Ending the STI Epidemic Through Prevention: The Role of Doxy-PEP

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Objectives

1. Review the state of the HIV/STI Epidemic
2. Summarize the current landscape of HIV/STI prevention options
3. Appraise new methods for STI prevention like Doxy-PEP
4. Discuss implementation of Doxy-PEP

PTC Disclaimer

Some terms in this presentation may have been modified to align with executive order requirements that this CDC-funded grant has received.

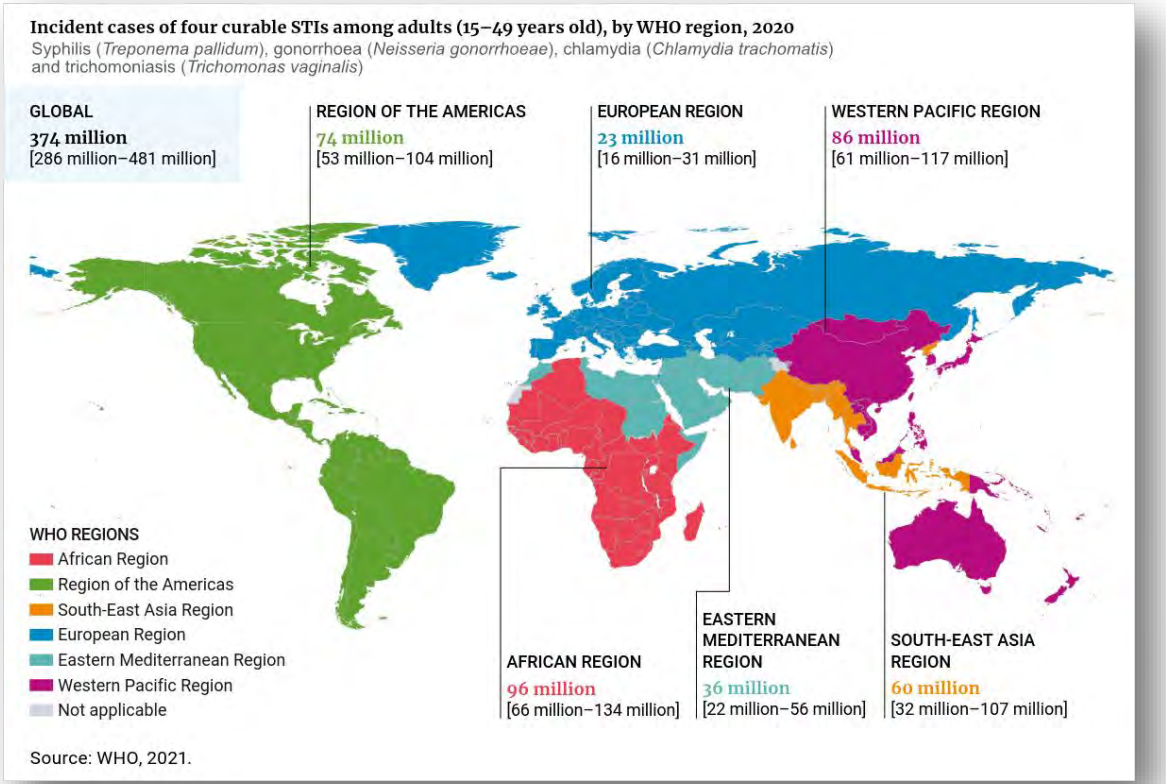
Audience Poll #1

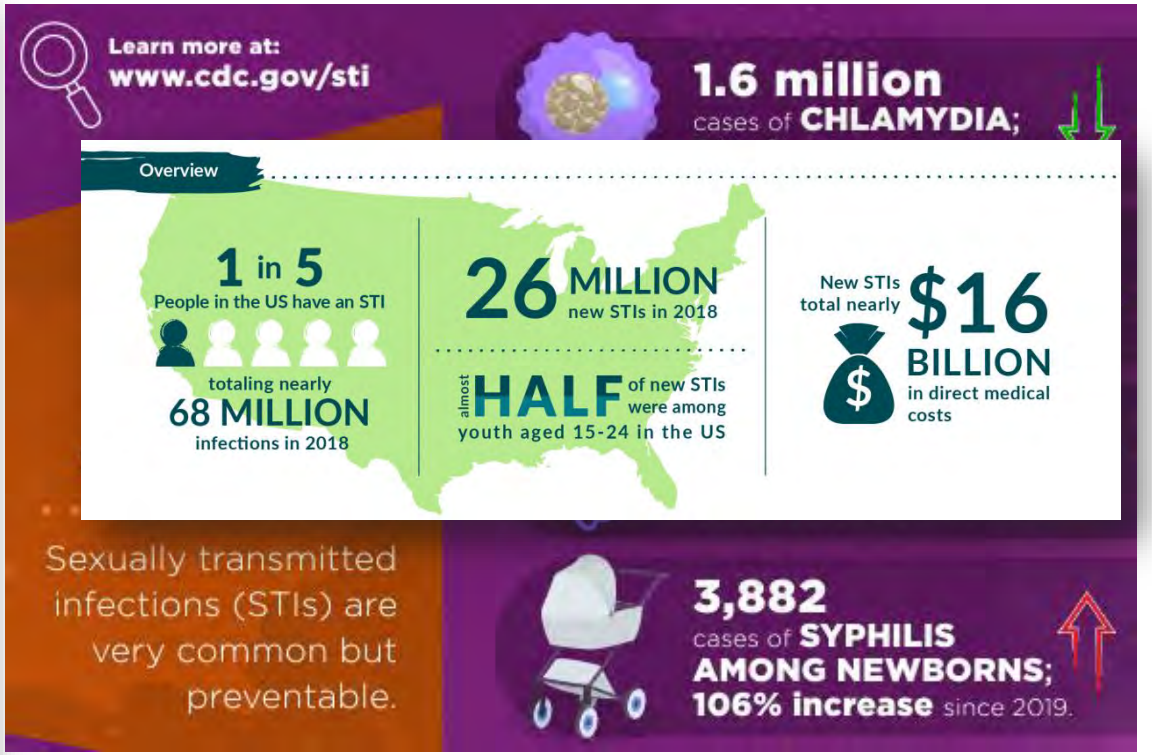
Where is your clinic on your Doxy-PEP Journey? (Choose the closest)

1. We offer Doxy-PEP routinely to all patients
2. We offer Doxy-PEP routinely to patients with an STI in the prior 12 months
3. We offer Doxy-PEP in patients who ask for it
4. We don't offer Doxy-PEP currently but are planning to in the next 6 months
5. We don't offer Doxy-PEP currently but may in the future
6. We do not have plans to offer Doxy-PEP

