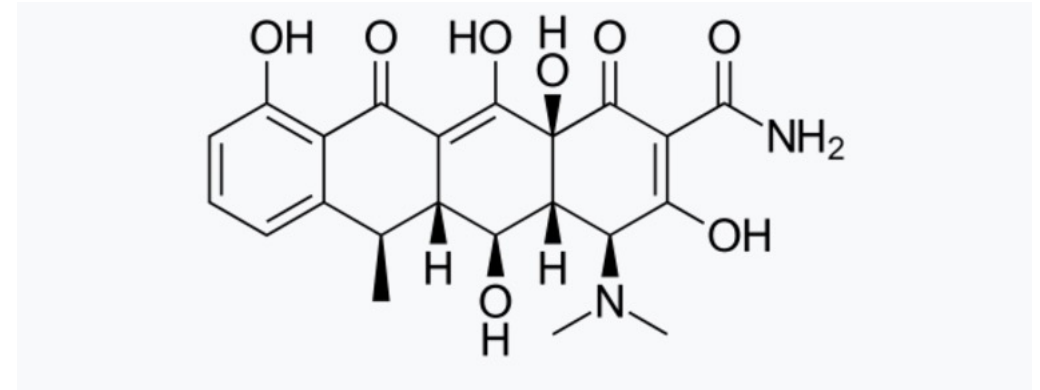


Addressing STIs beyond HIV and viral hepatitis



STIs and doxyPEP/PrEP: recap of scientific evidence

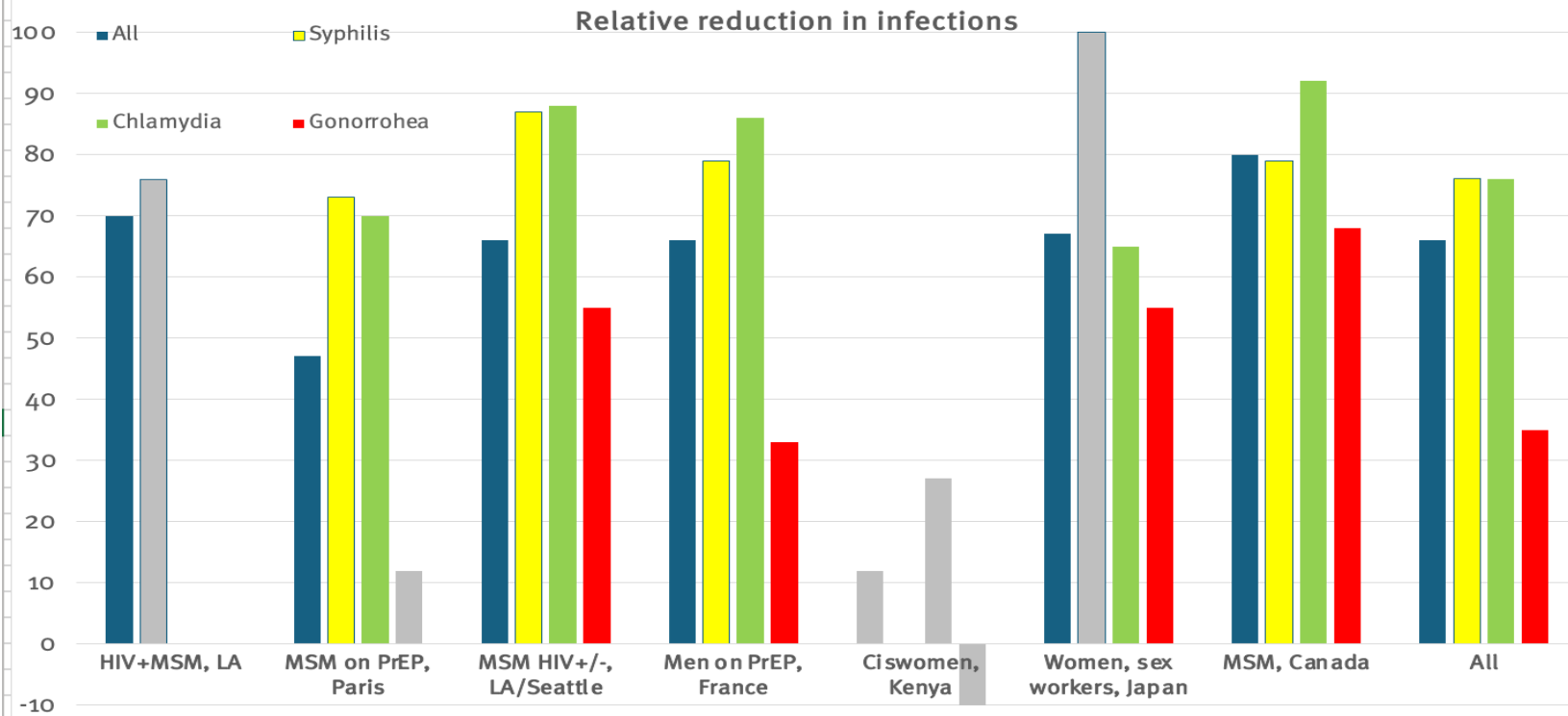
Gus Cairns, co-chair, Combination Prevention Programme Committee, EATG

