Event-driven HIV and STI Prevention for People Assigned Female Sex at Birth

Jenell Stewart, DO, MPH
Assistant Professor, Infectious Diseases, Hennepin Healthcare and University of Minnesota

Last Updated: May 20, 2024
Disclosures

No conflicts of interest or conflicts to disclose.
Funding for this presentation was made possible by U1OHA29296 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.
Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities
HIV PREVENTION

Event-Driven PrEP
Proven efficacy in placebo-controlled RCT

On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

P=0.002 by log-rank test

- 400 MSM mostly in France (43 in Canada)
- 16 HIV infections with 2 assigned to event-driven PrEP for 86% reduction in HIV (P=0.002)
- Breakthrough infections were due to nonuse
- Median of 4 pills per week

ANRS IPERGAY
Molina et al, NEJM, 2015
Decreased coverage with event-driven pre/post PrEP compared with daily PrEP (52% vs 75%) 

Randomized, open-label 1:1:1 assigned to daily, weekly, or pre/post PrEP (2012-2014) 

191 cisgender women in Cape Town, South Africa 

Women in Cape Town had 4 seroconversions 
- 2 among weekly group and 2 among with pre/post use 

ADAPT [HPTN-067] 
Bekker et al, Lancet HIV, 2018
TDF drug levels are higher in rectum than vagina

47 cisgender women given TDF/FTC to predict time to protective EC90

Daily TDF/FTC is proven to be protective for vaginal/front sex
Clinical data incongruent with vaginal drug levels

Estimates of dose-dependent effectiveness based on vaginal PK data

Estimates of dose-dependent effectiveness based on PBMC PK data

Figures replicated with permission
Zhang et al, Nature Medicine, 2023
Do vaginas demand perfection?

Figure 4. HIV Incidence Rates Among Cisgender Women by Adherence Trajectory (n = 2954)

<table>
<thead>
<tr>
<th>Adherence</th>
<th>HIV incidence rate per 100 person-years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consistently daily</td>
<td>0 [Reference]</td>
</tr>
<tr>
<td>Consistently high</td>
<td>0.13 (0.02-0.92)</td>
</tr>
<tr>
<td>High but declining</td>
<td>0.49 (0.22-1.08)</td>
</tr>
<tr>
<td>Consistently low</td>
<td>1.27 (0.53-3.04)</td>
</tr>
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</table>

Pooled data from 11 F/TDF PrEP studies among cisgender women in 6 countries [2012 to 2020]

Marrazzo et al, JAMA, March 1, 2024
Imperfect adherence is protective so might event-driven PrEP

- Imperfect adherence is protective for cisgender men
- Event-driven PrEP works for cisgender men
- Imperfect adherence is protective for women
- Event-driven PrEP may work for women
DoxyPEP

STI PREVENTION
Doxycycline Post-Exposure Prophylaxis for STI Prevention among Cisgender Women
Background

STIs are on the rise, notably among people who might benefit from PrEP regardless of sex or gender.

Sequalae of bacterial STIs can be severe and chronic among cisgender women or in the uterus.

Doxycycline PEP significantly reduced incident bacterial STIs by 60-70% in people assigned male sex at birth in France\(^1\) and the USA\(^2\).

Doxycycline drug levels are more variable but high in vaginal secretions.\(^3\)

\(^1\) Molina et al, Lancet ID, 2018
\(^2\) Luetktemeyer et al, NEJM, 2023
\(^3\) Haaland et al, EBioMedicine, 2024
Methods

Design: Open-label 1:1 randomized trial
Intervention: 200mg doxycycline hyclate within 72 hours of sex
Standard of Care: Quarterly STI testing and treatment


Approach: Quarterly follow-up with STI (endocervical) NAAT testing and treatment and surveys.
# Results: Baseline Characteristics

<table>
<thead>
<tr>
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<th>Doxycycline PEP (N=224)</th>
<th>Standard of Care (N = 225)</th>
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<tr>
<td><strong>Age, Median [IQR], years</strong></td>
<td>24 [22-27]</td>
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<td><strong>Bacterial STI at baseline</strong></td>
<td></td>
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<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>13% (30)</td>
<td>15% (33)</td>
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<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>5% (10)</td>
<td>3% (7)</td>
</tr>
<tr>
<td><em>Treponema pallidum</em></td>
<td>0% (0)</td>
<td>1% (2)</td>
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66% never married, 69% had prior pregnancies, 61% were using hormonal contraception, and 37% reported transactional sex
Results: Retention and Follow-up

97% of follow-up visits completed

82% of weekly SMS surveys completed

44 pregnancies accounting for 10% of follow-up time with other holds accounting for 5% in intervention group
Results: Sexual Behavior & PrEP use

In weekly SMS surveys, zero sexual exposures reported in 28.4% (2222/7818) of weeks.

>1 partner at 45.6% of the follow-up visits:
17.5% (305/1740) with 2 partners and 28.1% (489/1740) with ≥3

13% self-reported PrEP discontinuation. 0 incident HIV cases.
Results: Incident STIs

Overall STI incidence of 27 per 100 person-years

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Relative risk calculated using generalized estimation equation (GEE) with modified Poisson regression.
# Results: Incident STIs

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Subgroup analyses of STI incidence by age, hormonal contraception use, transactional sex, and STI detected at baseline found similar results.
Results: Secondary Outcomes

- No severe adverse reactions related to doxycycline.
- 4 participants reported social harms related to PEP use.
- No incident HIV.
- 100% (n=6) tetracycline-resistant (tetM) Neisseria gonorrhoeae at baseline and 100% at follow-up (n=22).
- 0% (n=66) detection of tetC in Chlamydia trachomatis.

Gene-mediating, high-level tetracycline-resistance, tetM, in N. gonorrhoeae or tetC in Chlamydia suis. Pitt et al, 2019; Wanninger et al, 2016
Results: Objective hair drug testing

- In a randomly selected subset of 50 participants assigned to doxycycline PEP
  - 56.0% (28/50) of participants had doxycycline detected at least once
  - 29.0% (58/200) of all quarterly visits had doxycycline detected,
    - 32.6% (58/178) when medication holds excluded
- 6.7% (3/45) of enrollment visits had doxycycline detected
- 5.1% (2/39) of follow up visits among SOC group had doxycycline detected
Conclusion

Our findings emphasize the need for STI preventive options for women that are effective and acceptable.

Adherence to preventive medicines needs to be better understood and supported for biomedical prevention to be effective.

Differing results between trials among MSM and this trial among cisgender women are likely explained by low use of doxycycline PEP.

Additional trials of doxycycline PEP for people AFAB regardless of gender are forthcoming.
Acknowledgements

We thank the young women who volunteered to participate in this study.


University of California – San Francisco: Monica Gandhi, Karen Kuncze, Alexander Louie, Hideaki Okomi, and Matthew Spinelli

Funding: US National Institutes of Health (grants R01AI145971, P30AI027757, K23MH124466, 3R01AI098472)

JMB is an employee of Gilead Sciences outside of the presented work.
Acknowledgment

This 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 $3,333,289 with 0% financed with non-governmental sources.

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