Sexually Transmitted Infections (STIs) Are Prevalent

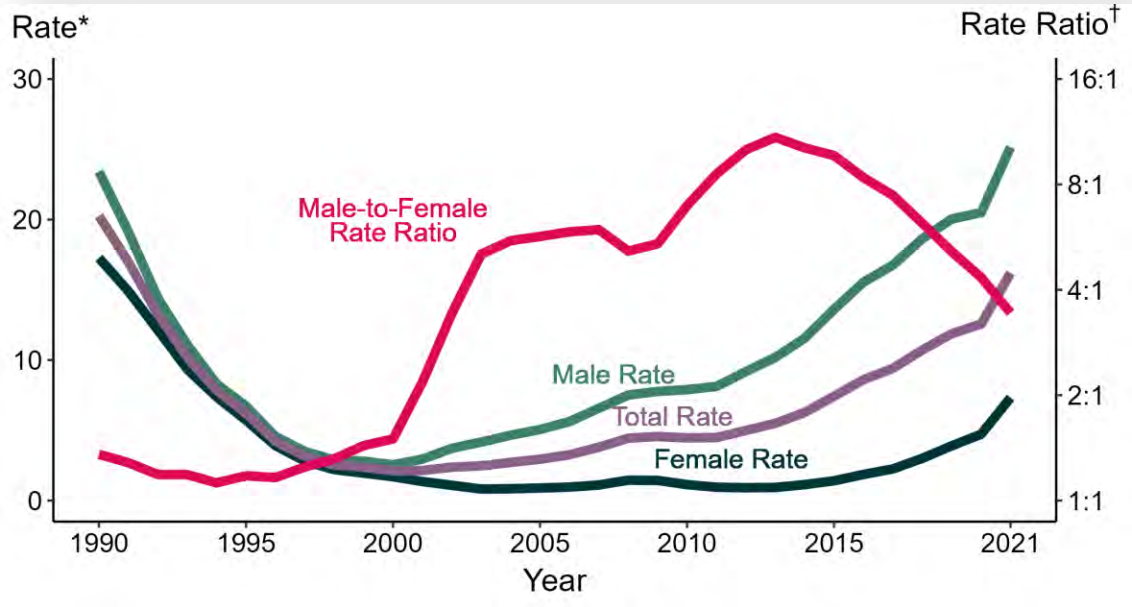
1 Million STIs are Acquired Every Day



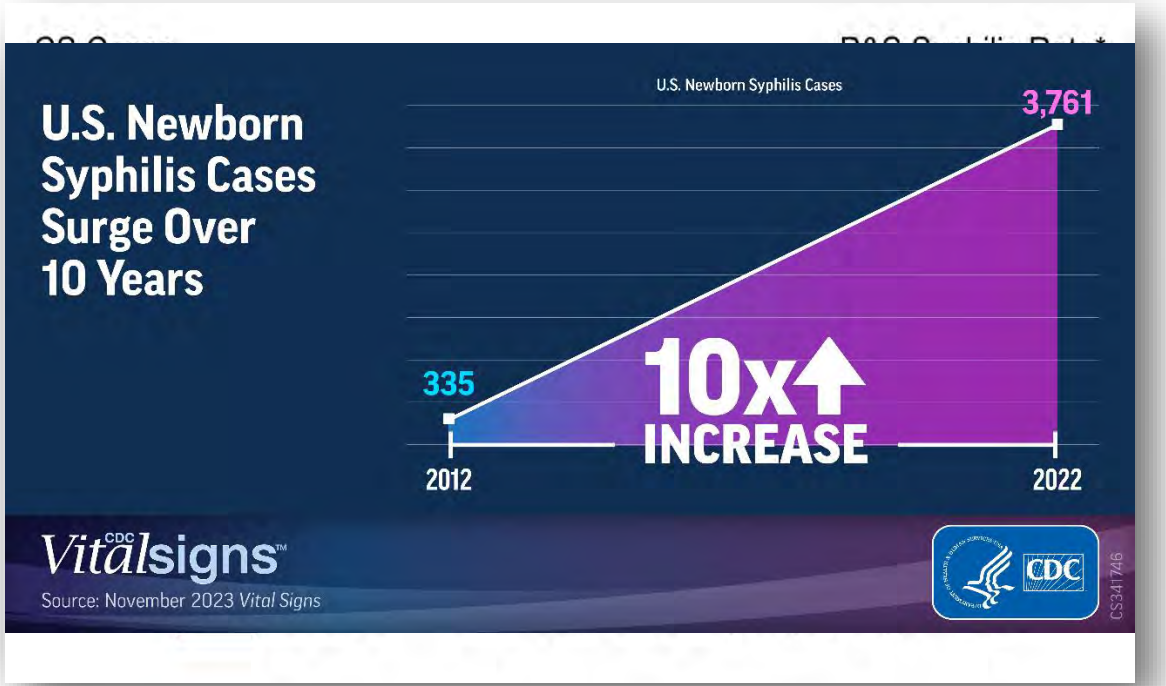


Why Do We Need to Prevent STIs?

Male to Female Ratio - Syphilis



Congenital Syphilis



- https://www.cdc. /std/statistics/2021/default.htm

Why Do We Need to Prevent STIs?

Rising Gonorrhea Resistance

The Commonwealth of Massachusetts
Executive Office of Health and Human Services
Department of Public Health
Bureau of Infectious Disease and Laboratory Sciences
305 South Street, Boston, MA 02130

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CLINICAL ALERT
January 19, 2023

MULTI-DRUG NON-SUSCEPTIBLE GONORRHEA IN MASSACHUSETTS

- A novel strain of multidrug-non-susceptible *Neisseria gonorrhoeae* with reduced susceptibility to ceftriaxone, cefixime, and azithromycin, and resistance to ciprofloxacin, penicillin, and tetracycline, has been identified in a Massachusetts resident. Although ceftriaxone 500 mg IM was effective at clearing infection for this case, this is the first isolate identified in the United States to demonstrate resistance or reduced susceptibility to all drugs that are recommended for treatment.
- Enhanced surveillance has identified a second isolate that, based on its genome, likely has similarly reduced susceptibility to ceftriaxone and cefixime.

Why Do We Need to Prevent STIs?

- **STIs Are Not Benign**
  - Pelvic inflammatory disease
  - Chronic pelvic pain
  - Infertility
  - Adverse pregnancy outcomes
    - Prematurity
    - Stillbirth
  - Urethral strictures
  - Gastrointestinal fistulas
  - Peri-rectal abscesses
  - Severe complications of syphilis
    - Permanent hearing or vision impairment

STI Prevention Landscape

- Illustrated by Barolini, Nicoletta. 2024.

Audience Poll #2

Which Prevention Method Are You Least Likely to Offer Patients Regularly? (Choose the closest)

1. Barrier protection (condoms)
2. Risk reduction counseling
3. Vaccination
4. Medication prophylaxis
5. Routine screening
6. Symptomatic treatment
7. Presumptive Treatment
8. Partner Services (bringing the partner into clinic)
9. Expedited partner therapy

Medication Prophylaxis

Medication Prophylaxis

1. **HIV post-exposure prophylaxis (PEP)**
2. HIV pre-exposure prophylaxis (PrEP)

Medication Prophylaxis

Medication Prophylaxis

1. HIV post-exposure prophylaxis (PEP)
2. **HIV pre-exposure prophylaxis (PrEP)**

Medication Prophylaxis

Medication Prophylaxis

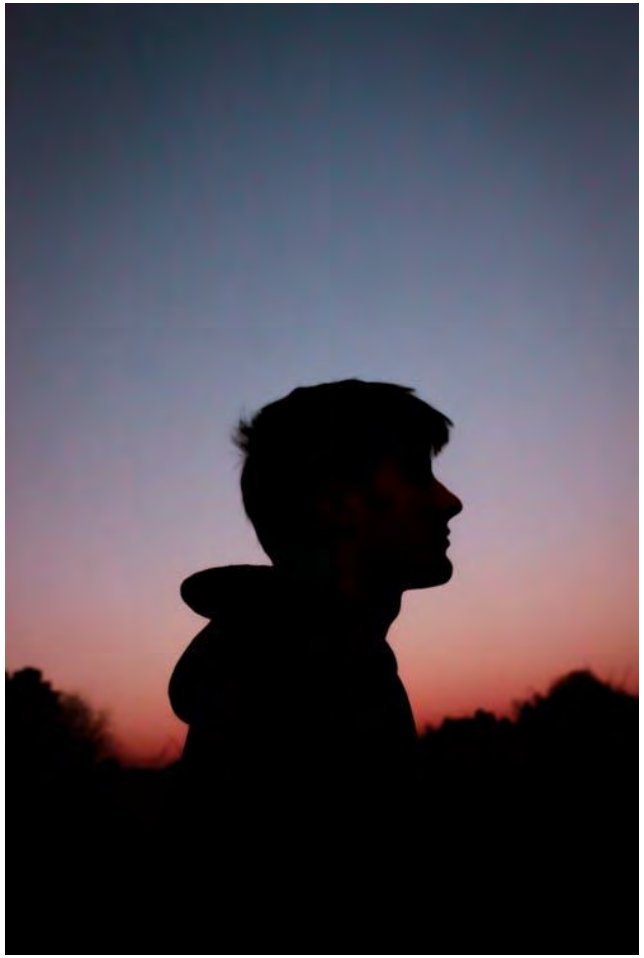
1. HIV post-exposure prophylaxis (PEP)
2. HIV pre-exposure prophylaxis (PrEP)
3. **Doxy-PEP**

Meet Marcus

- 29-year-old male in New York City
- Takes HIV PrEP for HIV prevention
- Sexually active with men
  - Four partners since his last visit, no condom usage
- Walks into clinic due with 2 days of green penile discharge

- **Routine testing for HIV, syphilis, and three-site gonorrhea/chlamydia testing performed**

