PROMOTING EQUITY IS ESSENTIAL TO EFFECTIVELY IMPLEMENT DOXYCYCLINE AS STI PEP

DOXYCYCLINE, A COMMONLY PRESCRIBED ANTIBIOTIC that has been in use for more than fifty years, recently has been shown to be useful in preventing the bacterial sexually transmitted infections (STIs) chlamydia, gonorrhea, and syphilis. This offers a new tool for preventing STIs when administered as post-exposure prophylaxis (PEP); that is, after sex, as part of a comprehensive sexual health intervention that also includes risk reduction counseling, STI screening and treatment, recommended vaccinations, and linkage to HIV pre-exposure prophylaxis (PrEP) and HIV PEP, HIV care, or other services. The Centers for Disease Control and Prevention (CDC) is considering public comments on draft guidelines for the use of doxycycline as STI PEP (hereafter doxy PEP) to guide prescribers, but additional policies and actions are needed for this intervention to be successfully implemented. The CDC draft guidelines recommend doxy PEP only for populations at elevated risk for these STIs, specifically gay, bisexual and other men who have sex with men (MSM) and transgender women with at least one bacterial STI in the last 12 months. These STIs are often asymptomatic and undetected in these populations, however, suggesting that a broader range of MSM and transgender women (and possibly other populations) could benefit from doxy PEP based on individual sexual behaviors.

THE U.S. HAS AN STI CRISIS

1 in 5 adults: The CDC estimates that at any given time, one in five U.S. adults has an STI.

Rapidly rising rates: Since 2000, the number of syphilis cases has increased more than five-and-a-half times (up 555%), chlamydia cases have nearly doubled (up 197%) and gonorrhea cases increased by half (up 51%).

MSM and transgender people heavily impacted: MSM make up 2-3% of the U.S. population yet accounted for 34% of primary and secondary syphilis cases in 2022 and roughly two-thirds of new HIV cases.

Significant Economic Impact: CDC estimates that STIs cost more than $16 billion per year in direct medical costs.

REDUCING STIs AMONG MSM AND TRANSGENDER WOMEN

How this new intervention is integrated into practice is critically important and calls for new approaches to prevention:

1. EMBRACE A SEXUAL HEALTH PARADIGM

The benefit of doxy PEP as an intervention to prevent STIs among MSM and transgender women is not only that is it a safe, widely available, and relatively inexpensive medication that is easy to use and distribute, but it is the first biomedical STI prevention tool that also is a necessary element of a comprehensive sexual health approach that has the potential to reduce the stigma and shame about sex that complicates STI prevention efforts.

POLICY ACTION: Center MSM and transgender women as the front-line educators, ambassadors, and implementers of doxy PEP

POLICY ACTION: Develop pro-active messaging for the general public to counter anti-LGBTQ+ messages and sexual shaming

POLICY ACTION: Standardize sexual health training during medical education and conduct detailing with clinical providers and clinics

2. FOCUS ON EQUITY

Time and again, when we have implemented interventions and assumed that all people could benefit, racial and ethnic minorities, lower-income people, and sexual and gender minorities have been left behind. CDC recently published estimates of HIV PrEP use in 2022 that show that while 94% of white people with an indication for PrEP were using it, only 24% of Latinx and 13% of Black people with an indication for PrEP were using it. AIDSVu analyzed these data and found that there were only 5 Black PrEP users for every Black HIV diagnosis and only 9 Latinx PrEP users for every Latinx HIV diagnosis, compared to 36 white PrEP users for every white HIV diagnosis. The success of doxy PEP may hinge on pro-actively countering these inequities from the beginning.

POLICY ACTION: CDC and other federal health agencies should fund and encourage their grantees to support and deliver doxy PEP implementation activities that focus on Black and Latinx MSM and transgender women

POLICY ACTION: HRSA should develop a strategy for implementing doxy PEP that leverages the resources of the Health Centers Program and Ryan White HIV/AIDS Program

POLICY ACTION: Non-governmental entities, including pharmaceutical manufacturers, foundations, and corporations should fund community efforts to educate and implement doxy PEP

IS DOXYCYCLINE SAFE AND EFFECTIVE?

