

CROI Update: Prevention

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Disclosures

I have conducted research with supplies donated by Hologic and Mayne Pharmaceuticals

Disclaimer

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Prevention



DOXY-PEP



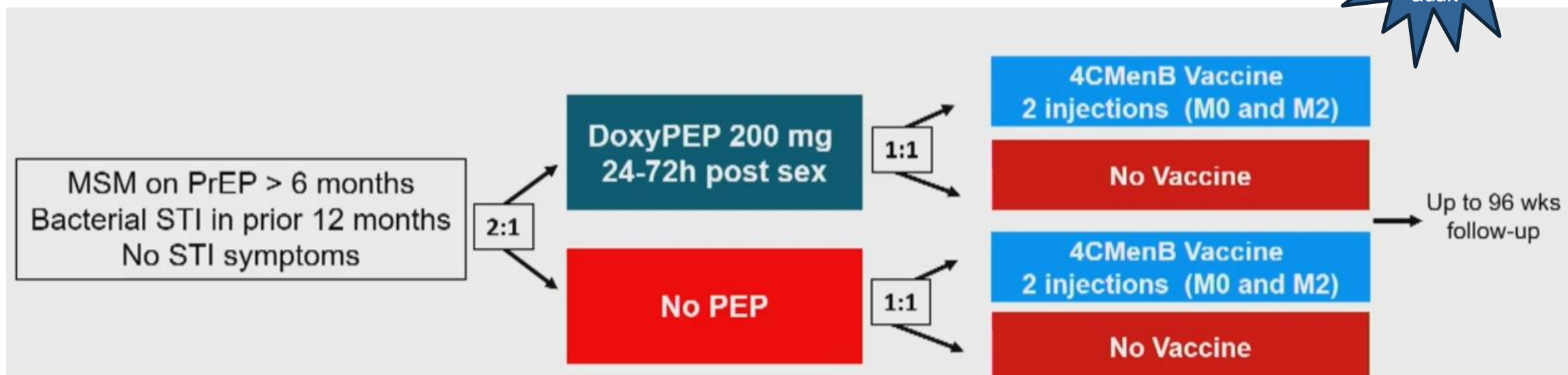
HIV PREP

Doxy-PEP: Clinical trial result updates, impact of use in clinical practice, & preliminary AMR data

Final Results of ANRS 174 DOXYVAC: A Randomized Trial to Prevent STI in MSM on PrEP

Molina, J-M G, et al. Abstract #124

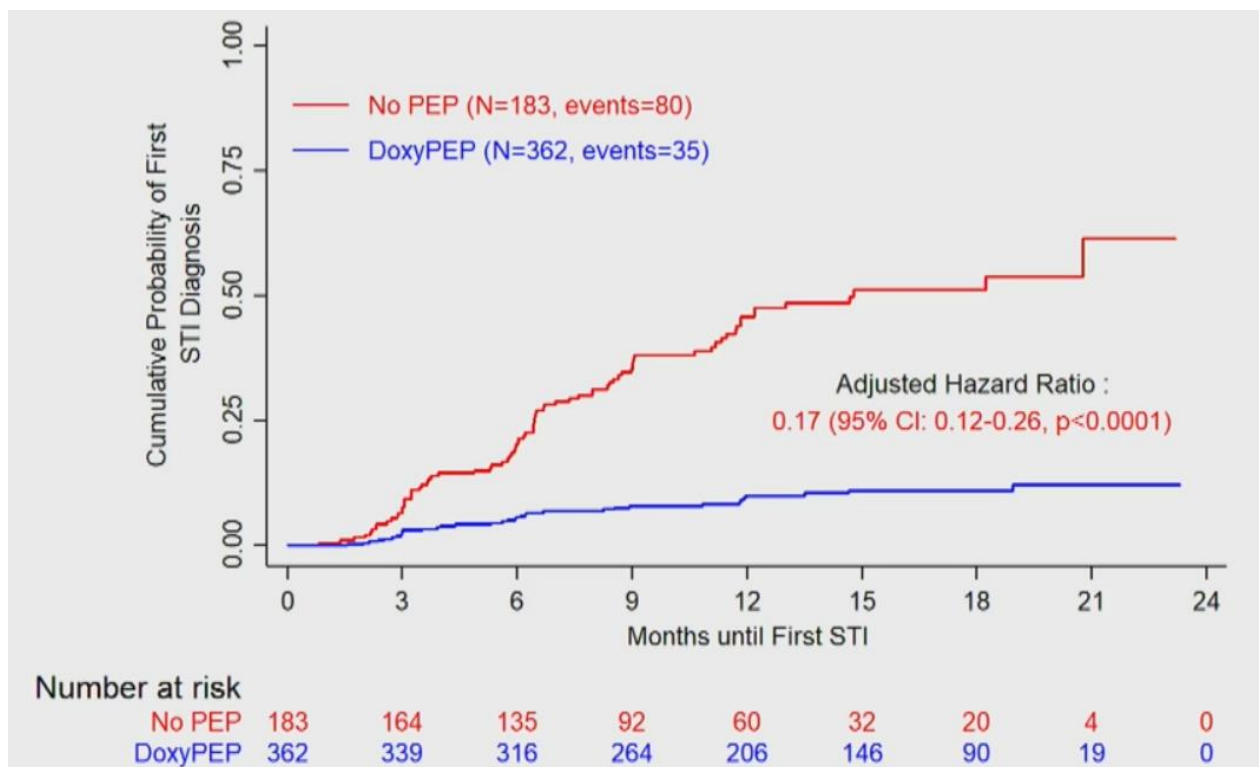
- Multicenter, 2 x 2 factorial randomized, open-label trial
- Primary efficacy endpoints:
 - Impact of Doxy-PEP on time to first episode of syphilis or chlamydia
 - **Impact of 4CMenB vaccine on time to first episode of gonorrhea**



Final Results of ANRS 174 DOXYVAC: A Randomized Trial to Prevent STI in MSM on PrEP