- **Treated empirically with Ceftriaxone and Doxycycline**



Marcus's Prevention Plan

Primary Prevention

Vaccination

- HPV
- Hepatitis A/B
- Meningococcal ACYW
- Mpox

Medication

- HIV PrEP

Secondary Prevention

Routine screening

- Q3 Month Screening

Syndromic testing/treatment

Presumptive treatment

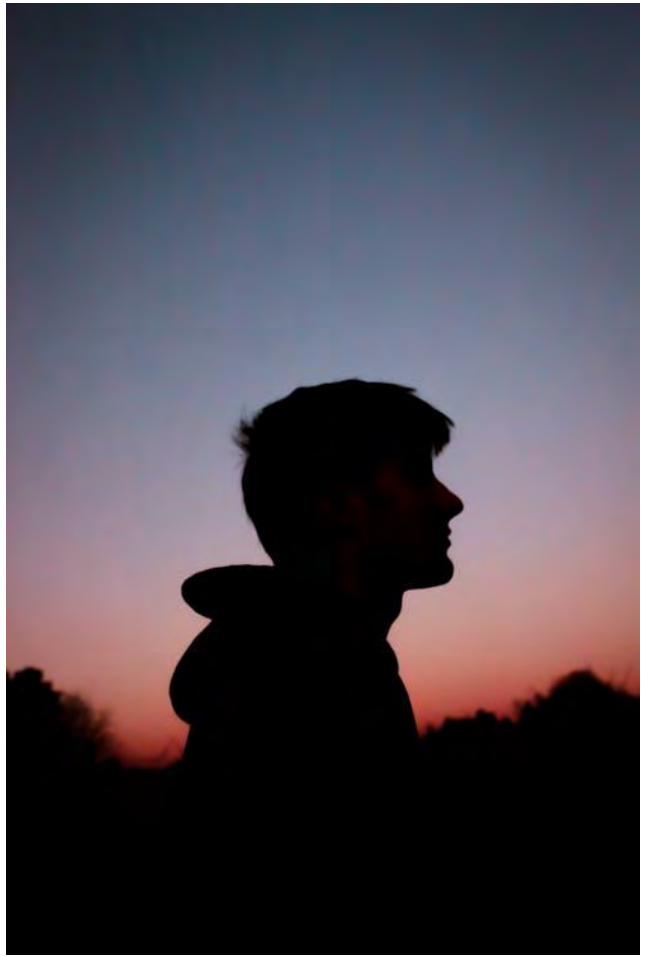
Marcus's Results

Lab results:
HIV Ab/Ag - Negative
Urine GC/CT – GC positive
Pharyngeal GC/CT – GC positive
Rectal GC/CT – GC positive
RPR – 1:128 - 1:4 - 2 months ago

Received additional 7 days (total 14 days) of doxycycline for early latent syphilis due to the BPG shortage at the time

Marcus

- Returned 6 weeks later
- **“I got totally better but now it hurts again when I pee”**
  - Seven partners since his last visit
  - Is sure that his regular partners got treated for gonorrhea and syphilis
  - Repeat routine testing for HIV, syphilis, and three-site gonorrhea/chlamydia testing was performed
  - Treated empirically with Ceftriaxone and Doxycycline



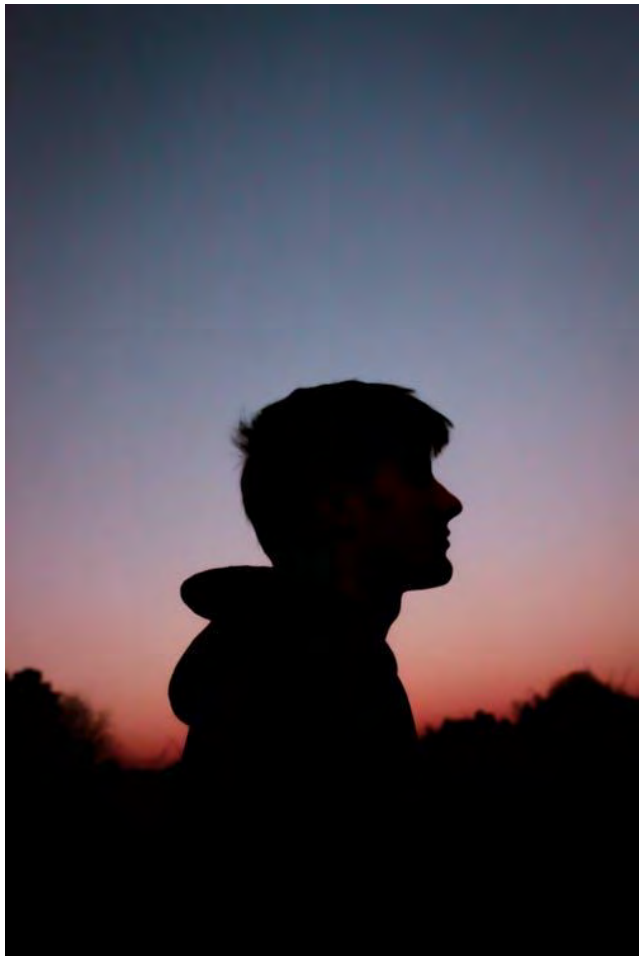
Marcus's Results

Lab results:
HIV Ab/Ag - Negative
Urine GC/CT – GC positive
Pharyngeal GC/CT – GC positive
Rectal GC/CT – CT positive
RPR – 1:32 - 1:128 – 6 weeks ago

Marcus

- Called to give Marcus his results and he was pretty upset

- **“This is frustrating, is there anything I can do so I stop getting STIs?”**



Medication Prophylaxis

Medication Prophylaxis

1. HIV post-exposure prophylaxis (PEP)
2. HIV pre-exposure prophylaxis (PrEP)
3. **Doxy-PEP**

What is Doxy-PEP?

- Doxycycline
- 200mg by mouth
- Up to 72 hours after
- A condomless sexual encounter at any anatomic site

What Do I Need To Know About Doxy-PEP?

- Benefits (i.e., does it work)
- Risks (i.e., does it harm)
- Implementation (i.e., how can I give it)

Benefits:
Does Doxy-PEP Prevent STIs?

Audience Poll #3

Approximately how effective is Doxy-PEP against chlamydia and syphilis? (Choose the closest)

1. 100%
2. 80%
3. 50%
4. 20%
5. 0%

Does Doxy-PEP Prevent STIs?

ORIGINAL ARTICLE

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

Anne F. Luetkemeyer, M.D., Deborah Donnell, Ph.D., Julia C. Dombrowski, M.D., M.P.H., Stephanie Cohen, M.D., M.P.H., Cole Grabow, M.P.H., Clare E. Brown, Ph.D., Cheryl Malinski, B.S., Rodney Perkins, R.N., M.P.H., Melody Nasser, B.A., Carolina Lopez, B.A., Eric Vittinghoff, Ph.D., Susan P. Buchbinder, M.D., Hyman Scott, M.D., M.P.H., Edwin D. Charlebois, Ph.D., M.P.H., Diane V. Havlir, M.D., Olusegun O. Soge, Ph.D., and Connie Celum, M.D., M.P.H., for the DoxyPEP Study Team*

Post-exposure prophylaxis with doxycycline to prevent sexually transmitted infections in men who have sex with men: an open-label randomised substudy of the ANRS IPERGAY trial

Jean-Michel Molina, Isabelle Charreau, Christian Chidiac, Gilles Pialoux, Eric Cua, Constance Delaugerre, Catherine Capitant, Daniela Rojas-Castro, Julien Fonsart, Béatrice Herrou, Cécile Bébéar, Laurent Cotte, Olivier Robineau, François Raffi, Pierre Chastenneau, Alexandre Aslan, Julie Chas, Laurence Nicolaïdis, Briana Spire, Luis Segpon-Teyssier, Diane Lorette, Soizic Le Mestre, Véronique Doré, Laurence Meyer, for the ANRS IPERGAY Study Group*

Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women

Jenell Stewart, D.O., M.P.H., Kevin Oware, M.A., Deborah Donnell, Ph.D., Lauren R. Violette, M.P.H., Josephine Odoyo, R.N., M.P.H., Olusegun O. Soge, Ph.D., Caitlin W. Scoville, M.P.H., Victor Omollo, M.B., Ch.B., M.P.H., Felix O. Mogaka, M.B., Ch.B., Fredericka A. Sesay, M.B., Ch.B., M.P.H., R. Scott McClelland, M.D., M.P.H., Matthew Spinelli, M.D., M.P.H., Monica Gandhi, M.D., M.P.H., Elizabeth A. Bukusi, M.B., Ch.B., M.Med., M.P.H., Ph.D., and Jared M. Baeten, M.D., Ph.D., for the dPEP Kenya Study Team*

Doxycycline to prevent bacterial sexually transmitted infections in the USA: final results from the DoxyPEP multicentre, open-label, randomised controlled trial and open-label extension

Anne F Luetkemeyer, Deborah Donnell, Stephanie E Cohen, Julia C Dombrowski, Cole Grabow, Grace Hasen, Clare Brown, Chase Cannon, Cheryl Malinski, Rodney Perkins, Melody Nasser, Carolina Lopez, Robert J Suchland, Eric Vittinghoff, Susan P Buchbinder, Hyman Scott, Edwin D Charlebois, Diane V Havlir, Olusegun O Soge, Connie Celum

Doxycycline prophylaxis and meningococcal group B vaccine to prevent bacterial sexually transmitted infections in France (ANRS 174 DOXYVAC): a multicentre, open-label, randomised trial with a 2×2 factorial design

Jean-Michel Molina, Beatrice Bercot, Lambert Assoumou, Emma Rubenstein, Michèle Algarte-Genin, Gilles Pialoux, Christine Katlama, Laure Surgers, Cécile Bébéar, Nicolas Dupin, Mousso Ouattara, Laurence Slama, Juliette Pavie, Claudine Duvivier, Bénédicte Laze, Lourenco Goldwirt, Severine Gibowski, Marion Ollivier, Jade Ghosn, Dominique Costagliola, for the ANRS 174 DOXYVAC Study Group*

What We Know About Doxy-PEP From Trials

Randomized Controlled Trials of Doxy-PEP		
Study	**Population**	**Effectiveness**
IPERGAY	MSM/TGW taking PrEP	**Reduction** in time to first STI HR 0.53 (0.33-0.85) reduction seen in CT and syphilis but **NOT** GC
DoxyPEP	MSM/TGW taking PrEP or PWH	**Reduction** in STI per quarter RR 0.38 (0.24-0.6)
DoxyVac	MSM taking PrEP	**Reduction** in time to first CT or syphilis HR 0.16 (0.08-0.30). Reduction in time to girst GC HR 0.49 (0.32 – 0.76)
dPEP	Females taking PrEP	**No reduction** in STI incidence RR 0.88 (0.6-1.29)

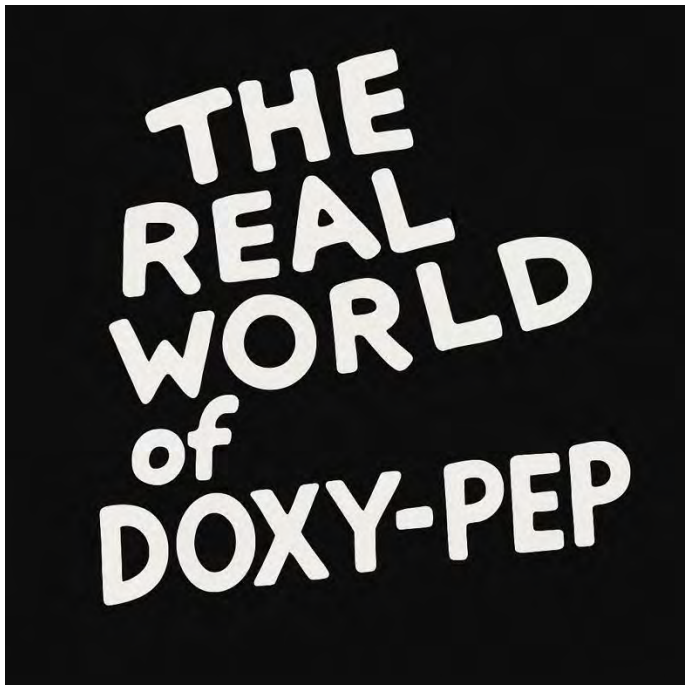
MSM = men who have sex with men, TGW = transgender women, PWH = Persons with HIV, GC = gonorrhea, CT = chlamydia, OR = odds ratio, HR = hazards ratio, RR = relative risk reduction

- Doxycycline **post-exposure prophylaxis** (PEP) is safe and well tolerated
- Doxy-PEP **prevents** STIs in MSM and transgender women
- Doxy-PEP **did not** prevent STIs in cis-women in the dPEP study

More To Come

- **Syphilaxis** (Australia) - Comparing Doxycycline PrEP vs PEP
- **CTN 313: The DaDHS Trial** – Comparing Doxycycline PrEP vs placebo
- **DISCO** - Comparing Doxycycline PrEP vs PEP
- **FoXXy Doxy** – ATN/HPTN trial in people with vaginas

Benefits:
Does Doxy-PEP Prevent STIs?



The Real World - Males

Study & Location	Population	Results	Timeframe
San Francisco (Public Health Clinics) Sankaran et al., JAMA Intern Med 2025	MSM, TGW	Chlamydia ↓ 50%; Syphilis ↓ 51%; Gonorrhea ↑ slightly	13 mo
California – Kaiser Permanente Traeger et al., JAMA Intern Med 2025	HIV PrEP users	Chlamydia ↓ 9.6%→2%; Syphilis ↓ 1.7%→0.3%; Gonorrhea ↓ slightly; stable in non-users	Quarterly
San Francisco (96 Weeks) Spinelli et al., Clin Infect Dis 2025	4,592 PrEP pts (55% Doxy-PEP; incl. PLWH, trans men, cis women)	Sustained ↓ Chlamydia & Syphilis (AOR 0.17); Gonorrhea ↓ initially then ↑ (AOR 1.28)	96 wk
Chicago (CDPH Clinics) Luc et al., Sex Transm Dis 2025	219 young MSM	Overall STI ↓ 77%; Chlamydia ↓ 78%; Syphilis: none; Gonorrhea ↓ 54%	2024
Philadelphia (Public STI Clinic) Lewis et al., Sex Transm Dis 2025	508 MSM on PrEP	Any STI ↓ 39%; Chlamydia ↓ 60%; Gonorrhea ↓ 51%; crossover confirmed	2019–23
New York City (CHP) Zucker et al., AJPH 2025	100 early adopters (gbMSM, TGW; 12% PLWH, rest on PrEP)	Any STI ↓ 14%→7.9%; Chlamydia ↓ 11.9%→2.8% (IRR 0.30); Gonorrhea NS	9 mo pre vs post
Boston (MGH Sexual Health Clinic) Raccagni et al., JAC-AMR 2025	670 pts (24% of clinic)	Chlamydia ↓ 8.5%→3.9%; Syphilis ↓ 2.4%→1.4%; Gonorrhea NS; spillover benefit seen in non-users	Year 1

Implementation – Barriers & Facilitators (Kenya Women's Trial)

- Qualitative sub-study of 69 young women (18–30, Kisumu, Kenya) in dPEP trial
- Barriers to adherence:
  - Side effects (esp. nausea on empty stomach)
  - Pill burden (dPEP + daily HIV PrEP)
  - Stigma, privacy concerns
  - Partner disapproval & conflict
  - Forgetfulness, routine disruptions
- Facilitators:
  - Belief in effectiveness
  - Discreet pill carriers (lipstick containers)
  - Social/family encouragement
  - Integration into routines
- **Suggests adherence challenges, not drug ineffectiveness, explain null results**

Table 2 Barriers and Facilitators Identified in The Interviews, Grouped by Time Points

