

FROM DATA TO PRACTICE: MAXIMIZING THE IMPACT OF DOXYPEP THROUGH EQUITY-CENTERED IMPLEMENTATION

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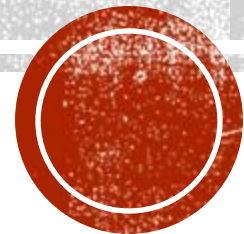
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AT THE FOREFRONT
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THE
STATE OF STIs
IN THE
UNITED STATES,
2022

**CDC's 2022 STI Surveillance
Report underscores that STIs
must be a public health
priority**



1.6 million
CASES OF CHLAMYDIA
6.2% decrease since 2018



648,056
CASES OF GONORRHEA
11% increase since 2018



207,255
CASES OF SYPHILIS
80% increase since 2018

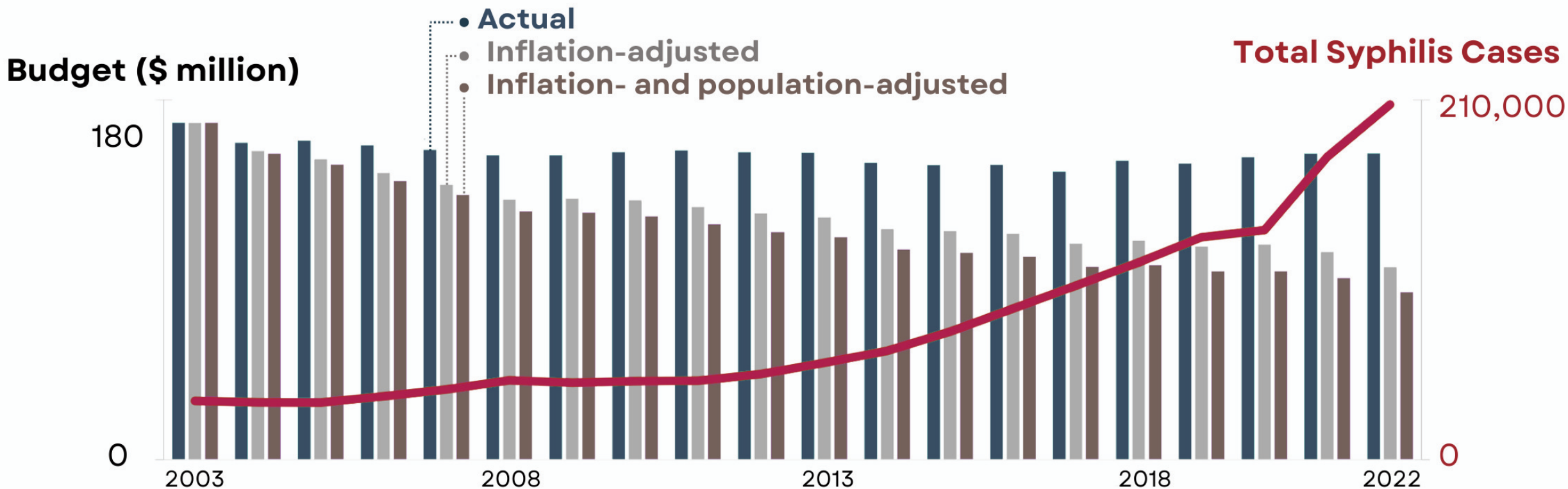


3,755
CASES OF SYPHILIS
AMONG NEWBORNS
183% increase since 2018

LEARN MORE AT: www.cdc.gov/std/

Annual CDC STD Prevention Budget, FY 2003–FY 2022 and Total Syphilis Cases

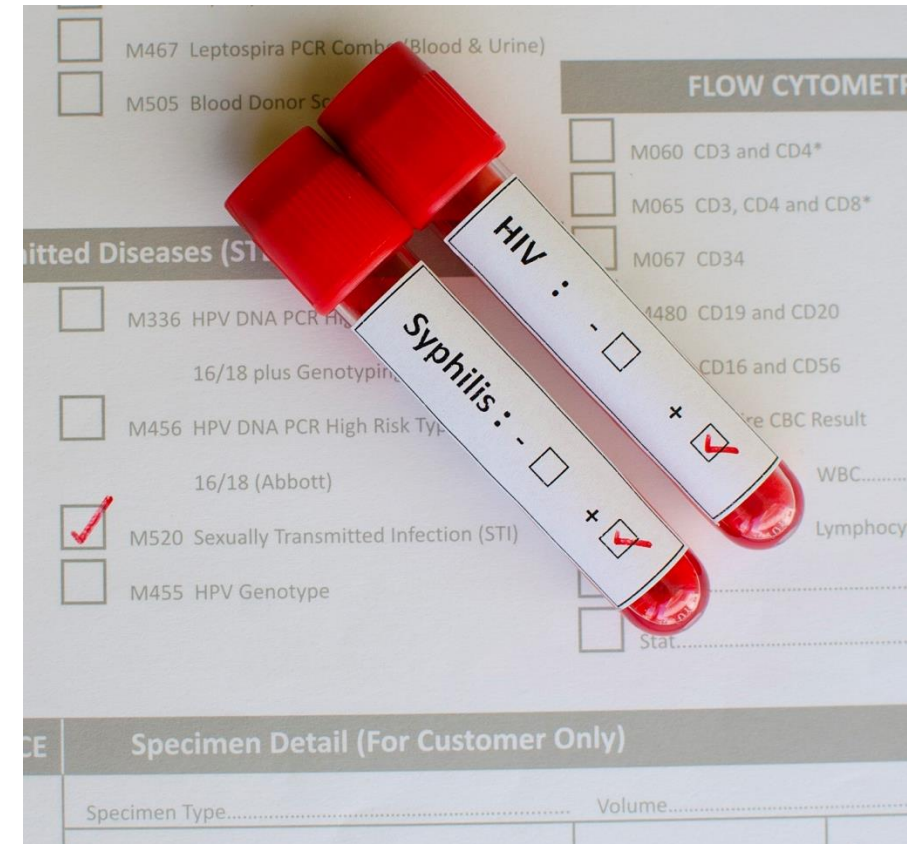
*50% drop in per-capita purchasing power since 2003**