Molina, J-M G, et al. Abstract #124

Time to first episode of syphilis or chlamydia



Time to first GC

Intervention	Adjusted Hazard Ratio & p-value
Doxy-PEP	0.67 (95% CI: 0.52 – 0.87), p=0.003
4CMenB	0.78 (95% CI: 0.60 – 1.01), p=0.061

High-level TCN-resistant GC

- 12.5% no doxy-PEP (N=40)
- 35.5% doxy-PEP (N=31)
- P-value for difference: 0.043

Doxy-PEP Effectiveness in Men Who Have Sex with Men (MSM) and Transgender Women (TGW) on HIV PrEP

Bacon O, et al. Abstract #1151

- San Francisco City Clinic, Pre- (11/2021 – 11/2022) & Post- (11/2022 – 11/2023) Doxy-PEP implementation
- Compared STI test positivity among doxy-PEP users vs. non-users
- Analysis: difference in differences

Figure 1: Chlamydia Positivity

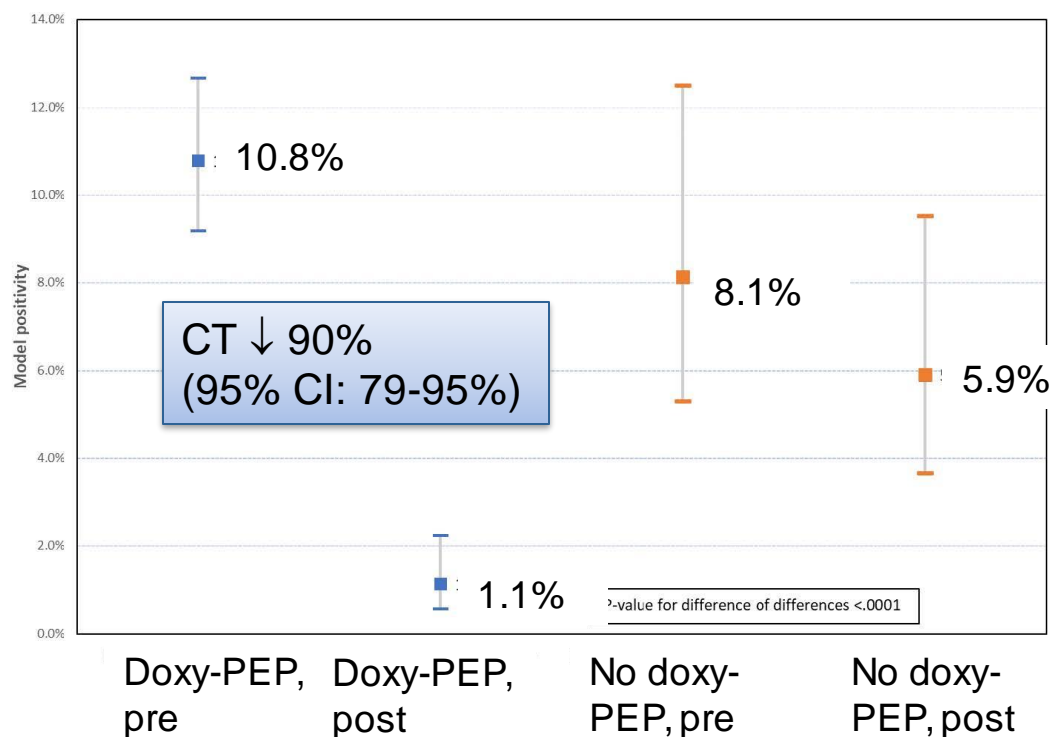
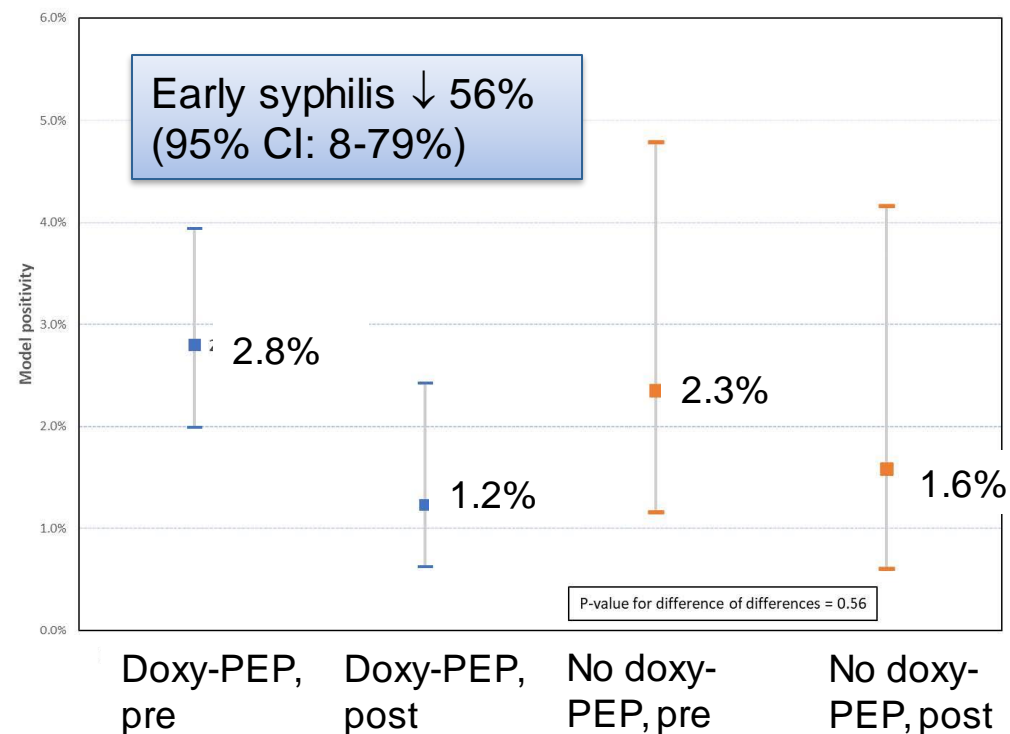


