

USE OF DOXYCYCLINE AS PRE- AND POST-EXPOSURE PROPHYLAXIS FOR STIs

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DISCLOSURES

I have no relevant disclosures or conflicts of interest to declare

WHAT IS STI PROPHYLAXIS?
'DOXYPEP' OR 'DOXYPREP'

DOXYCYCLINE PROPHYLAXIS

- Use of Doxycycline to prevent bacterial sexually transmitted infections
- Post-exposure prophylaxis (PEP) 200mg taken within 24-72 hours of sex
- Pre-exposure prophylaxis (PrEP) 100mg taken daily
- Predominantly used and studied in men who have sex with men
- Self sourced online (legal & illegal pharmacies) or use leftover antibiotics
- Doxycycline (Tetracycline)
 - Used to treat Chlamydia, Syphilis, Mycoplasma Genitalium
 - Not recommended for Gonorrhoea treatment: >50% resistance reported in most studies
 - Also used for acne, malaria prophylaxis, Lyme disease, respiratory infections, rosacea, cellulitis
 - SEs: GI upset, headache, photosensitivity, skin reactions, oesophageal ulceration

WHY?

- Bacterial STIs are increasing, particularly among MSM
- HIV PrEP and contraception provide a roadmap for alternatives to condoms
- Allows combination interventions & provides choice
- Antibiotic resistance in Chlamydia and Syphilis rare
- 8% ocular or neurological Syphilis complications

WHAT IS THE EVIDENCE?

RANDOMISED CONTROL TRIALS

- Bolan et al. (2015)
 - Los Angeles; 30 MSM living with HIV.
 - Doxycycline 100mg daily for 48 weeks (PrEP)
 - **73%** reduction in bacterial STI (Chlamydia, Syphilis, Gonorrhoea)
- Molina et al. (2018)
 - France; 232 participants on HIV-PrEP
 - Single-dose 200mg Doxycycline within 24-72h after sex
 - **47% relative risk reduction** of first STI
 - **70%** RR reduction in Chlamydia. **73%** RR reduction in Syphilis
 - No reduction in Gonorrhoea

RANDOMISED CONTROL TRIALS

- Luetkemeyer et al. DOXYPEP. (2022, International AIDS Conference)
 - USA; MSM and Trans women on HIV-PrEP or living with HIV.
 - Single-dose 200mg Doxycycline within 24 after condomless sexual contact
 - **65%** reduction in STI incidence / quarter
 - **55-57%** reduction in Gonorrhoea
 - **74-88%** reduction in Chlamydia
 - **77-87%** reduction in Syphilis
 - 54% took <10 doses / month

DOES DOXY-PEP WORK AGAINST GONORRHOEA?

- 55-57% reduction in Gonorrhoea in DOXYPEP study (USA)
 - 25% baseline Gonorrhoea tetracycline resistance
 - Consistent with US national population level data (20%)
- No reduction in Molina et al. DoxyPEP study
 - Smaller trial
 - 56% Gonorrhoea tetracycline resistance
- UK Health Security Agency data (2020) 65% tetracycline resistance

HOW MANY AND WHO EXACTLY?

HOW MANY MSM USING HIV PREP ARE USING ANTIBIOTIC PROPHYLAXIS?



8% - Dean St Survey, London 2018



9.9% - Melbourne 2018



2.2% - Netherlands 2020



5% - Brighton, UK 2022



3.2% - Belgium 2022



9% - Online UK 2020

WHO IS USING IT AND INTERESTED?

O'Halloran et al. 2020 (UK)

- Factors associated with use: 5+ condomless sex partners, chemsex, recent STI diagnosis

Park et al. 2021 (USA)

