Ending the STI Epidemic Through Prevention

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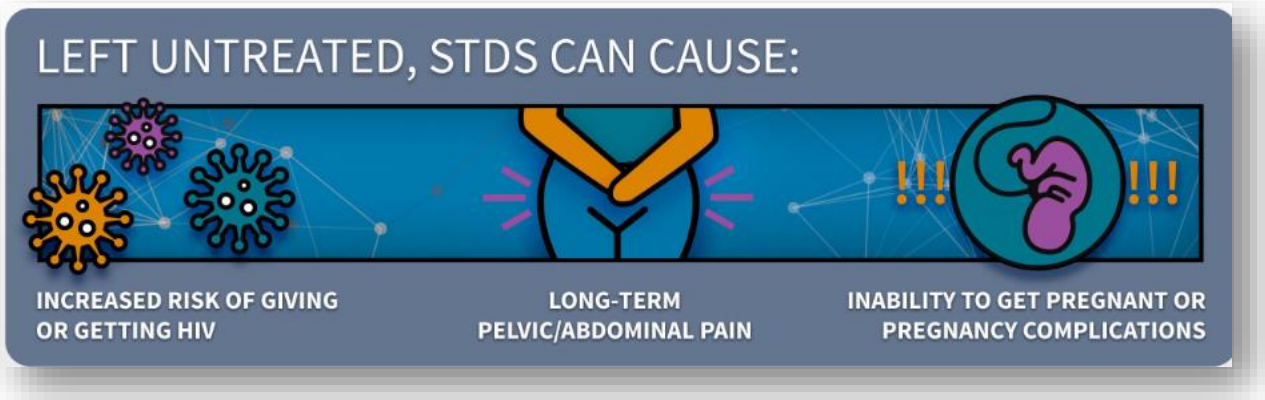
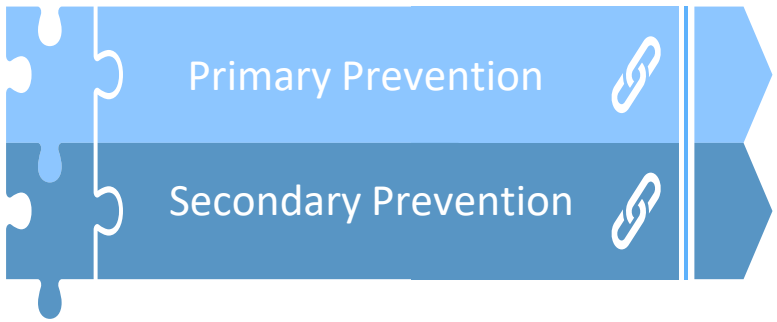
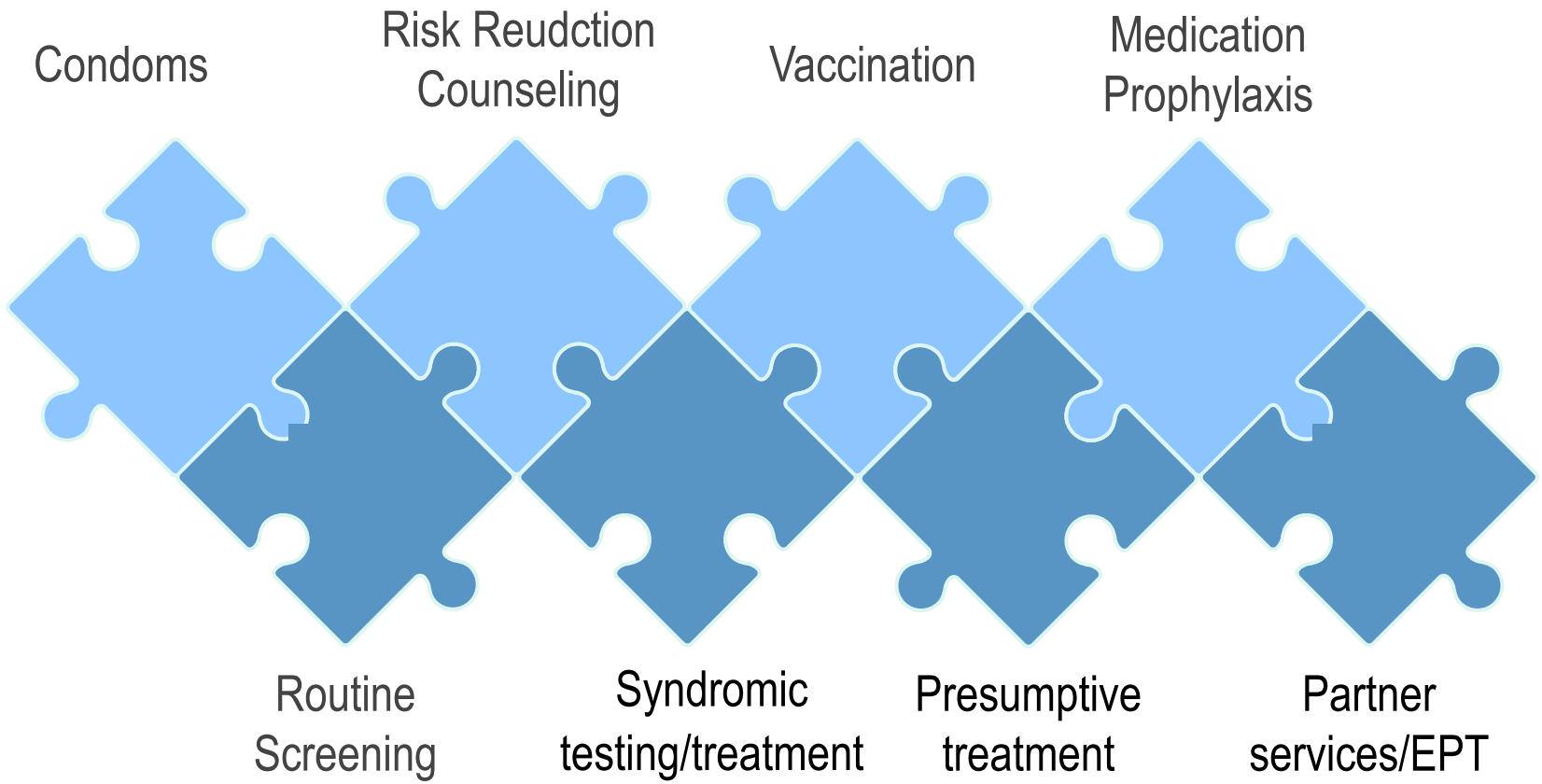
STIs Are Not Benign