What is doxyPEP/PrEP?

- **Doxycycline is a tetracycline-type antibiotic and antiparasitic drug**
- **Used to treat some bacterial pneumonias, acne, chlamydia and other urethritis, Lyme disease, syphilis as alternative to penicillin. Also typhus, cholera, plague...**
- **Has been used as prophylaxis against Lyme disease recurrence, malaria, nematode diseases (river blindness, elephantiasis)**
- **Effectively prevents syphilis and chlamydia infection and some gonorrhoea**
- **Dose as PEP: 200mg up to 72h after sexual exposure**
- **Dose as PrEP 100 – 200mg up to 24h before exposure**

The studies

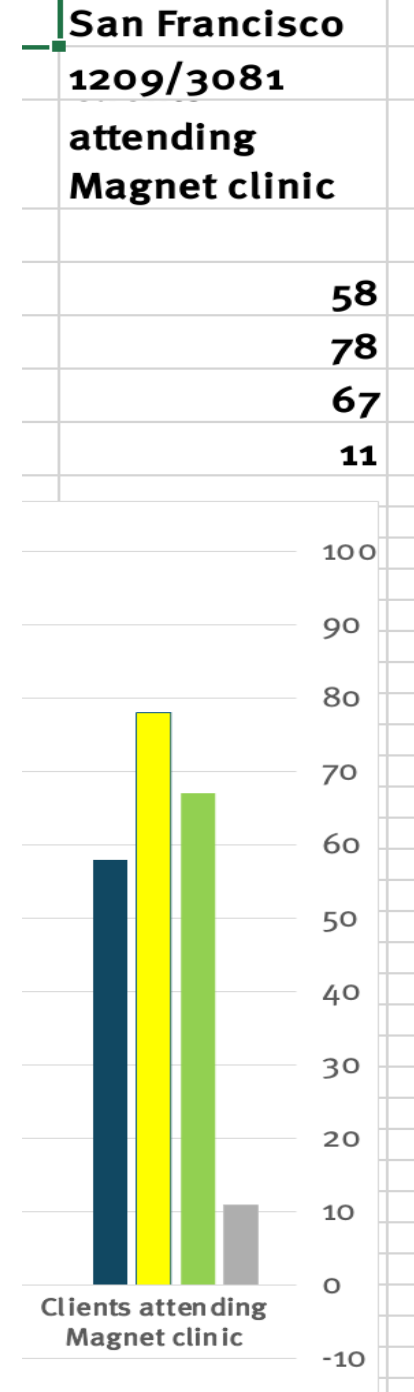
Title	DPMSM	IPERGAY	DOXYPEP	DOXYVAC	dPEP	Japan	DuDHS	ALL
N	30	232	501	545	440	40	52	
Who	HIV+MSM, LA	MSM on PrEP, Paris	MSM HIV+/-, LA/Seattle	Men on PrEP, France	Ciswomen, Kenya	Women, sex workers, Japan	MSM, Canada	All
Type	PrEP	PEP	PEP	PEP	PEP	PrEP	PrEP	
All	70	47	66	66	12	67	80	66
Syphilis	76	73	87	79	0	100	79	76
Chlamydia		70	88	86	27	65	92	76
Gonorrhoea		12	55	33	-12	55	68	35



