Doxycycline for STI prophylaxis: Solution or problem?

Key stewardship considerations

UW TASP Discussion

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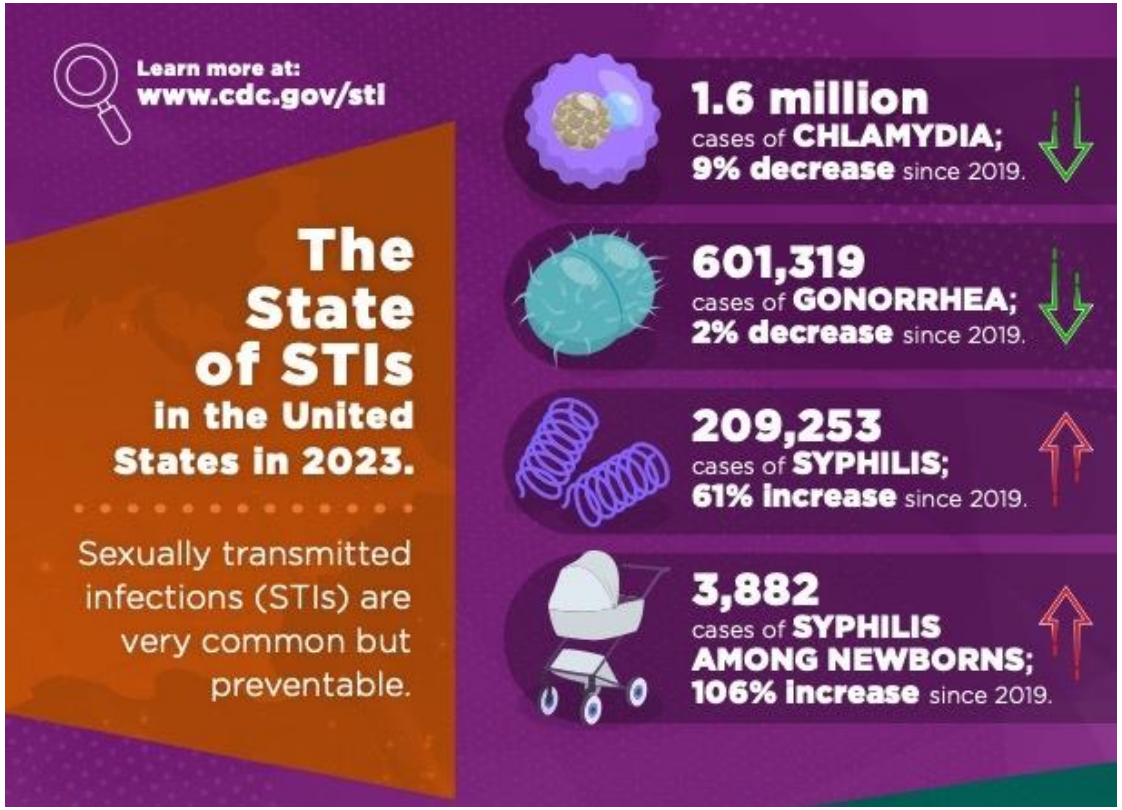
11 February 2025

Objectives

- Understand current evidence and indications for doxy-PEP
- Weigh pros and cons of using doxycycline for STI prophylaxis
- Describe potential antimicrobial stewardship concerns related to doxy-PEP