*Inflation adjustment is to 2003 dollars. Funding years for the bars are USG fiscal years. Inflation adjustment used the “all items” component of the consumer price index (CPI). Population adjustment for a given year was calculated by dividing national population in 2003 by national population in the given year.

SYPHILIS AND HIV

- Syphilis thought to facilitate HIV acquisition and transmission
 - HIV can be found on syphilitic lesions
 - Syphilis infection cause transient increase of HIV VL
- Epidemiological link between syphilis and HIV
 - High rates of HIV co-infection, particularly among MSM and TWSM
 - One study found median time to HIV diagnosis to be 1.6 years
- Increased morbidity in PWLH
 - Early neurosyphilis and ocular syphilis
 - Higher rates of treatment failure



Zetola NM, Klausner JD. Syphilis and HIV infection: an update. Clin Infect Dis. 2007 May 1;44(9):1222-8.

Pathela P et al. The high risk of an HIV diagnosis following a diagnosis of syphilis: a population-level analysis of New York City men. Clin Infect Dis. 2015 Jul 15;61(2):281-7.

A Vicious Cycle: STDs *predict* future HIV

Rectal GC
or CT



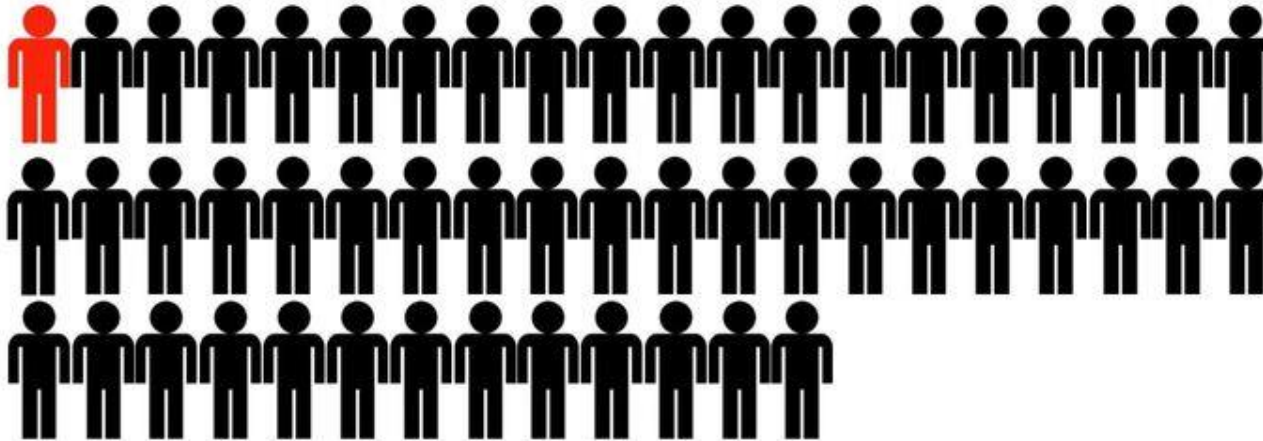
1 in 15 MSM were diagnosed with HIV within 1 year.*