Theme	Month 1 (Initial IDIs)	Month 6 (IDIs)	Month 12 (IDIs at Exit)	FGDs (after study exit)
Barriers				
Side Effects	✓ (28/40)	✓ (15/40)	✓ (25/40)	✓
Stigma and Privacy Concerns	✓ (21/40)	✓ (27/40)	✓ (15/40)	✓
Forgetfulness and Routine Disruptions	✓ (8/40)	✓ (16/40)	✓ (20/40)	✓
Partner Influence and Reactions	✓ (13/40)	✓ (14/40)		✓
Pregnancy and Health Concerns		✓ (5/40)		
Access Issues			✓ (5/40)	
Facilitators				
Perceived Effectiveness/Protection	✓ (12/40)	✓ (15/40)	✓ (30/40)	✓
Use of Discreet Pill Carriers	✓ (10/40)	✓ (16/40)	✓ (15/40)	✓
Social Support and Encouragement	✓ (9/40)	✓ (14/40)	✓ (20/40)	✓
Routine Integration	✓ (7/40)	✓ (14/40)	✓ (25/40)	✓
Health Education and Provider Support		✓ (8/40)		
Fear Reduction		✓ (1/40)		
Positive Experiences and Benefits		✓ (7/40)		

- Kwach B et al. *BMC Infect Dis.* 2025

The Real World - Females

- Multi-center case series:
  - 35 AFAB patients
  - (<1% of 5U,744 Doxy-PEP users) at 4 U.S. SHCs
- Demographics:
  - Median age: 29 years
  - 83% transgender men, 14% cisgender women
  - 97% condomless sex with cis men
  - 23% sex work
  - 43% chemsex
- **Use**: Median 236 days; ~2 doses/month

- STI outcomes:
  - Pre-PEP: 46% had ≥1 STI
  - Post-PEP: 20% had ≥1 STI
  - Gonorrhea & M. genitalium most common
  - No pregnancies observed; pregnancy screening inconsistent
  - **Urgent need for efficacy data in female populations**

- Hazra A et al. *Sex Transm Dis.* 2025

Risks:
What Do We Know About The Risks of Doxy-PEP?

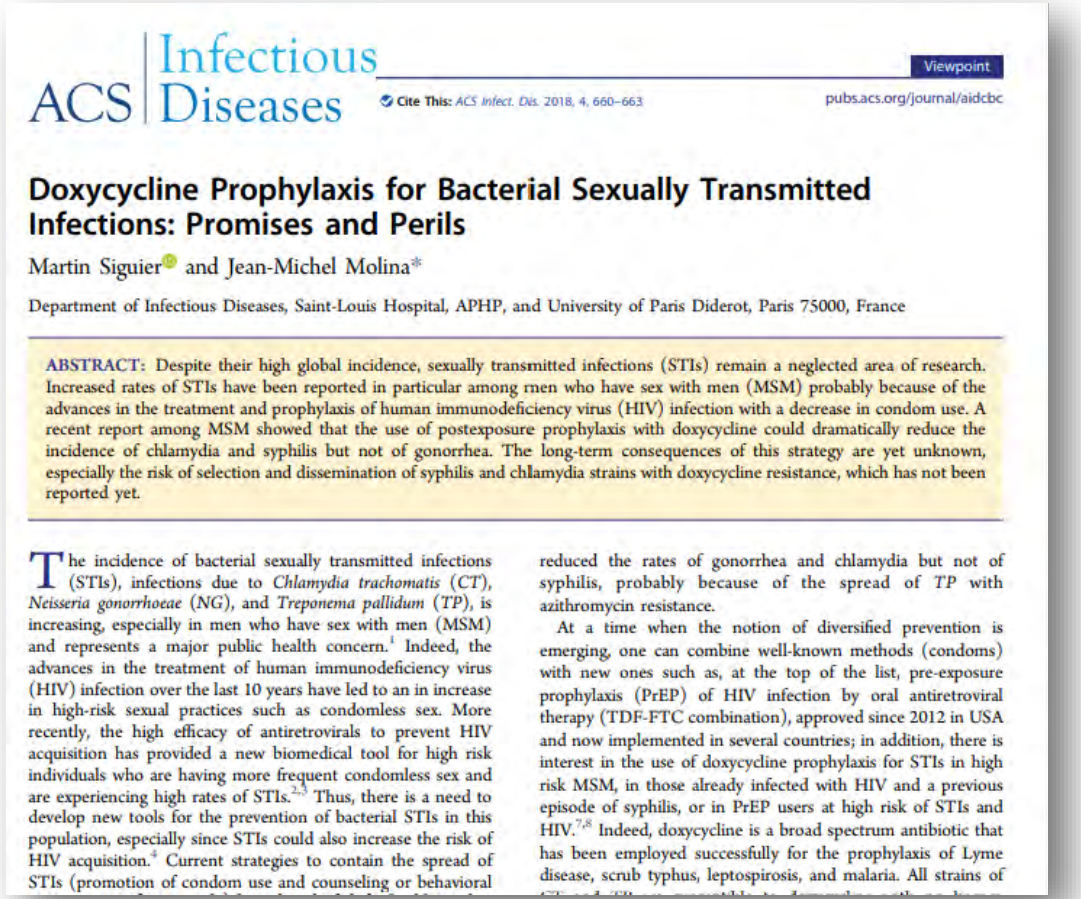
Audience Poll #4

What is your biggest concern about providing Doxy-PEP to patients?

(I know that many of them may apply)

1. It doesn't work (or won't work long-term)
2. Risk compensation (my patient may be more likely to have sex without barrier protection)
3. I am worried about it changing the presentation of STIs
4. I am worried about generating resistance to STIs
5. I am worried about generating resistance to commensal organisms like staph
6. Something else (please put it in the chat)

Doxy-PEP Concerns



ACS Infectious Diseases

Viewpoint

Cite This: ACS Infect. Dis. 2018, 4, 660−663

pubs.acs.org/journal/aidcbc

Doxycycline Prophylaxis for Bacterial Sexually Transmitted Infections: Promises and Perils

Martin Siguier and Jean-Michel Molina*

Department of Infectious Diseases, Saint-Louis Hospital, APHP, and University of Paris Diderot, Paris 75000, France

ABSTRACT: Despite their high global incidence, sexually transmitted infections (STIs) remain a neglected area of research. Increased rates of STIs have been reported in particular among men who have sex with men (MSM) probably because of the advances in the treatment and prophylaxis of human immunodeficiency virus (HIV) infection with a decrease in condom use. A recent report among MSM showed that the use of postexposure prophylaxis with doxycycline could dramatically reduce the incidence of chlamydia and syphilis but not of gonorrhea. The long-term consequences of this strategy are yet unknown, especially the risk of selection and dissemination of syphilis and chlamydia strains with doxycycline resistance, which has not been reported yet.

The incidence of bacterial sexually transmitted infections (STIs), infections due to *Chlamydia trachomatis* (*CT*), *Neisseria gonorrhoeae* (*NG*), and *Treponema pallidum* (*TP*), is increasing, especially in men who have sex with men (MSM) and represents a major public health concern.[1] Indeed, the advances in the treatment of human immunodeficiency virus (HIV) infection over the last 10 years have led to an in increase in high-risk sexual practices such as condomless sex. More recently, the high efficacy of antiretrovirals to prevent HIV acquisition has provided a new biomedical tool for high risk individuals who are having more frequent condomless sex and are experiencing high rates of STIs.[2,3] Thus, there is a need to develop new tools for the prevention of bacterial STIs in this population, especially since STIs could also increase the risk of HIV acquisition.[4] Current strategies to contain the spread of STIs (promotion of condom use and counseling or behavioral

reduced the rates of gonorrhea and chlamydia but not of syphilis, probably because of the spread of *TP* with azithromycin resistance.