Persistent STI rates demand new solutions

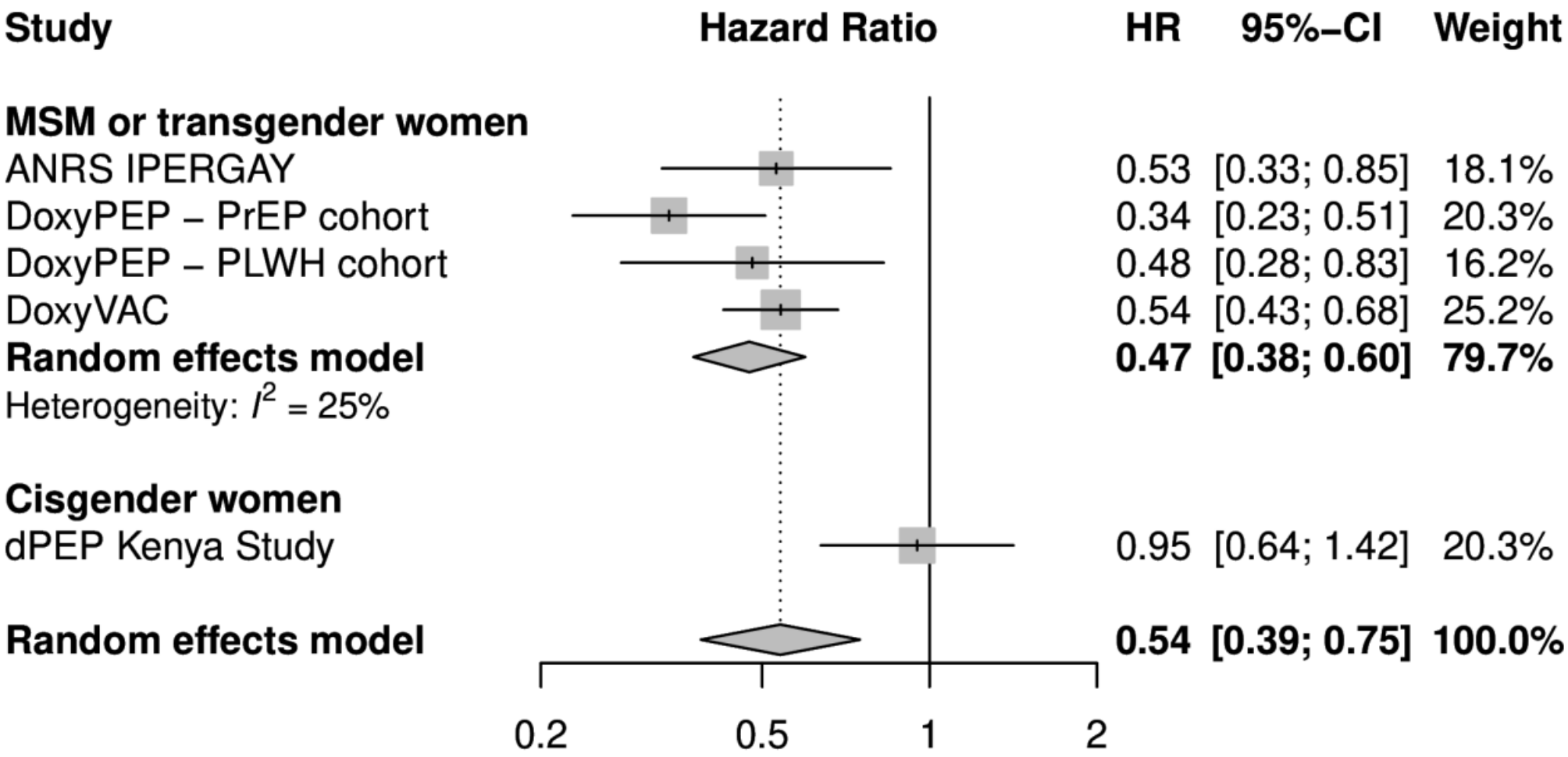


- STIs increasing for >10 years – most alarming for infectious and congenital syphilis
- Syphilis carries most morbidity – stillbirth, birth defects, neurosyphilis, hearing or vision loss, etc.
- All bacterial STI are preventable, but existing STI control strategies ("Talk, test, treat") are insufficient
- Need intervention that is cheap, accessible, acceptable, and (fairly easily) implementable