In DOXYVAC study, 22% additional reduction in gonorrhoea attributed to meningitis B vaccination (NS)

Real-life rollout: San Francisco

- SF offered dPEP to all sexual health clinic attendees taking HIV PrEP from October 2022
- Up till September 2023, 39% of 3081 offered dPEP started it
- Incidence of any STI decreased 58% when comparing dPEP vs no-PEP users
 - Syphilis down 78%
 - Chlamydia down 67%
 - Gonorrhoea down 11% (not significant)
- In all clinic users, STI incidence per visit went down from 18% to 8%
- In 3 city clinics seeing >3700 people, incidence of chlamydia and syphilis halved. Gonorrhoea – no significant decrease.



Latest study - Milan

- Retrospective study, published last month (19/11/2024). San Raffaele SHC.
- N = 754 GBMSM who had been prescribed dPEP between 01/08/2022 – 31/07/2024.
- HIV+ in care (26%) or HIV- HIVPrEP users (70%) or non-users (4%)
- NB of 754 prescribed dPEP only 219 (29%) had actually used it ≥ 1 time
- A proportion of dPEP users (70 = 32%) had also received the meningitis vaccine, which has partial protection against gonorrhoea

Milan study continued

- 549 STI diagnoses, 401 before dPEP prescription and 139 after
- 50% of diagnoses gonorrhoea, 22% chlamydia, 18% syphilis
- Post-dPEP reduction in incidence: 80% syphilis, 80% chlamydia
- 74% reduction in gonorrhoea, but 22% attributable to meningitis vaccine so 52% to dPEP