Figure 2: Early Syphilis Positivity

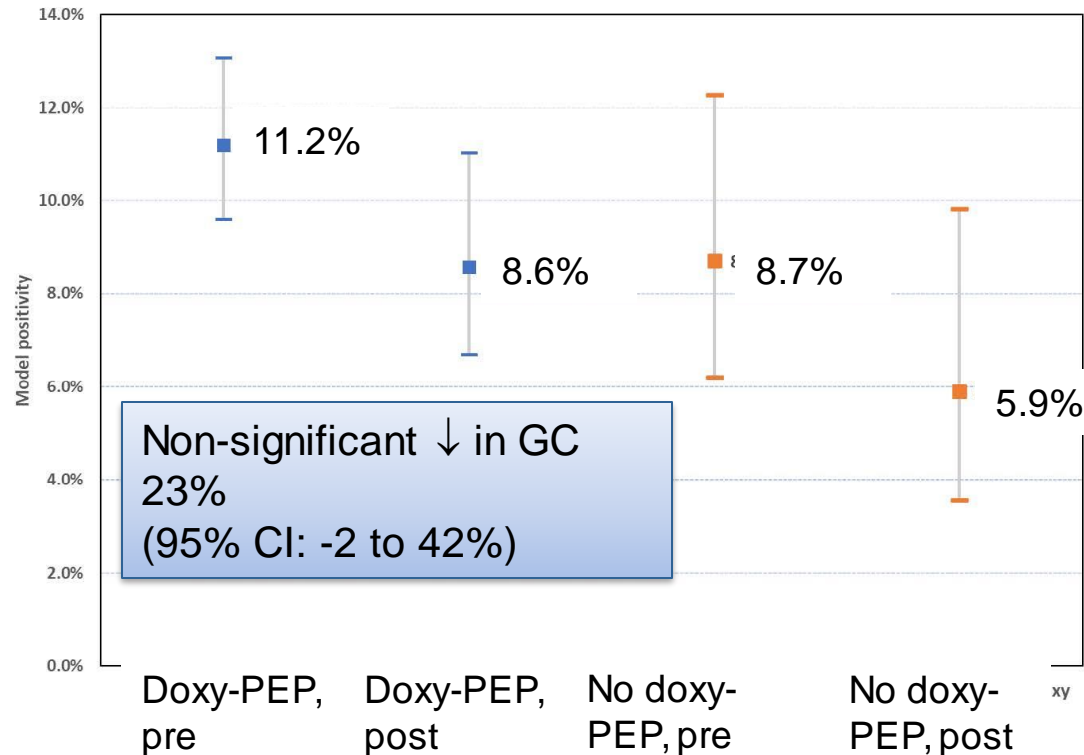


Doxy-PEP Effectiveness in Men Who Have Sex with Men (MSM) and Transgender Women (TGW) on HIV PrEP

Bacon O, et al. Abstract #126

- San Francisco City Clinic, Pre- (11/2021 – 11/2022) & Post- (11/2022 – 11/2023) Doxy-PEP implementation
- Compared STI test positivity among doxy-PEP users vs. non-users

