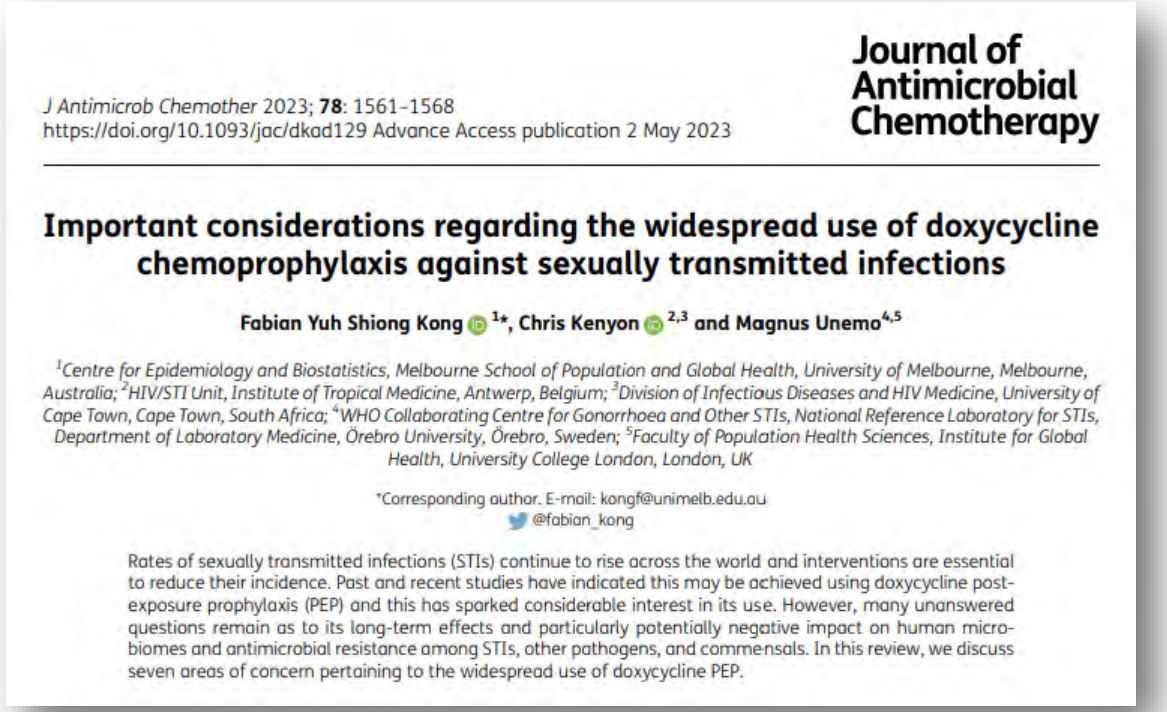
Clinical Questions

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

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 Gonorrhea*
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

Limited Antibiotics in the Pipeline

The Journal of Antibiotics (2023) 76:431–473
https://doi.org/10.1038/s41429-023-00629-8

Japan Antibiotics Research Association

The Society for Actinomycetes Japan

REVIEW ARTICLE

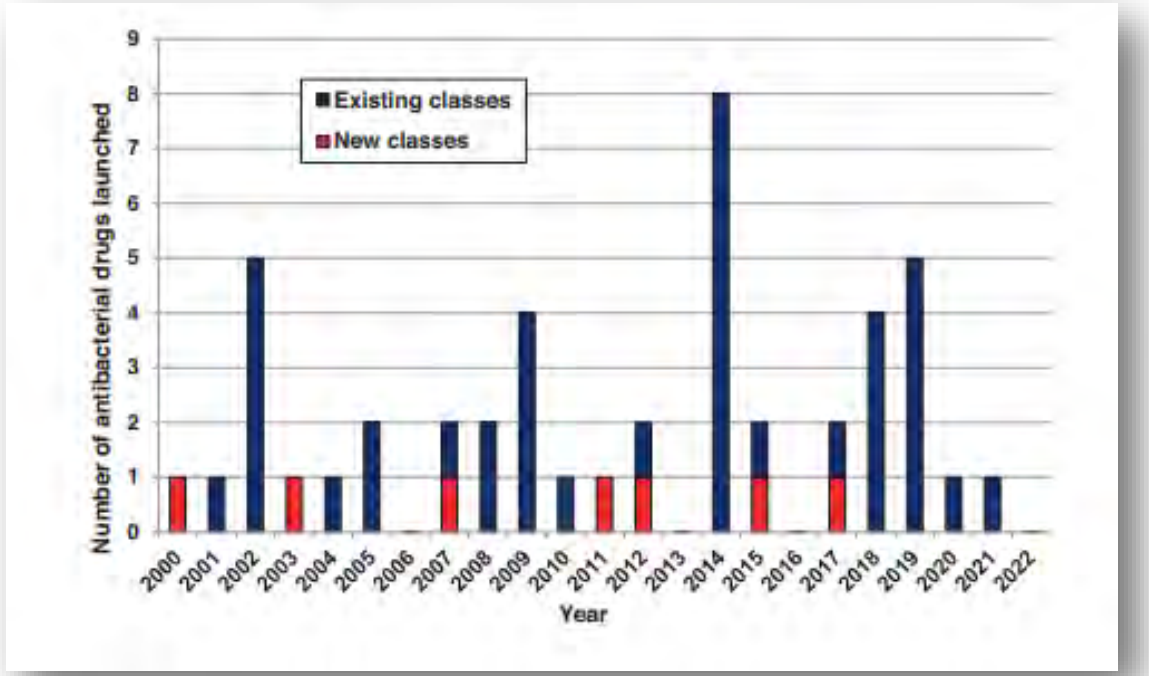
Antibiotics in the clinical pipeline as of December 2022

Mark S. Butler[1] · Ian R. Henderson[1] · Robert J. Capon[1] · Mark A. T. Blaskovich[1]

Received: 2 March 2023 / Revised: 20 April 2023 / Accepted: 25 April 2023 / Published online: 8 June 2023

Abstract

The need for new antibacterial drugs to treat the increasing global prevalence of drug-resistant bacterial infections has clearly attracted global attention, with a range of existing and upcoming funding, policy, and legislative initiatives designed to revive antibacterial R&D. It is essential to assess whether these programs are having any real-world impact and this review continues our systematic analyses that began in 2011. Direct-acting antibacterials (47), non-traditional small molecule antibacterials (5), and β-lactam/β-lactamase inhibitor combinations (10) under clinical development as of December 2022 are described, as are the three antibacterial drugs launched since 2020. Encouragingly, the increased number of early-stage clinical candidates observed in the 2019 review increased in 2022, although the number of first-time drug approvals from 2020 to 2022 was disappointingly low. It will be critical to monitor how many Phase-I and -II candidates move into Phase-III and beyond in the next few years. There was also an enhanced presence of novel antibacterial pharmacophores in early-stage trials, and at least 18 of the 26 phase-I candidates were targeted to treat Gram-negative bacteria infections. Despite the promising early-stage antibacterial pipeline, it is essential to maintain funding for antibacterial R&D and to ensure that plans to address late-stage pipeline issues succeed.



• Butler MS, Henderson IR, Capon RJ, Blaskovich MAT. Antibiotics in the clinical pipeline as of December 2022. J Antibiot (Tokyo). 2023;76(8):431-473. doi:10.1038/s41429-023-00629-8

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.

This work was supported by the US National Institute of Allergy and Infectious Diseases (grant numbers R01 AI132606 and R01 AI153521) and the US Centers for Disease Control and Prevention (contract number 200-2016-91779), paid to YHG. The findings, conclusions, and views expressed are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. KIOR declares no competing interests.

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Lancet Microbe 2023
Published Online October 23, 2023
https://doi.org/10.1016/S2666-5247(23)00314-2

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

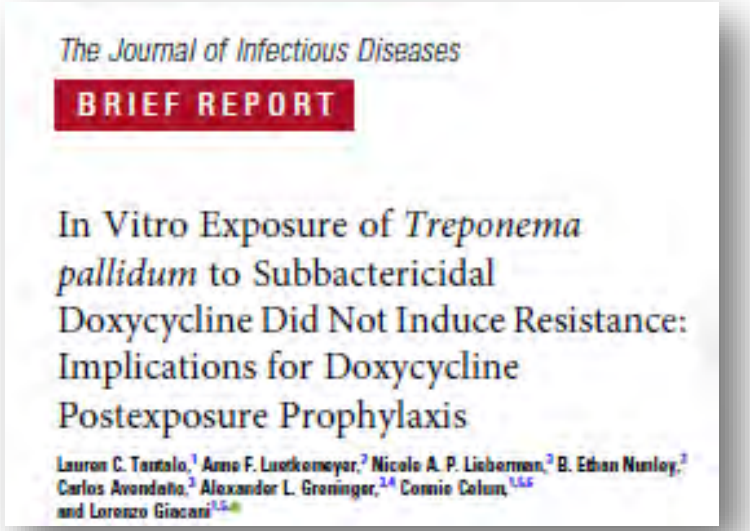
Antimicrobial Resistance

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]

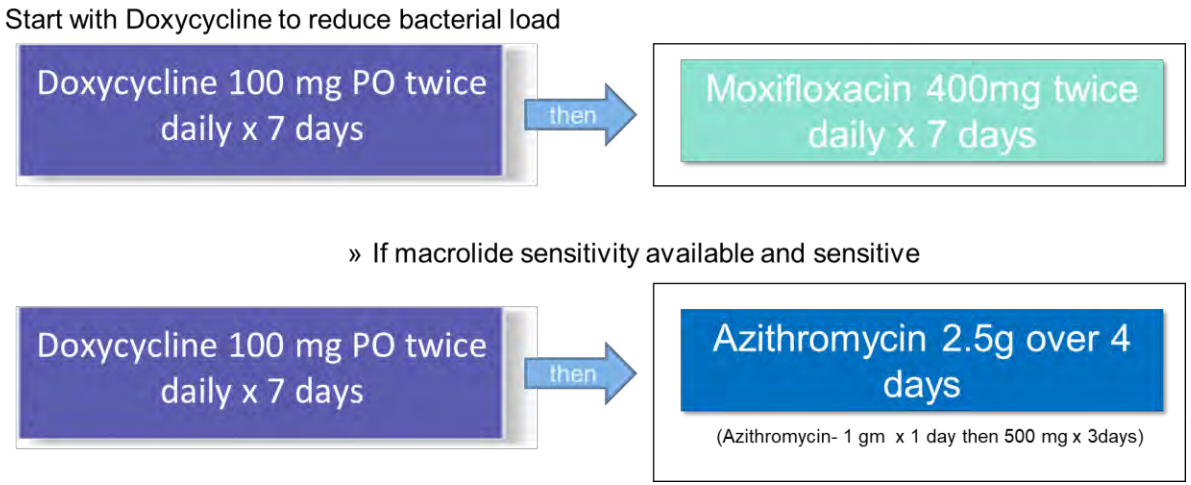
- Widespread macrolide resistance was seen with a single-point mutation

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]