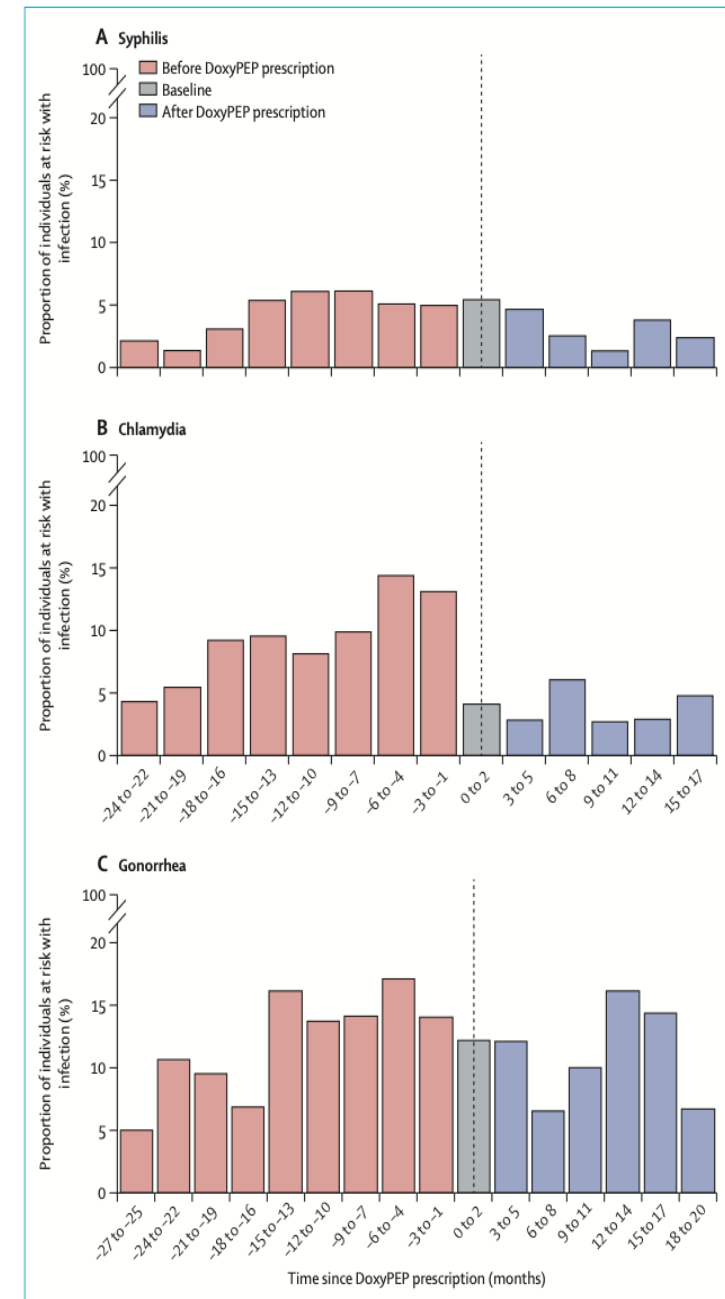


Figure: Proportions of cases of syphilis (A), chlamydia (B), and gonorrhoea (C) infections, before and after DoxyPEP prescription, in 3-month intervals, among DoxyPEP users (n=222). The solid black line at 0 indicates the date of DoxyPEP prescription. DoxyPEP=doxycycline post-exposure prophylaxis.

Safety / side effects (2 largest studies)

DoxyPEP

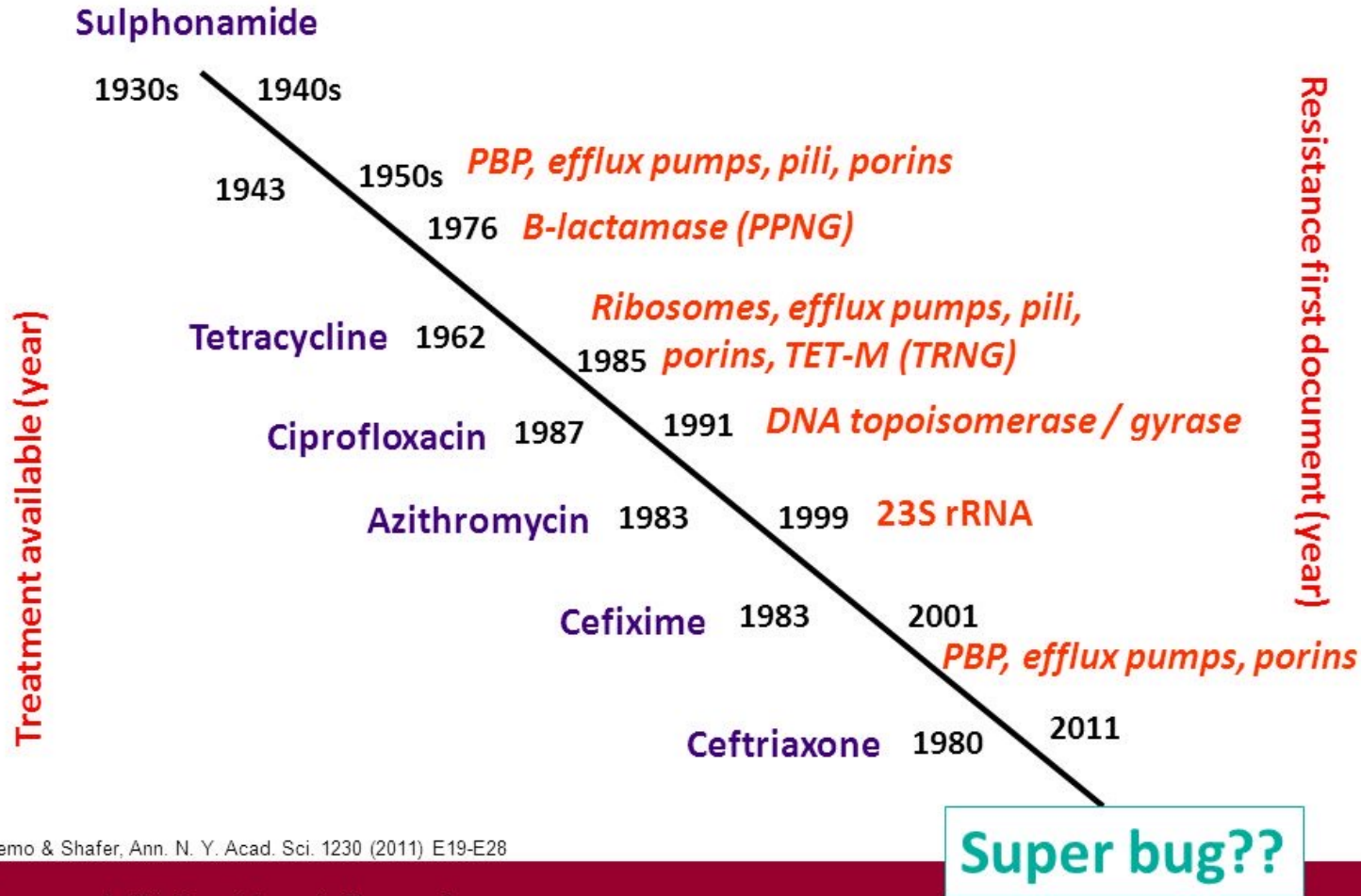
- **5 grade 3 events**
 - 3 diarrhoea
 - 2 headache
- **1 grade 2 lab event**
 - Raised liver enzymes
- **No adverse events rated 'severe'**
- **2% discontinuations**

