Doxycycline for STI Prevention Evidence and Current Research

WEBINAR 7 October 2022

The Choice Agenda welcomes you
dPEP peeps

- Australia
- Botswana
- Canada
- Côte d'Ivoire
- Eswatini
- France
- Gambia
- Ghana
- Guatemala
- India
- Indonesia
- Italy
- Kenya
- Myanmar
- Netherlands
- Nigeria

- Peru
- Philippines
- Russia
- Singapore
- Slovenia
- South Africa
- Switzerland
- Tanzania
- Thailand
- Uganda
- Ukraine
- United Kingdom
- United States
- Vietnam
- Zambia
- Zimbabwe

32 countries

327 webinar registrants
Webinar Logistics

- This call will be recorded. Your presence = consent.
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  - Please comment, ask questions, share info/resources in the chat.
  - Let’s hear your voice and see your face too. Raise hand to speak on camera.
- We will share links to recording and slides in follow-up email.
- Access TCA webinar resources here:
  - [www.avac.org/choice-agenda](http://www.avac.org/choice-agenda)
Press record!
Thank you to everyone who submitted questions during registration.
November 3 webinar

PEP Needs Some Pep!

Addressing PEP Neglect in HIV Prevention Research, Programming and Uptake

Register: tinyurl.com/pepneedspep
Agenda

- Dr. Connie Celum, UW
- Rodney Perkins, UW
- Dr. Jenelle Stewart, UM/HHRI
- Dr. Victor Omollo, KEMRI
- Jennifer Mahn, NCSD
Doxycycline post-exposure prophylaxis for prevention of STIs among MSM and TGW who are living with HIV or on PrEP

Results from the DoxyPEP study

Connie Celum, MD, MPH
Annie Luetkemeyer, MD
Co-Principal Investigators

DOXYPEP
Disclosures

• Doxycycline provided by Mayne Pharmaceuticals
• Laboratory support from Cepheid & Hologic
US is Experiencing Steep, Sustained Increases in Sexually Transmitted Infections

1.6 million CASES OF CHLAMYDIA
1.2% decrease since 2016

677,769 CASES OF GONORRHEA
45% increase since 2016

133,945 CASES OF SYPHILIS
52% increase since 2016

2,148 CASES OF SYPHILIS AMONG NEWBORNS
235% increase since 2016

THE STATE OF STDs IN THE UNITED STATES, 2020

STDs remain far too high, even in the face of a pandemic.

Note: These data reflect the effect of COVID-19 on STD surveillance trends.
The global epidemic of STIs disproportionately impacts men who have sex with men (MSM)

San Francisco DPH
STI surveillance data 2018

CDC 2020 STI surveillance
The oral antibiotic doxycycline has shown promise to reduce new sexually transmitted infections when taken after sex (post exposure prophylaxis or “PEP”).

Study was done to understand if taking doxy-PEP after sex would decrease the 3 most common bacterial STIs AND to understand the impact of intermittent doxy use on antibiotic resistance in STIs and other bacteria.

*Why Doxycycline?* It is generally safe, well tolerated, and inexpensive. It is active against chlamydia & syphilis. Some gonorrhea have resistance and it is unknown how much activity is needed for PEP.
**Intervention:** *Open label* doxycycline 200mg taken as PEP within 72 hours after condomless sexual contact  
*Maximum of 200 mg every 24 hours*

**Inclusion criteria:**
- Male sex at birth
- Living with HIV or on PrEP
- ≥ 1 STI in past 12 months
- Condomless sex with ≥ 1 male partner in past 12 months

**STI Testing:** Quarterly 3 site GC/CT testing + RPR, GC culture before treatment

**Sites:** San Francisco & Seattle HIV & STI clinics

**2:1 randomization**

**MSM & TGW living with HIV**  
(Planned n = 390)

<table>
<thead>
<tr>
<th>Month</th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxy PEP</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No PEP</td>
<td></td>
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</tbody>
</table>

**STI testing**

**MSM & TGW on HIV PrEP**  
(Planned n = 390)

<table>
<thead>
<tr>
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<th>3</th>
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<th>9</th>
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**STI testing**
**Doxy PEP – How to Take**

One pill of doxycycline ideally within 24 hours but no later than 72 hours after condomless sex