Primary or
Secondary
Syphilis



1 in 18 MSM were diagnosed with HIV within 1 year.**

No rectal STD
or syphilis
infection

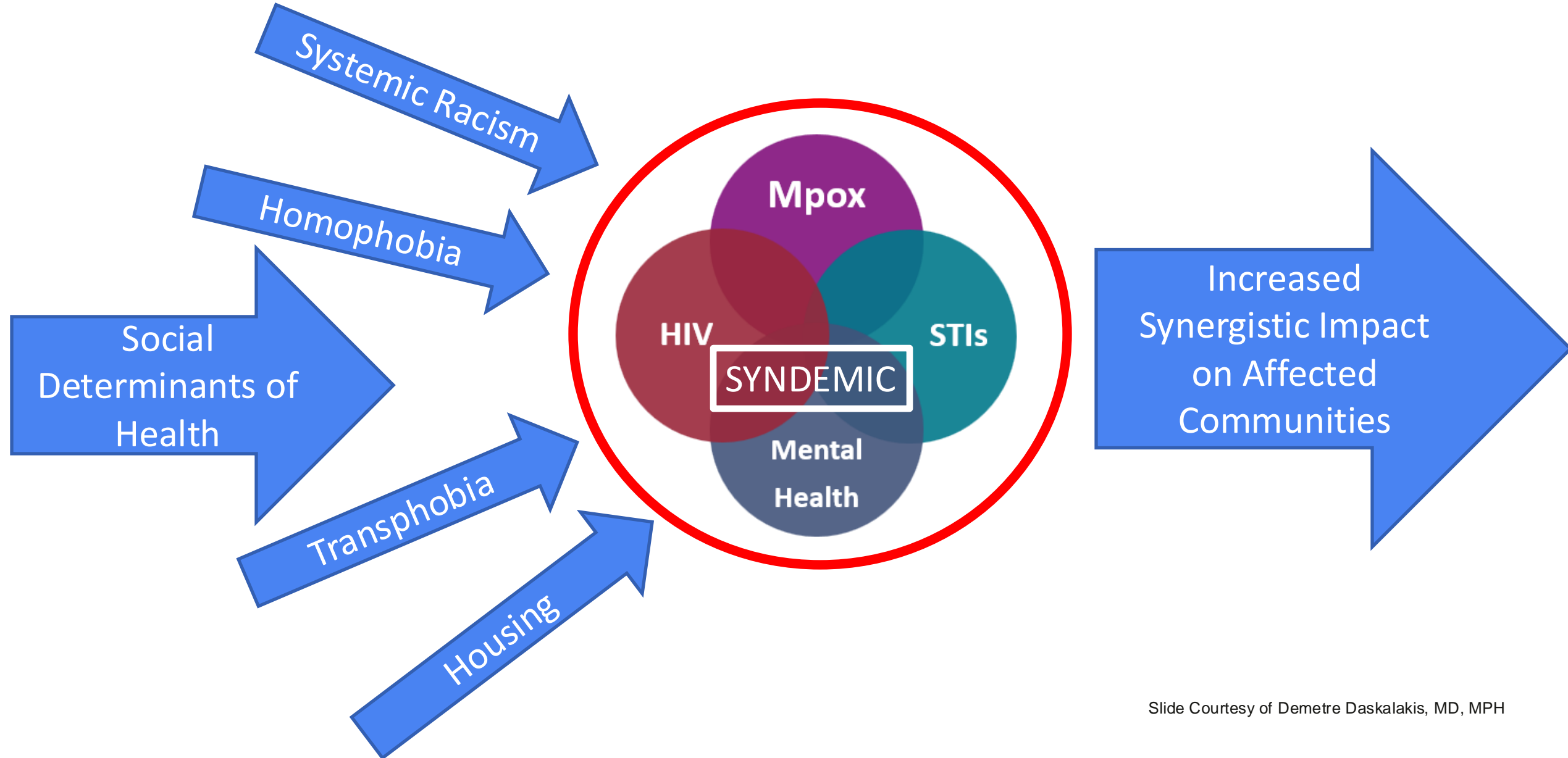


1 in 53 MSM were diagnosed with HIV within 1 year.*

*STD Clinic Patients, New York City. Pathela, CID 2013:57;

**Matched STD/HIV Surveillance Data, New York City. Pathela, CID 2015:61

Syndemic Problems Require Syndemic Solutions



DOXYCYCLINE

- Second-generation tetracycline antibiotic
- Widely available, inexpensive, and well-tolerated
- Broad spectrum of anti-microbial activity
- Used to treat multiple STIs
 - 1st line therapy for chlamydia trachomatis infections
 - Alternative therapy for P&S syphilis infections
 - No longer used to treat N.gonorrhoea due to tetracycline resistance
- **Teratogenic drug class**, contraindicated in pregnancy
 - Review by the Teratogen Information System (TERIS) concluded that therapeutic doses during pregnancy are unlikely to pose a substantial teratogenic risk
 - Data are insufficient to state that there is no risk



Study	Population (n)	DoxyPEP use	Primary Finding	Comments
IPERGAY Molina et al. Lancet ID 2018	HIV-neg MSM (n=232)	3.4 doses/mo (86% coverage)	47% reduction in 1 st CT or syphilis infection No difference in GC	homogenous study population
DoxyPEP Luetkemeyer et al. NEJM 2023	MSM/TWSM (HIV-neg n=327) (LWH n=174)	4 doses/mo (86% coverage)	66% reduction in 1 st STI GC, CT, and syphilis	<5% TWSM
DOXYVAC Molina et al. Lancet ID 2024	HIV-neg MSM (n=501)	3.5 doses/mo (83% coverage)	84% reduction in 1 st CT or syphilis infection 51% reduction in 1 st GC	homogenous study population
dPEP-KE Stewart et al. NEJM 2023	HIV-neg ciswomen (n=449)	? doses/mo (78% coverage)	No reduction in 1 st STI	4 social harms reported in doxyPEP group
SYPHILAXIS Haire et al. NCT03709459	HIV-neg MSM (enrolling)			
DISCO Grennan et al. NCT04762134	MSM (not yet enrolling)			