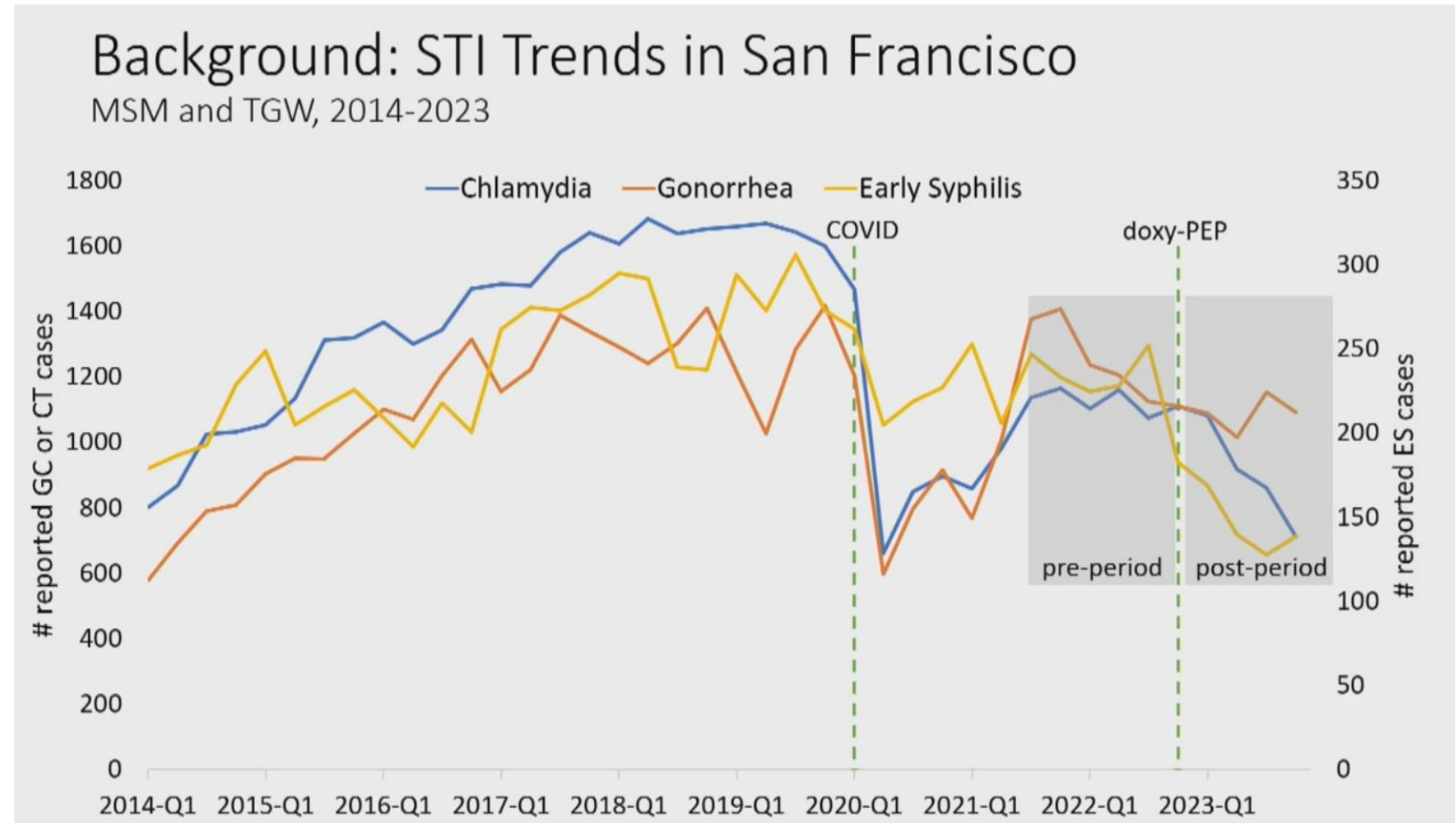
Figure 3: Gonorrhea Positivity



Doxy-PEP Associated with Declines in Chlamydia and Syphilis in MSM and Trans Women in San Francisco

Sankaran M, et al. Abstract #127

- Population level: San Francisco citywide surveillance data
- Ecological analysis
- Before & after doxy-PEP guidelines, focus on “post-COVID” era
- Interrupted time series
- Estimated >3700 people on doxy-PEP, ~20% of MSM & TGW

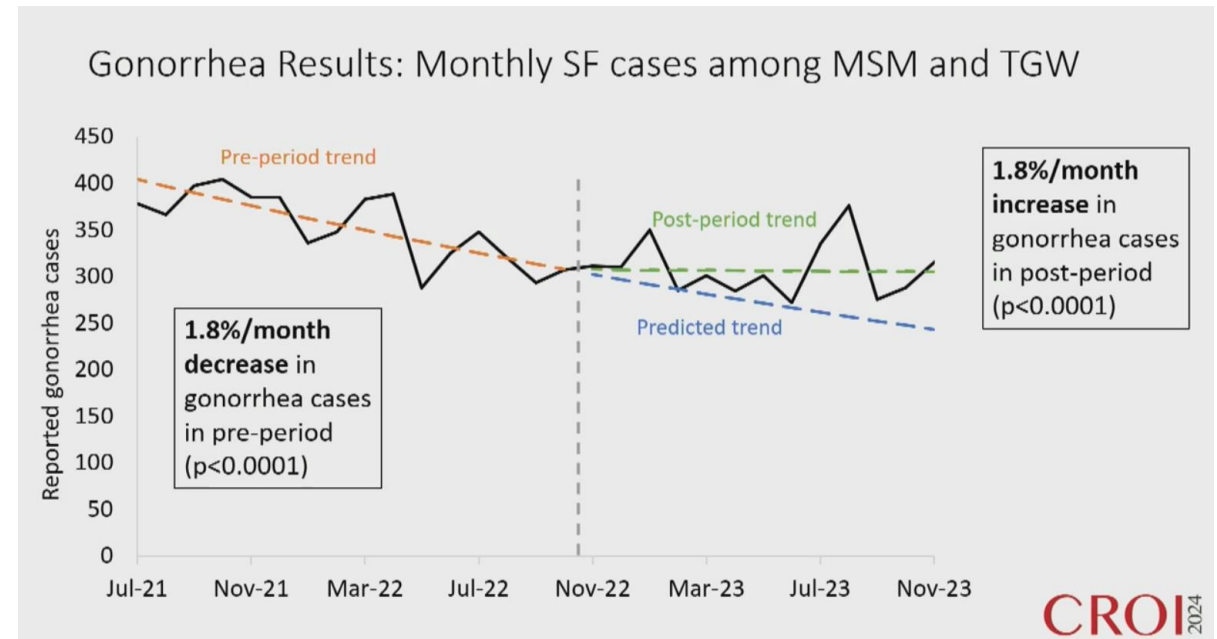
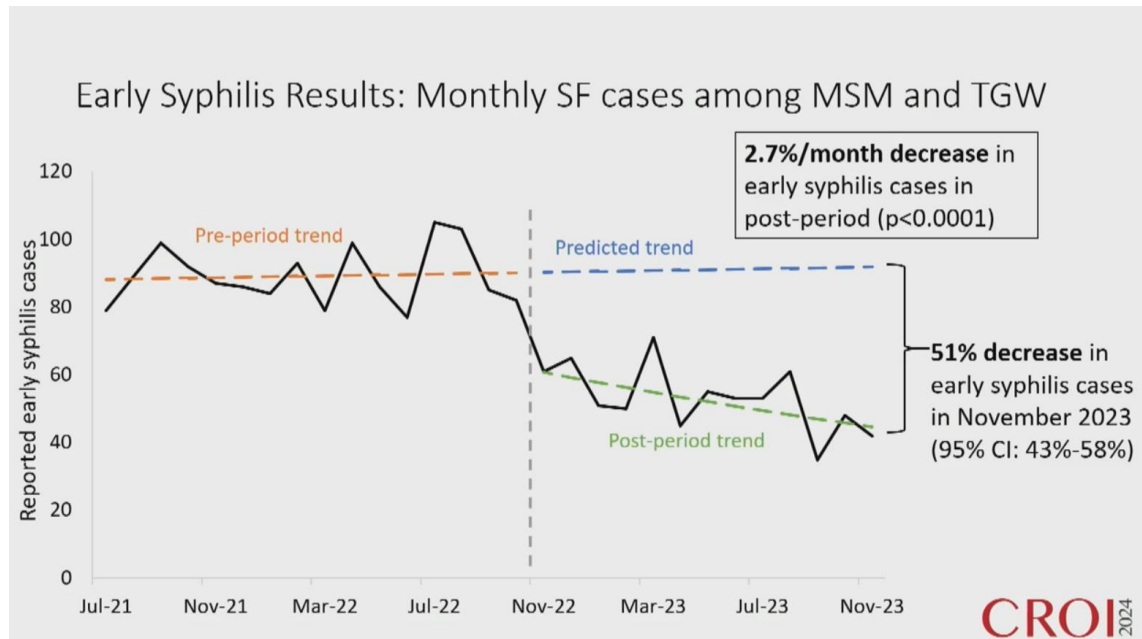