At a time when the notion of diversified prevention is emerging, one can combine well-known methods (condoms) with new ones such as, at the top of the list, pre-exposure prophylaxis (PrEP) of HIV infection by oral antiretroviral therapy (TDF-FTC combination), approved since 2012 in USA and now implemented in several countries; in addition, there is interest in the use of doxycycline prophylaxis for STIs in high risk MSM, in those already infected with HIV and a previous episode of syphilis, or in PrEP users at high risk of STIs and HIV.[7,8] Indeed, doxycycline is a broad spectrum antibiotic that has been employed successfully for the prophylaxis of Lyme disease, scrub typhus, leptospirosis, and malaria. All strains of

- However, even if these results are encouraging, they should be taken with great caution:

1. Previous trials of antibiotic prophylaxis have shown only <u>limited and transient benefits</u>
2. <u>Risk compensation</u>…might offset early benefits
3. Antibiotic prophylaxis might <u>change the presentation</u> of STIs
4. Impact of doxycycline use on the microbiome remains to be assessed
    - Might <u>select for antibiotic resistance</u> outside the field of STIs
    - The greatest fear is by far the risk of selection of <u>doxycycline resistance to chlamydia and syphilis</u>

- Siguier M, Molina JM. Doxycycline Prophylaxis for Bacterial Sexually Transmitted Infections: Promises and Perils. ACS Infect Dis. 2018;4(5):660-663. doi:10.1021/acsinfecdis.8b00043

Clinical Questions

How will Doxy-PEP impact sexual behavior?	• DoxyPEP and DoxyVAC
	  • No impact on sexual behavior
	  • Changes in sexual behavior could impact Doxy-PEPs effectiveness since it is not 100% protective

Antibiotic prophylaxis may change the presentation or diagnosis of STIs	• Notable concern about the impact on syphilis serological testing
	  • Partial treatment
	  • Delayed diagnosis
	  • False negatives

Syphilis Serology Impacted by Doxy-PEP/PrEP?

Case report

INTERNATIONAL JOURNAL OF STD & AIDS

DOXY do, or DOXY Don't? Syphilis and doxycycline post-exposure prophylaxis: A case report

Omar Chircop[1], Courtney Jaggers[2], Martha Spiteri[3], Aaron Schembri[4] and Valeska Padovese[5]

International Journal of STD & AIDS
2025, Vol. 36(4) 324–326

DOI: 10.1177/09564624241308026
journals.sagepub.com/home/std
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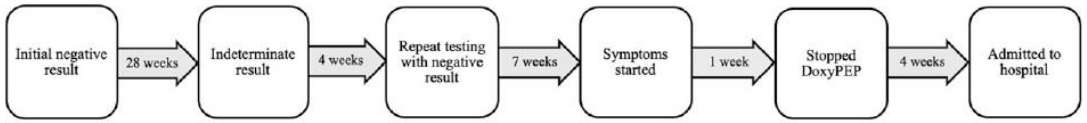


JOURNAL ARTICLE

A 24-year-old man taking PrEP with unusual syphilis test results

Get access ›

Marika L Forsythe, MD ✉, Hong-Kee Lee, PhD

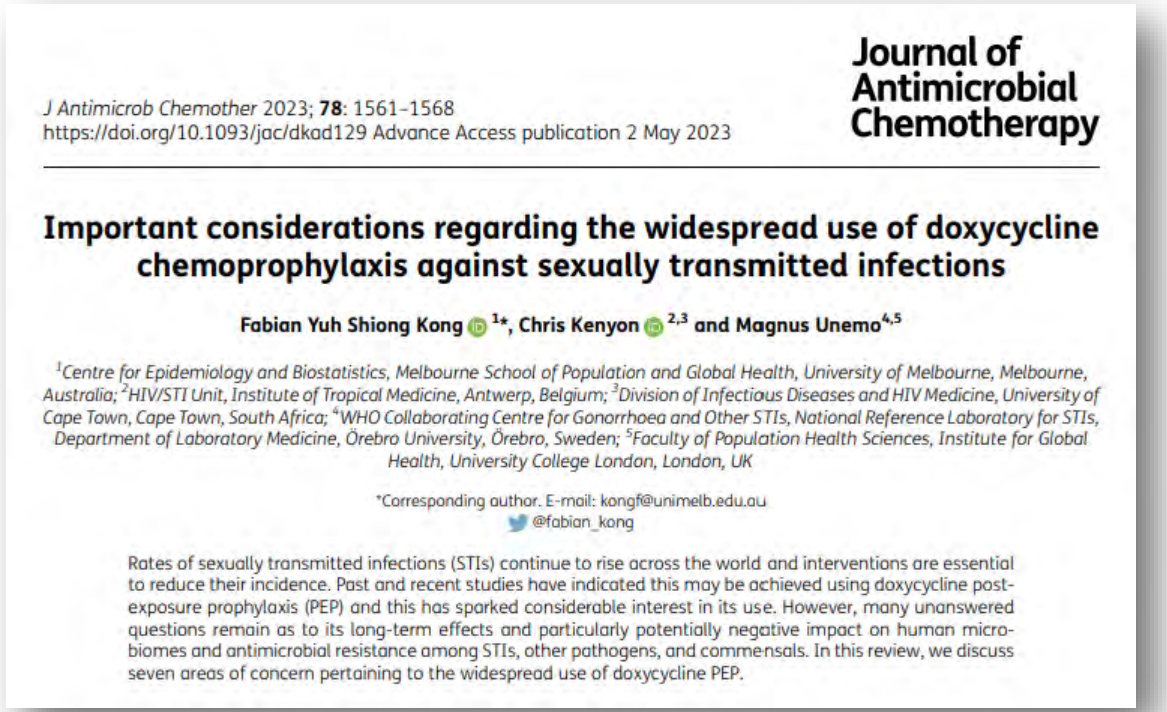
Laboratory Medicine, Volume 56, Issue 5, September 2025, Pages 550–553,
https://doi.org/10.1093/labmed/lmae114
Published: 29 March 2025

Table 1. Summary of the patient's laboratory results and subsequent interpretations regarding a syphilis diagnosis

Date	Test	Result, antibody index (AI)	Interpretation
July 16, 2022	Syphilis antibody, total	1.3 (reactive)	Negative
	RPR quantitative test	Nonreactive	
	Syphilis antibody, TP-PA	Nonreactive	
July 30, 2022	Syphilis antibody, total	1.0 (equivocal)	Negative
	RPR quantitative test	Nonreactive	
	Syphilis antibody, TP-PA	Nonreactive	
March 4, 2023	Syphilis antibody, total	>8.0 (reactive)	Negative
	RPR quantitative test	Nonreactive	
	Syphilis antibody, TP-PA	Nonreactive	
March 28, 2023	Syphilis antibody, total	6.0 (reactive)	Positive
	RPR quantitative test	Nonreactive	
	Syphilis antibody, Trep-Sure	Positive (reactive)	
November 10, 2023	Syphilis antibody, total	0.5 (nonreactive)	Negative
February 21, 2024	Syphilis antibody, total	0.4 (nonreactive)	Negative

RPR, rapid plasma reagin; TP-PA, *Treponema pallidum* particle agglutination.

Antimicrobial Resistance Questions



J Antimicrob Chemother 2023; **78**: 1561–1568
https://doi.org/10.1093/jac/dkad129 Advance Access publication 2 May 2023

Journal of Antimicrobial Chemotherapy

Important considerations regarding the widespread use of doxycycline chemoprophylaxis against sexually transmitted infections

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Rates of sexually transmitted infections (STIs) continue to rise across the world and interventions are essential to reduce their incidence. Past and recent studies have indicated this may be achieved using doxycycline post-exposure prophylaxis (PEP) and this has sparked considerable interest in its use. However, many unanswered questions remain as to its long-term effects and particularly potentially negative impact on human microbiomes and antimicrobial resistance among STIs, other pathogens, and commensals. In this review, we discuss seven areas of concern pertaining to the widespread use of doxycycline PEP.

1. Antimicrobial Resistance in STIs
    1. *Treponema pallidum*
    2. *Chlamydia trachomatis*
    3. *Mycoplasma genitalium*
    4. *Neisseria gonorrhoeae*
2. Antimicrobial Resistance in other bacterial species
    1. Commensal bacteria

- Kong FYS, Kenyon C, Unemo M. Important considerations regarding the widespread use of doxycycline chemoprophylaxis against sexually transmitted infections. J Antimicrob Chemother. 2023;78(7):1561-1568. doi:10.1093/jac/dkad129

Doxy-PEP **Will** Increase Doxycycline Usage

Correspondence

Estimating changes in antibiotic consumption in the USA with the introduction of doxycycline post-exposure prophylaxis

Doxycycline as a post-exposure prophylaxis (doxy-PEP) reduced the risk of bacterial sexually transmitted infections (STIs) in a randomised controlled trial of men who have sex with men taking HIV pre-exposure prophylaxis (PrEP), transgender women taking HIV PrEP, and people living with HIV.[1] There is concern that increased consumption of doxycycline might increase antimicrobial resistance, including doxycycline-resistant *Neisseria gonorrhoeae*, *Staphylococcus aureus*, and *Streptococcus pneumoniae*.[2-4]

Antibiotic use might change with the introduction of doxy-PEP; estimating this change could inform considerations of the risks of antimicrobial resistance and the benefits of STI prevention. We estimated the first-order expected increase in antibiotic consumption in the USA under several doxy-PEP prescribing scenarios (appendix pp 1–2). We accounted for defined STI in the past year.[1] If 75% of people in this population began to take doxy-PEP, monthly antibiotic consumption would increase by approximately 2·52 million doses (ie, doxy-PEP consumption of 2·58 million doses minus 62 100 antibiotic doses that would otherwise have been used for bacterial STI treatment; appendix p 6). If the entire eligible population began to take doxy-PEP, monthly antibiotic consumption would be expected to increase by 3·36 million doses (appendix p 7).