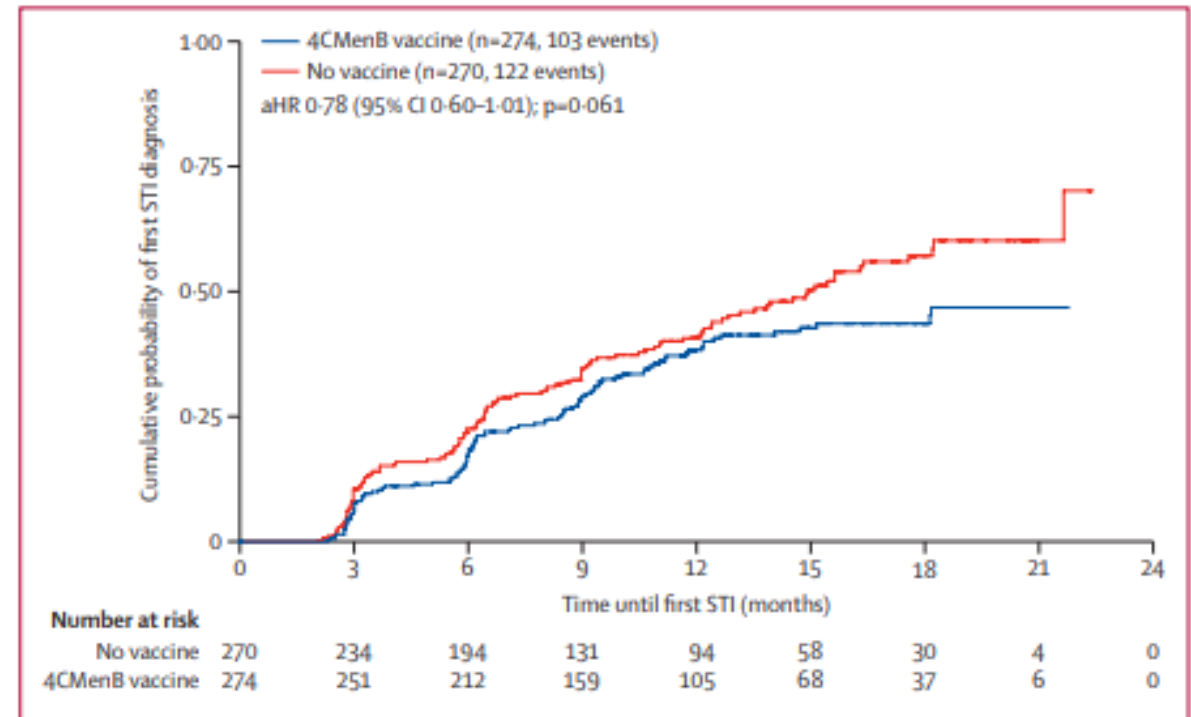
DOXYVAC RESULTS — MENB VACCINE

- Data for MenB vaccination to prevent GC was inconclusive
- Small benefit (~20-30%) possible
- Similar rates of cumulative as well as symptomatic infections