- 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



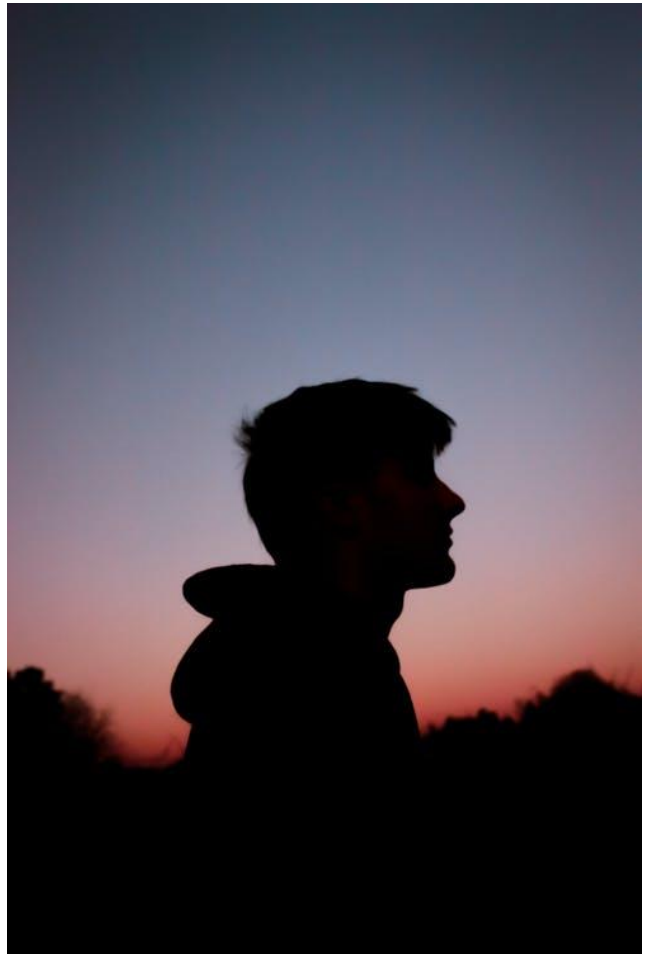


Meet Igor

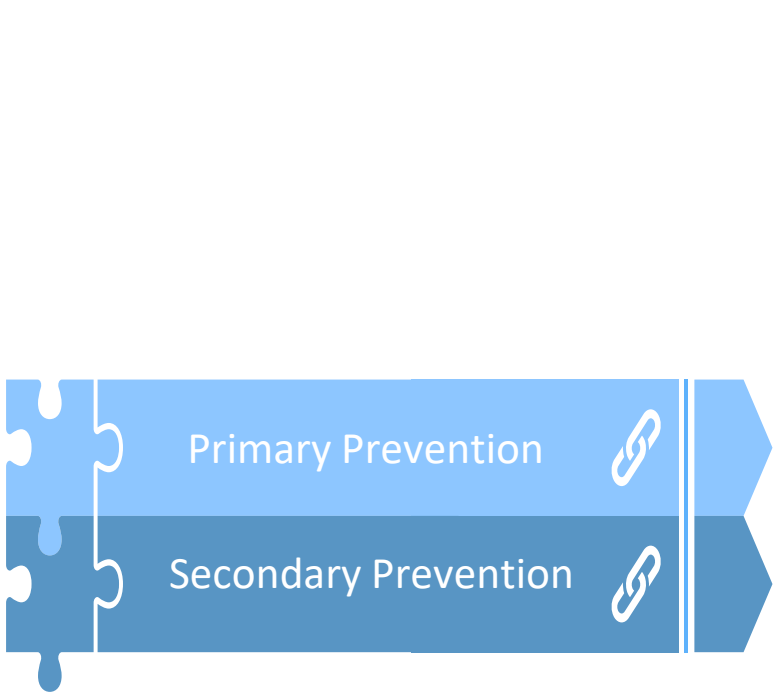
- 29-year-old male in New York City
- Takes HIV PrEP for HIV prevention
- Sexually active with men
  - Four partners since his last visit, no condom usage
- Walks in to clinic due with 2 days of green penile discharge

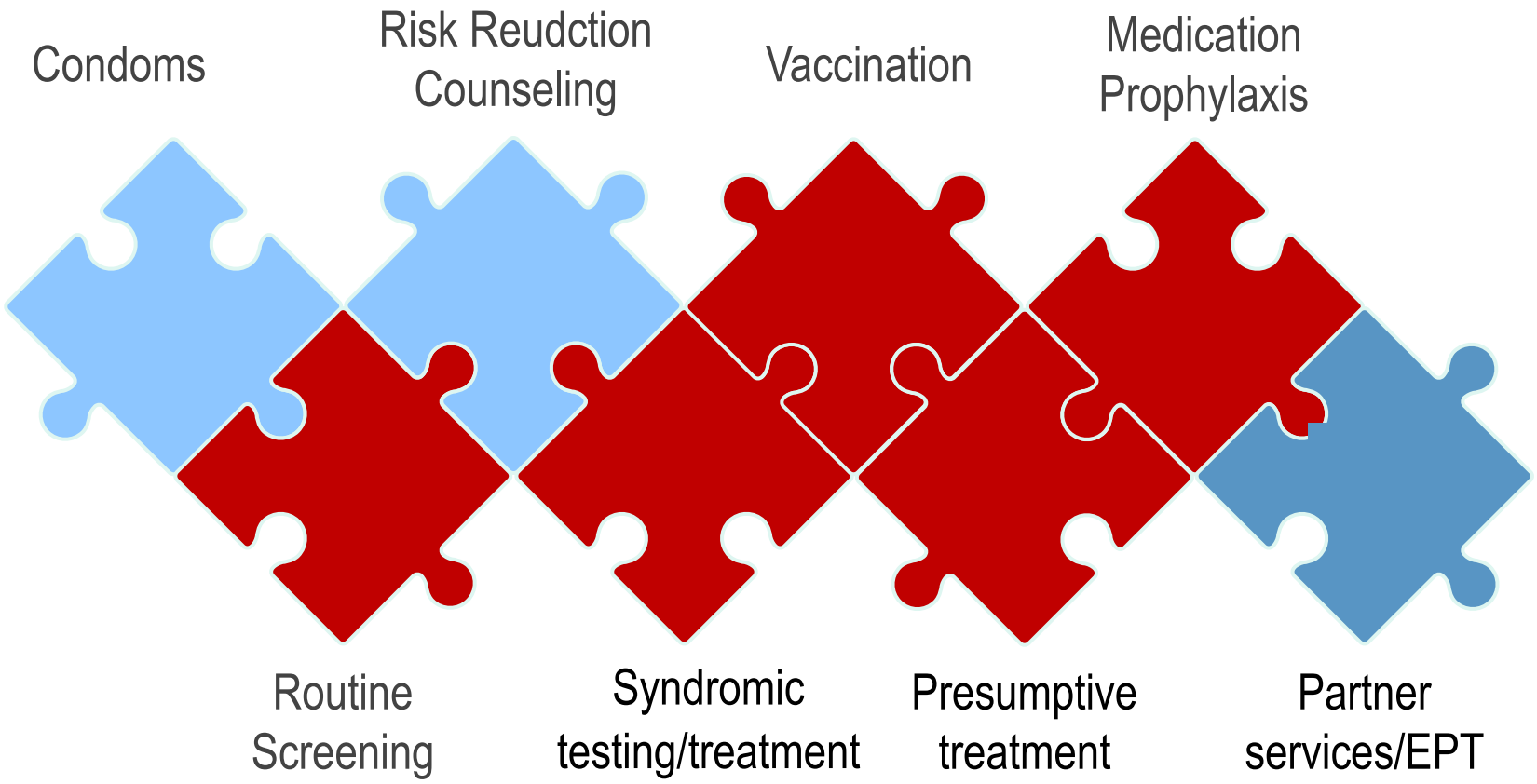
- **Routine testing for HIV, syphilis, and three-site gonorrhea/chlamydia testing performed**