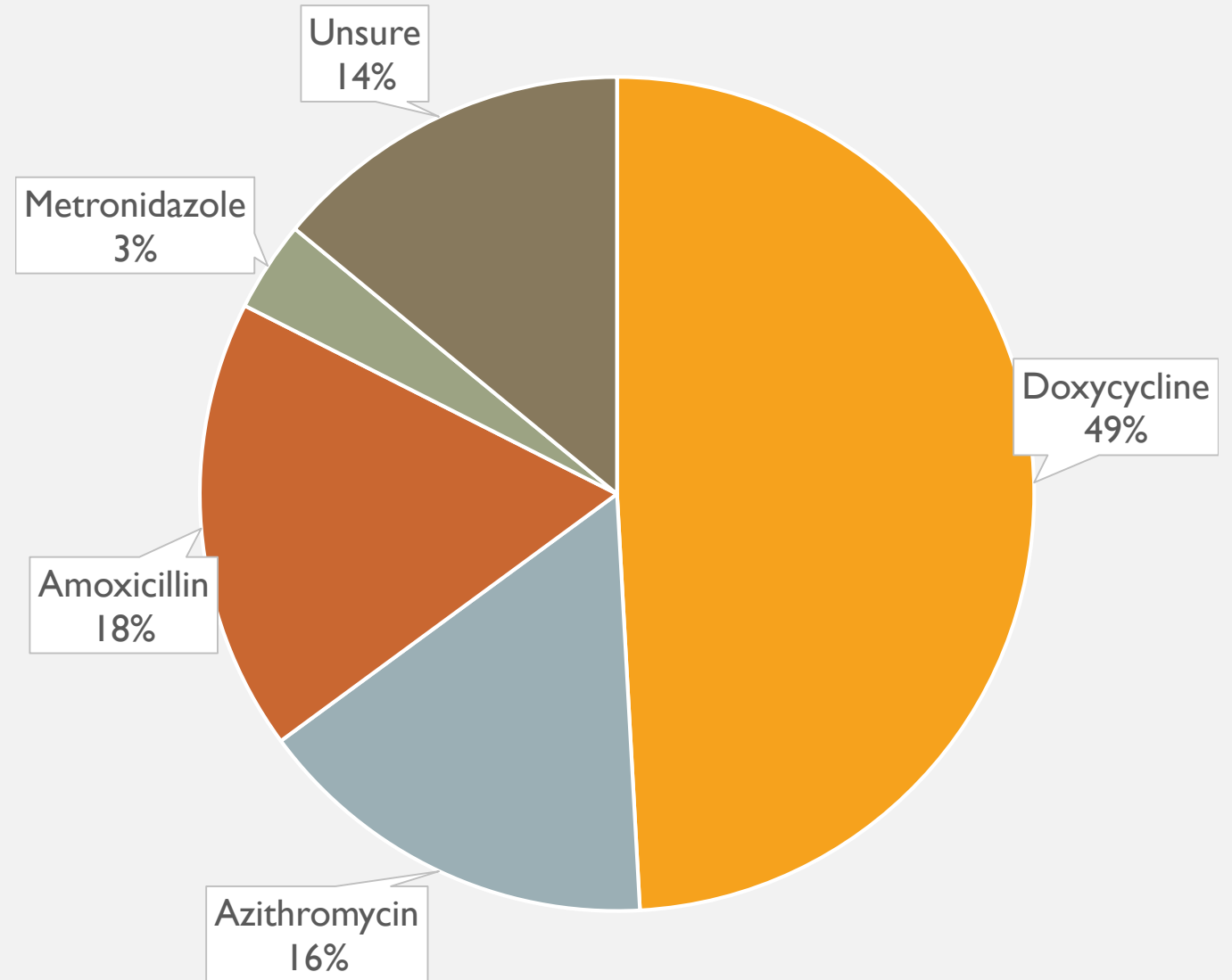
- 68% MSM would take if offered
- 90% Healthcare providers would prescribe if recommended by CDC
- Only 43% HCP willing if not recommended

Spinelli et al. 2019 (USA)

- 84% MSM surveyed on dating app interested in Doxy PEP/PrEP

WHAT ANTIBIOTICS?

- Data from UK online survey (Kohli et al. 2022)
- 1,520 MSM
- 3.6% ever used STI prophylaxis
 - HIV PrEP users – 6.2%
 - MSM living with HIV – 6.9%
 - HIV negative & not using HIV PrEP – 1.9%



WHAT ARE THE CONCERNS?

ANTIBIOTIC RESISTANCE

- Drive antibiotic resistance in other organisms
- No established standards for identifying emergent doxycycline resistance in syphilis, chlamydia or mycoplasma genitalium
- No tetracycline resistance in Syphilis found; macrolide resistance > a single point mutation
- Large systematic reviews & meta-analyses > resistant organisms post treatment for respiratory infections/UTIs at an individual level (Costelloe et al. 2010; Bryce et al. 2016)
- Doxycycline use for acne associated with resistance in other organisms (Farrah et al. 2016)
- No association seen with malaria prophylaxis and staph aureus tetracycline resistance (Mende et al. 2016)
- Macrolide (azithromycin) in enteric STIs such as Shigella

MORE DATA NEEDED

IMPACT ON GUT MICROBIOME
AND OTHER COMMENSALS

STATEMENTS AND GUIDANCE



Public Health
England



CDC Response to Doxy-PEP d International AIDS Conferenc July 27, 2022 – CDC Response to presentation of Doxy-PEP clinical

Position
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Key Points

- Doxycycline (STIs) is
- Any potential
- Further doxycycline level.
- We recommend professional

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In the coming months, CDC in collaboration with BASHH will develop interim clinical guidance, as well as to

Research questions on this topic will address:

- Clarifying frequency/population with which
- Understanding the individual health risks
- Weighing the public health risks vs. benefits
- Determining optimal groups for this target

Box 1: Recommendations for clinicians

- Make asking about the recent use of antibiotics, for any reason, routine. This includes

Sexually Transmitted Infections Treatment Guidelines, 2021

Doxy-PEP as an STI Prevention Strategy: Considerations for Individuals and Healthcare Providers of Gay or Bisexual Men or Transgender Women