- Phase 3 trial of gonorrhoea specific vaccine ongoing

GSK



GSK receives US FDA Fast Track designation for investigational vaccine against gonorrhoea

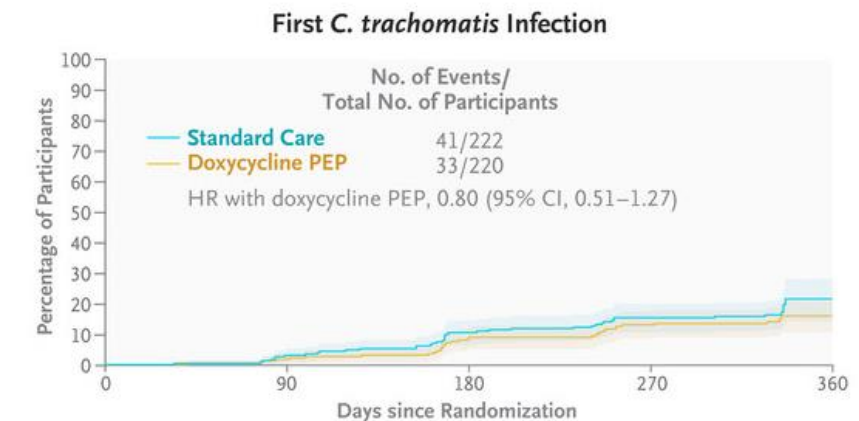
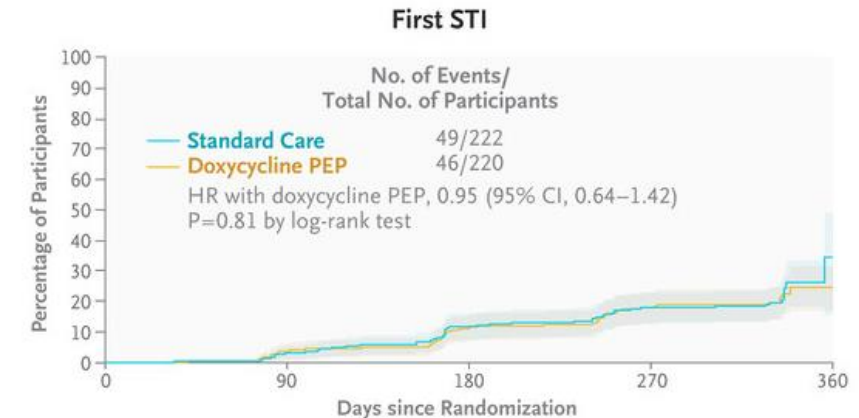
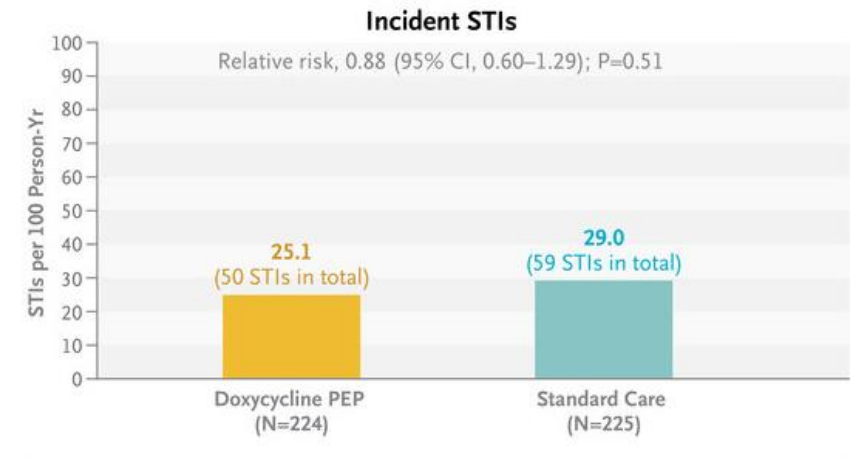