- **Treated empirically with Ceftriaxone and Doxycycline**



Igor's Prevention Plan





Igor'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

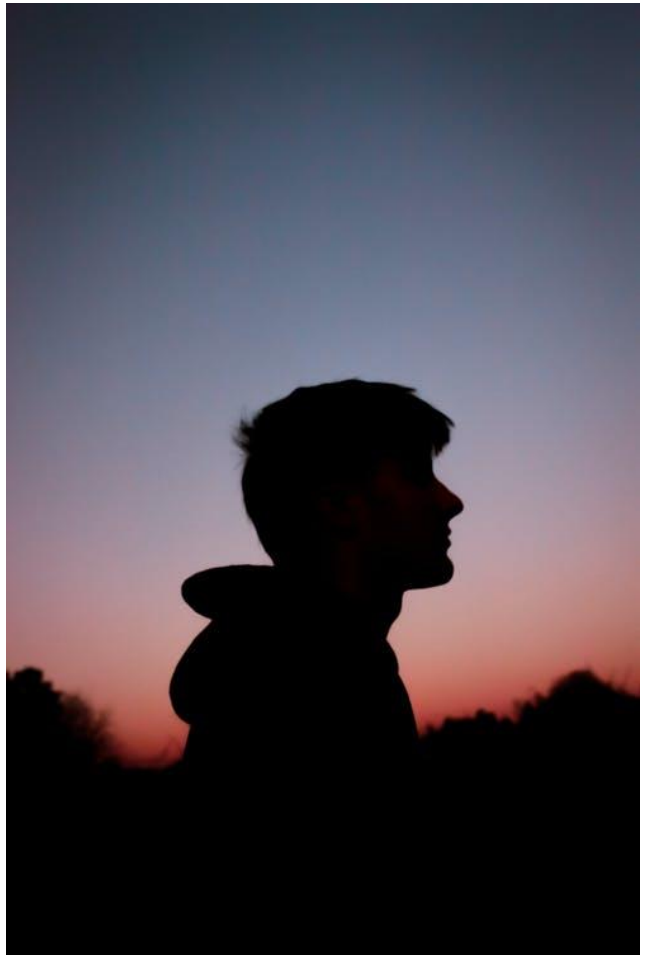
Igor's Results

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

Igor

- 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

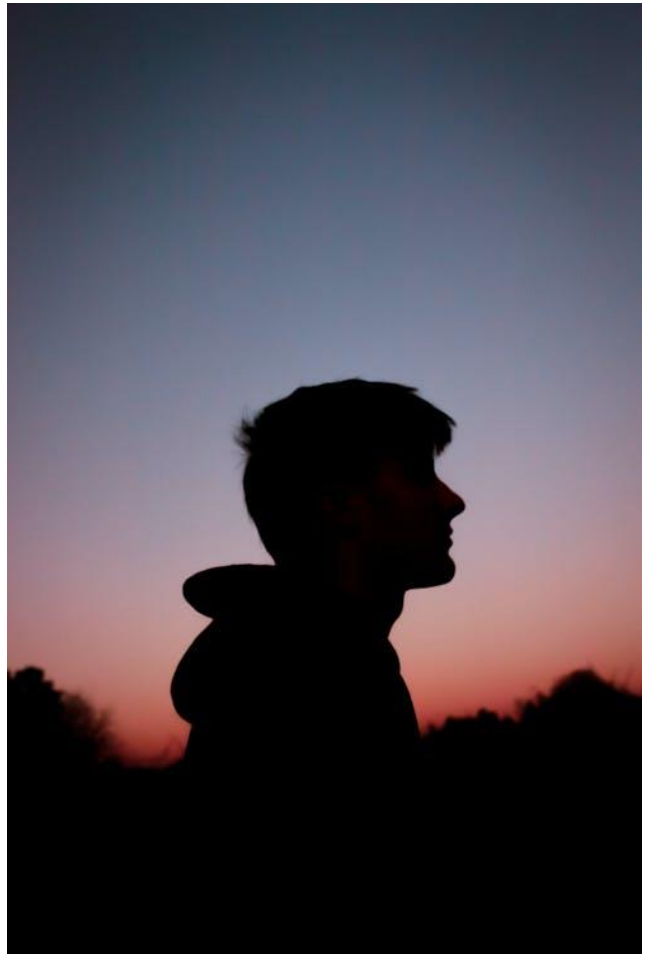


Igor's Results

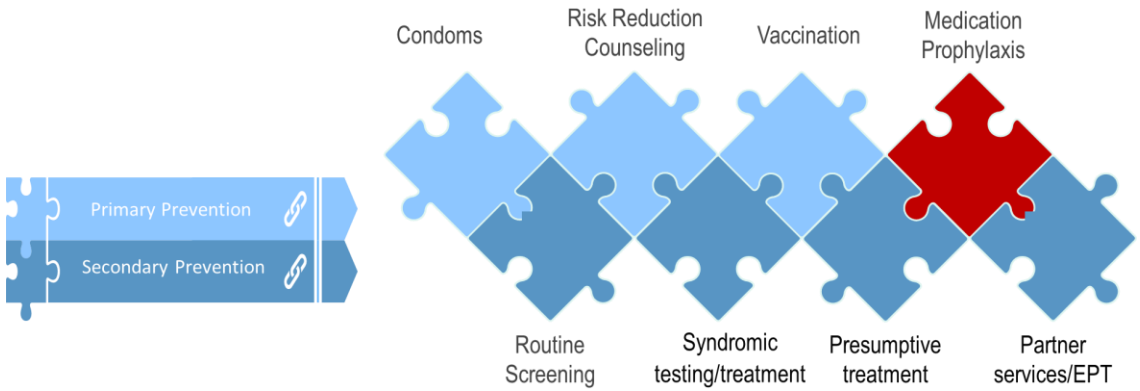
Lab results:
HIV Ab/Ag - Negative
Urine GC/CT – GC positive
Pharyngeal GC/CT – GC positive
Rectal GC/CT – CT positive
RPR – 1:32 - 1:128 – 6 weeks ago

Igor

- You call to give Igor his results and he's 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, ideally within 24 hours but up to 72 hours after a condomless sexual encounter

Does Doxy-PEP Prevent STIs?

What We Know About Doxy-PEP

Existing studies on Doxycycline as post-exposure (Doxy-PEP) or pre-exposure (Doxy-PrEP) prophylaxis				
Study		Population	Effectiveness	Pills/month
ANRS IPERGAY	PEP	MSM/TGW taking PrEP	**Reduction** in time to first STI HR 0.53 (0.33-0.85) Reduction seen for CT and syphilis but not GC	6.8
DoxyPEP	PEP	MSM/TGW Taking PrEP or PWH	**Reduction** in STI per quarter RR 0.38 (0.24 – 0.6)	4.O (IQR 1-10)
DoxyVac	PEP	MSM on PrEP	**Reduction** in time to first CT or syphilis HR 0.16 (0.08-0.30). Reduction in time to first GC HR 0.49 (0.32-0.76)	7.0 (IQR 4-11)
dPEP	PEP	Women	**No reduction** in STI incidence RR 0.88 (0.60-1.29)	Not reported

MSM = men who have sex with men, TGW = transgender women, PWH = Persons with HIV, CT = Chlamydia, GC = Gonorrhea, OR = odds ratio, HR = hazards ratio RR = Relative risk reduction () = Confidence intervals IQR() = Interquartile range

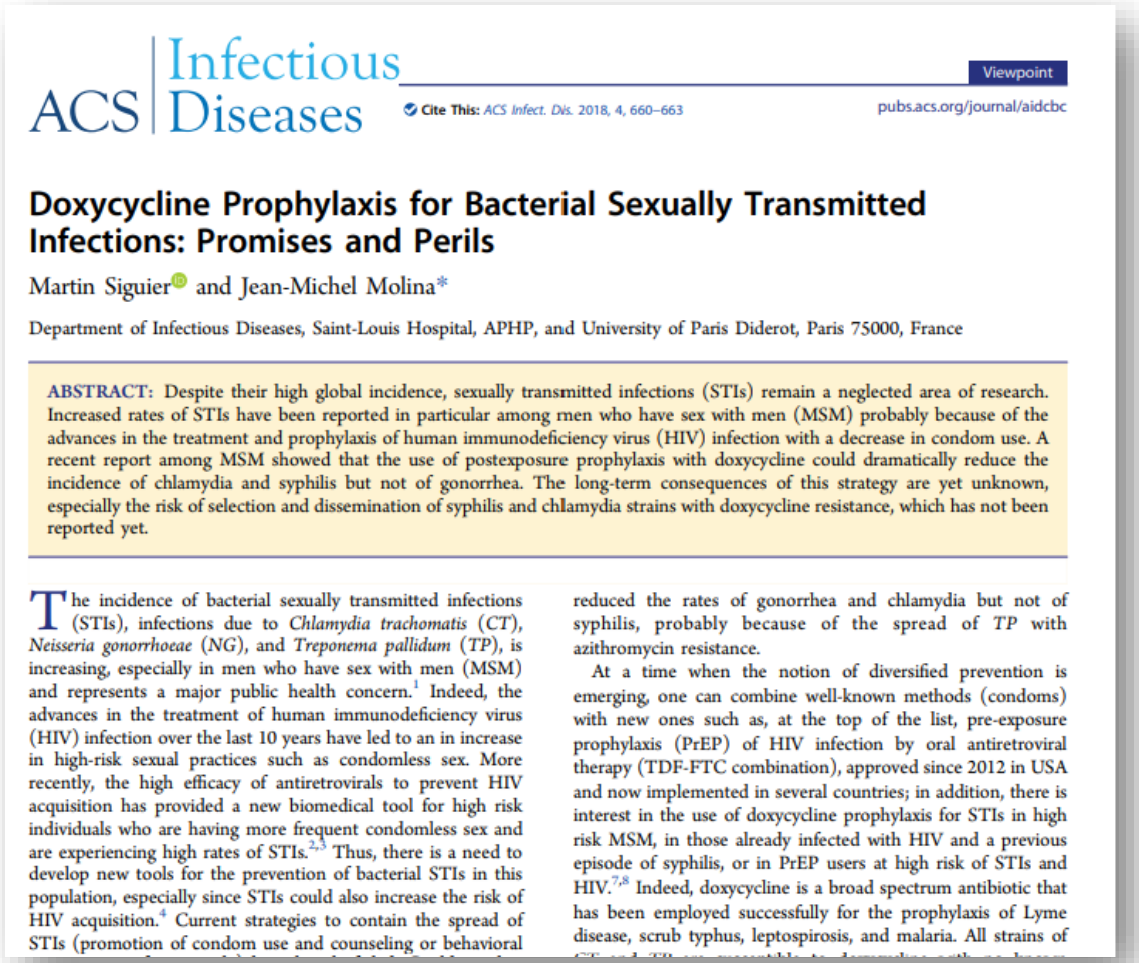
- Doxycycline **post-exposure prophylaxis** (PEP) is safe and well tolerated
- Doxy-PEP **prevents** STIs in MSM and transgender women
- Doxy-PEP **did not** prevent STIs in cis-women in the dPEP study