Example: Sex on Sat; take dose of doxy by Tues

Example: Sex on Thursday; take dose of doxy by Sunday

Example 2: Daily (or more) sex Sat-Tues; take daily dose of doxy and last dose within 24 hours but not later than 72 hours after last sex

No more than one pill (200 mg) every 24 hours
Primary endpoint and stopping rules

• **1º Endpoint**: At least one incident STI (GC/CT/syphilis) during a follow-up quarter
  - All STI endpoints adjudicated by blinded endpoint committee

• **Power**: 80% power to detect a decrease in quarterly STI prevalence from 10% to 5%, powered separately for PrEP & PLWH cohorts

• **Stopping rules**: only if both cohorts cross stopping boundary for proven effectiveness based on one-sided alpha of 0.025 for each cohort.

5/13/2022 Scheduled interim analysis: DSMB recommended stopping enrollment due to significant effectiveness in both cohorts
# Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>PrEP</th>
<th>Living with HIV</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong>* (ITT population)</td>
<td>327</td>
<td>174</td>
<td>501</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>36 (31 - 42)</td>
<td>43 (36 - 54)</td>
<td>38 (32 - 47)</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>210 (67%)</td>
<td>111 (66%)</td>
<td>321 (67%)</td>
</tr>
<tr>
<td>Black</td>
<td>14 (5%)</td>
<td>22 (13%)</td>
<td>36 (8%)</td>
</tr>
<tr>
<td>Asian/Pacific Islander</td>
<td>45 (14%)</td>
<td>8 (5%)</td>
<td>53 (11%)</td>
</tr>
<tr>
<td>Multiple races/other</td>
<td>44 (14%)</td>
<td>28 (17%)</td>
<td>72 (15%)</td>
</tr>
<tr>
<td><strong>Ethnicity: Hispanic/Latino</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>96 (29%)</td>
<td>55 (32%)</td>
<td>151 (30%)</td>
</tr>
<tr>
<td>Black</td>
<td>14 (5%)</td>
<td>22 (13%)</td>
<td>36 (8%)</td>
</tr>
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<td>Multiple races/other</td>
<td>44 (14%)</td>
<td>28 (17%)</td>
<td>72 (15%)</td>
</tr>
<tr>
<td><strong>Gender identity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Man</td>
<td>319 (98%)</td>
<td>163 (94%)</td>
<td>482 (96%)</td>
</tr>
<tr>
<td>Trans woman/gender diverse</td>
<td>8 (2%)</td>
<td>11 (6%)</td>
<td>19 (4%)</td>
</tr>
<tr>
<td><strong>Gender of sexual partners: Male only</strong></td>
<td>281 (86%)</td>
<td>153 (88%)</td>
<td>434 (87%)</td>
</tr>
<tr>
<td><strong>STI in past 12 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>233 (71%)</td>
<td>110 (63%)</td>
<td>343 (69%)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>207 (63%)</td>
<td>85 (49%)</td>
<td>292 (58%)</td>
</tr>
<tr>
<td>Syphilis†</td>
<td>48 (15%)</td>
<td>52 (30%)</td>
<td>100 (20%)</td>
</tr>
<tr>
<td><strong>Sexual partners in past 3 months</strong></td>
<td>9 (4 - 17)</td>
<td>8.5 (3 - 20)</td>
<td>9 (4 - 17)</td>
</tr>
<tr>
<td><strong>Substance use in past 3 months</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stimulants (methamphetamine, cocaine, crack)</td>
<td>178 (55%)</td>
<td>115 (68%)</td>
<td>293 (59%)</td>
</tr>
<tr>
<td>Ecstasy, GHB, ketamine</td>
<td>97 (30%)</td>
<td>60 (35%)</td>
<td>157 (32%)</td>
</tr>
<tr>
<td>Amyl Nitrates (poppers)</td>
<td>140 (43%)</td>
<td>84 (49%)</td>
<td>224 (45%)</td>
</tr>
</tbody>
</table>

* As of 5/13/22 with at least one follow-up visit  **Total may exceed 100% as more than 1 STI possible, †Syphilis: Limited to 1°, 2°, early Latent
Primary Endpoint: STI incidence per quarter

<table>
<thead>
<tr>
<th></th>
<th>PrEP cohort</th>
<th>PLWH cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>STI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea only</td>
<td>31.9% (82/257)</td>
<td>30.5% (39/129)</td>
</tr>
<tr>
<td>Chlamydia only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;=2 STIs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Percent of quarterly visits with an STI:

- Doxycycline PEP: 10.7% (61/570)
- Standard of care: 11.8% (36/305)

Risk reduction in STI incidence/quarter (95% CI):

- PrEP: 66% (54% - 76%)
- Living with HIV: 62% (40% - 76%)
- Total: 65% (54% - 73%)

*All p < 0.0001*
Doxy-PEP reduced EACH individual STI in both arms

Risk reduction in each STI per quarter

<table>
<thead>
<tr>
<th>Anatomic site</th>
<th>PrEP cohort</th>
<th>PLWH cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea</td>
<td>52/257 (20.2%)</td>
<td>26/128 (20.3%)</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>31/257 (12.1%)</td>
<td>19/128 (14.8%)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>7/257 (2.7%)</td>
<td>3/128 (2.3%)</td>
</tr>
</tbody>
</table>

**Risk reduction in each STI per quarter**

<table>
<thead>
<tr>
<th>STI</th>
<th>PrEP</th>
<th>PLWH</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC</td>
<td>55% (35%-68%)</td>
<td>57% (29%-74%)</td>
</tr>
<tr>
<td></td>
<td><em>p&lt;0.0001</em></td>
<td><em>p=0.001</em></td>
</tr>
<tr>
<td>CT</td>
<td>88% (75%-95%)</td>
<td>74% (43%-88%)</td>
</tr>
<tr>
<td></td>
<td><em>p&lt;0.0001</em></td>
<td><em>p=0.0007</em></td>
</tr>
<tr>
<td>Syphilis</td>
<td>87% (41%-97%)</td>
<td>77% (-71%, 96%)</td>
</tr>
<tr>
<td></td>
<td><em>p=0.0084</em></td>
<td><em>p=0.095</em></td>
</tr>
</tbody>
</table>
Lack of ‘risk compensation’ & High Adherence

**Sexual behavior:** At enrollment, median of 9 sexual partners (IQR 4,17) with 5 sexual acts per month (IQR 1.7, 10.7) and 90.1% of sex as condomless.

**Risk Compensation:** On study, no significant change in:
- # of sex partners during follow-up in doxy-PEP arm
- # of condomless anal, vaginal, and frontal sex and oral sex acts in doxy-PEP arm
- Differences in # of partners or # of condomless sex acts between doxy-PEP and standard of care arm

**Adherence:**
- 86% reported doxy-PEP always/often after anal/vaginal sex
- Median doxyPEP doses: 4.0 per month (IQR 1.0- 10.0), 25% with ≥10 doses/month, based on quarterly interview
Doxy PEP was safe, tolerable & highly acceptable

- **AEs attributed to doxycycline PEP:**
  - No grade 3+ adverse events, grade 2+ lab abnormalities, or SAEs

- **Tolerability**
  - 1.5% discontinued due to intolerance or participant preference

- **Acceptability:**
  - 88% reported doxycycline PEP was acceptable/very acceptable
Gonococcal Tetracycline (TCN) culture-based susceptibility

- Conducted through CDC SURRG & ARLN programs
- ~17% of baseline GC diagnoses and on-study GC endpoints have culture-based resistance data available
- Tetracycline susceptibility by ARLN agar dilution method (> 2 highly resistant) \(^1\)
- Baseline: ≈ 25% with TCN resistance, consistent with US GISP GC TCN resistance data \(^2\)
- Population level GC TCN resistance: 20% in US < 56% in France during IPERGAY \(^3\)

\(^1\) https://www.cdc.gov/std/gonorrhea/arg/carb.htm
\(^2\) CDC STD Surveillance Report 2020, \(^3\) LaRuche et al Eurosurveillance 2014;19(34)
What we know

• DoxyPEP works very well to prevent STI’s in this study population: ↓by more than 60% each quarter
• ↓ in each bacterial STI per quarter, including gonorrhea
• Need to treat about 5 people to prevent a quarter with an STI, in a population with a high STI incidence (30% per quarter)
• Generally safe & well tolerated

What we don’t know yet

• Efficacy & risk/benefit ratio in cis-women & men who have sex with women
• Impact on bystander bacteria like Staph aureus and on gut
• Impact on doxy-susceptibility for Chlamydia, Gonorrhea, Syphilis and Mycoplasma genitalium

Figure courtesy Stephanie Cohen
Current State of Implementation

- Current CDC STI Treatment Guidelines do not include a recommendation for or against Doxy PEP