As CDC and others work quickly to [evaluate data](#) to inform clinical guidance on the safe and effective use of doxycycline post-exposure prophylaxis (doxy-PEP) to prevent gonorrhea, chlamydia, and syphilis, we acknowledge there are individuals and clinicians who are already engaged in the off-label use of doxycycline as bacterial STI post-exposure prophylaxis or considering it. As such, we are providing the following considerations to inform those decisions:

- [Current efficacy data](#) [↗](#) only applies to gay and bisexual men and transgender women. Studies among heterosexual cis-gender women are ongoing.
- Doxycycline 200 mg administered within 24-72 hours of condomless sex was the regimen evaluated in this study. Other antibiotics should not be considered for PEP.
- In addition to informing patients about the potential STI prevention benefits of doxy-PEP, providers should also counsel patients about potential adverse side effects of doxycycline including phototoxicity, gastrointestinal symptoms, and more rarely esophageal ulceration.
- Providers should continue to screen, test, and treat for bacterial STIs in accordance with [CDC's STI Treatment Guidelines](#) and [CDC's PrEP for the Prevention of HIV guidelines](#) [↗](#), even among people who may be using doxycycline as PEP or PrEP.

CLINICAL TRIALS .GOV

	Title	Status	Conditions	Interventions
1	Combined Prevention of Sexually Transmitted Infections (STIs) in Men Who Have Sex With Men and Using Oral Tenofovir Disoproxil Fumarate/ Emtricitabine (TDF/FTC) for HIV Pre-Exposure Prophylaxis (PrEP)	Recruiting	<ul style="list-style-type: none"> •Unsafe Sex •Risk-Taking 	<ul style="list-style-type: none"> •Drug: Experimental: doxycycline •Biological: Bexsero® vaccine
2	Impact of the Daily Doxycycline Pre-exposure Prophylaxis (PrEP) on the Incidence of Syphilis, Gonorrhoea and Chlamydia	Recruiting	<ul style="list-style-type: none"> •STIs Prevention 	<ul style="list-style-type: none"> •Drug: Doxycycline
3	Evaluation of Doxycycline Post-exposure Prophylaxis to Reduce Sexually Transmitted Infections in PrEP Users and HIV-infected Men Who Have Sex With Men	Active, not recruiting	<ul style="list-style-type: none"> •Gonorrhea •Chlamydia •Syphilis 	<ul style="list-style-type: none"> •Drug: Doxycycline Hyclate Delayed-Release 200 mg
4	Combo-PEP: Multipurpose Prevention of Post-Exposure Prophylaxis Regimens	Recruiting	<ul style="list-style-type: none"> •Sexually Transmitted Diseases 	<ul style="list-style-type: none"> •Drug: Doxycycline •Drug: Biktarvy
5	Doxycycline Intervention for Bacterial STI Chemoprophylaxis (DISCO)	Not yet recruiting	<ul style="list-style-type: none"> •Bacterial Sexually Transmitted Diseases 	<ul style="list-style-type: none"> •Drug: Doxycycline Hyclate
6	Doxycycline PEP for Prevention of Sexually Transmitted Infections Among Kenyan Women Using HIV PrEP	Active, not recruiting	<ul style="list-style-type: none"> •HIV Infections •HIV/AIDS •Neisseria Gonorrhoeae Infection •Chlamydia Trachomatis Infection •Syphilis Infection 	<ul style="list-style-type: none"> •Drug: Doxycycline
7	Oral Doxycycline for the Prevention of Syphilis in Men Who Have Sex With Men (DaDHS)	Unknown status	<ul style="list-style-type: none"> •Syphilis •Sexually Transmitted Infections 	<ul style="list-style-type: none"> •Drug: Doxycycline •Other: Placebo
8	Tenofovir/Emtricitabine With Doxycycline for Combination HIV and Syphilis Pre-exposure Prophylaxis in HIV-negative MSM	Unknown status	<ul style="list-style-type: none"> •HIV •Syphilis 	<ul style="list-style-type: none"> •Drug: Doxycycline 100mg PO daily x 12 months •Drug: Tenofovir/emtricitabine 200/300mg PO daily •Drug: Doxycycline 100mg PO daily x 6 months

SUMMARY

- Increasing evidence of effectiveness for doxycycline, with more studies ongoing
- High interest among MSM surveyed
- Self-sourcing antibiotics – mainly but not exclusively doxycycline
- Not currently endorsed by UKHSA or BASHH
- Some guidance available and more in development (CDC)
- Questions remain
 - Gonorrhoea in all contexts?
 - Antibiotic resistance emergence risk?
 - Impact on other bacteria / microbiome?
 - Self sourcing vs clinician led? Patient choice?
 - Do benefits actually outweigh risks?
- Doxycycline used long-term for other conditions, why not for STI prevention?

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THANK YOU!

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