More To Come

- **Syphilaxis** (Australia) - “An antibiotic every day or two antibiotic pills after sex”
  - Comparing Doxycycline PrEP vs PEP
- **CTN 313: The DaDHS Trial** – “Daily doxycycline or placebo”
  - Comparing Doxycycline PrEP vs placebo
- **DISCO** - Comparing Doxycycline PrEP vs PEP

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

Doxy-PEP Concerns



ACS Infectious Diseases

Viewpoint

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pubs.acs.org/journal/aidcbc

Doxycycline Prophylaxis for Bacterial Sexually Transmitted Infections: Promises and Perils

Martin Siguier and Jean-Michel Molina*

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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 limited and transient benefits
2. Risk compensation…might offset early benefits
3. Antibiotic prophylaxis might change the presentation of STIs
4. Impact of doxycycline use on the microbiome remains to be assessed
   - Might select for antibiotic resistance outside the field of STIs
   - The greatest fear is by far the risk of selection of doxycycline resistance to Chlamydia and Syphilis

1. 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

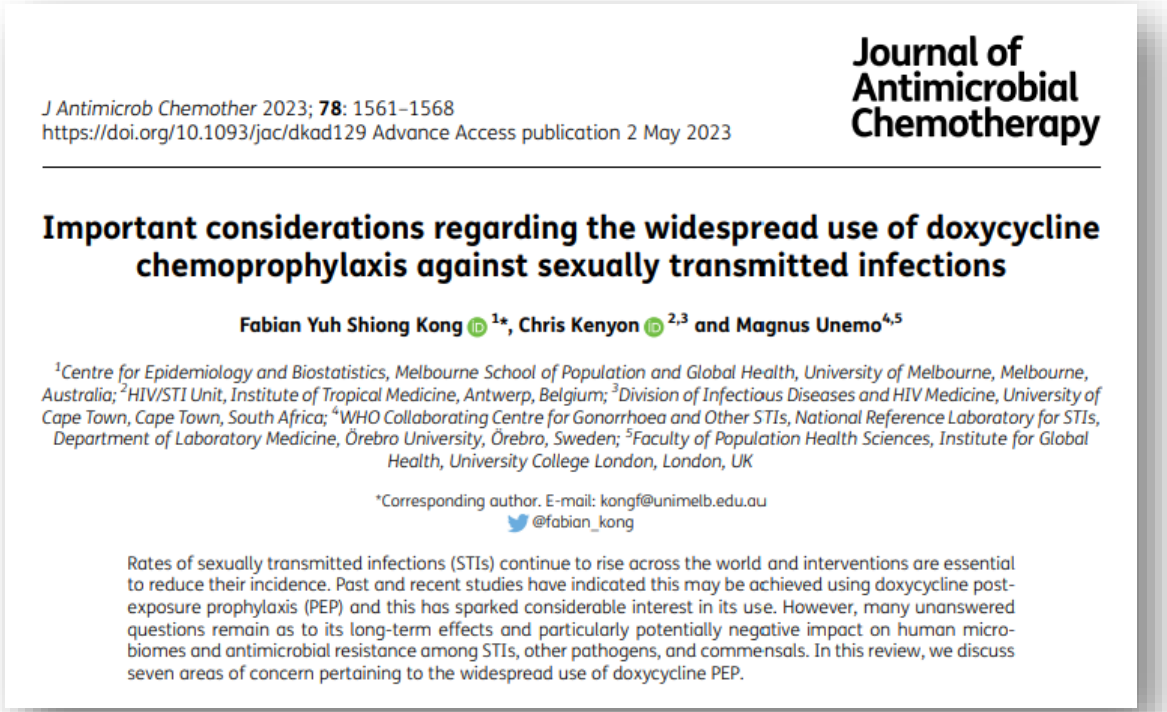
Clinical Questions

- Antibiotic prophylaxis may change the presentation or diagnosis of STIs

- No data so far

- Notable concern about the impact on syphilis serological testing
  - Partial treatment
  - Delayed diagnosis
  - False negatives

Antimicrobial Resistance Concerns



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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
        1. Staph aureus
        2. Commensal Neisseria
        3. Enterobacterales

1. 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

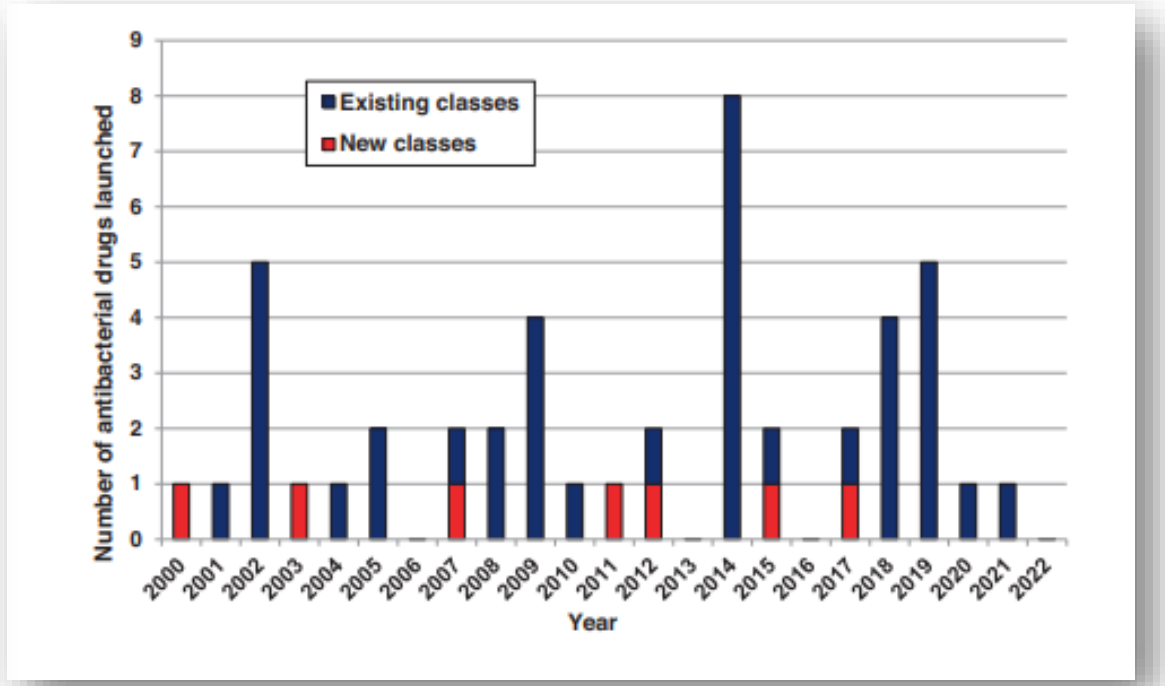
Antibiotics in the clinical pipeline as of December 2022

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.



1. 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

COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

NEW YORK CITY STD HIV PREVENTION TRAINING CENTER

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*
- 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

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

1.Lau A, Bradshaw CS, Lewis D, Fairley CK, Chen MY, Kong FY, Hocking JS. The Efficacy of Azithromycin for the Treatment of Genital Mycoplasma genitalium: A Systematic Review and Meta-analysis. Clin Infect Dis. 2015 Nov 1;61(9):1389-99. doi: 10.1093/cid/civ644. Epub 2015 Aug 3. PMID: 26240201.
2.Li Y, Le WJ, Li S, Cao YP, Su XH. Meta-analysis of the efficacy of moxifloxacin in treating Mycoplasma genitalium infection. Int J STD AIDS. 2017 Oct;28(11):1106-1114. doi: 10.1177/0956462416688562. Epub 2017 Jan 24. PMID: 28118803.
3.Gossé, M., Nordbø, S.A. & Pukstad, B. Evaluation of treatment with two weeks of doxycycline on macrolide-resistant strains of Mycoplasma genitalium: a retrospective observational study. BMC Infect Dis 21, 1225 (2021).