Doxy-PEP Associated with Declines in Chlamydia and Syphilis in MSM and Trans Women in San Francisco

Sankaran M, et al. Abstract #127

50% decrease in chlamydia ($p < 0.001$)*
51% decrease in early syphilis ($p < 0.001$)

1.8% per month increase in gonorrhea
($p < 0.001$)



*no change in CT cases among cisgender women in the same time period

Impact of Doxycycline as STI Postexposure Prophylaxis on the Gut Microbiome and Antimicrobial Resistance Gene Expression

Chu V, et al. Abstract #1154

- Doxy-PEP study collected rectal swabs at enrollment & 6 months
- DNA and RNA metagenomic sequencing of samples from participants with the highest reported doxy-PEP use vs. standard-of-care

Microbiome (not shown)

Bacterial diversity & total bacterial abundance **did not differ** between doxy-PEP and SOC or over time by arm

Tetracycline ARG expression

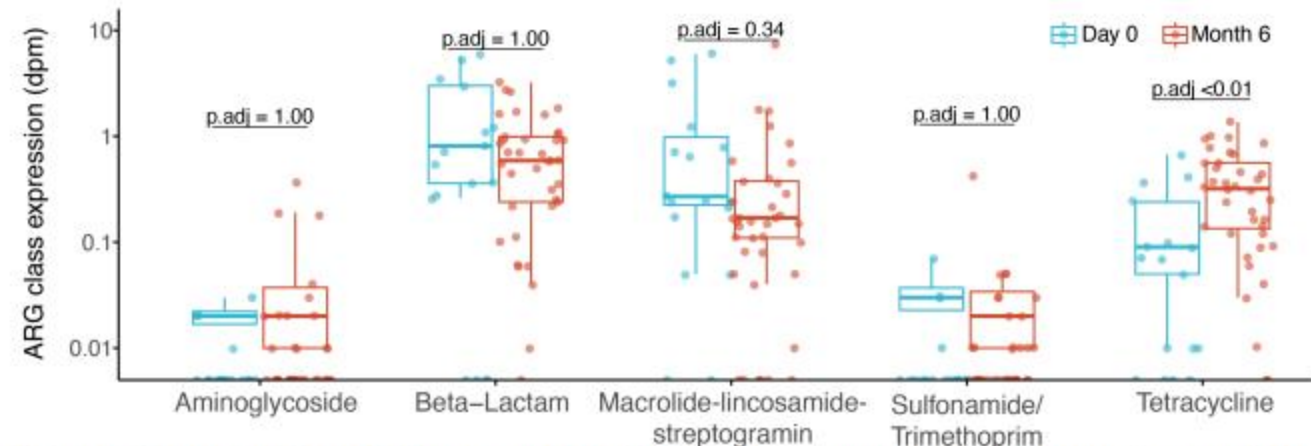


Figure 2. Impact of doxy-PEP use on ARG class expression, normalized by reads per million sequenced and gene length (depth per million, dpm) in the doxy-PEP RNA-seq samples (n=55). Tetracycline ARG expression significantly increased between Day 0 and Month 6, while no difference was observed among non-tetracycline ARG classes.

Impact of Doxycycline as STI Postexposure Prophylaxis on the Gut Microbiome and Antimicrobial Resistance Gene Expression

Chu V, et al. Abstract #1154

- Doxy-PEP was associated with a dose-dependent increase in tetracycline antimicrobial resistance gene abundance.

GUT RESISTOME

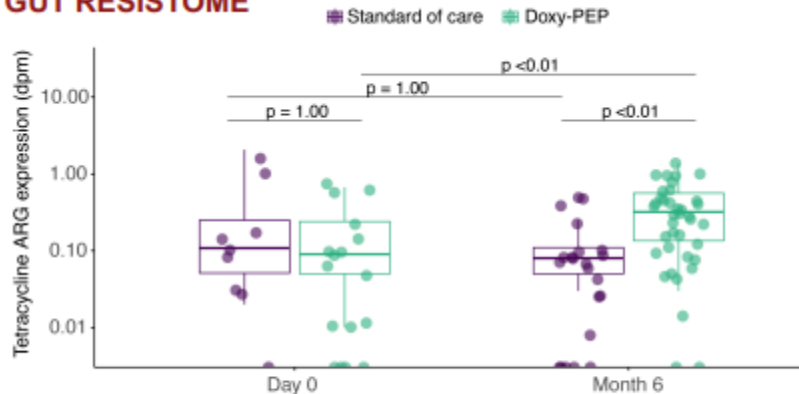


Figure 3. Tetracycline ARG expression by study arm and visit in the RNA-seq samples (n=86). Tetracycline ARG expression increased in the doxy-PEP Month 6 group compared with the SOC Month 6 and the doxy-PEP Day 0 groups.