Molina JM, et al. Lancet Infect Dis. 2024 May 23:S1473-3099(24)00236-6

DPEP-KE

- 1:1 open-label randomized trial
 - Intervention: 200mg doxycycline within 72hrs of sex
 - SOC: quarterly STI screening and treatment
- Population (n=449) in Kimusu, Kenya
 - Average age 24
 - 70% never married
 - Average 2 partners in the past 3 months
 - 18% with STI at enrollment
 - Median of 4 doxyPEP doses/month
 - 80% sex acted covered with doxyPEP by self-report
- No difference in 1st STI or CT
 - Drug only detected in 56% of participants
 - 4 social harms reported in setting of unintentional disclosure of doxyPEP use

Stewart J, et al. N Engl J Med. 2023 Dec 21;389(25):2331-2340



GAUGING CURRENT INTEREST

- Survey of MSM and TWSM seen at STI Clinics in Toronto and Vancouver found:
 - 60.1% would be willing to use doxy PEP
 - 44.1% would be willing to use doxy PrEP
- Survey of Australian MSM found:
 - 52.7% would be very or slightly likely to use doxycycline to prevent syphilis
 - 75.8% felt very or slightly strongly that chemoprophylaxis would help reduce syphilis infections in their communities

Fusca L, Hull M, Ross P, et al. Exposure Prophylaxis Among Gay, Bisexual and Other Men Who Have Sex With Men in Vancouver and Toronto. *Sex Transm Dis*. 2020 Jan 17. Epub ahead of print

Wilson DP, Prestage GP, Gray RT, et al. Chemoprophylaxis is likely to be acceptable and could mitigate syphilis epidemics among populations of gay men. *Sex Transm Dis* 2011; 38:573–9

GAUGING CURRENT INTEREST & USE

- Large multi-city sample of individuals using a gay social networking app
 - 84% of participants expressed interest in trying doxy PEP
 - **African-American and Hispanic/Latinx respondents had higher interest in doxycycline-PEP than White respondents**
- Prevalence of doxycycline PEP/PrEP use in Seattle
 - **9.3% reported already using doxycycline prophylaxis**
 - Willingness to take doxycycline prophylaxis was more common among those with HIV (62%) or on PrEP (60%)

Spinelli MA, et al. High Interest in Doxycycline for Sexually Transmitted Infection Postexposure Prophylaxis in a Multicity Survey of Men Who Have Sex With Men Using a Social Networking Application. *Sex Transm Dis.* 2019;46(4):e32-e34.