A new intervention for STI prevention

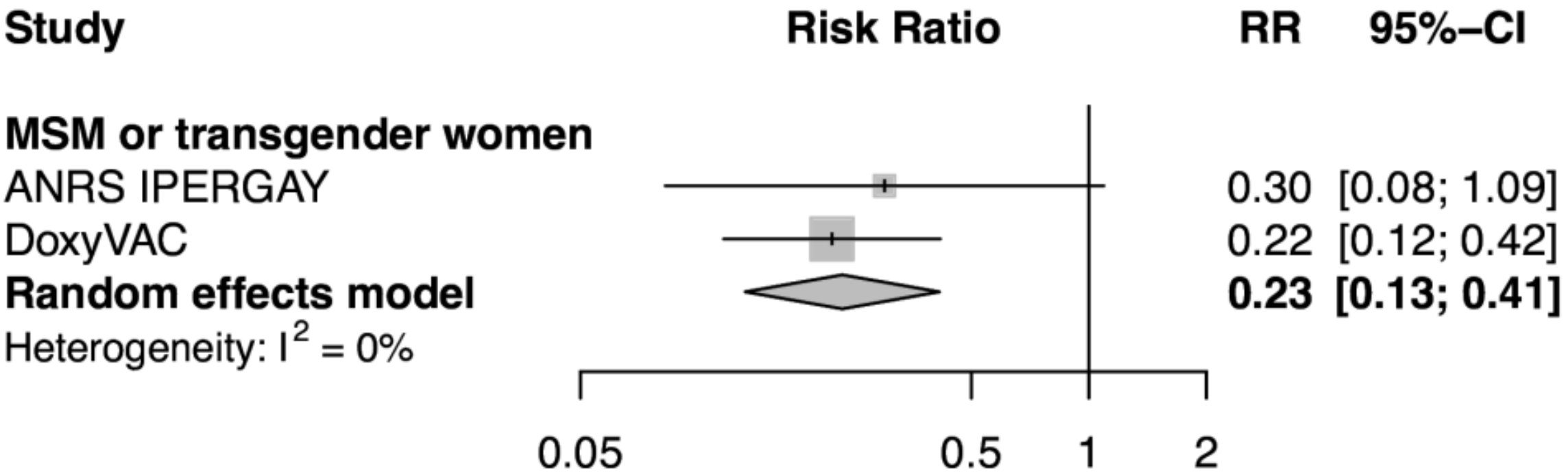
- **Doxy-PEP** = strategy of taking 200mg of doxycycline PO within 24-72 hrs after condomless sex to prevent bacterial STI
  - Sex-positive, user-controlled tool for persons at increased bacterial STI risk
  - Safe, cheap, well tolerated, highly acceptable in RCT participants and real-world users
  - Uncertainties: eligible populations, longer term risks and impacts, longevity of effectiveness for all STIs
- **Doxy-PrEP** = strategy of taking 100mg of doxycycline PO daily to prevent bacterial STI

Doxy-PEP reduces overall STI risk by **46%**



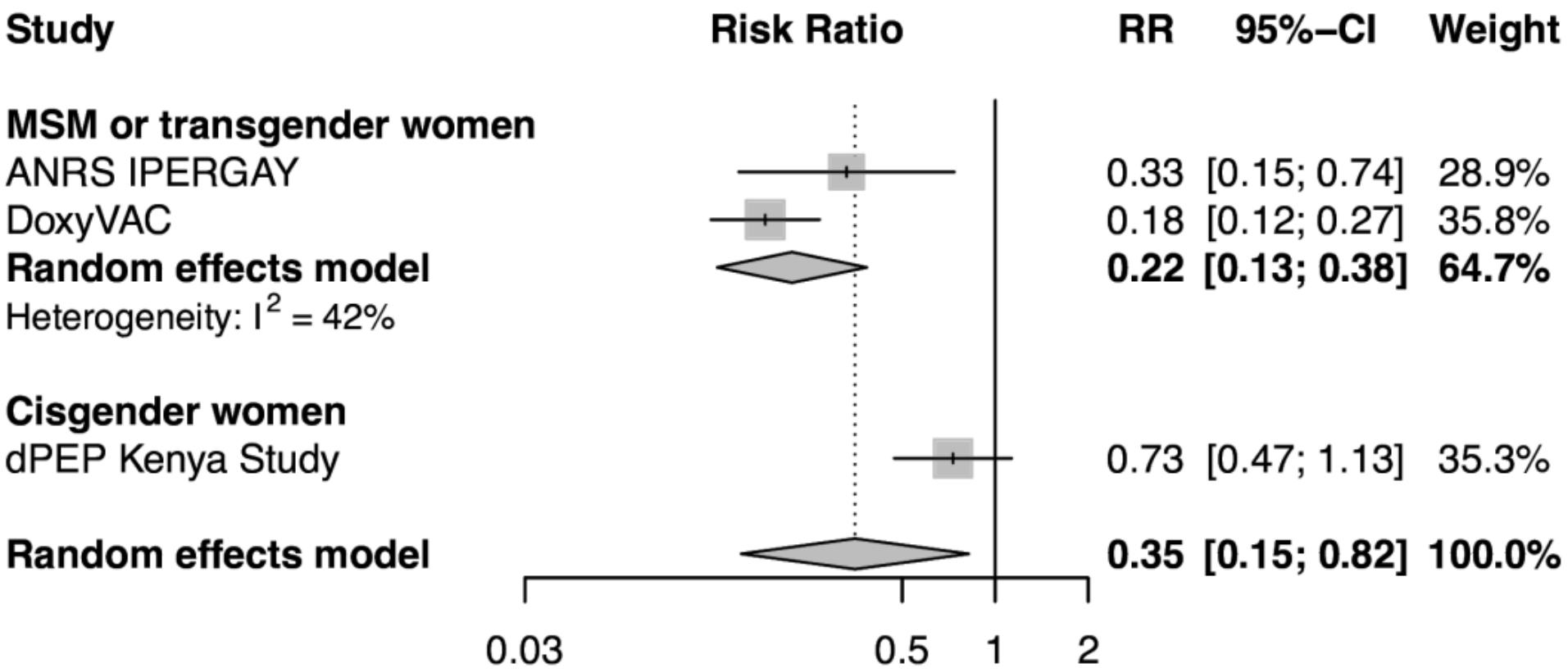
Sokoll PR et al, *Sex Transm Infect* 2024