A retrospective analysis of ten prescribing strategies based on the PrEP use, HIV status, and bacterial STI history of people predicted substantial variation across the strategies in the number of infections averted per person taking doxy-PEP.[5] The prescribing strategy with the lowest number needed to treat to prevent a chlamydia infection was a diagnosis of two bacterial STIs within a 6-month period. 75% implementation of this strategy among men who have sex with men taking HIV PrEP and people living with HIV would lead to an increase in monthly antibiotic consumption of 0·28 million doses in the USA, whereas widespread (ie, 100%) implementation would lead to an increase of 0·37 million doses (appendix p 7). Among bacterial STI history-based prescribing strategies, year while maintaining similar levels of monthly doxy-PEP consumption and reductions in chlamydia infection risk as reported for people taking HIV PrEP (appendix p 3).

These estimates suggest that doxycycline consumption in the USA will increase with the introduction of doxy-PEP, even when accounting for the reduction in antibiotics used to treat chlamydia, gonorrhoea, and syphilis; the extent of this increase will depend on the size of the population taking doxy-PEP. Monitoring changes in antibiotic consumption, disease incidence, and burden of resistance will be important to understand the effects of doxy-PEP.

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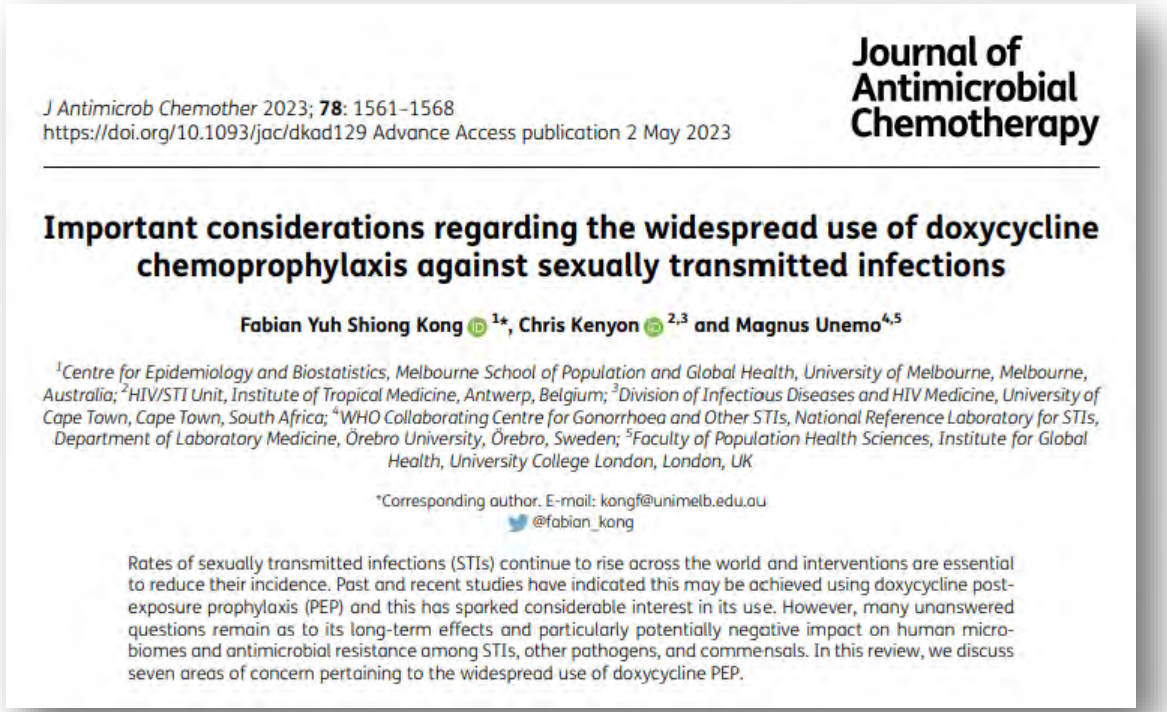
See Online for appendix

- Projected increase in antibiotic use with Doxy-PEP rollout
  - If 75% of eligible users adopt Doxy-PEP: +2.52 million doses/month
  - If 100% adopt: +3.36 million doses/month
- Targeting users with ≥2 STIs in 6 months reduces the increase to 0.18–0.24 million doses/month
- **Doxy-PEP will increase Doxycycline usage, even when accounting for the reduction in antibiotics used**

Roster KIO, Grad YH. Estimating changes in antibiotic consumption in the USA with the introduction of doxycycline post-exposure prophylaxis. The Lancet Microbe [Internet]. 2024;5(1):e9. Available from: http://dx.doi.org/10.1016/S2666-5247(23)00314-2

Antimicrobial Resistance Questions



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Journal of Antimicrobial Chemotherapy

Important considerations regarding the widespread use of doxycycline chemoprophylaxis against sexually transmitted infections

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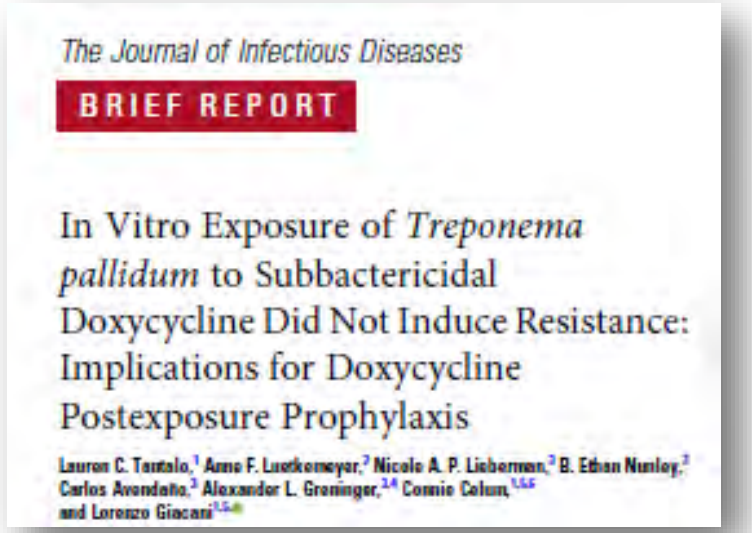
Antimicrobial Resistance

Chlamydia

- No clinical resistance to tetracyclines in *Chlamydia trachomatis*
- Tetracycline resistance has been seen in C.suis (pigs)
  - tetC (efflux pump)

Syphilis

- No clinical resistance to tetracyclines in *Treponema pallidum*


The Journal of Infectious Diseases

BRIEF REPORT

In Vitro Exposure of *Treponema pallidum* to Subbactericidal Doxycycline Did Not Induce Resistance: Implications for Doxycycline Postexposure Prophylaxis

Lauren C. Tantalo,[1] Anne F. Luetkemeyer,[2] Nicole A. P. Lieberman,[2] B. Ethan Nunley,[2] Carlos Avendaño,[3] Alexander L. Greninger,[2,4] Connie Celum,[1,5,6] and Lorenzo Giacani[1,5,6]