- CDPH working on guidance

- Some clinicians prescribing, mostly on a case-by-case basis

- Community interest high

Note added to CDC STI Treatment Guidelines in July 2022

Doxy-PEP as an STI Prevention Strategy: Considerations for Individuals and Healthcare Providers of Gay or Bisexual Men or Transgender Women

As CDC and others work quickly to evaluate data to inform clinical guidance on the safe and effective use of doxycycline post-exposure prophylaxis (doxy-PEP) to prevent gonorrhea, chlamydia, and syphilis, we acknowledge there are individuals and clinicians who are already engaged in the off-label use of doxycycline as bacterial STI post-exposure prophylaxis or considering it. As such, we are providing the following considerations to inform those decisions:

- Current efficacy data only applies to gay and bisexual men and transgender women. Studies among heterosexual cis-gender women are ongoing.
- Doxycycline 200 mg administered within 24-72 hours of condomless sex was the regimen evaluated in this study. Other antibiotics should not be considered for PEP.
- In addition to informing patients about the potential STI prevention benefits of doxy-PEP, providers should also counsel patients about potential adverse side effects of doxycycline including phototoxicity, gastrointestinal symptoms, and more rarely esophageal ulceration.
- Providers should continue to screen, test, and treat for bacterial STIs in accordance with CDC's STI Treatment Guidelines and CDC's PrEP for the Prevention of HIV guidelines, even among people who may be using doxycycline as PEP or PrEP.

Snapshot from: https://www.cdc.gov/std/treatment-guidelines/clinical-primary.htm#CautionsForDoxyPEP
Next steps

• Control arm has been offered doxyPEP, which will provide data on incident STIs, antimicrobial resistance, and sexual behavior after initiating doxyPEP in context of known efficacy

• Evaluation of impact on antibiotic resistance is underway: *S. aureus*, commensal *Neisseria*, gut microbiome

• Additional studies of doxycycline for STI prevention are underway
  • dPEP study among Kenyan AGYW on HIV PrEP
  • DoxyVacc factorial design: DoxyPEP +/- Bexsero vaccine among MSM in France
  • DISCO study of DoxyPEP vs Doxy PrEP among MSM in Canada
  • Syphiliaxis study in Australia: observational cohort of DoxyPEP/PrEP in MSM & TGW

• Stakeholder discussions and normative guidance

• Larger studies and ongoing surveillance needed in doxycycline PEP users to assess impact on TCN resistance development in GC
DOXYPEP
Acknowledgments

With profound thanks to our study participants for their time & commitment

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Oliver Bacon
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The San Francisco & Seattle Departments of Public Health

With profound thanks to our study participants for their time & commitment
Community Perspectives on *DoxyPEP* Use Among Men Who Have Sex with Men (MSM) and Transgender Women (TW) in San Francisco and Seattle

Rodney Perkins, MPH, MSN, RN
PhD Candidate, Nursing Science
Fellow, Research in Nursing and Global Health (RINGH)
University of Washington
Disclosures

• None
Research Questions

• **Main Study**
  - Attitudes towards *doxyPEP* and the clinical trial
  - Sexual and STI prevention history and attitudes about STIs
  - Attitudes about ART/PrEP and HIV status disclosure
  - Experience taking *doxyPEP*, including adherence, side effects, sexual behavior
  - Beliefs about *doxyPEP*, efficacy, when needed, concerns
  - Partner and peer attitudes about *doxyPEP*

• **Sub-Study**
  - Relationship between *doxyPEP* use and sexual satisfaction
  - Meaning of sexual pleasure/intimacy
  - Healthcare provider perspectives and willingness to prescribe
Community Perspectives on DoxyPEP

• What are the motivations for *doxyPEP* and the study?
  • Reduce own STI incidence
  • Perceived STI risk, most perceived as very high-risk
  • Protect others, altruism

• Was a lot of community education needed, or were participants already aware of *doxyPEP*?
  • DoxyPEP trial provided instructions on the side effects and guidance on the 72-hour regimen
  • Some participants had heard of the use of *doxyPEP*, especially overtime
  • Some confusion regarding when *doxyPEP* was needed, timing use after oral sex or kissing
Community Perspectives on DoxyPEP

- What were the concerns participants had regarding the study?
  - Several were concerned about antibiotic resistance
  - Some expressed concern over unforeseen harm
  - Some concerns regarding the long-term effects of continued use