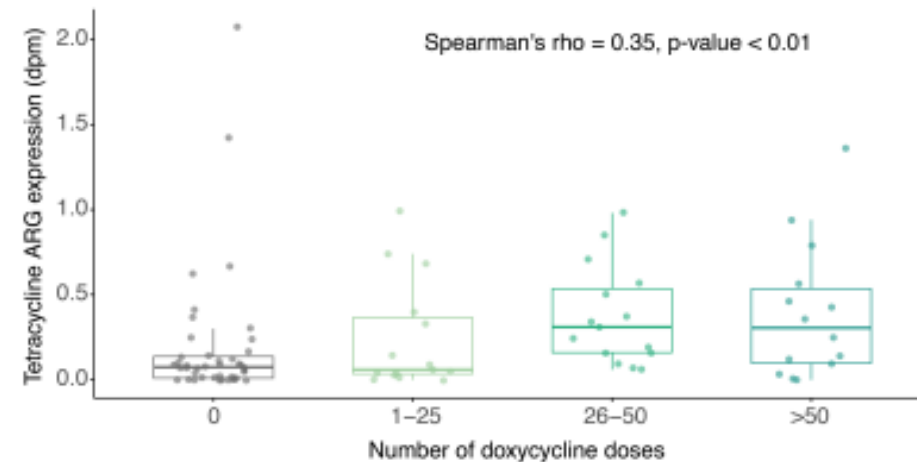


Figure 4. Tetracycline ARG expression increased with number of doxycycline doses since enrollment in the RNA-seq samples (n=86).

Doxy-PEP Section Summary

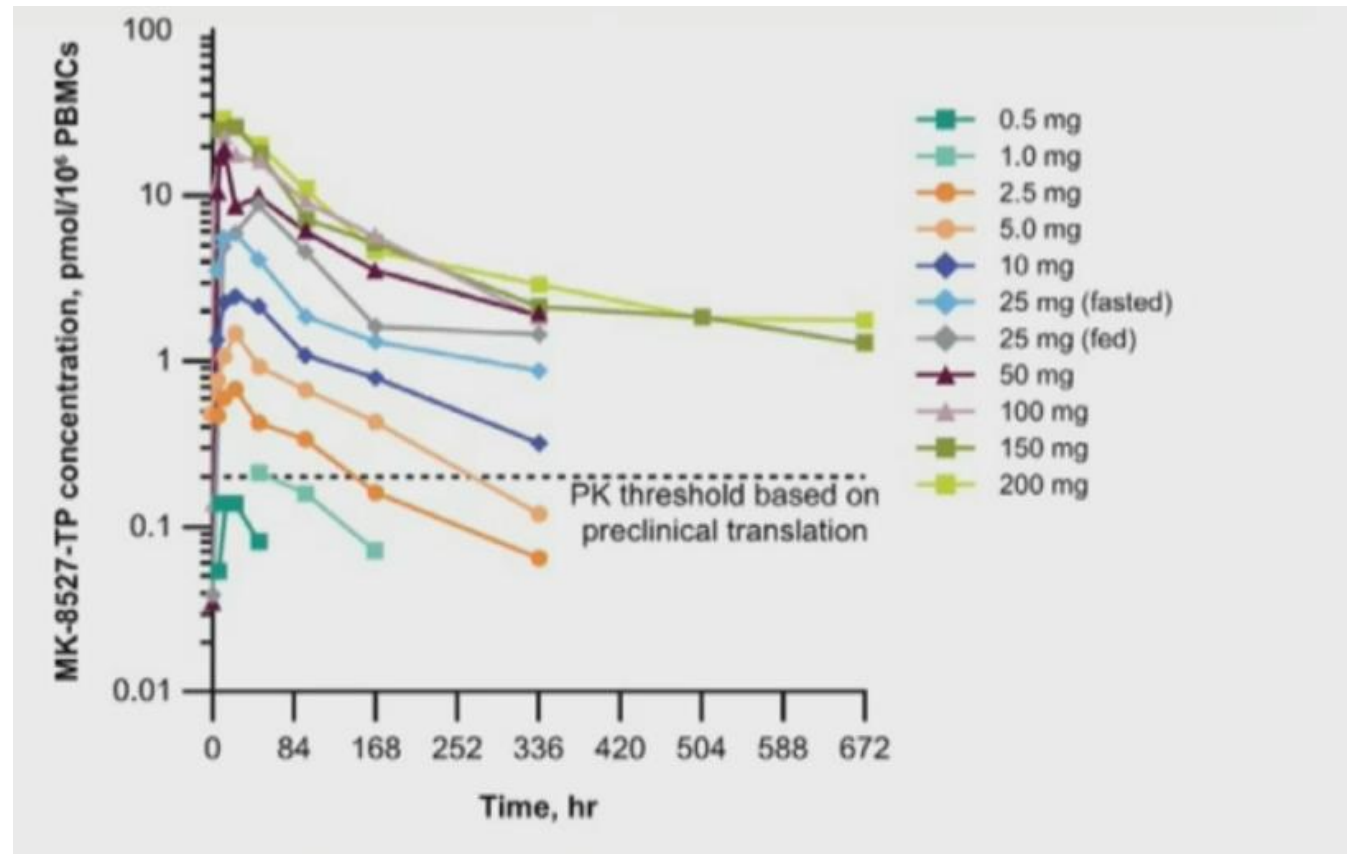
- Doxy-PEP decreases STI rates in MSM and transgender women
 - Clear impact on chlamydia and syphilis in both clinical trial & practice data
 - Decreased gonorrhea risk in clinical trials but no clear impact in practice
- Scale-up occurred quickly in San Francisco (high interest in the intervention)
- Doxy-PEP use does not appear to impact gut bacterial diversity over 6 months, but is associated with a dose-dependent increase in tetracycline AMR genes in the gut
 - Clinical significance & impact of longer term use unknown

PrEP: Novel Formulations

PrEP: What's in the pipeline?