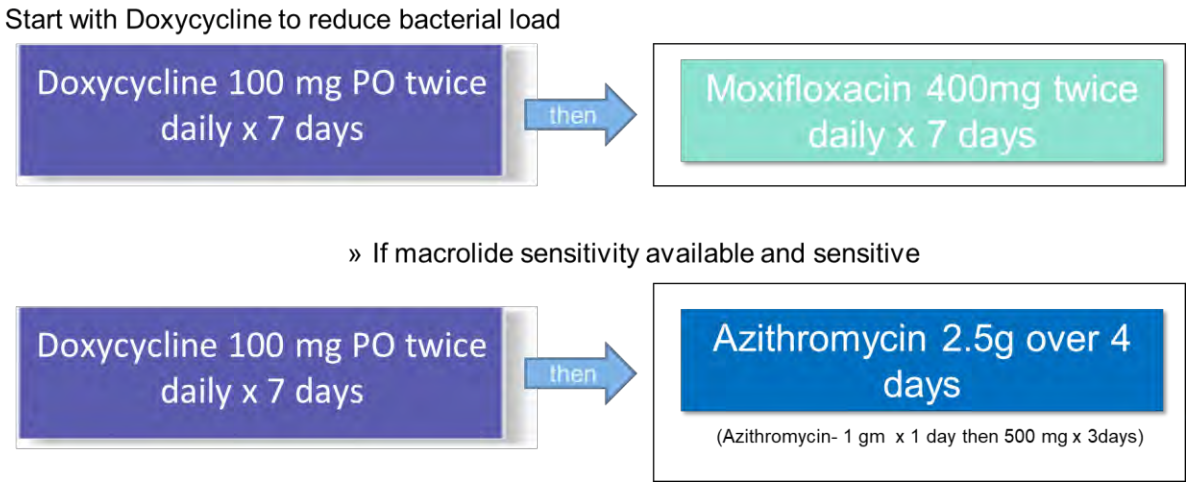
- Widespread macrolide resistance was seen with a single-point mutation

Benamri I, Azzouzi M, Sanak K, Moussa A, Radouani F. An overview of genes and mutations associated with Chlamydiae species' resistance to antibiotics. Ann Clin Microbiol Antimicrob. 2021;20(1):59. Published 2021 Sep 3. doi:10.1186/s12941-021-00465-4

Beale MA, Marks M, Sahi SK, et al. Genomic epidemiology of syphilis reveals independent emergence of macrolide resistance across multiple circulating lineages. Nat Commun. 2019;10(1):3255. Published 2019 Jul 22. doi:10.1038/s41467-019-11216-7

Antimicrobial Resistance – *M. genitalium*

- ***Mycoplasma genitalium***
  - Previously an "emerging" STI
  - Persistent urethritis in men and women
  - Test using first-void urine or urethral swab, send for NAAT
  - Treatment based on testing availability



- Intrinsically <u>resistant</u> to:
  - Cell wall and folic acid inhibitors
- High <u>resistance</u> rates to:
  - Protein synthesis inhibitors
    - Macrolides 77%
    - **Tetracyclines, 60%**
  - Nucleic acid synthesis inhibitors
    - quinolones, 90%

Antimicrobial Resistance – *M. genitalium*

Clinical Infectious Diseases

MAJOR ARTICLE

Outcomes of Resistance-guided Sequential Treatment of *Mycoplasma genitalium* Infections: A Prospective Evaluation

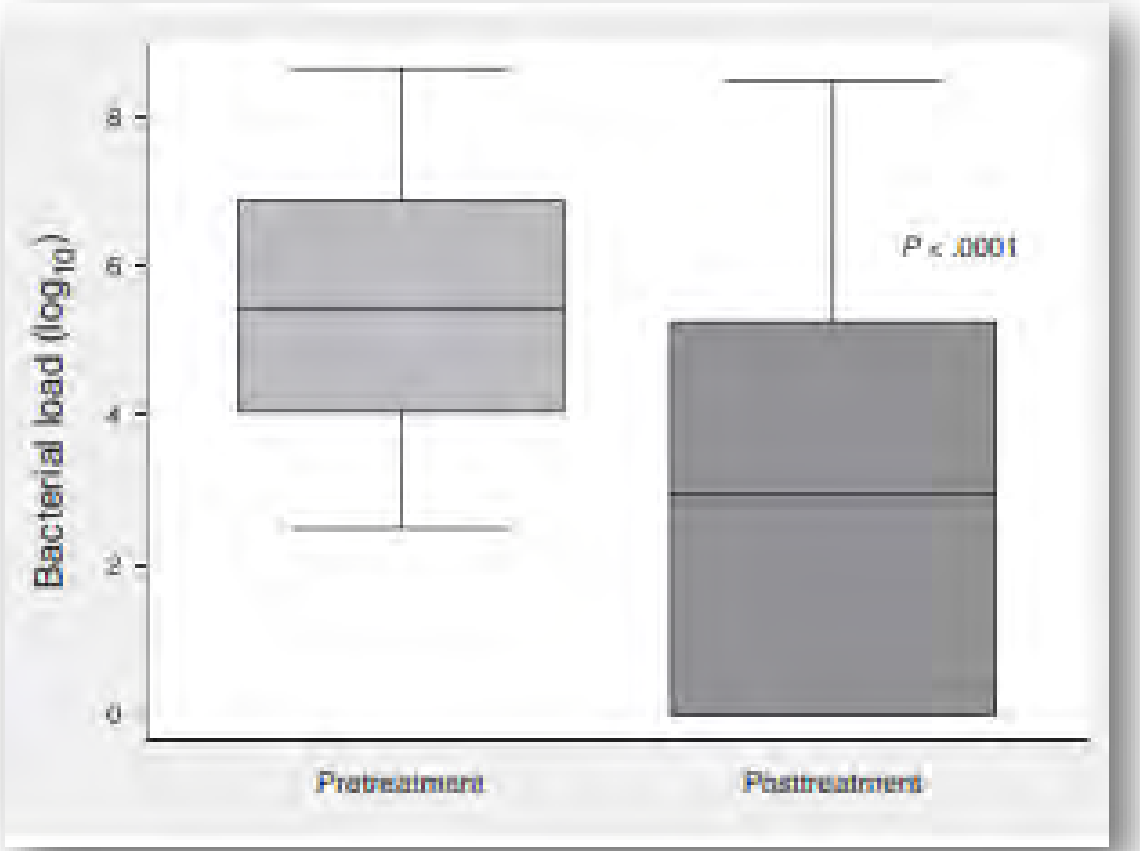
Tim R. H. Read,[1,2] Christopher K. Fairley,[1,2] Gerald L. Murray,[3,4,5,6] Jorgen S. Jensen,[7] Jennifer Danielewski,[3,4] Karen Worthington,[2] Michelle Doyle,[2] Elisa Mokany,[8] Litty Tan,[8] Eric P. F. Chow,[1,2] Suzanne M. Garland,[3,4,6,9] and Catriona S. Bradshaw[1,2]

[1]Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, [2]Melbourne Sexual Health Centre, Alfred Health, Carlton, [3]Murdoch Children's Research Institute, Parkville, [4]Department of Microbiology and Infectious Diseases, Royal Women's Hospital, Melbourne, [5]Infection and Immunity Program, Monash Biomedicine Discovery Institute, and [6]Royal Children's Hospital, Melbourne, Victoria, Australia; [7]Statens Serum Institut, Copenhagen, Denmark; [8]SpeeDx Pty Ltd, Eveleigh, New South Wales, and [9]Department of Obstetrics and Gynaecology, University of Melbourne, Victoria, Australia

(See the Major Article by Braun et al on pages 569-76 and Editorial commentary by Sulkowski on pages 577-9.)

Background. Rising macrolide and quinolone resistance in *Mycoplasma genitalium* necessitate new treatment approaches. We evaluated outcomes of sequential antimicrobial therapy for *M. genitalium* guided by a macrolide-resistance assay.

Methods. In mid-2016, Melbourne Sexual Health Centre switched from azithromycin to doxycycline (100 mg twice daily for 7 days) for nongonococcal urethritis, cervicitis, and proctitis. Cases were tested for *M. genitalium* and macrolide-resistance mutations (MRMs) by polymerase chain reaction. Directly after doxycycline, MRM-negative infections received 2.5 g azithromycin (1 g, then 500 mg daily for 3 days), and MRM-positive infections received sitafloxacin (100 mg twice daily for 7 days). Assessment of test of cure and reinfection risk occurred 14–90 days after the second antibiotic.



Read TRH, Fairley CK, Murray GL, et al. Outcomes of Resistance-guided Sequential Treatment of Mycoplasma genitalium Infections: A Prospective Evaluation. Clin Infect Dis. 2019;68(4):554-560. doi:10.1093/cid/ciy477