Doxy-PEP reduces syphilis by **77%**



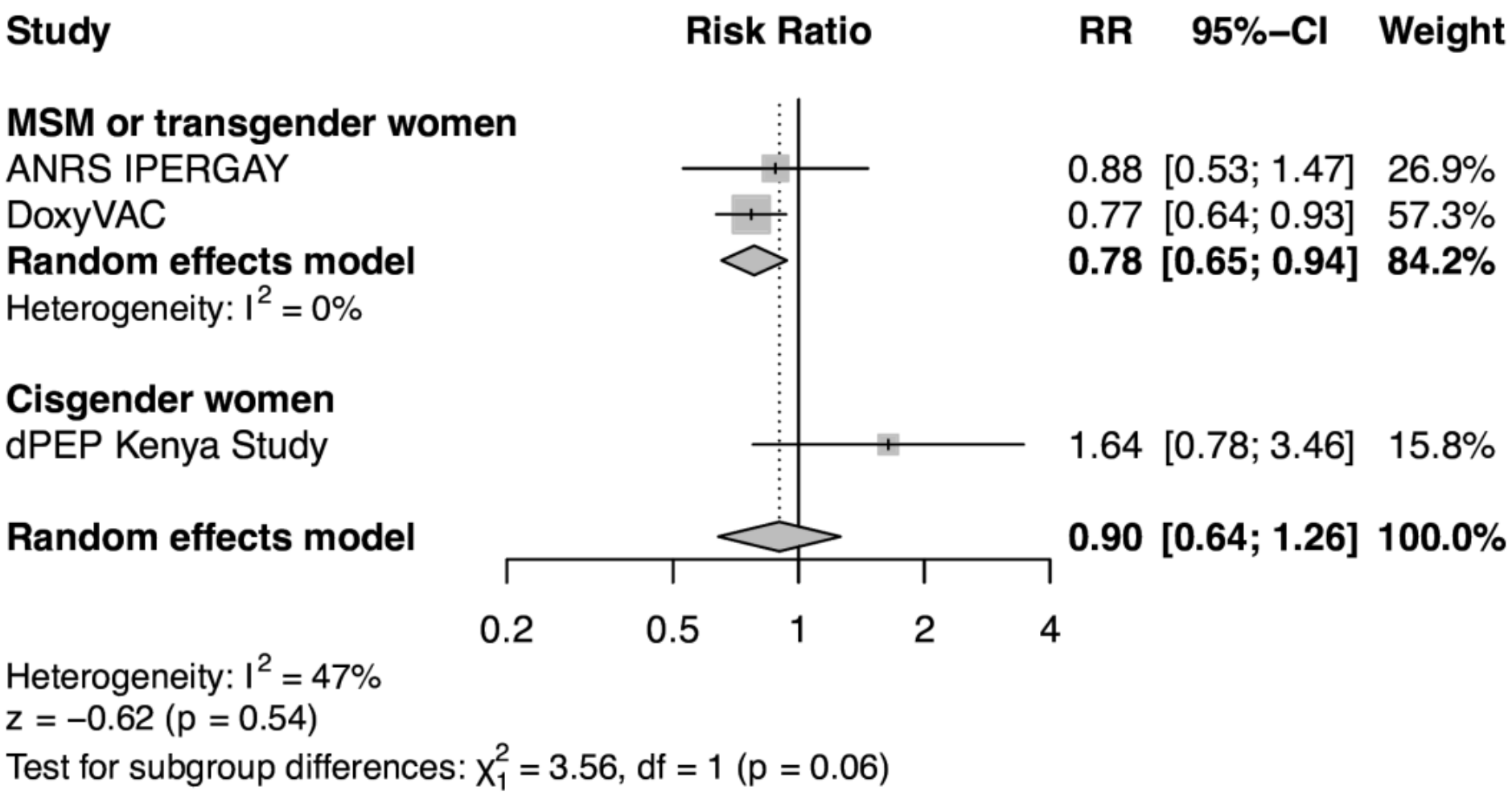
Sokoll PR et al, *Sex Transm Infect* 2024