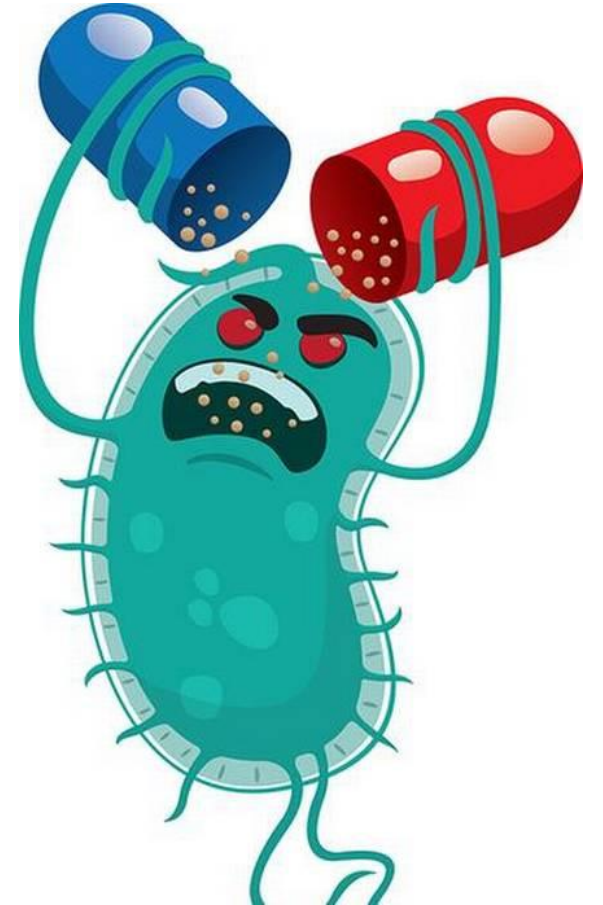
Dombrowski JC. Doxycycline Prophylaxis Use among Cisgender Men and Transgender Persons who have Sex with Men in Seattle. *CDC STD Prevention Conference 2020.*

TARGET POPULATION FOR DOXY PEP/PREP

- Large proportion of STIs occur among those with repeat infections
- In Massachusetts between 2014-2016
 - 0.2% of the general population acquired ≥ 1 repeat STI diagnoses
 - Accounted for 27.7% of all STIs during the same period
- “Core” disease transmitters disproportionately effected by STI morbidity
- Novel STI prevention efforts need to start with this population

CONCERN FOR ANTIMICROBIAL RESISTANCE

- Tetracycline resistance already seen in gonorrhea (higher in MSM)
- Chlamydia treatment failure seen in 5-23% of cases, however clear resistance to tetracycline not identified
- Mycoplasma genitalium (MG) emerging cause of NGU in MSM, seeing resistance to tetracycline
- No established standards for identifying or measuring doxycycline resistance in NG, CT, MG, or TP
- Concern for resistance of commensal flora (staphylococcus, streptococcus, etc)



OTHER RESISTANCE CONCERNS

- Widespread use of doxyPEP will select for tetracycline-resistant gonorrhoea
- Limited long-term benefit for extragenital GC
- DoxyPEP will **not** be our answer to reducing GC infections
- Theoretical risk of selective dual-resistance GC isolates (bacteria resistant to TCN as well as cephalosporin)

- **We must weigh these real AMR concerns with the significant reductions seen in syphilis and chlamydia infections**

SO WHERE DO WE GO FROM HERE?

Several questions/concerns remain:

- Long term safety and AE data needed
- Clearly identify target population
- Monitoring resistance to STIs as well as commensal flora
- Education efforts, distinguishing HIV PEP/PrEP from Doxy PEP

Urgency of ongoing STI burden on MSM and TWSM compels us to act now

DOXYPEP USE AT HBH

- Protocol implemented in 6/2021, initial uptake slow due to competing demands
- Initial focused on patients with recent history of syphilis, expanded to align with current CDPH and CDC guidelines
- As of 6/6/2024, **1482** patients initiated on doxyPEP
 - 1468 (99.1%) Assigned Male at Birth
 - 1329 (89.7%) Male-identified
 - 908 (61.3%) White
 - 987 (66.6%) Non-Hispanic
 - 273 (18.4%) living with HIV
- Currently reviewing system-wide STI positivity to assess for any changes