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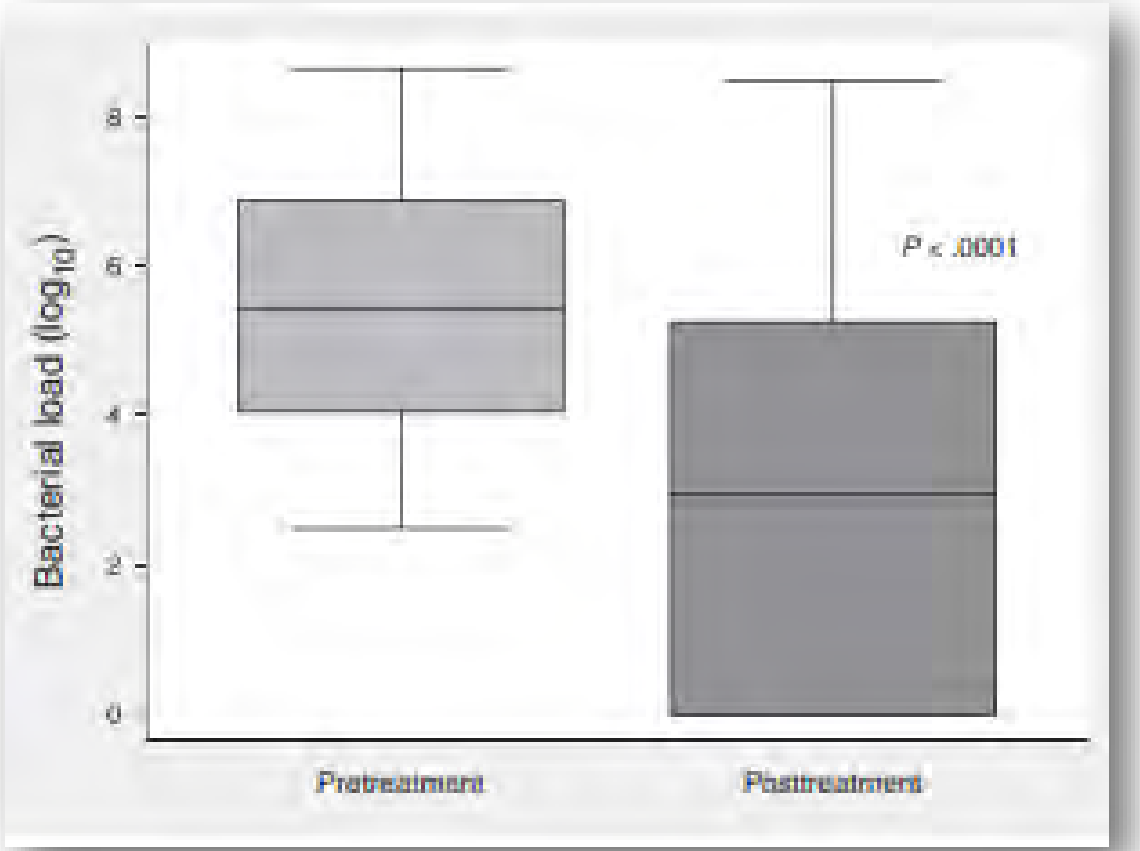
(See the Major Article by Braun et al on pages 569-76 and Editorial commentary by Sulkowski on pages 577-9.)

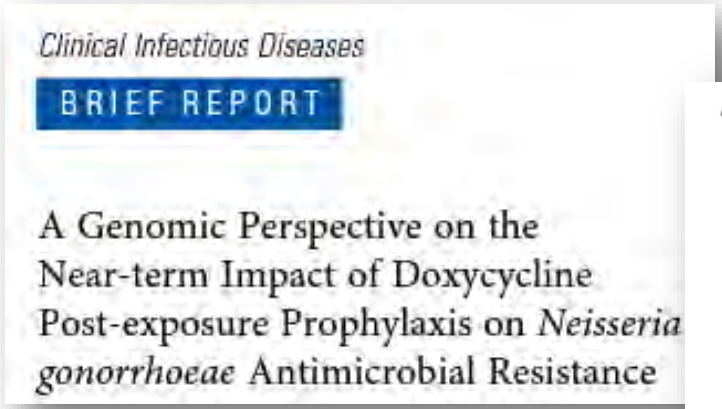
Background. Rising macrolide and quinolone resistance in *Mycoplasma genitalium* necessitate new treatment approaches. We evaluated outcomes of sequential antimicrobial therapy for *M. genitalium* guided by a macrolide-resistance assay.

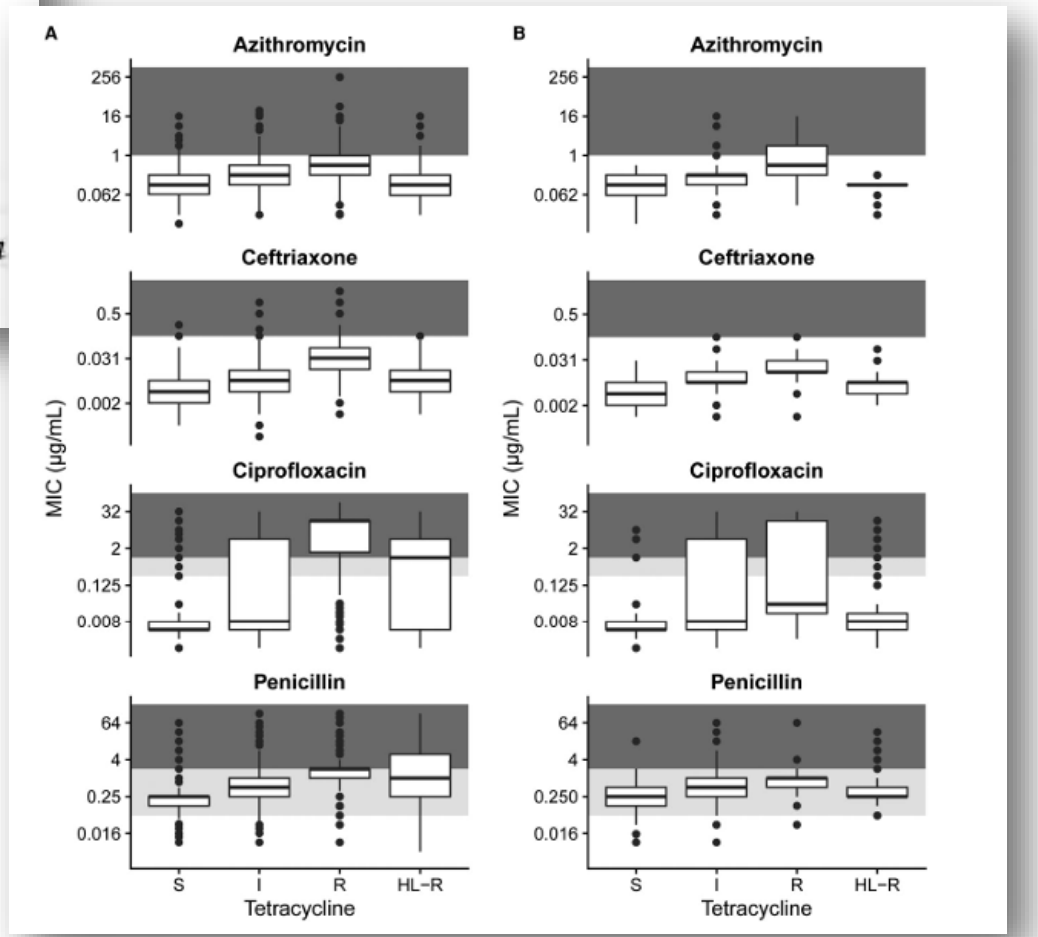
Methods. In mid-2016, Melbourne Sexual Health Centre switched from azithromycin to doxycycline (100 mg twice daily for 7 days) for nongonococcal urethritis, cervicitis, and proctitis. Cases were tested for *M. genitalium* and macrolide-resistance mutations (MRMs) by polymerase chain reaction. Directly 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

Antimicrobial Resistance - Gonorrhea

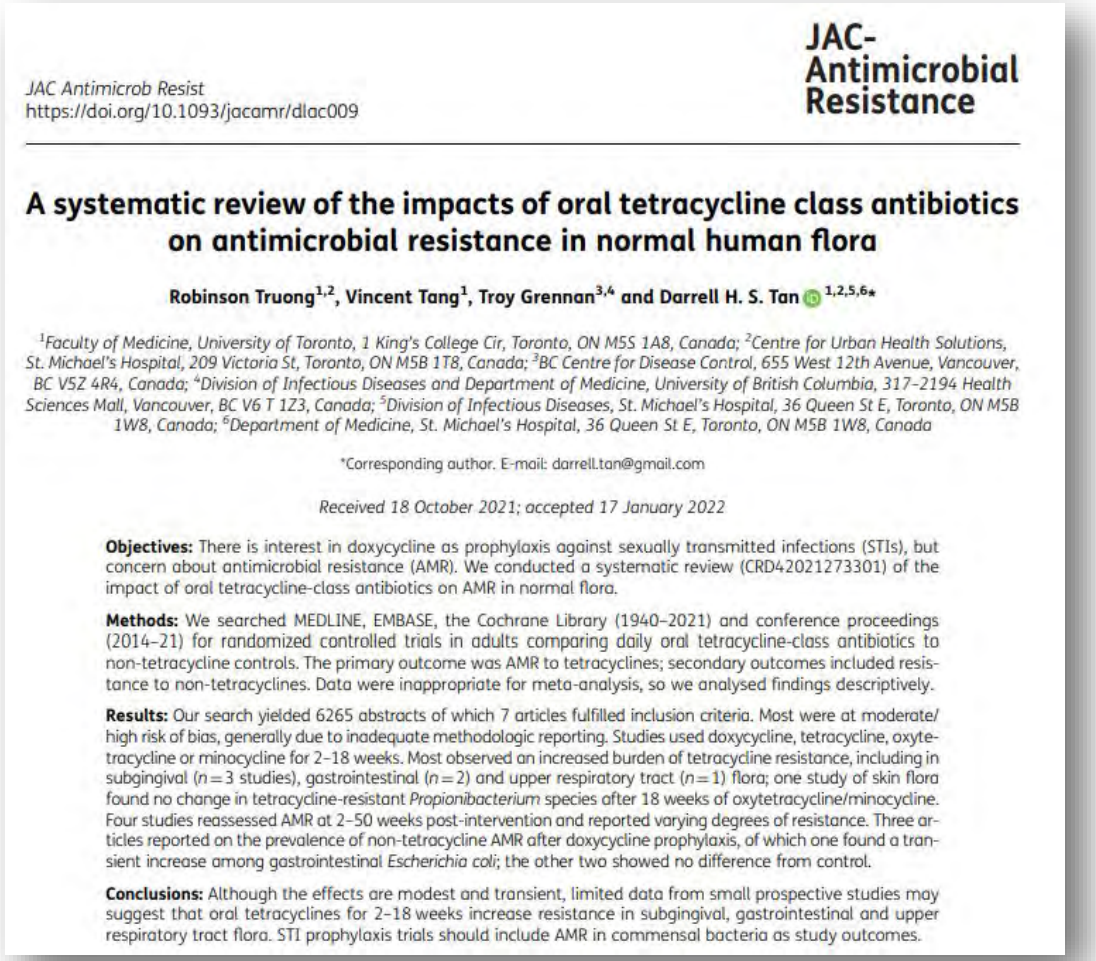




- Risk of **resistance to tetracyclines** (doxycycline) in gonorrhea
- Risk of **cross resistance** to other antimicrobials including beta-lactams like Ceftriaxone

Mortimer TD, Grad YH. A genomic perspective on the near-term impact of doxycycline post-exposure prophylaxis on Neisseria gonorrhoeae antimicrobial resistance [published online ahead of print, 2023 May 4]. Clin Infect Dis. 2023;ciad279. doi:10.1093/cid/ciad279

Antimicrobial Resistance - Commensals



JAC Antimicrob Resist
https://doi.org/10.1093/jacamr/dlac009

JAC-Antimicrobial Resistance

A systematic review of the impacts of oral tetracycline class antibiotics on antimicrobial resistance in normal human flora

Robinson Truong[1,2], Vincent Tang[1], Troy Grennan[3,4] and Darrell H. S. Tan[1,2,5,6]*

[1]Faculty of Medicine, University of Toronto, 1 King's College Cir, Toronto, ON M5S 1A8, Canada; [2]Centre for Urban Health Solutions, St. Michael's Hospital, 209 Victoria St, Toronto, ON M5B 1T8, Canada; [3]BC Centre for Disease Control, 655 West 12th Avenue, Vancouver, BC V5Z 4R4, Canada; [4]Division of Infectious Diseases and Department of Medicine, University of British Columbia, 317-2194 Health Sciences Mall, Vancouver, BC V6 T 1Z3, Canada; [5]Division of Infectious Diseases, St. Michael's Hospital, 36 Queen St E, Toronto, ON M5B 1W8, Canada; [6]Department of Medicine, St. Michael's Hospital, 36 Queen St E, Toronto, ON M5B 1W8, Canada

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Received 18 October 2021; accepted 17 January 2022

Objectives: There is interest in doxycycline as prophylaxis against sexually transmitted infections (STIs), but concern about antimicrobial resistance (AMR). We conducted a systematic review (CRD42021273301) of the impact of oral tetracycline-class antibiotics on AMR in normal flora.