DoxyVac

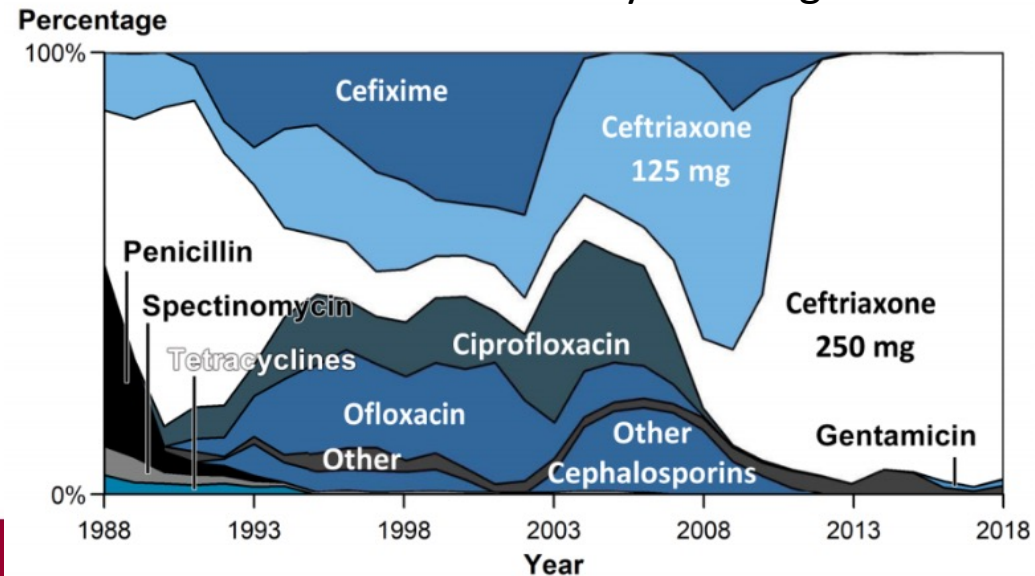
- **22 grade 3 events (6%)**
 - Some were injection reactions
 - 3 diarrhoea (1%)
 - 1 each vomiting, abdo pain, unspecified
- **One reaction to doxycycline rated 'severe' (fixed-drug eruption)**
- **2% discontinuations**