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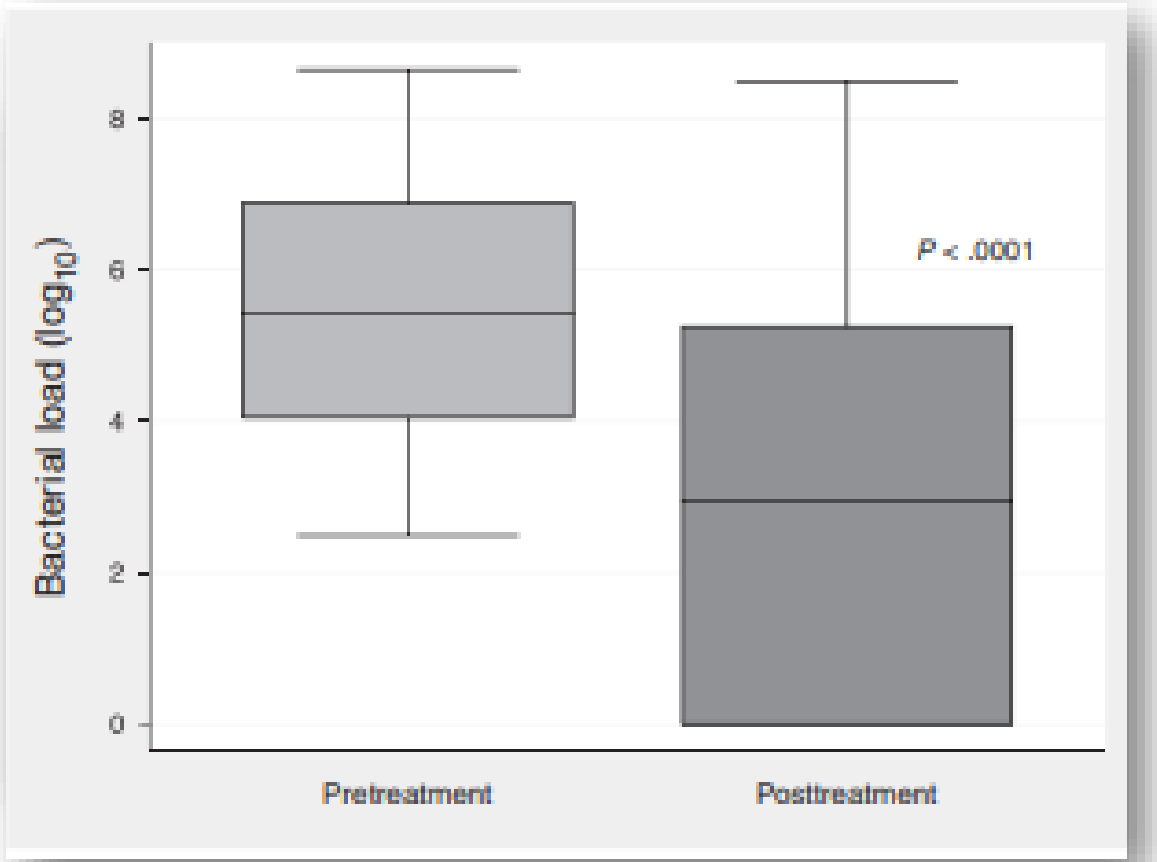
(See the Major Article by Braun et al on pages 569-76 and Editorial commentary by Sulkowski on pages 577-9.)

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.



1. 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

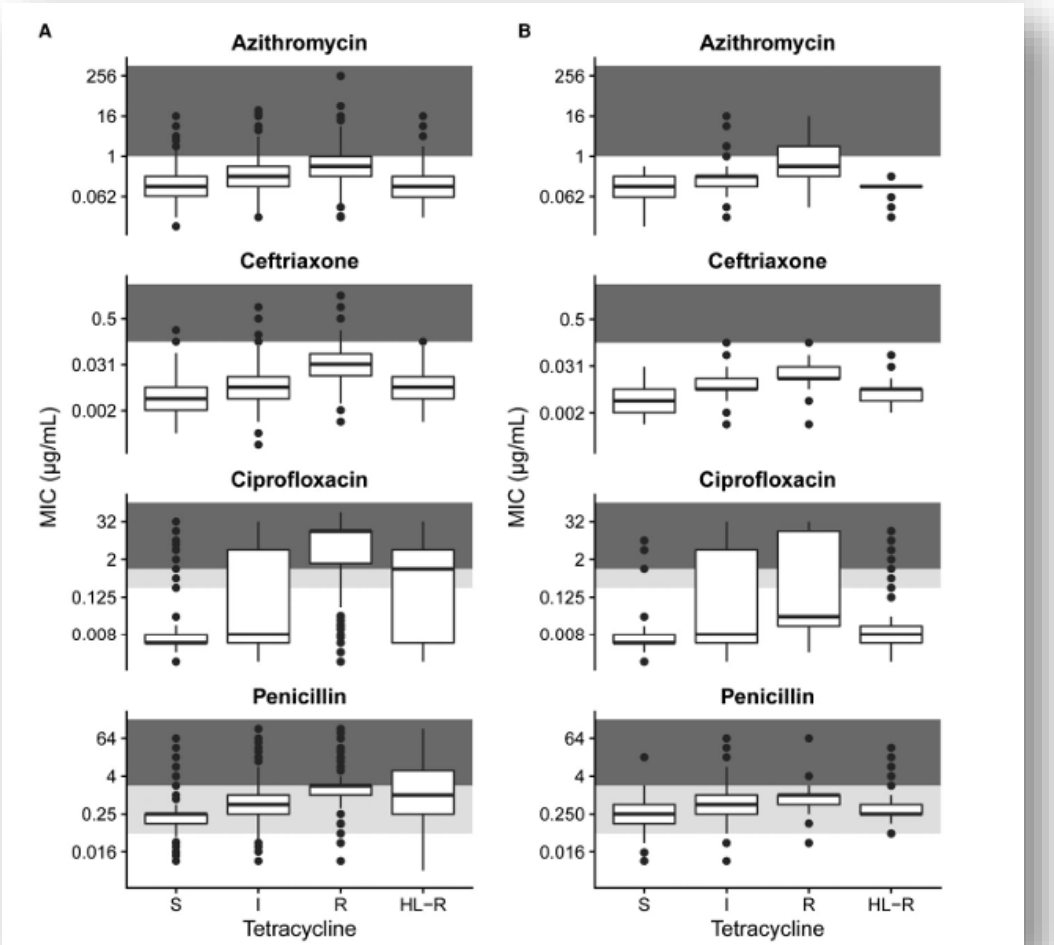
Clinical Infectious Diseases

BRIEF REPORT

A Genomic Perspective on the Near-term Impact of Doxycycline Post-exposure Prophylaxis on *Neisseria gonorrhoeae* Antimicrobial Resistance