Methods: We searched MEDLINE, EMBASE, the Cochrane Library (1940–2021) and conference proceedings (2014–21) for randomized controlled trials in adults comparing daily oral tetracycline-class antibiotics to non-tetracycline controls. The primary outcome was AMR to tetracyclines; secondary outcomes included resistance to non-tetracyclines. Data were inappropriate for meta-analysis, so we analysed findings descriptively.

Results: Our search yielded 6265 abstracts of which 7 articles fulfilled inclusion criteria. Most were at moderate/high risk of bias, generally due to inadequate methodologic reporting. Studies used doxycycline, tetracycline, oxytetracycline or minocycline for 2–18 weeks. Most observed an increased burden of tetracycline resistance, including in subgingival ($n=3$ studies), gastrointestinal ($n=2$) and upper respiratory tract ($n=1$) flora; one study of skin flora found no change in tetracycline-resistant *Propionibacterium* species after 18 weeks of oxytetracycline/minocycline. Four studies reassessed AMR at 2–50 weeks post-intervention and reported varying degrees of resistance. Three articles reported on the prevalence of non-tetracycline AMR after doxycycline prophylaxis, of which one found a transient increase among gastrointestinal *Escherichia coli*; the other two showed no difference from control.

Conclusions: Although the effects are modest and transient, limited data from small prospective studies may suggest that oral tetracyclines for 2–18 weeks increase resistance in subgingival, gastrointestinal and upper respiratory tract flora. STI prophylaxis trials should include AMR in commensal bacteria as study outcomes.

- Limited data from small prospective studies may suggest that oral tetracyclines for 2–18 weeks increase resistance in subgingival, gastrointestinal and upper respiratory tract flora.

- Truong R, Tang V, Grennan T, Tan DHS. A systematic review of the impacts of oral tetracycline class antibiotics on antimicrobial resistance in normal human flora. JAC Antimicrob Resist. 2022;4(1):dlac009. Published 2022 Feb 15. doi:10.1093/jacamr/dlac009

Doxy-PEP Increases Resistance Genes

nature medicine

Article

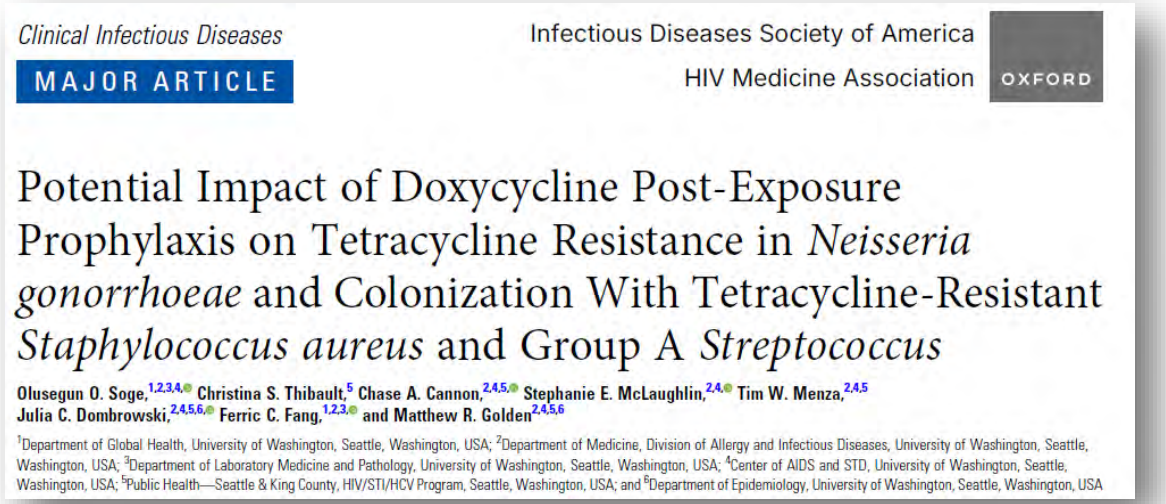
https://doi.org/10.1038/s41591-024-03274-2

Impact of doxycycline post-exposure prophylaxis for sexually transmitted infections on the gut microbiome and antimicrobial resistome

- Metagenomic + transcriptomic analysis of rectal swabs (DoxyPEP trial)
  - Compared doxy-PEP users (n=100) to controls (n=50) over 6 months
- Increased proportion and activity of tetracycline resistance genes (ARGs)
  - Tetracycline ARGs: 46% → 51% (DNA); 4% → 15% (RNA)
  - **Strongest expression increase seen in participants taking >25 doses**
  - No increase in ARGs for other antibiotic classes
- No significant change in gut bacterial diversity or total bacterial mass

• Args T. Impact of doxycycline post-exposure prophylaxis for sexually transmitted infections on the gut microbiome and antimicrobial resistome. 2025;31(January).

Doxy-PEP and Gonorrhea: A Tetracycline Resistance Surge



Clinical Infectious Diseases

MAJOR ARTICLE

Infectious Diseases Society of America
HIV Medicine Association

OXFORD

Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in *Neisseria gonorrhoeae* and Colonization With Tetracycline-Resistant *Staphylococcus aureus* and Group A *Streptococcus*

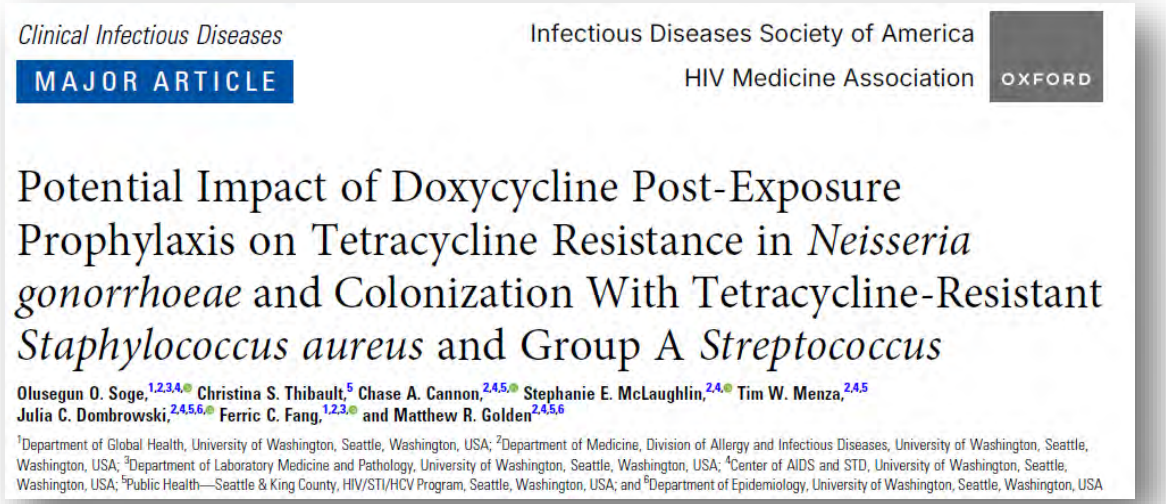
Olusegun O. Soge,[1,2,3,4] Christina S. Thibault,[5] Chase A. Cannon,[2,4,5] Stephanie E. McLaughlin,[2,4] Tim W. Menza,[2,4,5] Julia C. Dombrowski,[2,4,5,6] Ferric C. Fang,[1,2,3] and Matthew R. Golden[2,4,5,6]

[1]Department of Global Health, University of Washington, Seattle, Washington, USA; [2]Department of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington, USA; [3]Department of Laboratory Medicine and Pathology, University of Washington, Seattle, Washington, USA; [4]Center of AIDS and STD, University of Washington, Seattle, Washington, USA; [5]Public Health—Seattle & King County, HIV/STI/HCV Program, Seattle, Washington, USA; and [6]Department of Epidemiology, University of Washington, Seattle, Washington, USA

- Tetracycline resistance in *Neisseria gonorrhoeae* (NG), King County MSM (2017–2024)
  - TetR stable until 2023, then rose from 27% to 70%
  - High-level tetR (HL tetR) rose from 2% (2021) to 65% (2024)
  - Strongest associations with >3 doxy-PEP doses/month
- **Conclusion:**
  - Doxy-PEP likely accelerating tetracycline resistance in NG
  - May limit doxy-PEP's preventive value for gonorrhea

Soge OO, Thibault CS, Cannon CA, McLaughlin SE, Menza TW, Dombrowski JC, et al. Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in Neisseria gonorrhoeae and Colonization with Tetracycline-Resistant Staphylococcus aureus and Group A Streptococcus. Clin Infect Dis [Internet]. 2025;1–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/40036749

Off-Target Effects: Resistant S. aureus and Group A Strep in Doxy-PEP Users



Clinical Infectious Diseases

MAJOR ARTICLE

Infectious Diseases Society of America
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OXFORD

Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in *Neisseria gonorrhoeae* and Colonization With Tetracycline-Resistant *Staphylococcus aureus* and Group A *Streptococcus*