CDC REVIEWED THREE RECENT STUDIES OF DOXYCYCLINE AS PEP FOR MSM AND TRANSGENDER WOMEN.

IPERGAY (open-label extension)

Results show a 70% reduction in chlamydia and syphilis and a non-statistically significant reduction in gonorrhea cases.

San Francisco/Seattle DoxyPEP

Results show more than a 70% reduction in chlamydia, more than a 75% reduction in early syphilis, and more than a 55% reduction in gonorrhea. Study stopped early due to effectiveness.

French ANRS DOXYVAC

Results showed nearly a 90% reduction in chlamydia, nearly an 80% reduction in syphilis, and a 50% reduction in gonorrhea. Study stopped early due to effectiveness.

WHAT HAS BEEN OBSERVED REGARDING DOXY PEP AND DRUG RESISTANCE?

Antimicrobial resistance is a serious issue that threatens the safety and effectiveness of a broad range of antibiotics and other therapeutics. This causes legitimate questions to be raised over whether the benefits of use of doxycycline outweigh the potential risks of resistance.

Annie Leutkemeyer, MD a co-principal investigator of the San Francisco/Seattle DoxyPEP study stated that, "this isn't a choice between antibiotics and no antibiotics in men and transgender women with a history of recurrent STIs. The alternative here for many is repeated STIs that lead to recurrent antibiotics. Doxy PEP may mitigate the amount of antibiotics used, including broader spectrum antibiotics like ceftriaxone, the use of which was reduced by 50% by those taking doxy PEP."

San Francisco/Seattle researchers found:

- More tetracycline resistant gonorrhea (30% vs 11%) in those taking doxy PEP than those not taking it, which suggests that doxy PEP may be less protective against strains of gonorrhea that already have tetracycline resistance.
- Doxy PEP reduced colonization by *Staphylococcus aureus* from 44% to 31%, but the cultures resistant to doxycycline went up from 5% to 13%, a small but statistically significant increase. There was no increase in methicillin-resistant *Staphylococcus aureus* (MRSA) overall or with doxycycline-resistant MRSA.
- *Neisseria* species found in the throat did not appear to be affected by doxy PEP use.

Limiting antimicrobial exposure is an important objective to prevent antibiotic resistance and must be carefully balanced with the potential benefits of doxy PEP. The high prevalence of STIs among MSM and transgender women influences the calculation of net benefit for these populations. The balance may be different for other populations with lower STI prevalence.

3. BRIDGE KNOWLEDGE GAPS

Available evidence suggests that doxy PEP is safe and effective at preventing STIs in MSM and transgender women when administered after sex, yet we have much to learn about how to maximize its public health impact.

POLICY ACTION: CDC and NIH should convene a cross-agency working group to fund priority studies to maximize the benefits of doxy PEP

DOXYCYCLINE AS PEP offers an important new tool to prevent STIs. Policymakers must prioritize the Black and Latinx communities that rarely receive sufficient culturally and linguistically congruent health services by partnering with individuals and organizations to deliver affirming messaging and sexual health services. While acknowledging uncertainty and carefully monitoring for the emergence of drug resistance, policymakers and health care providers must not allow unsubstantiated fears to negate the potential benefits of doxy PEP for MSM and transgender women.

CRITICAL QUESTIONS REQUIRE A COMPREHENSIVE RESEARCH AGENDA

It will be important to develop a prioritized research agenda that tackles critical questions, including:

1. **Is doxycycline viable as STI PrEP?**
2. **What are key elements of a doxycycline resistance monitoring plan?**
3. **Is long-term use of doxycycline safe and what is the impact on the microbiome?**
4. **What are optimal ways to use doxycycline to BOTH achieve public health impact and reduce the risk of resistance?**
5. **Is doxy PEP appropriate for other populations?**

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http://bit.ly/USHIVpolicyproject