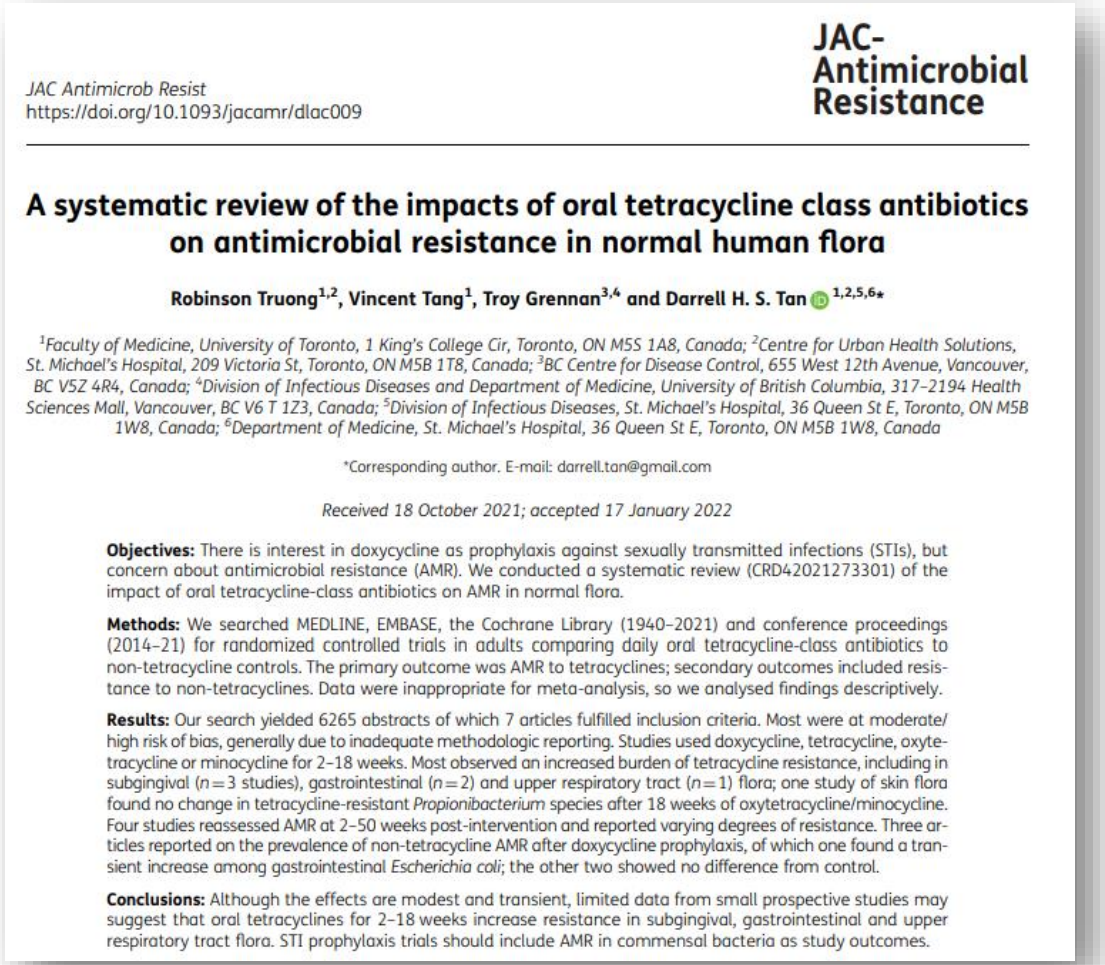
Tatum D. Mortimer and Yonatan H. Grad

Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA



1. 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*]

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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.

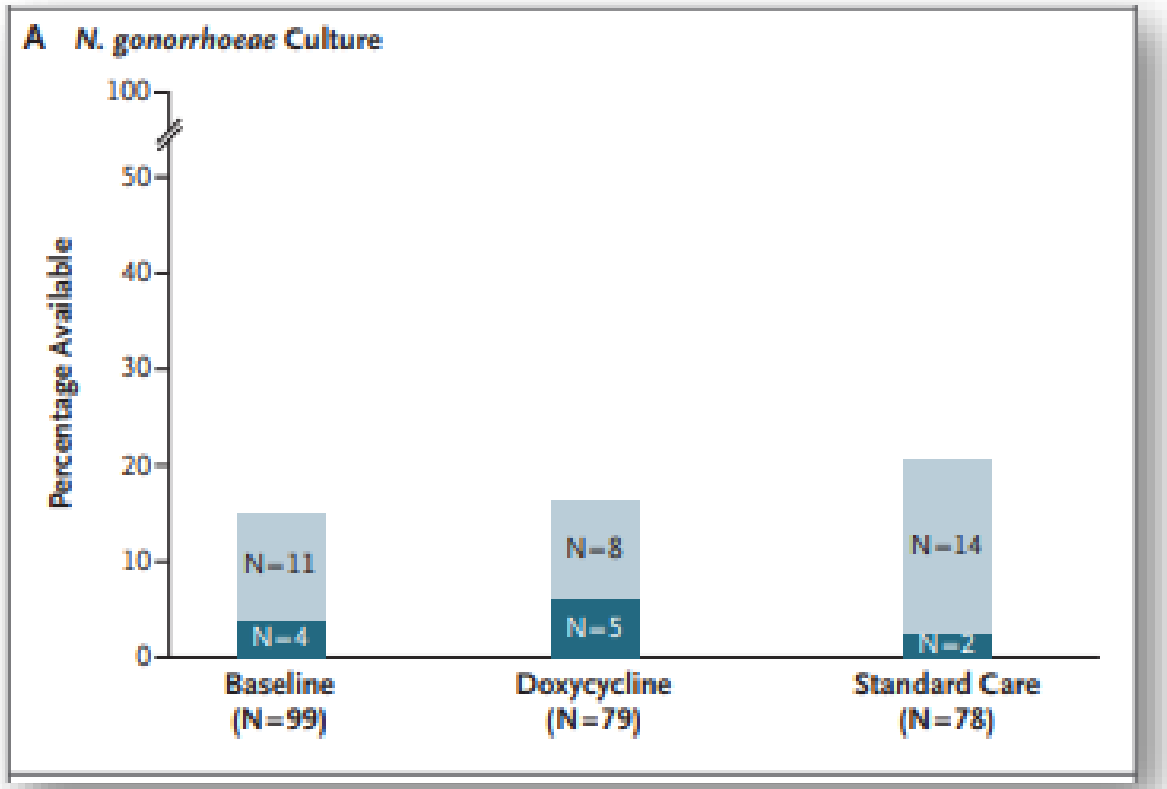
Results: Our search yielded 6265 abstracts of which 7 articles fulfilled inclusion criteria. Most were at moderate/high risk of bias, generally due to inadequate methodologic reporting. Studies used doxycycline, tetracycline, oxytetracycline or minocycline for 2–18 weeks. Most observed an increased burden 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.

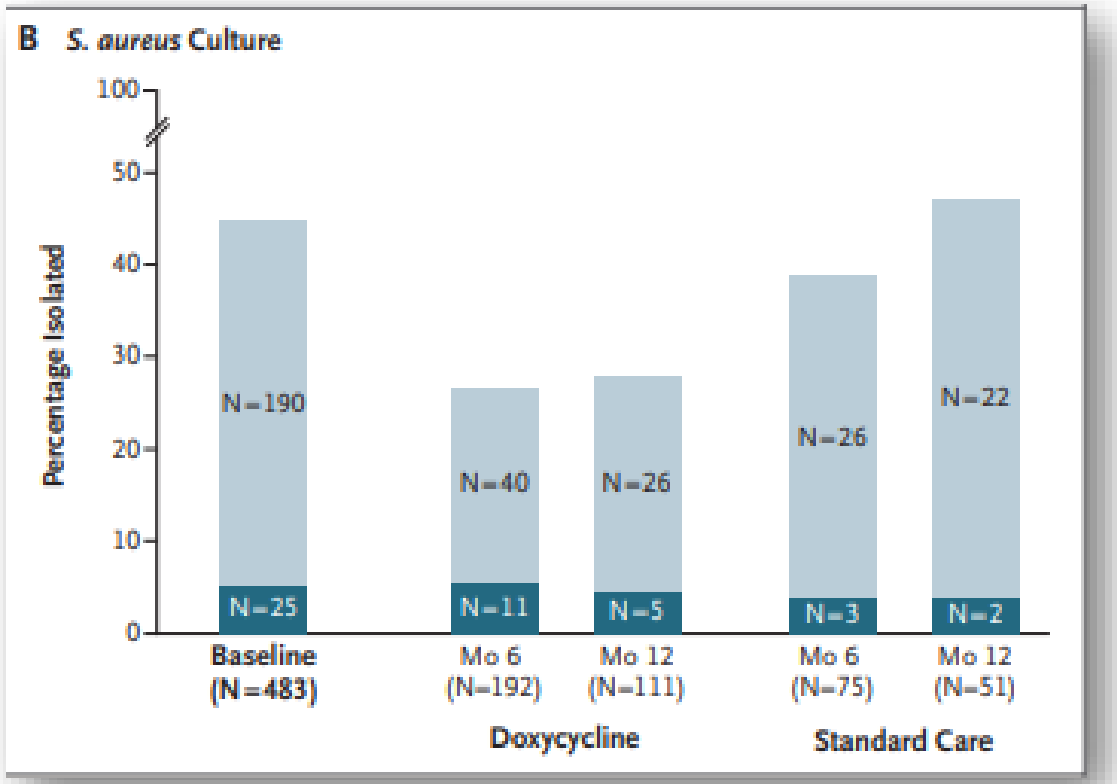
Conclusions: Although the effects are modest and transient, limited data from small prospective studies may suggest that oral tetracyclines for 2–18 weeks increase resistance in subgingival, gastrointestinal and upper respiratory tract flora. STI prophylaxis trials should include AMR in commensal bacteria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