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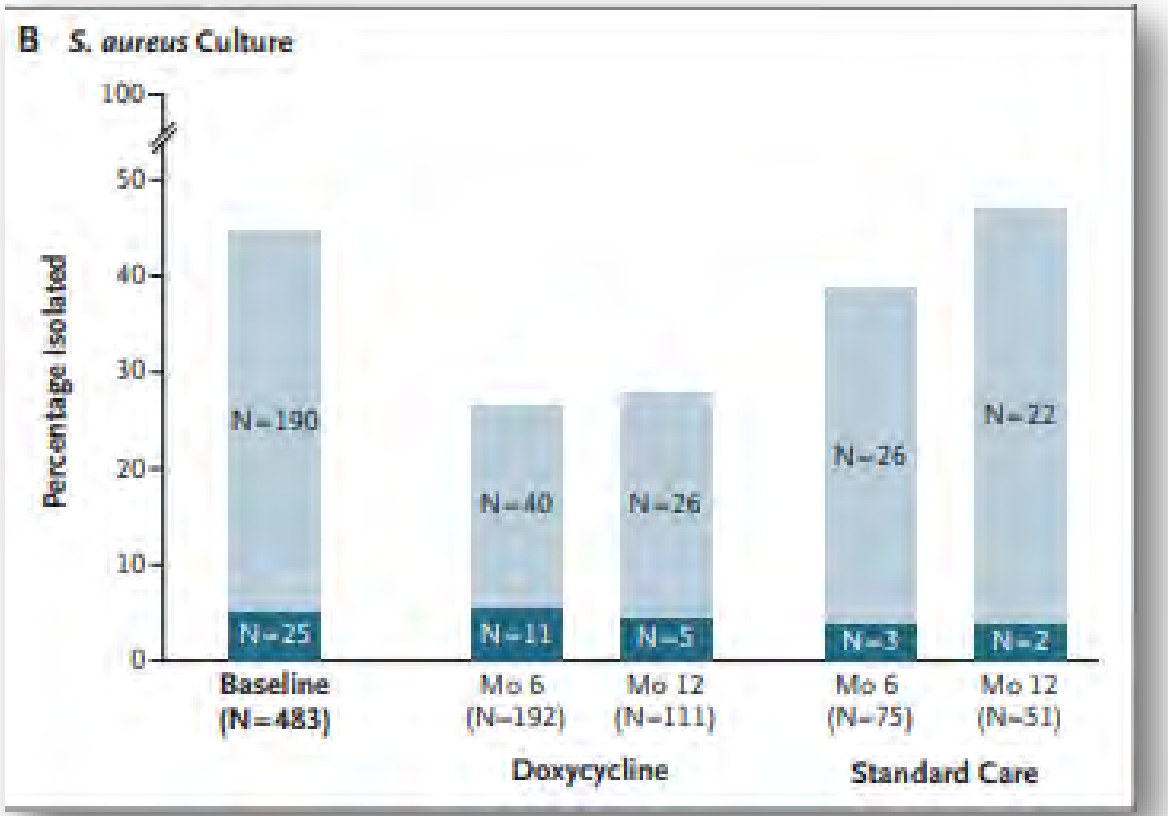
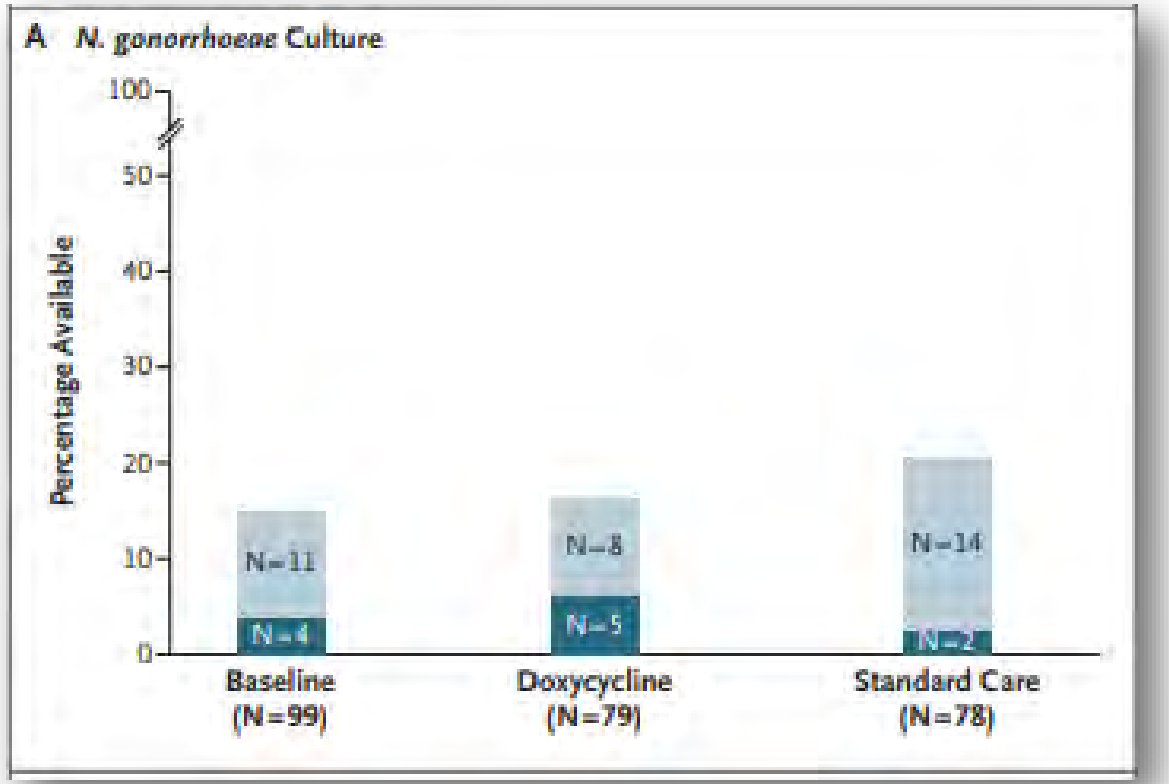
[1]Department of Global Health, University of Washington, Seattle, Washington, USA; [2]Department of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington, USA; [3]Department of Laboratory Medicine and Pathology, University of Washington, Seattle, Washington, USA; [4]Center of AIDS and STD, University of Washington, Seattle, Washington, USA; [5]Public Health—Seattle & King County, HIV/STI/HCV Program, Seattle, Washington, USA; and [6]Department of Epidemiology, University of Washington, Seattle, Washington, USA

- Colonization in MSM sexual health clinic attendees (2023–2024)
  - *S. aureus* overall colonization lower in Doxy-PEP users (27% vs 36%)
    - *Tetracycline-resistant S. aureus* higher in Doxy-PEP users (18% vs 8%)
  - *Group A Strep* (GAS) colonization: higher in Doxy-PEP users (9% vs 4%)
    - 82% of GAS isolates were tetracycline-resistant
- **Conclusion:**
  - Doxy-PEP selects for tetracycline-resistant off-target bacteria, even as it lowers overall colonization

Soge OO, Thibault CS, Cannon CA, McLaughlin SE, Menza TW, Dombrowski JC, et al. Potential Impact of Doxycycline Post-Exposure Prophylaxis on Tetracycline Resistance in Neisseria gonorrhoeae and Colonization with Tetracycline-Resistant Staphylococcus aureus and Group A Streptococcus. Clin Infect Dis [Internet]. 2025;1–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/40036749

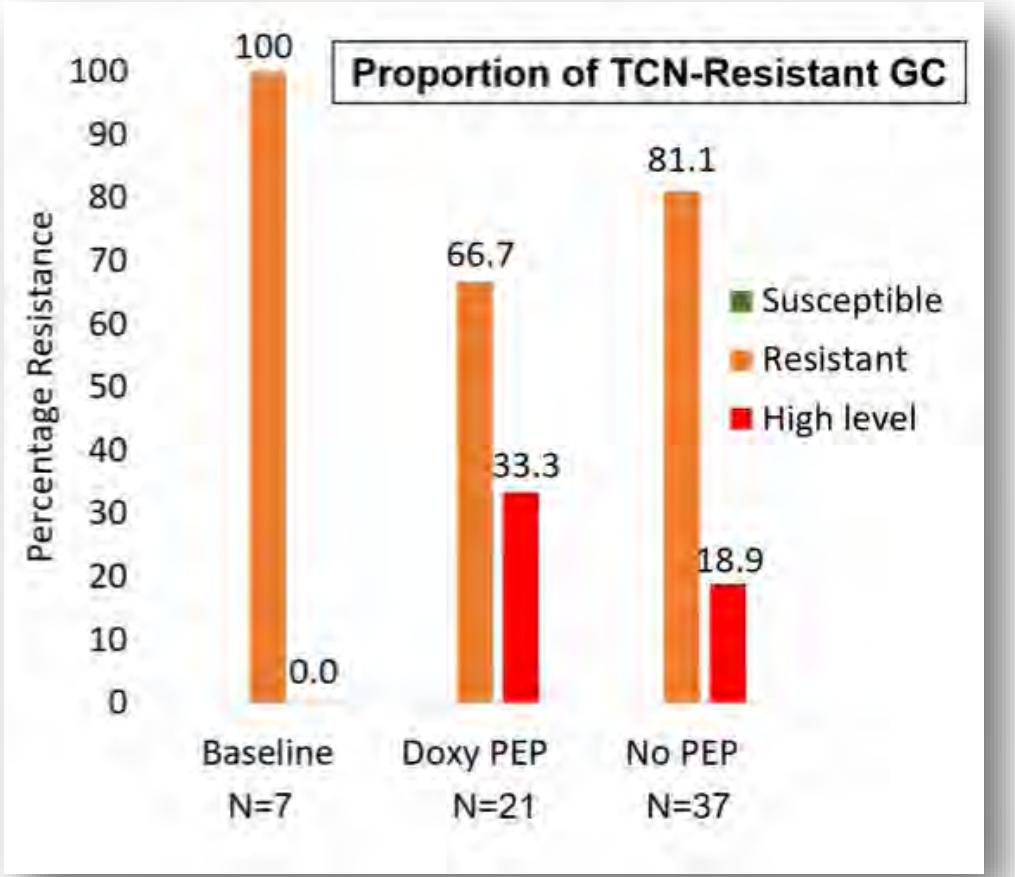
Antimicrobial Resistance – DoxyPEP Study

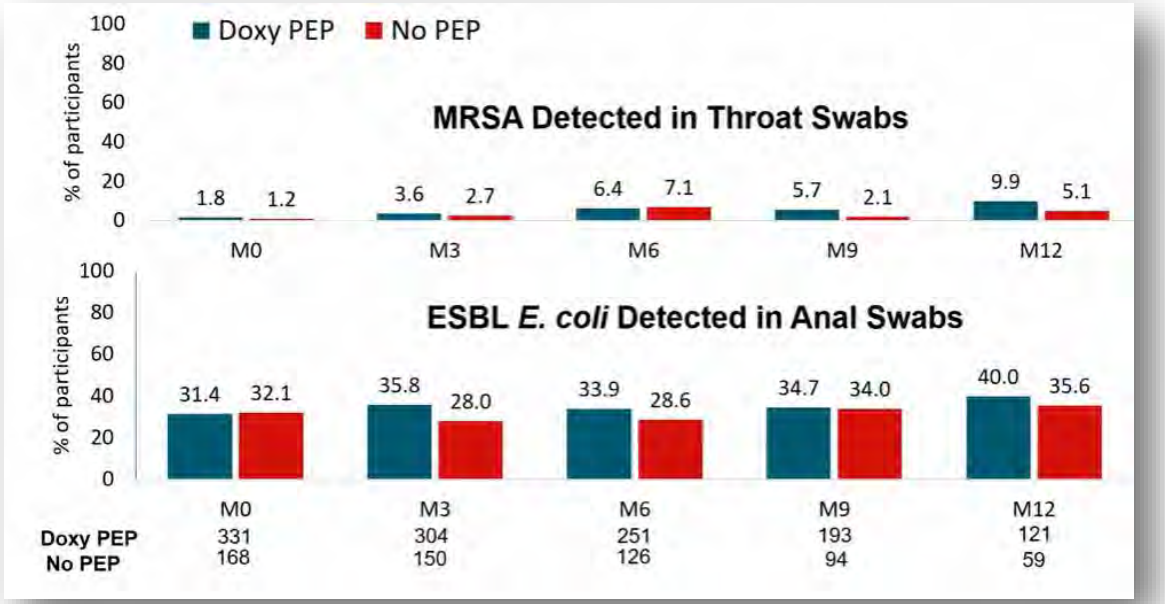




- Luetkemeyer AF, Donnell D, Dombrowski JC, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. N Engl J Med. 2023;388(14):1296-1306. doi:10.1056/NEJMoa2211934

Antimicrobial Resistance – DoxyVac Study





- Molina et al DOXYVAC CROI 2023 Abstract 119
- Liu AY, Buchbinder SP. CROI 2023: Epidemiologic Trends and Prevention for HIV and Other Sexually Transmitted Infections. Top Antivir Med. 2023;31(3):468-492.

Does Doxy-PEP Drive Ceftriaxone Resistance in Gonorrhea?

Doxy-PEP could select for ceftriaxone resistance in *Neisseria gonorrhoeae*

Authors' reply

We share Vanbaelen and colleagues' interest in understanding evolving gonococcal antimicrobial resistance and potential association with doxycycline prophylaxis for prevention of sexually transmitted infections, which we studied as doxycycline post-

	Spearman's correlation (95% CI)	p value
All gonococcal isolates regardless of doxy-PEP use (N=69)		
Cefixime	0·57 (0·38–0·71)	<0·0001
Ceftriaxone	0·50 (0·30–0·66)	<0·0001
Penicillin	0·41 (0·19–0·59)	0·0005
Gonococcal isolates from those using doxy-PEP (N=29)		
Cefixime	0·34 (−0·03–0·63)	0·07
Ceftriaxone	0·30 (−0·07–0·60)	0·11
Penicillin	0·22 (−0·16–0·54)	0·26
Gonococcal isolates from those not using doxy-PEP (N=40)		
Cefixime	0·73 (0·54–0·85)	<0·0001
Ceftriaxone	0·64 (0·42–0·80)	0·0001
Penicillin	0·54 (0·28–0·73)	0·0003

Doxy-PEP=doxycycline post-exposure prophylaxis. MIC=minimum inhibitory concentration.