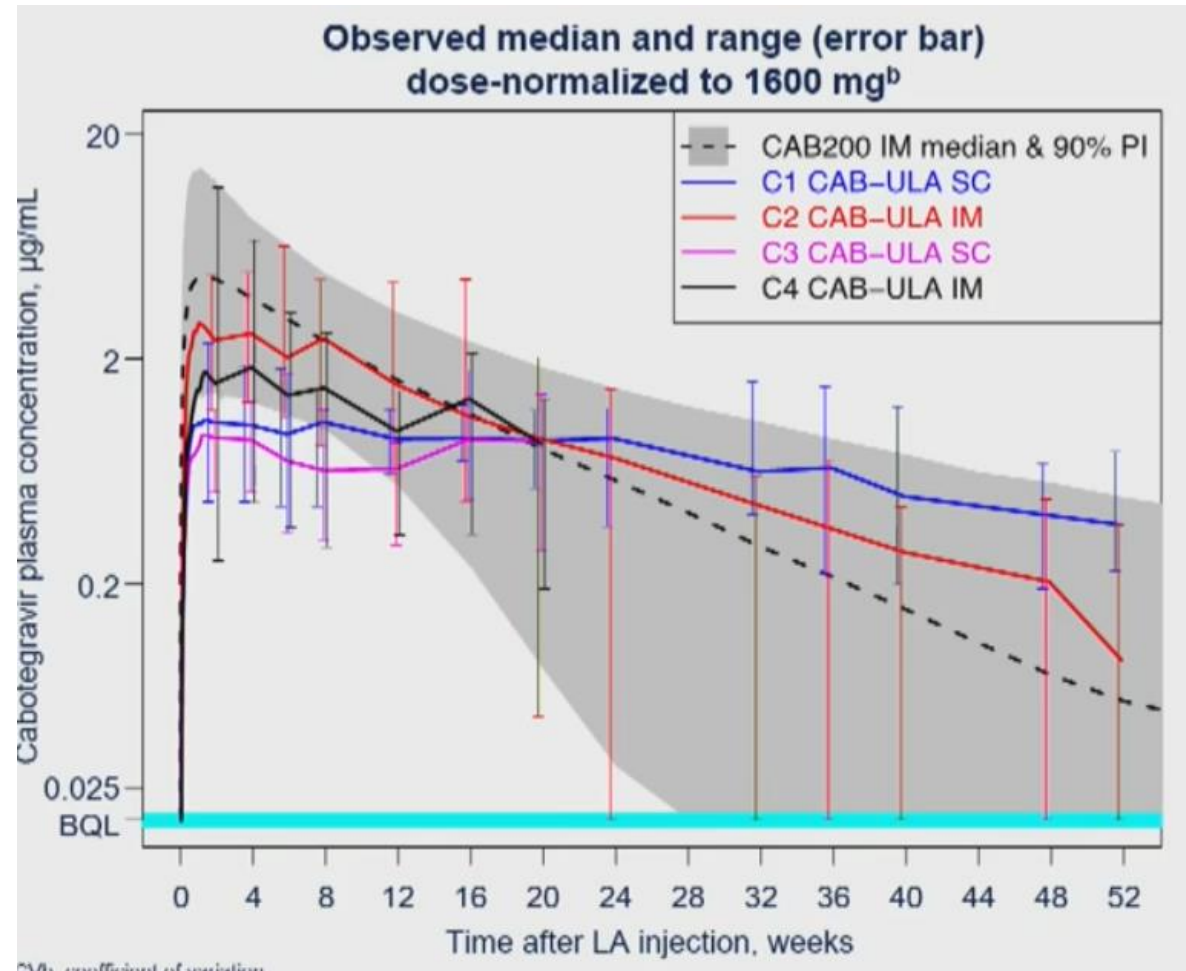
- **Weekly oral medication**
- Novel oral nucleoside reverse transcriptase translocation inhibitor (NRTTI) – MK-8527
- Phase 1 study
- Safe & well-tolerated
- PK profile supports weekly (or less frequent dosing)

Mean MK-8527 concentration following a single dose



PrEP: What's in the pipeline?

- **Longer acting injectable**
- Approved cabotegravir formulation + recombinant human hyaluronidase
- A new ultra-long-acting CAB formulation
- Phase 1 study
- IM version of ultra-long acting well-tolerated
- Dosing interval ≥ 4 months



PrEP: What's in the pipeline?