1. 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

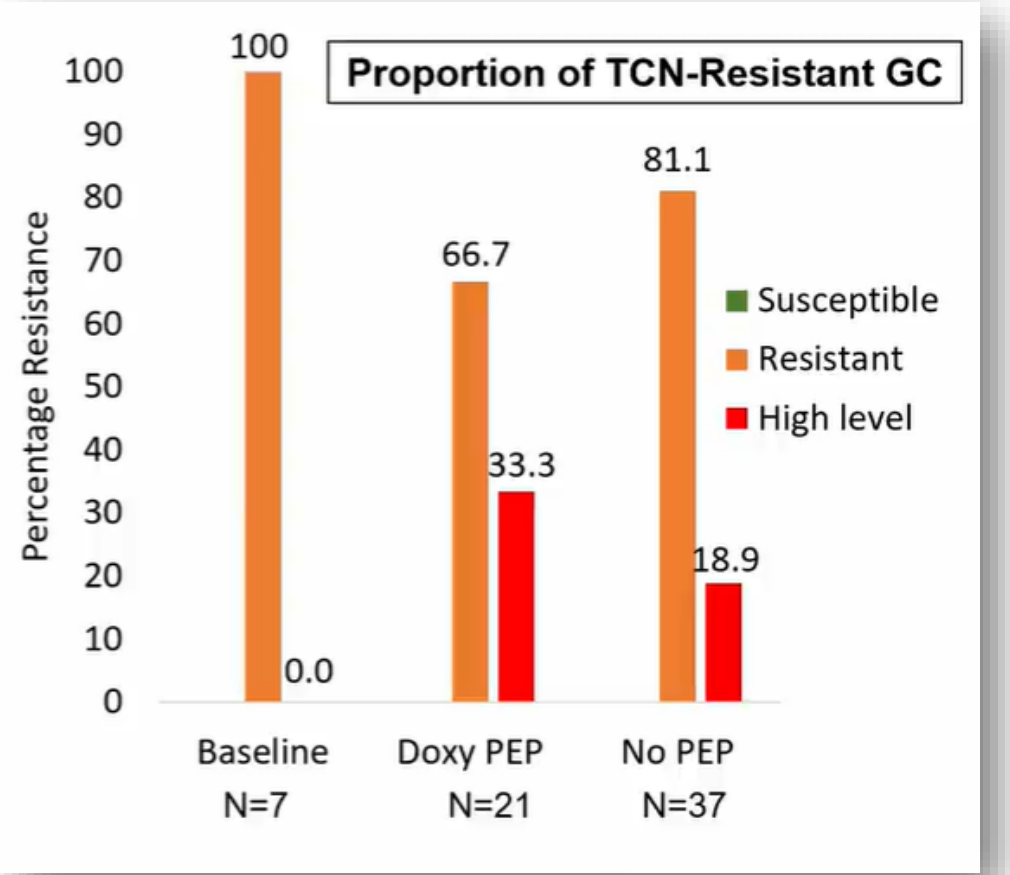
Antimicrobial Resistance – DoxyPEP Study

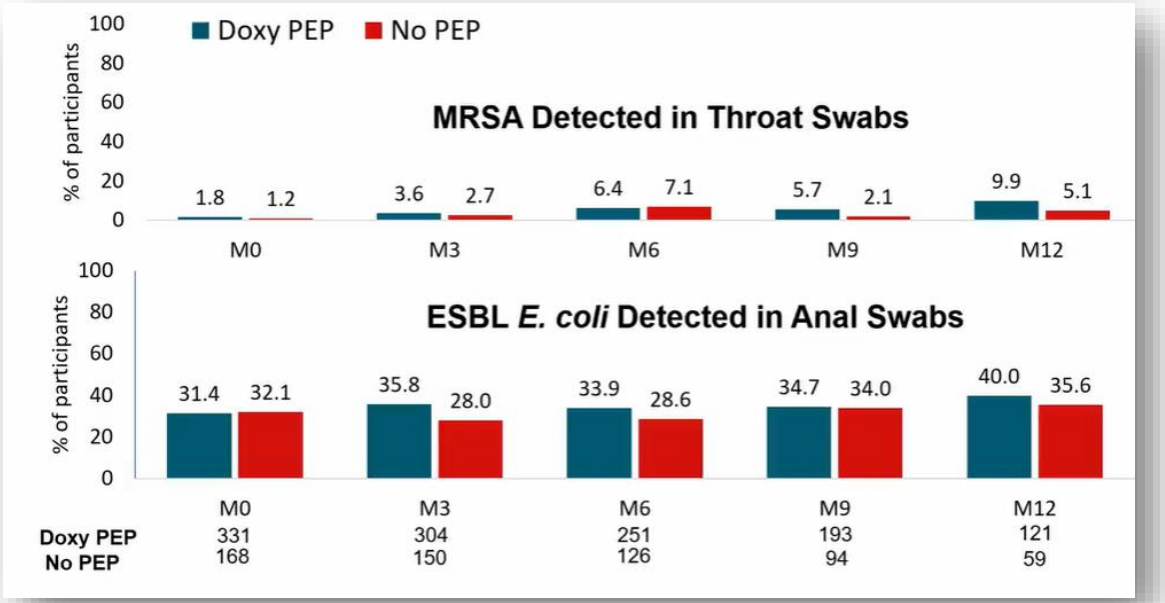




1. Luetkemeyer AF, Donnell D, Dombrowski JC, et al. Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections. *N Engl J Med*. 2023;388(14):1296-1306. doi:10.1056/NEJMoa2211934