Gonorrhoea resistance + treatment

N. gonorrhoeae treatments & resistance timeline



- Chlamydia and syphilis almost never develop resistance to doxycycline
- By early 90s, tetracyclines no longer used to treat gonorrhoea (see below)
- Latest gonorrhoea treatment: BASHH: ciprofloxacin 500mg if tested for resistance
- If not tested, ceftriaxone (CTX) 1g IM
- IUSTI: CTX 1g IM + azithromycin (AZM) 2g oral
- CTX and AZM resistance rarely seen together



Gonorrhoea resistance in doxyPEP studies

DoxyPEP

- 17% of gonorrhoea had *phenotypic* resistance at baseline
 - i.e. in cultures, but many didn't grow
- 27% had *genotypic* resistance mutations at baseline
 - During study, 38% of infections acquired on dPEP had resistance
 - 12% not on dPEP had resistance
 - But remember ½ as many infections on dPEP

DoxyVac

- All gonorrhoea isolates had some genotypic mutations at baseline
- During follow-up at 12m:
 - 36% on dPEP had 'high level' geno resistance
 - 13% on no PEP had high level resistance
- 2/3 as many infections on dPEP

Implications

- dPEP unlikely to impact on gonorrhoea *treatment* because it's not used
- May hasten lack of efficacy in *prevention* in places where it still works

How many use dPEP in Europe?

- **UK PrEP user survey 2019: 1856 PrEP users. 9% had bought antibiotics to prevent STIS (not all doxycycline)**
- **Germany Q3 2023. 438 gay and bi men. 40% heard of doxyPEP, 9% had used it**
- **UK: BiiSH survey. Nov-Dec 2023. 1106 GBMSM. 51% would use dPEP, 8% had used ABs, 84% started last year, 31% used other antibiotics. 64% would use GC vaccine.**
- **Belgium April 2024: 875 GBMSM and TGW. 40% had heard of dPEP, 9.4% had used it, 80% would but worry re side-effects/resistance**

BUT

- **Spain, July 2024: community-initiated survey, N=150 GBMSM of whom 82 (55%) had used dPEP (c. 20% dPrEP). Self-reported reduction in STIs. “A practice already in use”.**

The gonorrhoea vaccine

- The *Neisseria gonorrhoeae* bacterium is from the same family as the meningitis B organism
- Studies of the 4CMenB vaccine (*Bexsero*) suggested efficacy could be c. 37-44% effective against gonorrhoea
- Two studies of its use alongside dPEP now both suggest 22% efficacy
- However GSK have their GMMA vaccine, which is specifically attuned to NG antigens, is in a phase 2 trial. Primary results due 23/05/2025

Do we need to prevent all STIs?

- **Dutch study: three-monthly-screening for STIs vs six-monthly would prevent an extra 18,250 gonorrhoea & syphilis infections**
- **But would cost €430,000 per QALY-adjust life year gained**
- **79% of extra infections diagnosed would be asymptomatic**
- **Half of gonorrhoea and chlamydia cases self-resolve in 10 weeks and 13 weeks respectively**
- **7-10% of gonorrhoea in men -> orchitis, epididymitis if left completely untreated – but will be symptomatic**
- **How many GBMSM pass on STIs to women?**
- **One study found dPEP for people already treated of 1 or 2 STIs would be more cost effective**

Conclusions

- **DoxyPEP or PrEP appear very effective (70-85%) against chlamydia and syphilis. No sign of toxicity**
- **Some studies report 50-60% efficacy against gonorrhoea, others none. dPEP may contribute to increasing tetracycline resistance**
- **Antimicrobial resistance unlikely to endanger treatment for gonorrhoea because class no longer used. Prevention: has largely already happened**
- **It's very important other antibiotic classes are not used, especially ciprofloxacin, azithromycin, cephalosporins**
- **Usage appears to be increasing**
- **Some clinics already dispensing**
- **Evidence of public-health effectiveness**
- **Gonorrhoea vaccine combined with dPEP could be a game changer**
- **Questions remain about cost and cost-effectiveness**