Doxy-PEP reduces chlamydia by **65%**



Sokoll PR et al, *Sex Transm Infect* 2024

Doxy-PEP *may reduce* gonorrhea



Sokoll PR et al, *Sex Transm Infect* 2024

CDC issues highest evidence grade for doxy-PEP

CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024

Recommendations and Reports / June 6, 2024 / 73(2);1–8

Print

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Counsel all GBMSM and TGW with ≥1 bacterial STI in last 12 mo about benefits and harms of doxy-PEP and offer it through shared decision making **(AI)**. Evidence insufficient for other groups.

Weighing evidence for doxy-PEP

- **Proven efficacy for bacterial STI reduction**; NNT = 5
  - ✓ Syphilis and chlamydia rates (65-77%)
  - ✓ Lower for gonorrhea (~46%)

Luetkemeyer A et al, *NEJM* 2023
Dombrowski J et al, *Clin Infect Dis* 2024
Cannon C & Celum C, *Top Antivir Med* 2023

Weighing evidence for doxy-PEP

- **Proven efficacy for bacterial STI reduction**; NNT = 5
  - ✓ Syphilis and chlamydia rates (65-77%)
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- **Stewardship considerations**
  - ✓ Based on median of 4 doses (800 mg) per month, DPEP users took 45 extra days of doxy to prevent ~1 STI/year compared to SOC
  - ✓ Reduced ceftriaxone use by 50% (0.8 tx-days/yr DPEP vs 0.4 tx-days/yr SOC)
  - ✓ PEP vs PrEP: fewer total days of doxycycline exposure (48 days vs 365 days)
  - ✓Antibiotic exposure is common among MSM even if not using doxy-PEP

Luetkemeyer A et al, *NEJM* 2023
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Withholding empiric STI treatment as antibiotic stewardship

- Epi ("epidemiologic") or empiric STI treatment was instituted in era of poor GC/CT diagnostics
- Over 65% of MSM who are contacts to STI test negative for GC/CT but receive empiric antibiotics unnecessarily
- Overtreatment of contacts represents an estimated 2-4% of the 47 million doses of overused antibiotics in US

STI	Positive test rate among MSM contacts	RRR from doxy-PEP	Estimated positive test rate in contacts on doxy PEP
GC	34%	56%	**15%**
CT	34%	81%	**6.5%**

Syphilis: test + empiric treatment due to transmission risk

Cannon & Celum, *Top Antivir Med* 2023
Rowlinson E et al, *STD* 2020
US CDC. Antibiotic Use… 2018
Luetkemeyer A et al, *NEJM* 2023

Weighing evidence for doxy-PEP

- **Antibiotic exposure = ↑ risk for antimicrobial resistance**
  - ✓ Rising TCN-R in N. gonorrhoeae in MSM on doxy-PEP in Seattle & San Francisco
    - High-level tetR (≥16 µg/mL) is 55% in Seattle/King County MSM -- 52% in DPEP users vs 35% in non-users (*P*=0.01) within our SHC
    - Due to frequent screening and treating asymptomatic STI? Clonal spread of tetR isolates in networks?

