in mucosal secretions
 - Incident STIs
 - CCR5 and CD69 expression on cervical CD4 cells (subset)
 - Inflammation mediators
 - Cellular repair markers

Secondary Objective: Behavioral Assessments

- To compare the acceptability of daily FTC/TDF oral tablet to the dapivirine VR inserted once every 4 weeks during 24 weeks of study product use in an adolescent and young female population

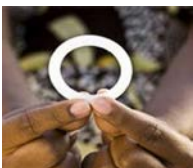


Approach

- **Design** - Prospective from baseline to exit
- **Data collection** - Quantitative: ACASI, CRFs
 - Qualitative: Serial IDIs +FGDs
- **Assessments:** Baseline, Monthly/Quarterly and exit

MTN 034: Acceptability Measures

- Uptake and time to discontinuation
- Facilitators and barriers to use
- Acceptability during sex and menses for IVR
- Correlates of acceptability
 - Behavioral risk and risk perception
 - Understanding of effectiveness of oral TDF/FTC PrEP and dapivirine VR
 - Stigma associated with product use
- Product use concerns
 - Partner's reaction
 - Side effects
 - Concerns about systemic vs topical exposure to ARVs



MTN 034: User Experiences

- Reports of product use & adherence patterns
- Disclosure to partner, family, and friends
- Product storage
- Vaginal hygiene practices
- Condom use
- FP method use
- Ring insertion, removal ease
- Frequency & context of VR expulsion incidents



MTN 034: User Preferences



**Daily oral
TDF/FTC
PrEP**



**Monthly
dapivirine VR**

- Preference at beginning of study (after counseling & being shown TDF/FTC pill & dapivirine VR)
- Change in preferences over 6 months after each phase of oral PrEP or dapivirine VR
- Choice of product after using both oral PrEP and dapivirine VR

Summary of MTN 034 Behavioral Questions

Topic	Sample Questions
Acceptability	What did adolescents and young women experience with product use?
Adherence	Do they use the methods often enough? Correlates, barriers & facilitators to consistent use
User experiences	Use as relates to sexual behavior? Condoms? Contraceptives? Vaginal hygiene practices?
Preferences	Which method do adolescents and young women choose? Why?



Conclusions

- Young women in SSA are at high risk for HIV acquisition; effective prevention tools are needed
- MTN 034 will assess behavior (patterns of use, preferences) and biology (safety, PK, STIs, microbiome) with dapivirine VR and TDF/FTC
- MTN 034 safety data needed for regulatory approval of oral PrEP and dapivirine VR for African adolescents and young women
- MTN 034 will characterize and probe user experiences and preferences after experiencing both dapivirine VR & oral PrEP

Acknowledgements

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