- Any pushback?
  - Experience with the study was uniformly positive
Community Perspectives on DoxyPEP

• Any sex shaming – as we have seen with HIV PrEP and MPV?
  • Partner and peer attitudes were positive
  • *doxyPEP* is trending on hook-up site profiles, sparked conversation and interest
  • Social media chat groups – ‘popping doxy’
  • Articles on ‘*doxyPEP* holiday’

Community Perspectives on DoxyPEP

• How would you characterize community interest/community demand for *doxyPEP*?
  • For some, increased frequency of sex, # of partners and types of sex
  • Greatly *reduced anxiety* over STI transmission
  • For some, *increased communication* with partners about sexual needs, boundaries and STI prevention
  • Pre-trial, STI transmission broadly was addressed by ‘test & treat’ rather than condoms
Community Perspectives on DoxyPEP

- How would you characterize community interest/community demand for *doxyPEP*? cont.
  - DoxyPEP is well-tolerated and perceived as *highly effective*
  - Easily adhered to
  - Nearly all participants reported interest in continuing
  - Nearly all participants reported being comfortable talking with their provider about *doxyPEP*
Community Perspectives on DoxyPEP

• Acceptance from the medical community and insurance coverage?
  • Concerns are very similar to most questions presented for the Webinar
    • Antibiotic resistance
    • Inadequate treatment for syphilis
  • Conservatively optimistic, more data and guidance from CDC
  • Providers with patients on doxyPEP
  • Unable to confirm coverage, insurance versus pay out of pocket
Healthcare Providers Needed!

For a **60-minute interview** on doxycycline postexposure prophylaxis (doxyPEP) in-person or via zoom

We seek **physicians, nurse practitioners, physician assistants, and pharmacists** with pre-exposure prophylaxis (PrEP) prescribing expertise and experience treating patient with sexually transmitted infections (STIs) to understand their perspective and willingness to prescribe doxyPEP as an STI prevention method

Financial compensation is provided for participation
To learn more information, contact

Rodney Perkins, Ph.D. Candidate
doxypep@uw.edu
206 265 9153
DOXYPEP
Acknowledgments

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Zuckerberg San Francisco General Hospital and Trauma Center

HAL LAB

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Public Health
Seattle & King County

Population Health Division
San Francisco Department of Public Health

HAL LAB
Doxycycline for STI prevention for Cisgender Women

Victor Omollo, MBChB, MPH, Kenya Medical Research Institute
Jenell Stewart, DO, MPH, Hennepin Healthcare, University of Minnesota
Acknowledgements

The dPEP Kenya Trial study participants and staff

**MPI:** Elizabeth Bukusi and Jared M Baeten, **Co-Investigators and key personnel:** Josephine B Odoyo, Kevin Oware, Caitlin Scoville, Lauren R Violette, Olusegun Soge, Scott McClelland, Jane Simoni, Zachary Kwena, and Ruanne Barnabas.

The Director General of the Kenya Medical Research Institute and the Directors of the Center for Microbiology & Center for Clinical Research for administrative support

**Funding:** US National Institutes of Health (grants R01AI145971, P30AI027757, K23MH124466)
Incident cases of four curable STIs among adults
Proportions of new HIV infections by age group

• 42% incident HIV infections among adolescent and young people aged 15-24
• Adolescent girls and young women disproportionately affected
• Priority population for PrEP by Kenya NASCOP
Unprecedented rates of curable STIs among women

<table>
<thead>
<tr>
<th>Study</th>
<th><em>Chlamydia trachomatis</em></th>
<th><em>Neisseria gonorrhoeae</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>MTN-020/ASPIRE (Dapivirine ring trial) South Africa, Zimbabwe, Zambia, Malawi, and Uganda</td>
<td>Prevalence = 12% Incidence = 27% per year</td>
<td>Prevalence = 4% Incidence = 11% per year</td>
</tr>
<tr>
<td>HPTN 082 (PrEP demonstration project) South Africa and Zimbabwe</td>
<td>Prevalence = 29% Incidence = 33% per year</td>
<td>Prevalence = 8% Incidence = 14% per year</td>
</tr>
<tr>
<td>POWER (PrEP implementation project) Kenya and South Africa</td>
<td>Prevalence = 26% Incidence = 53% per year</td>
<td>Prevalence = 10% Incidence = 20% per year</td>
</tr>
</tbody>
</table>