Soge OO et al, *CID* 2024 (in press)
Kohn R et al, CDC STI Prevention Conference 2024
Cohen S et al, CDC STI Prevention Conference 2024
Molina JM, et al. *Lancet Infect Dis* 2024

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    - Due to frequent screening and treating asymptomatic STI? Clonal spread of tetR isolates in networks?
  - ✓ Decreased overall *S. aureus* colonization but ↑ carriage of tetR (≥8 µg/mL) *S. aureus*
  - ✓ Low MRSA prevalence in Seattle/SF (1-6%) vs 10-12% in France; no difference btwn groups
  - ✓ Increase GAS carriage in DPEP users vs non-users (9% vs 4%, *P*=0.008) and tetR (8% vs 3%, *P*=0.025) in our SHC

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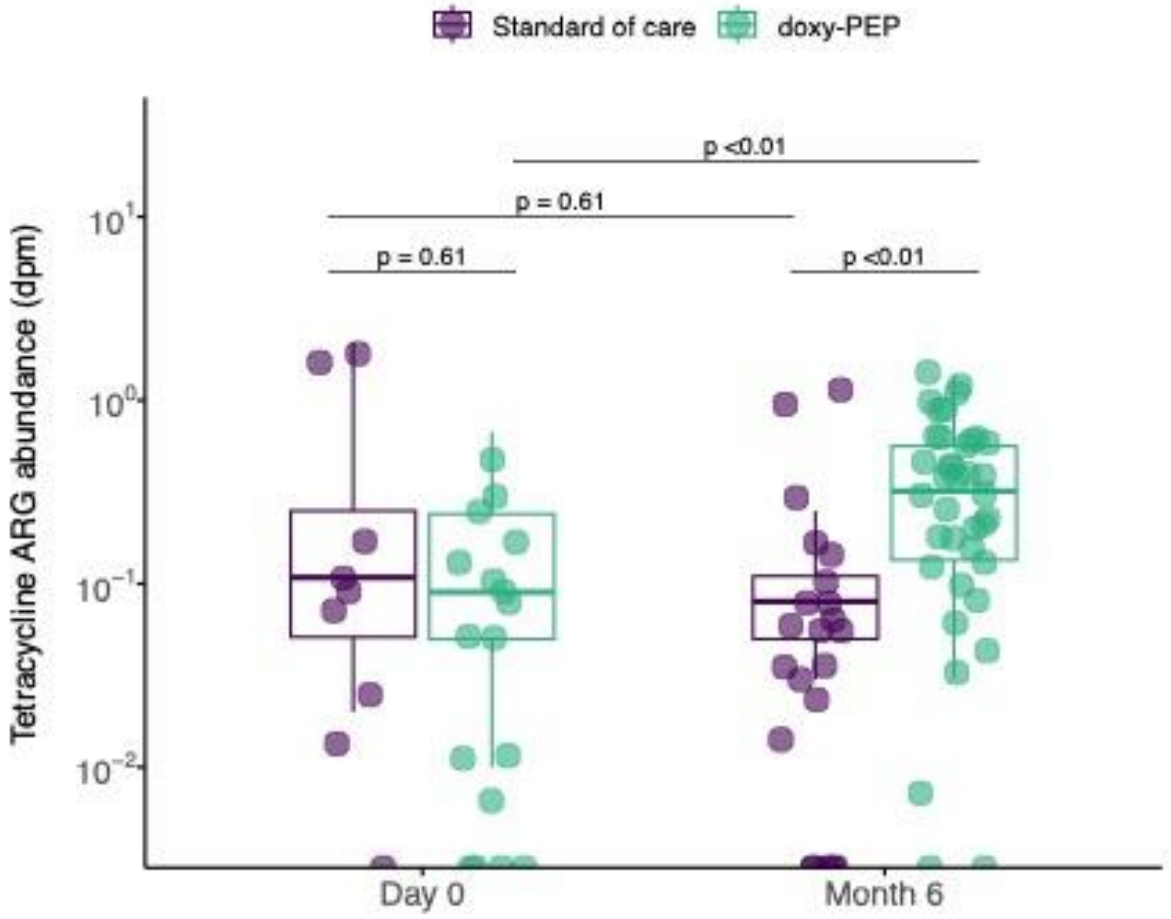
Doxy-PEP and the microbiome