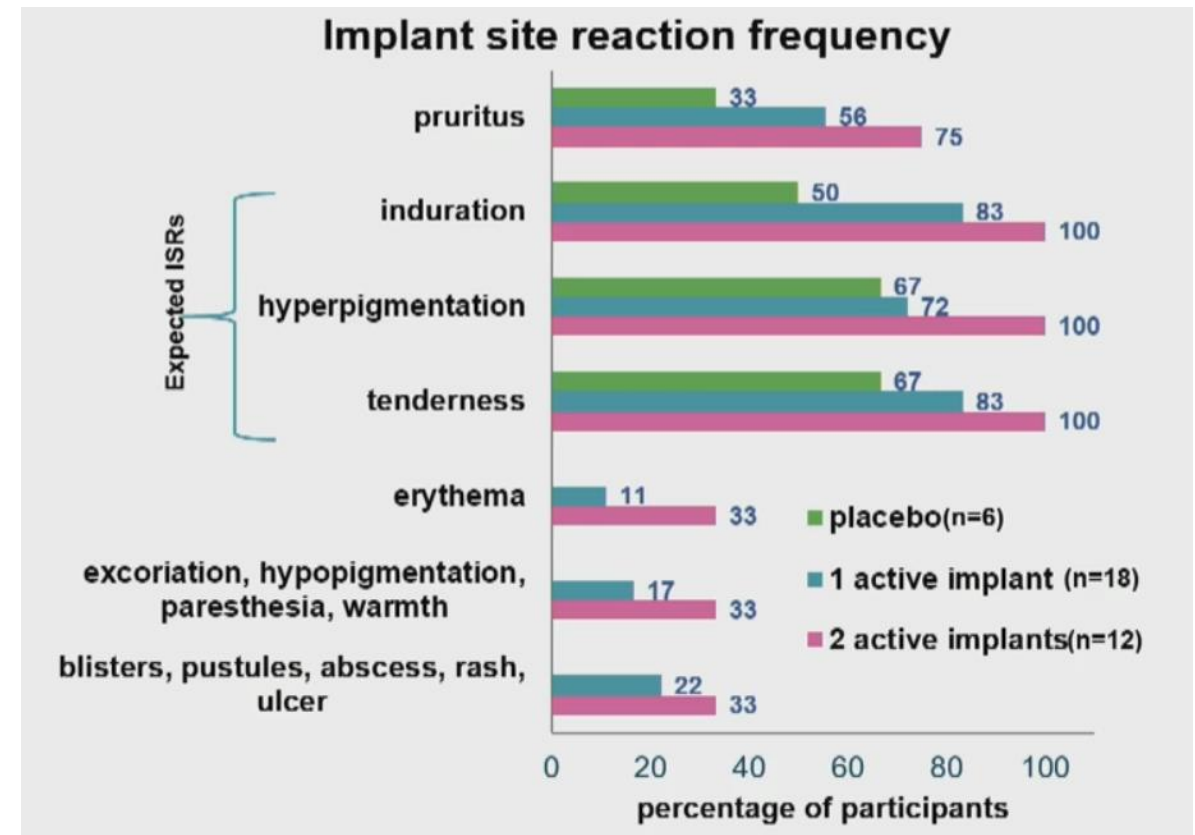
- Annual TAF implant



First in-human
Phase 1 Study:
48 weeks

31% removed
early, median 19
weeks

Lower than
planned drug
release

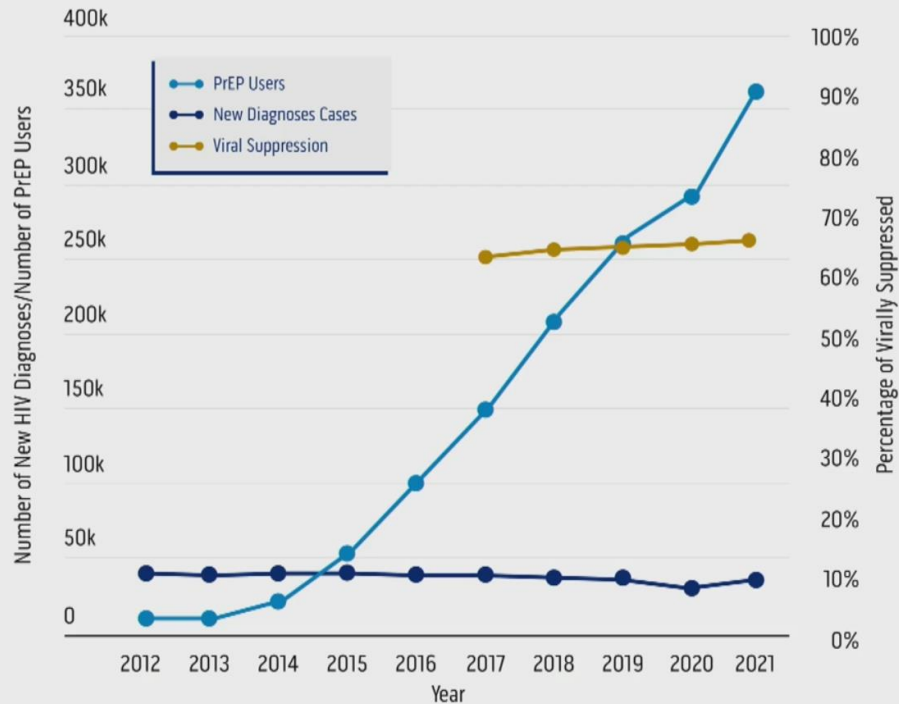


Association of State-Level PrEP Coverage and State-Level HIV Diagnoses, US, 2012-2021

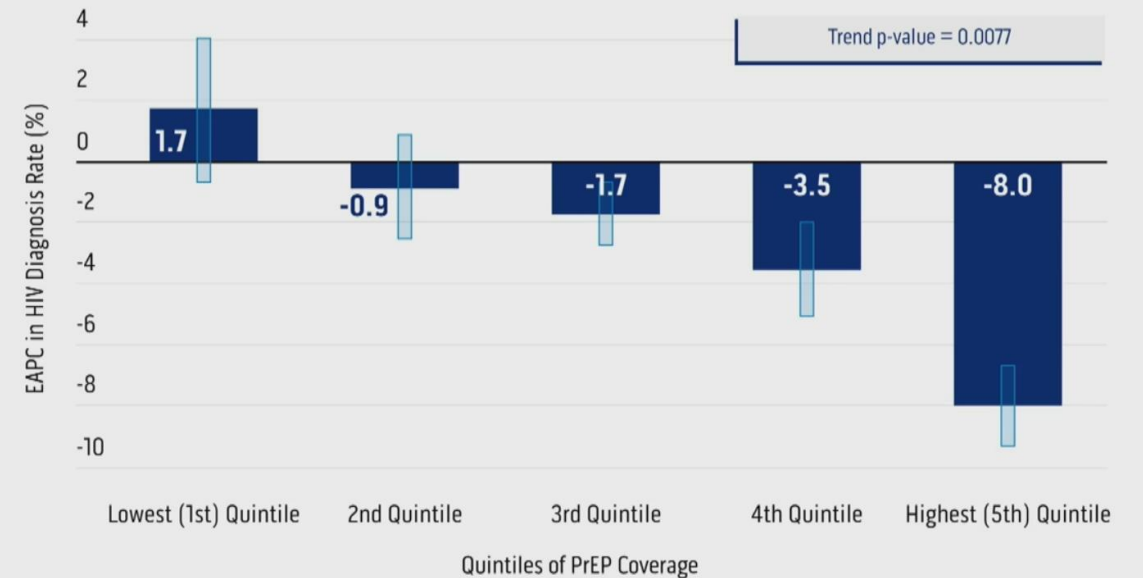
Sullivan P et al., Abstract #165

- Ecological study of association between PrEP coverage & new diagnoses
- PrEP use: commercial data sets
- PrEP coverage: # of PrEP users/100 persons with indications (CDC & AIDSvu data)

PrEP users, new HIV diagnoses and VS overall, United States 2012-2021



Estimated Annual Percent Change in HIV Diagnoses, by State Quintile of PrEP Use, 2012-2021, United States



Thank you!
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