High STI rates among young African women in three PrEP cohorts
# Evidence for Doxycycline PEP

## Completed studies on Doxycycline STI prophylaxis

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bolan (Open-label RCT)</td>
<td>30 MSM living with HIV infection; 2 or more treated syphilis diagnoses since HIV diagnosis in USA</td>
<td>Daily doxycycline hyclate, 100 mg tablet</td>
<td>0.27 (0.09–0.83)</td>
</tr>
<tr>
<td>ANRS IPERGAY Doxy study (Open-label RCT)</td>
<td>232 MSM and transgender women without HIV on HIV PrEP having condomless sex with men in France</td>
<td>Doxycycline hyclate, 200 mg tablet, single dose within 72 hours post–condomless sex; maximum 3/week</td>
<td>0.57 (0.13–0.62)</td>
</tr>
<tr>
<td>DoxyPEP (Open-label RCT)</td>
<td>780 people with male sex at birth (on HIV PrEP and living with HIV) in USA</td>
<td>Doxycycline hyclate, 200 mg tablet, single dose within 72 hours after condomless sex</td>
<td>0.65 (0.54-0.73)</td>
</tr>
</tbody>
</table>
# Ongoing doxycycline prophylaxis studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Location</th>
<th>Population</th>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combo-PEP</td>
<td>Atlanta, Georgia US</td>
<td>20 Adult (M/F)</td>
<td>Vaginal, Rectal and Plasma doxycycline concentration</td>
</tr>
<tr>
<td>ANRS 174 Doxyvac</td>
<td>Paris, France</td>
<td>720 MSM</td>
<td>Incidence; culture and antimicrobial resistance</td>
</tr>
<tr>
<td>Syphilaxis</td>
<td>New Wales, Sydney, Melbourne in Australia</td>
<td>125 MSM living with HIV and without HIV</td>
<td>Use, acceptability, incidence, microbiome, and resistance</td>
</tr>
<tr>
<td>dPEP Kenya</td>
<td>Kisumu, Kenya</td>
<td>449 cisgender women using HIV PrEP</td>
<td>Incidence of NG, CT, or syphilis, resistance, adherence effectiveness, microbiome, and costing</td>
</tr>
</tbody>
</table>
Potential benefits of dPEP for African women

<table>
<thead>
<tr>
<th>Benefit</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>High need</td>
<td>High burden of STIs and their consequences</td>
</tr>
<tr>
<td>Bypass unavailable diagnostics</td>
<td>Syndromic assessment is standard; etiologic testing is rarely done; dPEP could prevent STIs that would otherwise go undetected</td>
</tr>
<tr>
<td>Valued</td>
<td>Women report high value to quality STI services</td>
</tr>
<tr>
<td>Affordable</td>
<td>Doxycycline available in Africa, at a price that is affordable, even for women to self-pay</td>
</tr>
<tr>
<td>Woman-controlled</td>
<td>Women control their own STI prevention</td>
</tr>
</tbody>
</table>

Untreated STI can lead to pelvic inflammatory disease which can cause:
- Blocked fallopian tubes
- Inability to get pregnant
- Ectopic pregnancy
- Long-term pelvic/abdominal pain
Trial Design

• 1:1 open-label randomized trial of dPEP (200mg doxycycline hyclate) taken within 72 hours after sex

• N=446 cisgender women taking HIV PrEP, aged 18-30

• Quarterly follow-up with Xpert STI testing and treatment for 12 months in Kisumu, Kenya
Primary Outcomes

**Aim 1**

**Efficacy of dPEP on STI prevention**

**Endpoint**
- Primary endpoint = combined STI incidence
  - *C. trachomatis*
  - *N. gonorrhoeae*
  - *T. pallidum*

**Aim 2**

**Safety**

**Acceptability**

**Adherence**

**Resistance**

**Endpoint**
- Related Adverse Events
- Self-reported adherence, sexual behavior
- Hair drug levels
- Qualitative analysis of acceptability
- Incidence of molecular resistance in CT/NG

**Aim 3**

**Cost-effectiveness of dPEP**

**Endpoint**
- Cost per incident STI case and complications averted
Key Methods

STI Testing
- Same day results with Xpert machine testing
- Confirmation of treatment with ToC
- Blinded Endpoint Adjudication Committee

Resistance Testing
- Trend prevalence using molecular testing for *tetM* [and *tetC*] at baseline, quarterly, and ToC visits.