Increase in tet AMR genes beteen M0 to M6 among DoxyPEP participants

- Comparison of actively expressed AMR genes in 46 dPEP and 24 SOC ppts
- No difference in gut bacterial microbiome α- or β-diversity or total abundance between arms at M0 or M6, or over time by arm
- Actively expressed TCN-R genes increased by median of 2 in dPEP group (*P*<0.01) without change to non-TCN classes
- Doxy-PEP associated with higher # of AMR genes but no significant alteration in microbiome diversity

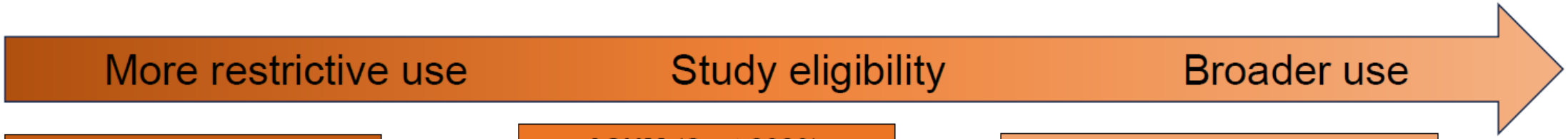
Chu et al, CROI 2024 (Abstract 3404) and *Nature Medicine* 2024
dPEP = doxycycline post-exposure prophylaxis
SOC = standard care group

Comparable examples of long-term antimicrobial use

Condition	Morbidity/Mortality	Impact (Absolute Effects)	Guidelines
Opportunistic infections of AIDS (PJP, toxoplasmosis, MAC)	Very High	53% ↓ in PJP (before effective HIV medications)	Recommended for low CD4 Selected immunocompromised
Malaria prophylaxis	High	0.8 cases per year (Indonesian RCT, 2001)	Recommended for travelers, Peace Corp, military in select destinations
Recurrent leg cellulitis	Intermediate	15% ↓ Recurrence ~2 yrs	Consider if 3-4 episodes/yr
Moderate to severe acne	Intermediate/Low	7-9% ↑ Skin Clearance	Limited to 3-4 months
Genital herpes	Intermediate/Low	↓ Time to recurrence & transmission	Widely used for people with frequent recurrences
Recurrent UTI (after sex)	Intermediate/Low	↓3.3 infections/year	Consider ≥2 episodes/year

Slide courtesy of Matt Golden

Who should be offered doxy-PEP?
Variation in international guidelines



Public Health England/BASHH (2017): Not endorsed; re-evaluating

IAS-USA (Dec 2022): Case-by case

Seattle King County (June 2023): *Inform*; prioritize hx of syphilis or multiple STIs

German STI Society (Aug 2023): Case-by-case; Reserved for selected individuals

ASHM (Sept 2023): Use doxy-PEP *primarily* for prevention of syphilis in GBMSM; Use for defined period of time

US CDC *Draft* (Oct 2023): A1 recommendation to consider for MSM and transwomen with at least 1 STI in past year; Insufficient evidence for other groups

San Francisco DPH (Oct 2022): Tiered: *Recommend* to study population; *Offer* to broader group (Trans women, trans men and MSM with multiple cis male partners but without STI diagnosis in prior 12 months)

California DPH (April 2023): Tiered: Offer to all non pregnant individuals at increased risk for bacterial STIs and those requesting doxy-PEP

Image: Pexels

Thoughts? Questions? Comments?

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