REAL WORLD DATA FROM SFDPH

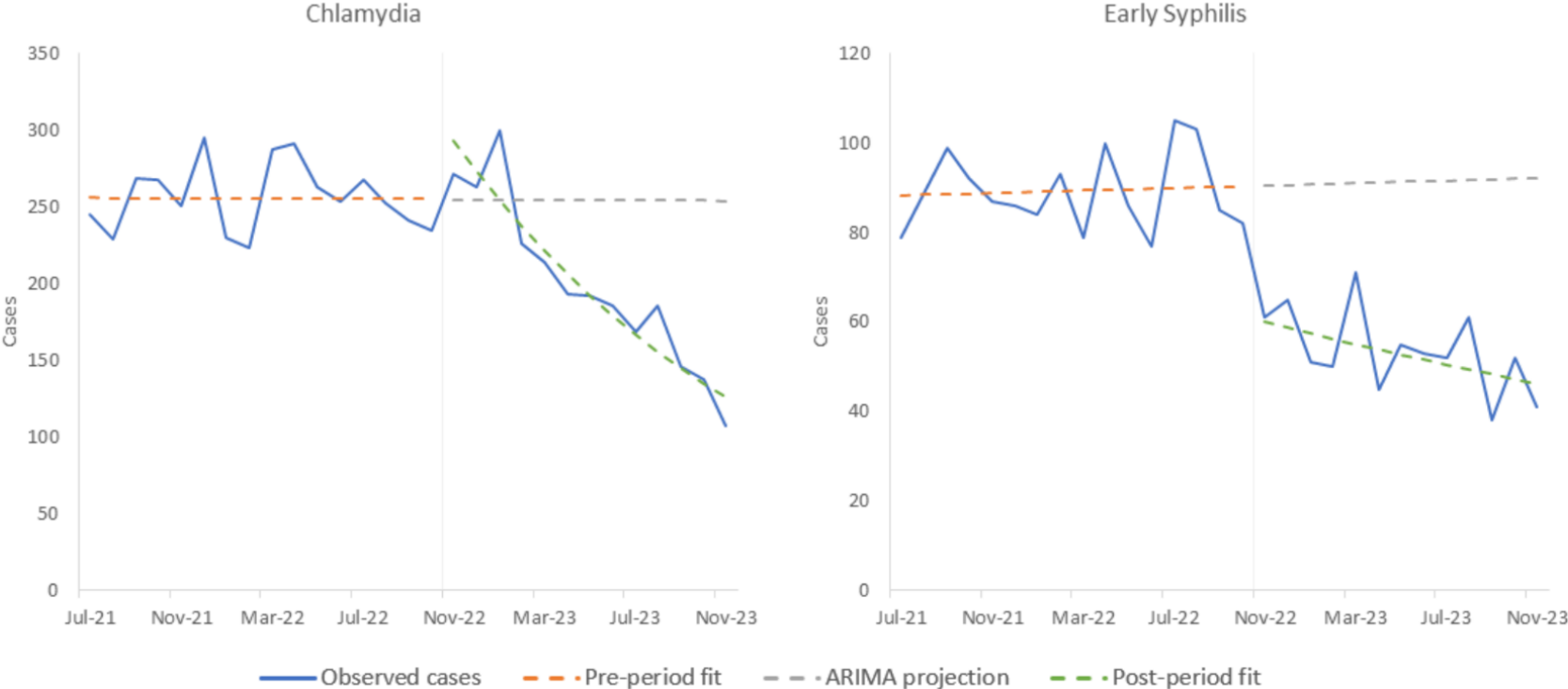


Figure. Observed and modelled chlamydia and early syphilis cases among MSM and TGW in San Francisco pre and post doxy-PEP implementation

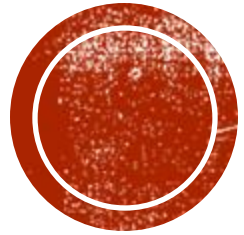
DÉJÀ-VU ALL OVER AGAIN?

Striking similarities between HIV PrEP and DoxyPEP

- Novel biomedical intervention w/significant impact in priority populations
- Concerns of anti-microbial resistance/misuse
- Equity concerns regarding utilization and uptake
- Data in cisgender women are lacking

So, what's different now?

- Signals of higher interest in Black and Hispanic/Latinx men
- **WE SHOULD KNOW AND DO BETTER**



QUESTIONS?



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