Table: **Spearman's correlation of tetracycline MIC with cephalosporin and penicillin MICs among gonococcal isolates from the DoxyPEP study[1]**

- Post hoc analysis from DoxyPEP trial
  - Correlation seen between tetracycline MIC and ceftriaxone/cefixime/penicillin MICs
    - **But only in participants not on Doxy-PEP**
  - Among Doxy-PEP users, no significant MIC correlation with cephalosporins
- Low culture recovery rates limit conclusions
- Majority of infections were rectal/pharyngeal, where culture yield is low
- **Conclusion:** No current signal that Doxy-PEP is selecting for ceftriaxone resistance

Vanbaelen T, Manoharan-Basil SS, Kenyon C. Doxy-PEP could select for ceftriaxone resistance in Neisseria gonorrhoeae. Lancet Infect Dis [Internet]. 2025;25(6):e316. Available from: http://dx.doi.org/10.1016/S1473-3099(25)00235-X

Doxy-PEP Harms Summary

Well known side effects:

- Gastrointestinal distress
- Photosensitivity
- Pill esophagitis

Growing understanding:

- No resistance seen with chlamydia and syphilis
- Decreased colonization with S. Aureus but increased GAS
- Growing resistance to Doxycycline in STIs (GC) and commensals (S. Aureus)

Unknowns:

- Impact on M. Gen
- Impact on the microbiome
- Impact on STI presentations
- Cross-resistance with other antibiotics

Implementation:
How Do I Implement Doxy-PEP In My Practice?

Implementation – Who Should Get Doxy-PEP?

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

Recommendation*	Strength of recommendation and quality of evidence†
• Providers should counsel all gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW) with a history of at least one bacterial sexually transmitted infection (STI) (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months about the benefits and harms of using doxycycline (any formulation) 200 mg once within 72 hours (not to exceed 200 mg per 24 hours) of oral, vaginal, or anal sex and should offer doxycycline postexposure prophylaxis (doxy PEP) through shared decision-making. Ongoing need for doxy PEP should be assessed every 3–6 months.	AI High-quality evidence supports this strong recommendation to counsel MSM and TGW and offer doxy PEP.
• No recommendation can be given at this time on the use of doxy PEP for cisgender women, cisgender heterosexual men, transgender men, and other queer and nonbinary persons.	Evidence is insufficient to assess the balance of benefits and harms of the use of doxy PEP

*Although not directly assessed in the trials included in these guidelines, doxy PEP could be discussed with MSM and TGW who have not had a bacterial STI diagnosed during the previous year but will be participating in sexual activities that are known to increase likelihood of exposure to STIs.
† See Table.

Implementation – Screening

- Screen for sexually transmitted infections (STIs) as indicated:
  - HIV Testing
  - Gonorrhea/Chlamydia NAAT testing (including extra-genital)
  - Syphilis testing
  - Hepatitis testing
  - Vaccination status
  - Counsel on
    - Prevention strategies
    - Risks and harms of Doxy-PEP
      - As well as using it for it's intended purpose
    - Drug-drug interactions (antacids, cations)

Implementation – Counseling

Well known side effects:

- Gastrointestinal distress
- Photosensitivity
- Pill esophagitis

Growing understanding:

- No resistance seen with chlamydia and syphilis
- Decreased colonization with S. Aureus but increased GAS
- Growing resistance to Doxycycline in STIs (GC) and commensals (S. Aureus)

Unknowns:

- Impact on M. Gen
- Impact on the microbiome
- Impact on STI presentations
- Cross-resistance with other antibiotics

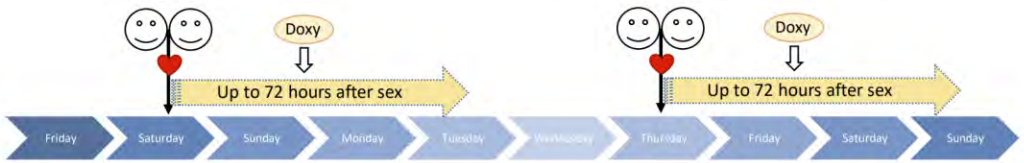
Patient Decision Aids

Doxy PEP – How to Take

= sex without a condom, including oral sex

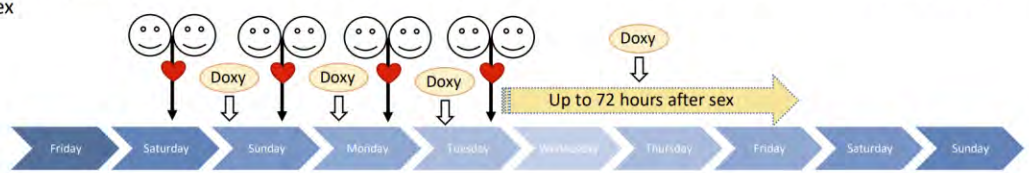
Two 100 mg pills of doxycycline ideally within 24 hours but no later than 72 hours after condomless oral, anal or vaginal sex

Example: Sex on Sat; take dose of doxy by Tues



Example: Sex on Thursday; take dose of doxy by Sunday

Example 2: Daily (or more) sex Sat-Tues; take daily dose of doxy and last dose within 24 hours *but not later than 72 hours* after last sex



***No more than* 200 mg every 24 hours**

About Doxy-PEP

What is doxy-PEP?

- Doxy-PEP means taking the antibiotic doxycycline after sex, to prevent getting an STI. It is like a morning-after pill but for STIs. Taking doxy-PEP reduces your chance of acquiring syphilis, gonorrhea, and chlamydia by about two-thirds.

When should I take doxy-PEP?

- Two 100 mg pills of doxycycline should be taken ideally within 24 hours but no later than 72 hours after condomless sex. Condomless sex means oral, anal or vaginal/front-hole sex where a condom isn't used for the entire time.

What about when I have sex again?

- If you have sex again within 24 hours of taking doxycycline, take another dose 24 hours after your last dose. You can take doxycycline as often as every day when you are having condomless sex but don't take more than 200 mg (two 100 mg pills) every 24 hours.

How should I take doxy-PEP?

- Take doxycycline with plenty of water or something else to drink so that it does not get stuck when you swallow. If your stomach is upset by doxycycline, taking it with food may help.
- Some people are more sensitive to the sun when they take doxycycline, so wear sunscreen.
- Please do not share doxycycline with others.
- Avoid dairy products, calcium, antacids, or multivitamins 2 hours before after taking doxycycline.

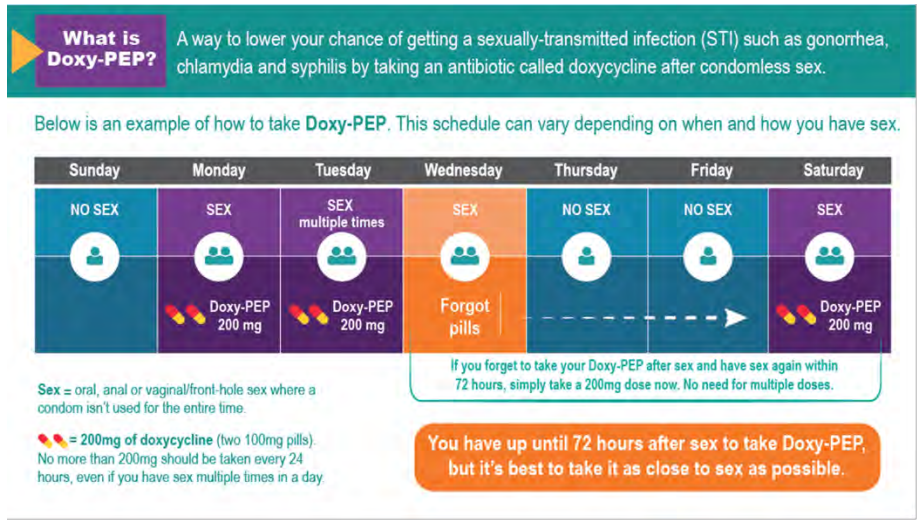
What are we still learning about doxy-PEP?

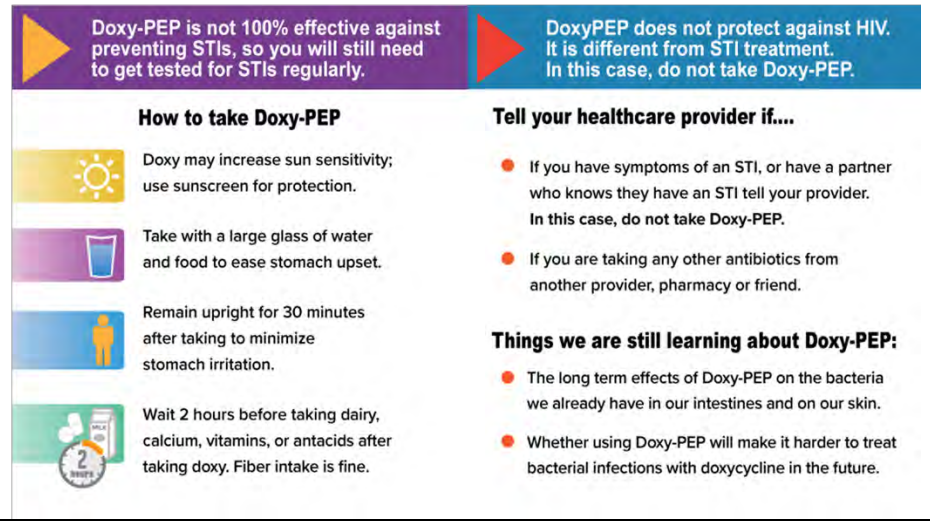
- Does it affect normal ("good") bacteria in our intestines?
- Could it increase or decrease the bacteria that live on our skin, or make them resistant to doxycycline (for example staph)?
- Will doxy-PEP increase doxycycline resistance in bacteria that cause STIs?
  - Although doxycycline has been used for decades, there is not resistance to doxycycline in chlamydia or syphilis.
  - About 25% of gonorrhea in the US is already resistant to doxy; doxy-PEP may not work against these strains. The DoxyPEP study and other studies will help understand whether using doxy-PEP changes resistance in gonorrhea.

Reminders

- Call us at 628-217-6692 if you run out of doxycycline, if you are having any side effects, or if you think you may have an STI.
- Please continue to get tested for STIs every 3 months and whenever you have symptoms.
- Doxy-PEP doesn't protect against MPX (monkeypox), HIV, or other viral infections

Patient Decision Aids





How Do I Prescribe Doxy-PEP?

FOR _____ DATE _____

ADDRESS _____

REFILL _____ TIMES

A generically equivalent drug product may be dispensed unless the practitioner hand writes the words "Brand Necessary" or "Brand Medically Necessary" on the face of the prescription.

℞

Doxycycline Monohydrate 100mg tabs
Take 2 tabs by mouth as needed every 24 hours
Take 2 capsules by mouth, once daily as needed (take within 72 hours of condomless sex),
Take no more then 2 capsules in any 24 hour period. Take with water and remain upright for 30 mins after taking
Dispense: #60 tabs
Refills: 0

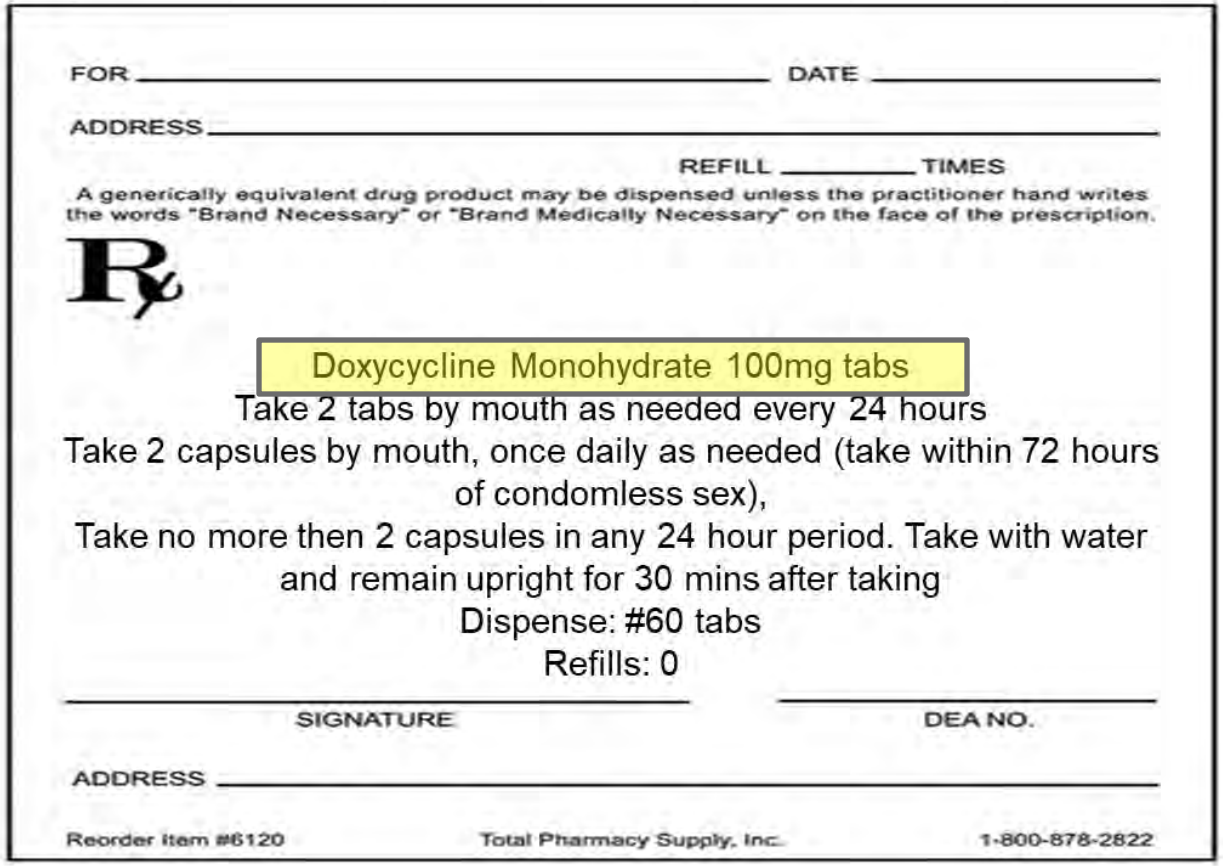
_____ _____

SIGNATURE DEA NO.