Additional Analyses
- Adherence-effectiveness analysis (using hair drug levels)
- Impact of dPEP on *Trichomonas* infections
- Impact of dPEP on *Mycoplasma genitalium*
- Impact on vaginal microbiome
The dPEP Kenya: Enrollment Characteristics

- Enrolled: 449 cisgender women on HIV PrEP
- Age: median (IQR) of 24 years (21-27)
- Marital status: 66% never married
- Number of children: 69% have delivered one child or more
- Contraception: 57% using LARC

- Condom use: 32% use at last sex
- Transactional sex: 37% in prior 3 months
- STIs: 17.9% prevalence of any treatable STI
dPEP for Cisgender Women: Challenges and Opportunities

Challenges
- Sexual health stigma
- No evidence that doxycycline is harmful in pregnancy but also not possible to exclude
- Lack of STI testing in majority of settings
- Implementation outside of research setting

Opportunities
- Increased emphasis on access to PrEP for cisgender women
- Growing interest in fertility protection among young women
- Address rising rates of congenital syphilis
- Low cost of dPEP
Thank you

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*Discrete pill carriers provided to dPEP trial participants*
Doxycycline for STI Prevention: Policy and Program Implications for Health Departments and Sexual Health Clinics

Jenny Mahn, MPA
Director, Clinical and Sexual Health
National Coalition of STD Directors
What do we know?

The major study is on doxycycline as PEP (not PrEP) and there is currently very limited data on doxy PrEP.

Current studies support doxy as PEP- including the "doxyPEP" study that was done in the US and just presented at IAS in July (publishing in process).

However, doxy PrEP is another potential tool to address STIs.
Implementation Considerations: Medication

- Resistance – will increased use of doxycycline lead to more antimicrobial resistance?

- Side effects – generally a very safe medication but there can be side effects (GI upset, photosensitivity, esophageal irritation, etc.,)
  - Could this impact adherence?
Who do we focus this intervention on?

- People who have had a bacterial STI in the past year?
- Lessons from MPV: restricting eligibility criteria based on sexual behavior could have significant implications for stigma/reluctance to disclose sexual behavior to providers
- How do we ensure health equity?
- Proactive offer is key for equity and distinguishes a public health approach from a personal care service

Source: Dr. Julie Dombrowski, MD, MPH, University of Washington, Public Health – Seattle & King County; 2022 STD Prevention Conference
How do we identify candidates?

- Sexual health clinics
- PrEP clinics (community-based, embedded, pharmacies, etc.,)
- HIV care clinics
- Partner Services
- EHR

Source: Dr. Julie Dombrowski, MD, MPH, University of Washington, Public Health – Seattle & King County; 2022 STD Prevention Conference
How do we let people know about it?

• Will people want to use it? Will they use it correctly?

• Need to develop culturally-reflective, consumer-facing messaging materials:
  • Rationale
  • Potential side effects
  • Research updates
  • STI testing recommendations

• Importance of staff training from front to back (fielding phone calls, website information, etc.,)
What will it take?

• Additional resources from programs (i.e., administrative capacity, updated standing orders/SOPs, clinical and pharmacy costs, etc.)

• Capacity building – provider/staff training, workflows, buy-in; importance of on-site champion

• Optimized EHR/data-capture system

• Dedicated staff/program manager/RN

• Doxy is relatively inexpensive (~ $.06 per each 100 mg pill under 340b and $.08/pill with GoodRx card but we don’t know about insurance coverage for doxy PrEP

• How should DIS interact with individuals on doxy PrEP?

• Important to consider existing capacity of sexual health clinics (COVID-19, MPV, vaccinations, staffing shortages etc.)
What about testing?

• Providers should continue to screen, test, and treat for bacterial STIs in accordance with CDC’s STI Treatment Guidelines and CDC’s PrEP for the Prevention of HIV guidelines, even among people who may be using doxycycline as PEP or PrEP

• Opportunity to utilize testing innovations such as non-clinic-based, self-collect STI testing
What’s the bottom line?

• We need more research on doxy PrEP, but it could potentially be a useful tool in addressing STIs

• Implementing a doxy PrEP program would require significant administrative infrastructure

• Sexual health clinics need additional resources → dedicated federal funding stream
Questions?

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