ADDRESS _____

Reorder Item #6120 Total Pharmacy Supply, Inc. 1-800-878-2822

How Do I Prescribe Doxy-PEP?



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Dispense: #60 tabs

Refills: 0

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SIGNATURE DEA NO.

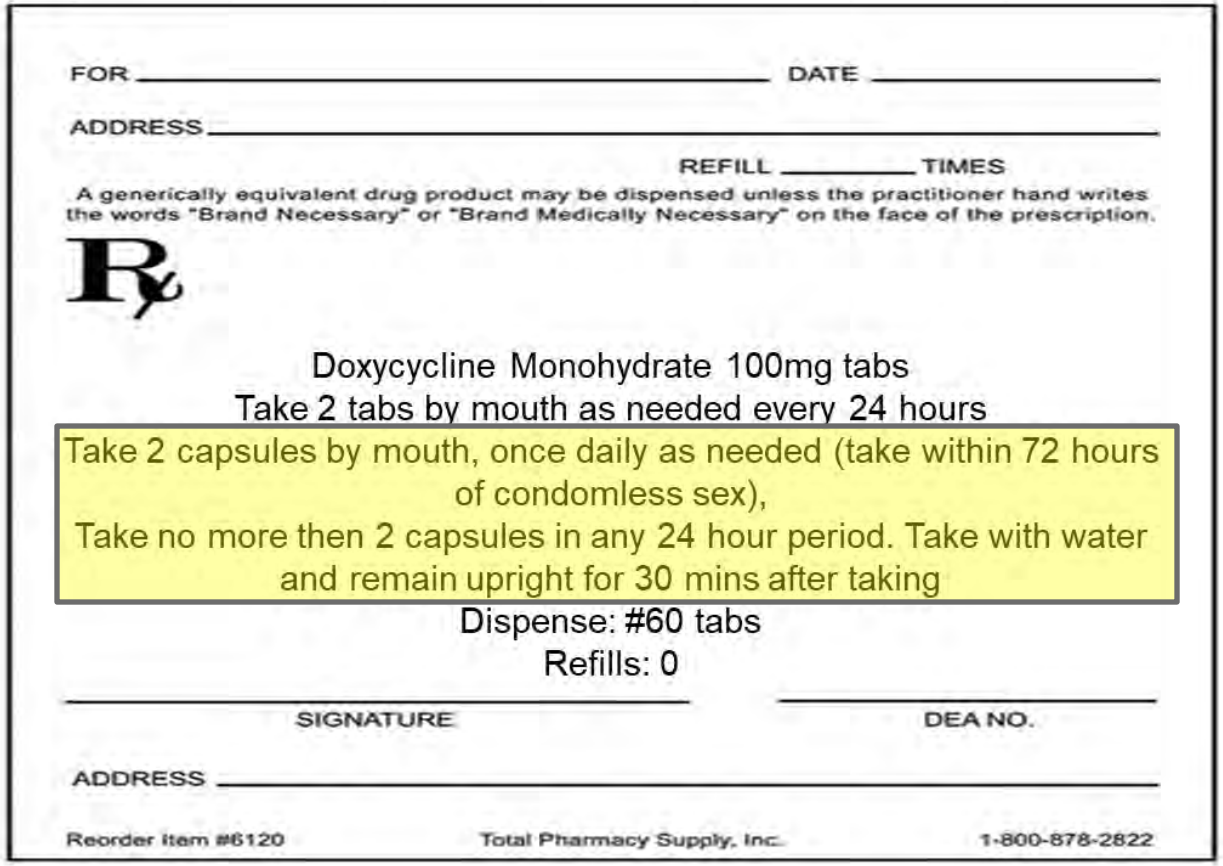
ADDRESS _____

Reorder Item #6120 Total Pharmacy Supply, Inc. 1-800-878-2822

Hyclate or Monohydrate

- Hyclate – cheaper
- Monohydrate – less GI distress

How Do I Prescribe Doxy-PEP?



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Refills: 0

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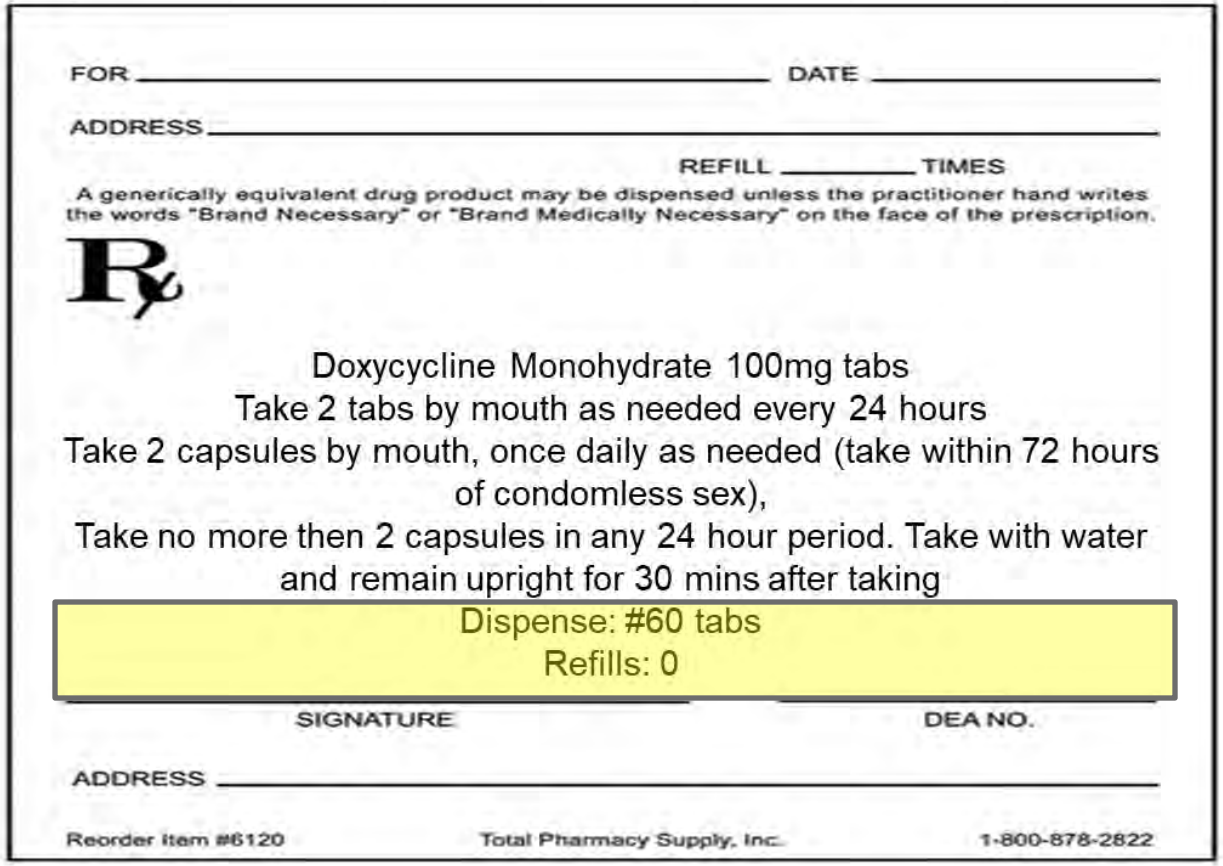
SIGNATURE DEA NO.

ADDRESS _____

Reorder Item #6120 Total Pharmacy Supply, Inc. 1-800-878-2822

- Detailed instructions

How Do I Prescribe Doxy-PEP?



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ADDRESS _____

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Take 2 capsules by mouth, once daily as needed (take within 72 hours of condomless sex),
Take no more then 2 capsules in any 24 hour period. Take with water and remain upright for 30 mins after taking

Dispense: #60 tabs
Refills: 0

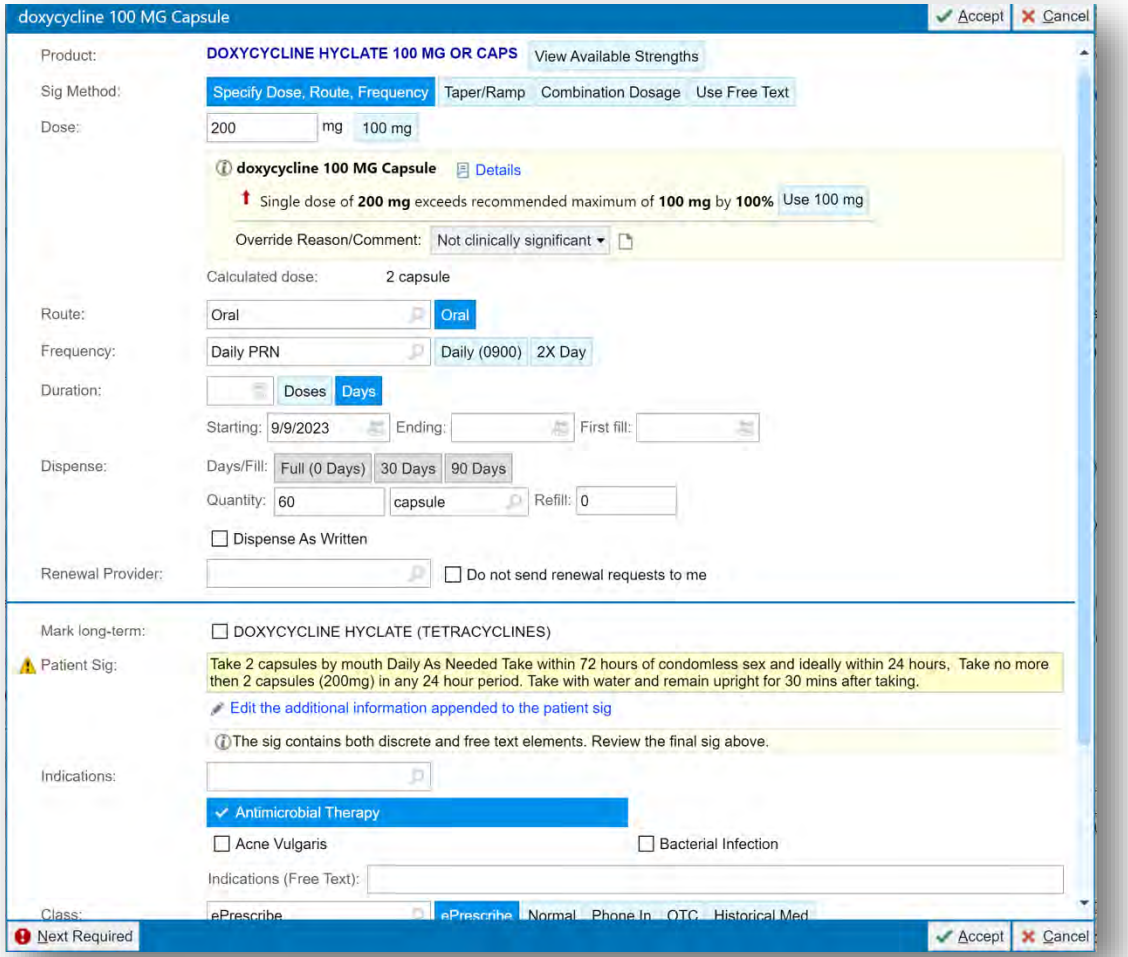
SIGNATURE DEA NO.

ADDRESS _____

Reorder Item #6120 Total Pharmacy Supply, Inc. 1-800-878-2822

- Dispense and refills
- 25% of patients used >= 10 doses per month

How Do I Prescribe Doxy-PEP?



How Do I Follow Patients on Doxy-PEP?

Follow-up

- Visits every 3-6 months
  - Repeat HIV and STI screening
  - Assess for side effects
  - Repeat counseling
  - Re-assess need for prevention modalities
  - Prescribe as appropriate

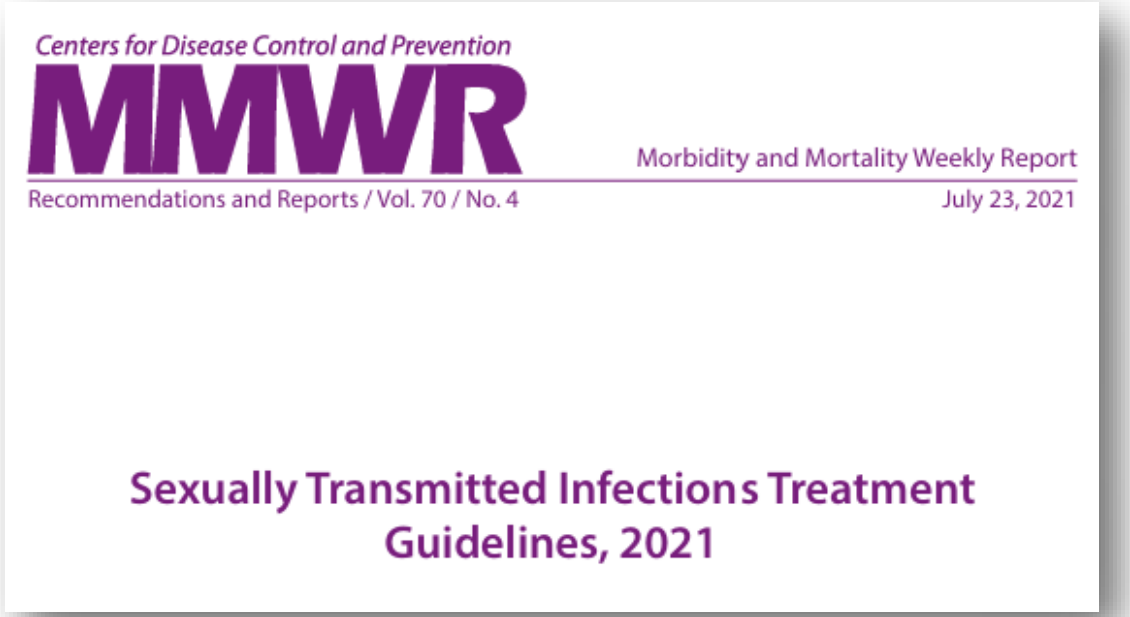
Population	Recommendations
Men who have sex with men	At least annually, test at each site of exposure (urethra, rectum) for sexually active MSM regardless of condom use or every 3-6 months **if at increased risk**.
Patients taking PrEP	All patients starting and taking oral PrEP should have genitourinary and extra-genital testing performed at baseline and every 3 months.
Persons living with HIV	For sexually active individuals, screen at first HIV evaluation and at least annually thereafter. More frequent screening might be appropriate depending **on individual risk behaviors** and local epidemiology
Non-pregnant Women	Test at least annually for sexually active women under 25 years of age and those aged 25 years and older **if at increased risk** Rectal chlamydial testing can be considered in females **based on sexual behaviors and exposure** through shared clinical decision making.
Men who have sex with women***	Consider screening young men in high prevalence clinical settings (adolescent and STI clinics and correctional facilities)
Pregnant Women	All pregnant women under 25 years of age and those aged 25 years and older **if at increased risk**. retest during 3rd trimester if under 25 years of age or at risk.

• Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

How Do I Treat Patients With STIs Taking Doxy-PEP?

Treat As Needed

- Treat as per the 2021 STI Guidelines
  - ***Exception: Consider in-person and exam and deferring empiric treatment for "exposure"***



• Workowski KA, Bachmann LH, Chan PA, et al. Sexually Transmitted Infections Treatment Guidelines, 2021. MMWR Recomm Rep. 2021;70(4):1-187. Published 2021 Jul 23. doi:10.15585/mmwr.rr7004a1

Clinical Conundrums

- What do I do if?
  - My patients test comes back positive for chlamydia after I've prescribed Doxy-PEP?
    - Doxycycline 100mg by mouth twice daily for 7 days
  - My patient is taking Doxy-PEP incorrectly
    - Repeat counseling and provide documents to assist with taking it properly
  - My patient's partner was diagnosed with an STI
    - Assess if your patient took Doxy-PEP "appropriately" after every recent encounter with that partner
    - Consider in person assessment and testing as opposed to empiric treatment

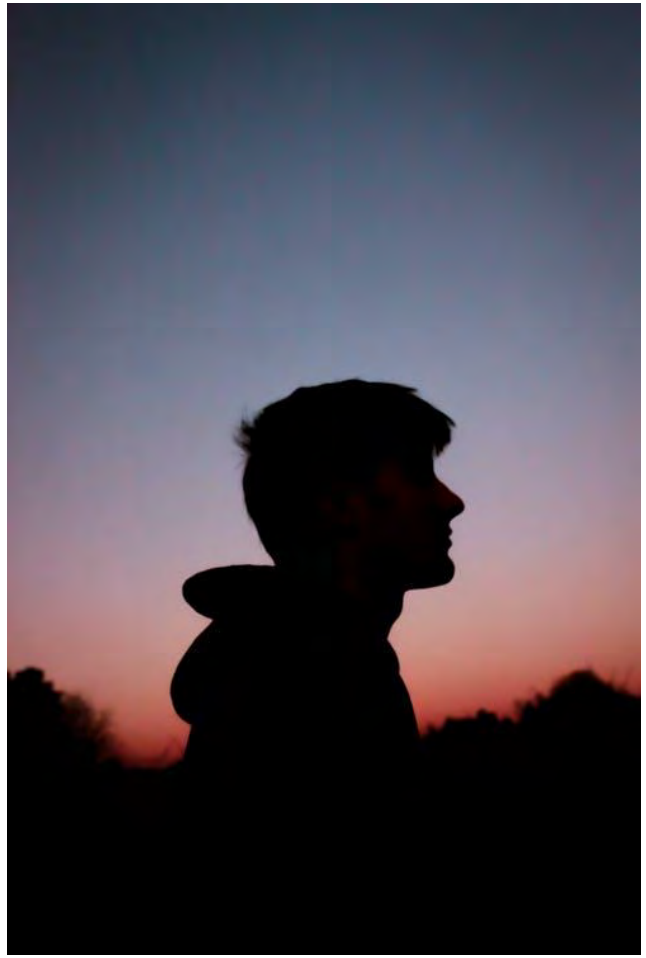
Audience Poll #5

Would you offer Marcus Doxy-PEP?

1. Yes
2. No

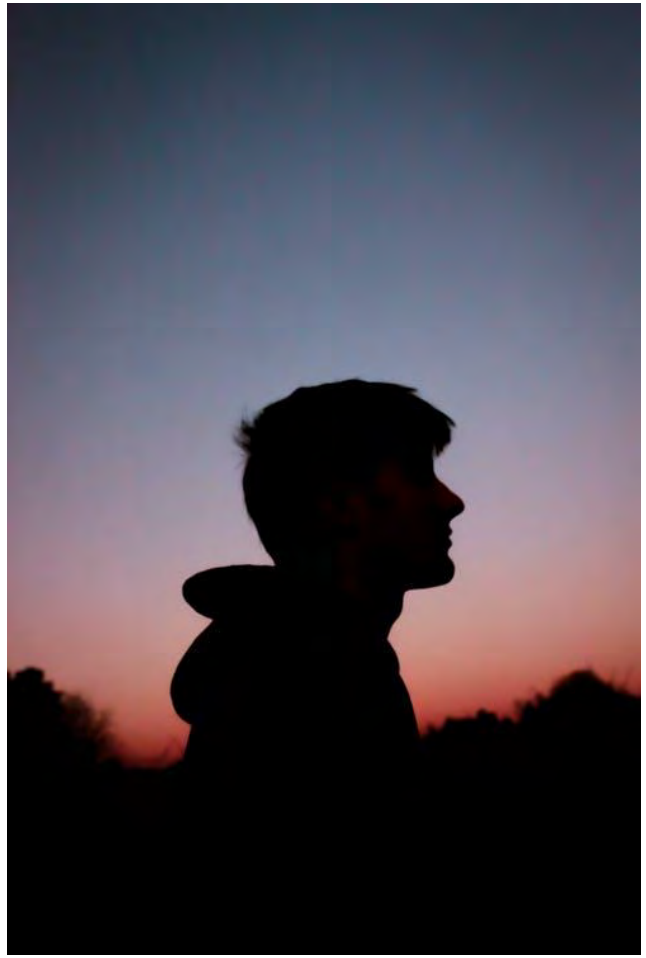
Marcus

- Marcus starts Doxy-PEP



Marcus Comes Back

- Return to clinic 4 weeks later
- “It hurts when I pee, and I have a lot of green discharge”
- Labs repeated
  - Plus, gonorrhea culture
- Treated with Gentamicin and Azithromycin



Marcus's Results

Lab results:
HIV Ab/Ag - Negative
Urine GC/CT – GC positive
Pharyngeal GC/CT – GC positive
Rectal GC/CT – negative
RPR – 1:16 - 1:128 – 10 weeks ago, 1:32 4 weeks ago

Marcus's Gonorrhea Culture

Lab results:

Azithromycin – susceptible (MIC 0.125)

Ciprofloxacin – resistant (MIC 1)

Ceftriaxone – susceptible (MIC 0.016)

Cefixime – Susceptible (48mm)

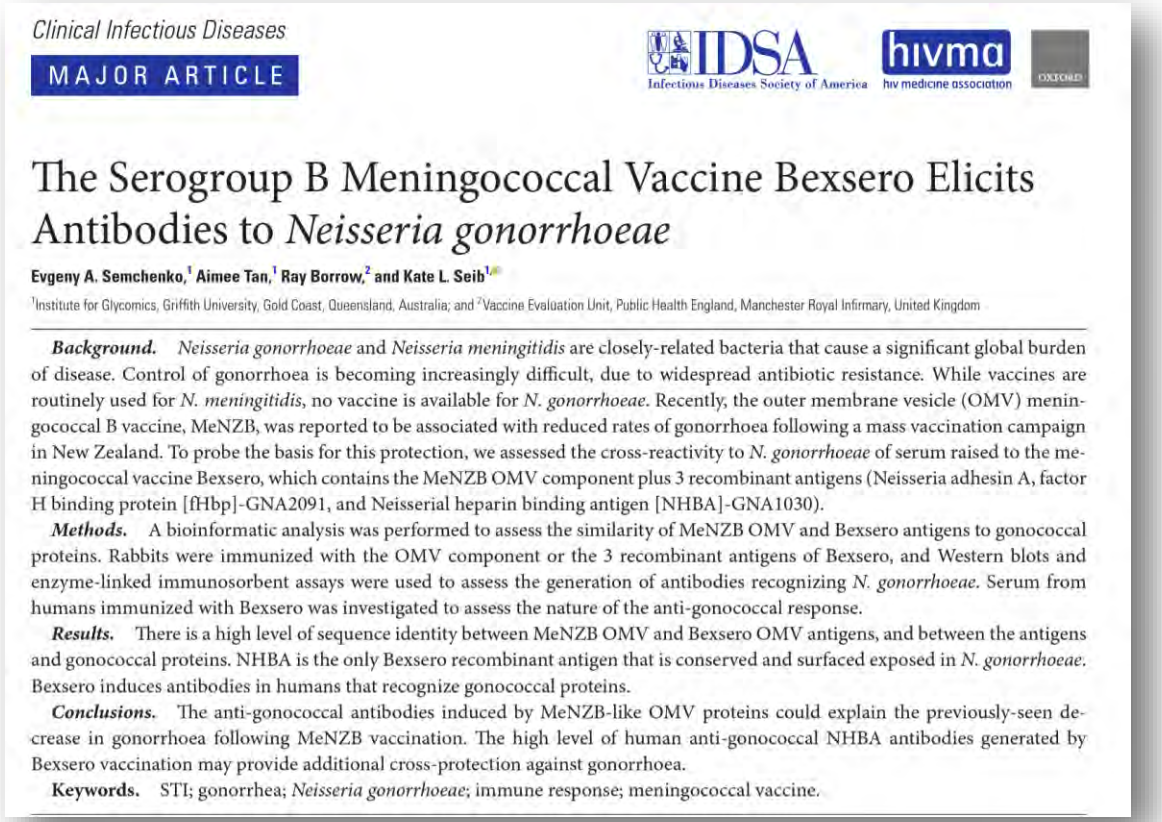
Tetracycline – resistant (MIC 12)

Tetracycline Resistant Gonorrhea

- Will it work for prophylaxis?
- What else can you offer him?

Why Would 4CMenB Prevent *N. Gonorrhea*

- Meningococcal serogroup B (MenB)-4C vaccine
  - 57 proteins were predicted to be surface expressed (outer membrane proteins [OMPs])
  - Majority of OMPs showed high sequence identity between the 2 bacterial species



Clinical Infectious Diseases

MAJOR ARTICLE

The Serogroup B Meningococcal Vaccine Bexsero Elicits Antibodies to *Neisseria gonorrhoeae*

Evgeny A. Semchenko,[1] Aimee Tan,[1] Ray Borrow,[2] and Kate L. Seib[1]

[1]Institute for Glycomics, Griffith University, Gold Coast, Queensland, Australia; and [2]Vaccine Evaluation Unit, Public Health England, Manchester Royal Infirmary, United Kingdom

Background. *Neisseria gonorrhoeae* and *Neisseria meningitidis* are closely-related bacteria that cause a significant global burden of disease. Control of gonorrhoea is becoming increasingly difficult, due to widespread antibiotic resistance. While vaccines are routinely used for *N. meningitidis*, no vaccine is available for *N. gonorrhoeae*. Recently, the outer membrane vesicle (OMV) meningococcal B vaccine, MeNZB, was reported to be associated with reduced rates of gonorrhoea following a mass vaccination campaign in New Zealand. To probe the basis for this protection, we assessed the cross-reactivity to *N. gonorrhoeae* of serum raised to the meningococcal vaccine Bexsero, which contains the MeNZB OMV component plus 3 recombinant antigens (Neisseria adhesin A, factor H binding protein [fHbp]-GNA2091, and Neisserial heparin binding antigen [NHBA]-GNA1030).

Methods. A bioinformatic analysis was performed to assess the similarity of MeNZB OMV and Bexsero antigens to gonococcal proteins. Rabbits were immunized with the OMV component or the 3 recombinant antigens of Bexsero, and Western blots and enzyme-linked immunosorbent assays were used to assess the generation of antibodies recognizing *N. gonorrhoeae*. Serum from humans immunized with Bexsero was investigated to assess the nature of the anti-gonococcal response.

Results. There is a high level of sequence identity between MeNZB OMV and Bexsero OMV antigens, and between the antigens and gonococcal proteins. NHBA is the only Bexsero recombinant antigen that is conserved and surfaced exposed in *N. gonorrhoeae*. Bexsero induces antibodies in humans that recognize gonococcal proteins.

Conclusions. The anti-gonococcal antibodies induced by MeNZB-like OMV proteins could explain the previously-seen decrease in gonorrhoea following MeNZB vaccination. The high level of human anti-gonococcal NHBA antibodies generated by Bexsero vaccination may provide additional cross-protection against gonorrhoea.

Keywords. STI; gonorrhea; *Neisseria gonorrhoeae*; immune response; meningococcal vaccine.

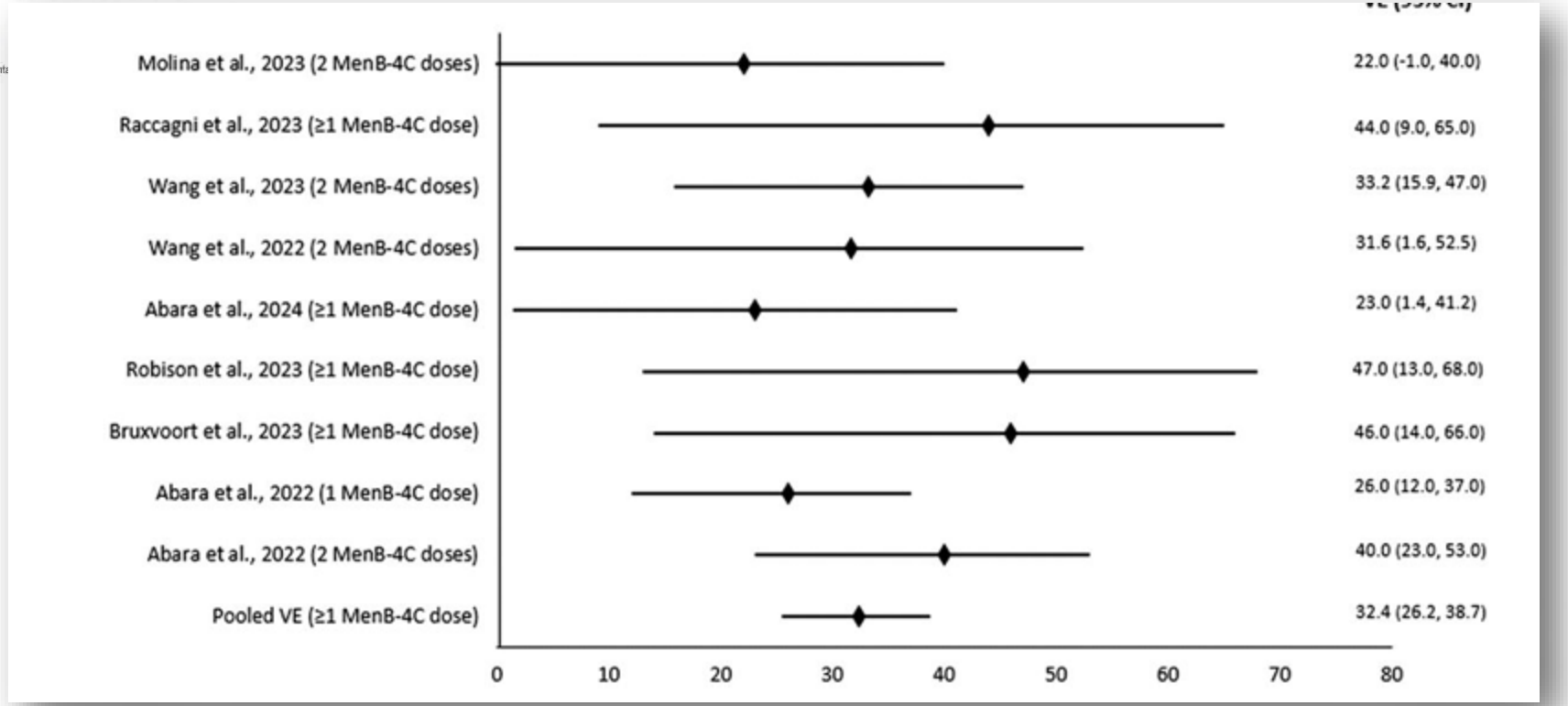
• Evgeny A Semchenko, Aimee Tan, Ray Borrow, Kate L Seib, The Serogroup B Meningococcal Vaccine Bexsero Elicits Antibodies to Neisseria gonorrhoeae, Clinical Infectious Diseases, Volume 69, Issue 7, 1 October 2019, Pages 1101–1111, https://doi.org/10.1093/cid/ciy1061

Does 4CMenB Vaccine Prevent Gonorrhea?

The Journal of Infectious Diseases
REVIEW

Effectiveness of MenB-4C Vaccine Against Gonorrhea: A Systematic Review and Meta-analysis

Winston E. Abara,[1,a] Robert D. Kirkcaldy,[2] Kyle T. Bernstein,[2] Eboni Galloway,[1] and Emily R. Learner[1]
[1]Division of STD Prevention, and [2]Center for Scientific Education and Leadership, US Centers for Disease Control and Prevention, Atlanta



- Abara WE, Kirkcaldy RD, Bernstein KT, Galloway E, Learner ER. Effectiveness of MenB-4C Vaccine Against Gonorrhea: A Systematic Review and Meta-analysis. J Infect Dis. 2025 Feb 4;231(1):61-70. doi: 10.1093/infdis/jiae383. PMID: 39082700; PMCID: PMC11782638.

England Rolling Out MenB Vaccination

BBC

World-first gonorrhoea vaccine launched by NHS England as infections soar

21 May 2025

Share Save

Andrew Rogers & James Gallagher
BBC News

Campaigner Max says he will definitely be getting the new vaccine

England will be the first country in the world to start vaccinating people against the sexually transmitted infection gonorrhoea.

It will not be available for everyone. The focus will mainly be on gay and bisexual men with a history of multiple sexual partners or an STI.

The vaccine is 30-40% effective, but NHS England hopes it will reverse soaring numbers of infections.

There were more than 85,000 cases in 2023 – the highest since records began in 1918.

Audience Poll #6

Would you offer Marcus Men B vaccination?

1. Yes
2. No

STI Prevention Summary

- We are in an era of STI prevention choice and patients should be aware of their options
- Doxy-PEP
  - Doxy-PEP **works** to prevent STIs in gay, bisexual, and other men who have sex with men living with and without HIV
  - Doxy-PEP **did not work** to prevent STIs in females in the dPEP study
  - There remain unknowns about the overall impact, risks, and unintended consequences of Doxy-PEP that potential users should be aware of (**Shared Decision Making**)
- 4CMenB has not been shown in randomized controlled trials to reduce gonorrhea incidence
- Flexibility is key, management will change as we learn more
- **Research is needed to help us better understand the risks and benefits of different STI prevention modalities**

Questions


STI PREVENTION LANDSCAPE
Primary Prevention
Condoms
Risk Reduction Counseling
Vaccination
Medication Prophylaxis
Secondary Prevention
Routine Screening
Syndromic Testing/Treatment
Presumptive Treatment
Partner Services/EPT

NYC STI Prevention Training Center (PTC)

The CDC-funded NYC STD Prevention Training Center at Columbia University provides a continuum of education, resources, consultation and technical assistance to health care providers, and clinical sites. *Region: Ohio, Indiana, Michigan, New York, New Jersey, Puerto Rico & the US Virgin Islands*

https://www.publichealth.columbia.edu/nycptc

National Network of STD Clinical Prevention Training Centers

Didactic Presentations

Webinars, conferences, trainings and grand rounds presentations to enhance and build knowledge

Clinical Consultation Warmline

Clinical guidance regarding STD cases; no identifying patient data is submitted

www.stdccn.org

Technical Assistance

Virtual and on-site technical assistance regarding quality improvement, clinic implementation and best practices around sexual health provision

For more information please contact:
nycptc@cumc.columbia.edu

Resources

Clinical guidance tools regarding the STD treatment guidelines, screening algorithms and knowledge books, such as the **Syphilis Monograph**.

To download a copy please visit:
http://bit.ly/SyphilisMonograph2019PTC