Antimicrobial Resistance – DoxyVac Study

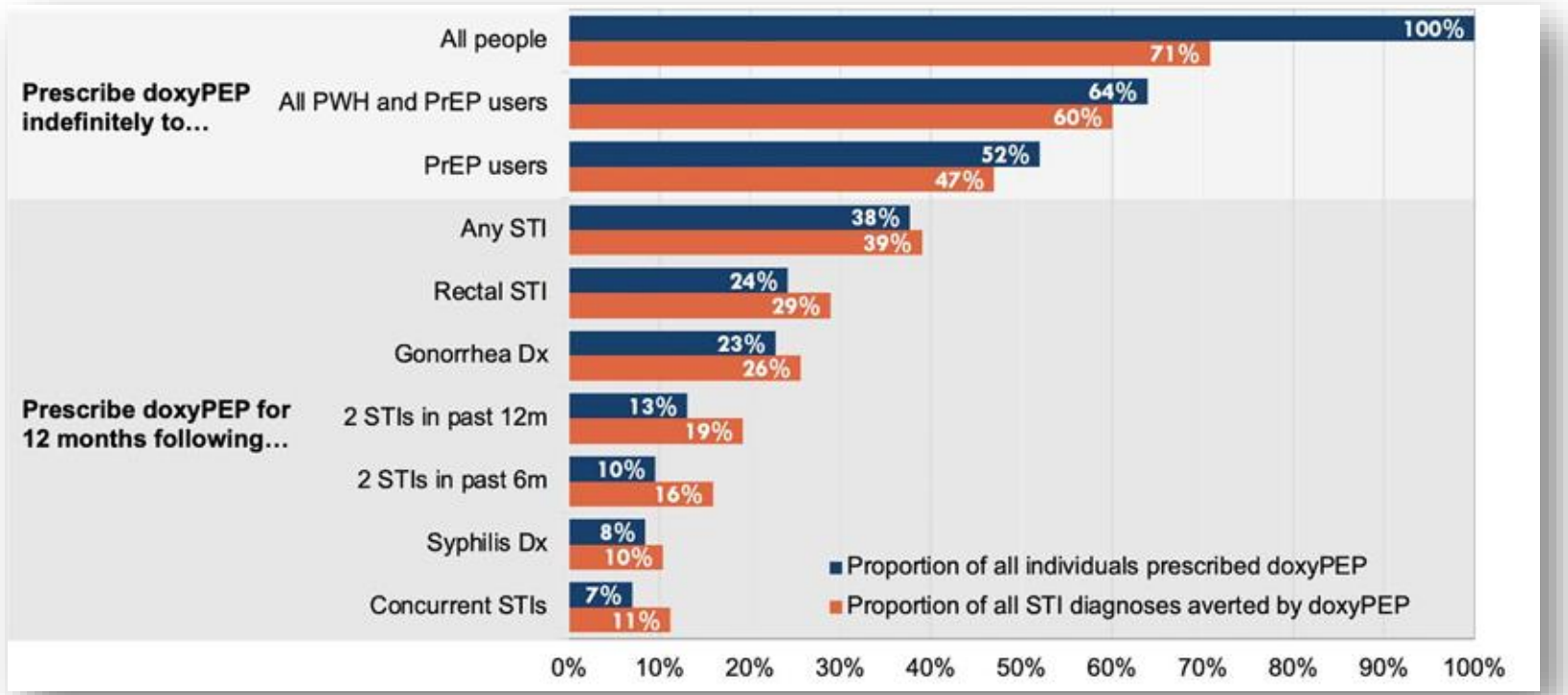




- Molina et al DOXYVAC CROI 2023 Abstract 119
- Liu AY, Buchbinder SP. CROI 2023: Epidemiologic Trends and Prevention for HIV and Other Sexually Transmitted Infections. Top Antivir Med. 2023;31(3):468-492.

Implementation Questions

- **Who should be given Doxy-PEP?**
- What is the proper interval for STI testing for individuals on Doxy-PEP?



1. Traeger MW, Mayer KH, Krakower DS, Gitin S, Jenness SM, Marcus JL. Potential impact of doxycycline post-exposure prophylaxis prescribing strategies on incidence of bacterial sexually transmitted infections [published online ahead of print, 2023 Aug 18]. Clin Infect Dis. 2023;ciad488. doi:10.1093/cid/ciad488

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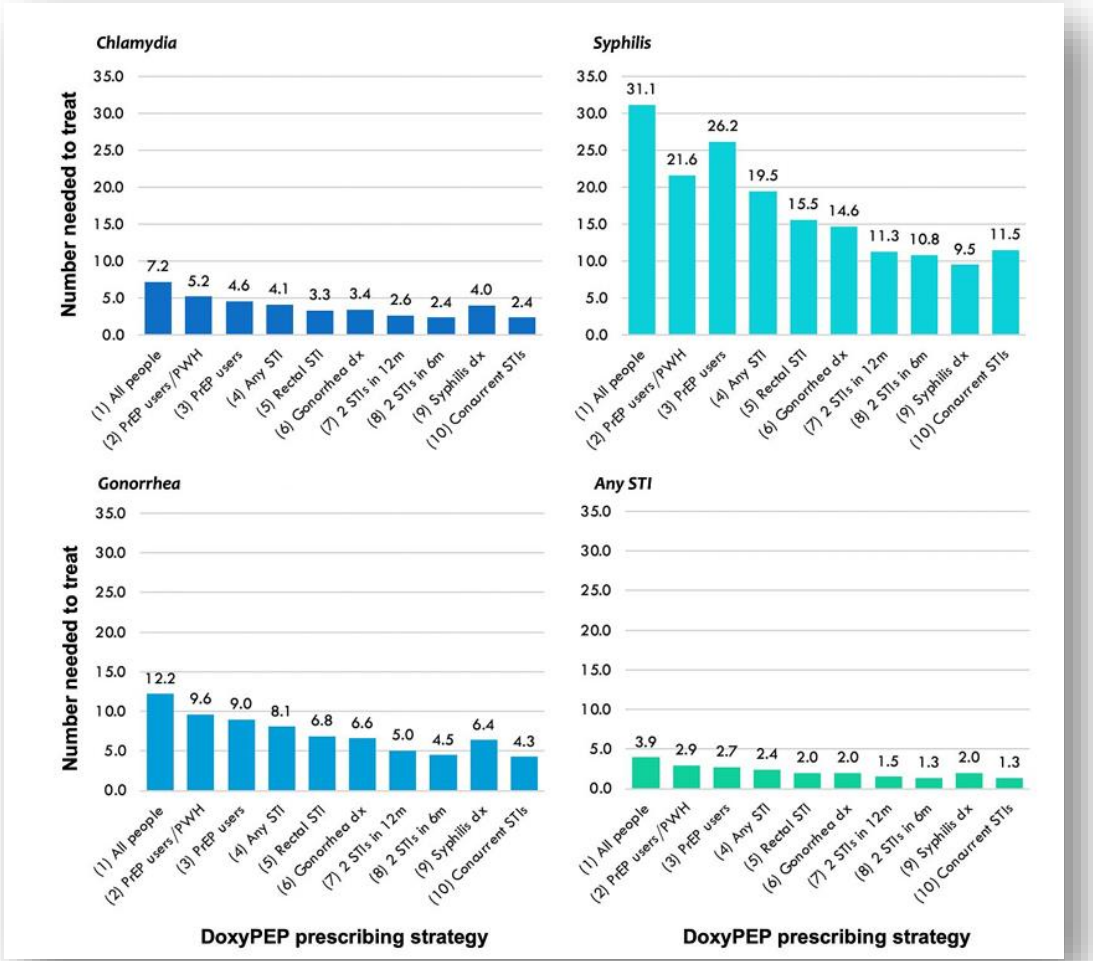

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Implementation Questions

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- **What is the proper interval for STI testing for individuals on Doxy-PEP?**

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

Updated Australian Recommendations

2023 Consensus Statement on doxycycline prophylaxis (Doxy-PEP) for the prevention of syphilis, chlamydia and gonorrhoea among gay, bisexual, and other men who have sex with men in Australia.

- "Doxy-PEP should be considered **primarily for the prevention of syphilis** in GBMSM who are at risk of this STI, although for some individuals the reduction in chlamydia, and the lesser reduction of gonorrhoea might be important."
  - Some stakeholders held the view that **Doxy-PEP should be considered only for the prevention of syphilis** in GBMSM, for the reasons listed above

- https://ashm.org.au/about/news/doxy-pep-statement/#:~:text=infections%20(STI).-,Among%20gay%2C%20bisexual%2C%20and%20other%20men%20who%20have%20sex%20with,to%20varying%20levels%20of%20tetracycline

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- GBMSM with a recent syphilis diagnosis
- GBMSM with two or more recent other (i.e., not syphilis) bacterial STI diagnoses
- GBMSM who identify an upcoming period of heightened STI risk, for example, attendance at a sex event, or holiday plans that likely involve sexual activity with multiple casual sexual partners
- GBMSM **with concurrent male and cisgender female sexual partners or other sexual partners with a uterus, recognising the additional health risks posed by chlamydia, gonorrhoea and syphilis for people with a uterus.**

- https://ashm.org.au/about/news/doxy-pep-statement/#:~:text=infections%20(STI).-,Among%20gay%2C%20bisexual%2C%20and%20other%20men%20who%20have%20sex%20with,to%20varying%20levels%20of%20tetracycline

Updated Australian Recommendations

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- Given that STI risk is often not static, it is recommended to **use Doxy-PEP for a predefined period, e.g., 3–6 months, followed by review of the need for ongoing use**

- Doxy-PEP users should be assisted **to maximise the benefits of Doxy-PEP while minimising overall antibiotic use.**
  - For example, if a Doxy-PEP user tends to have multiple sexual partners during weekends but few during the week, then a single Monday morning dose of 200mg Doxy-PEP should adequately cover their STI risk, rather than multiple doses over the weekend

- https://ashm.org.au/about/news/doxy-pep-statement/#:~:text=infections%20(STI).-,Among%20gay%2C%20bisexual%2C%20and%20other%20men%20who%20have%20sex%20with,to%20varying%20levels%20of%20tetracycline

CDC Preliminary Guidance

- Should be considered

Box. Population recommended for consideration for use of doxycycline as PEP for bacterial STI prevention

Recommendation	Strength of recommendation and quality of evidence
• Doxycycline 200mg taken once orally within 72 hours of oral, vaginal or anal sex should be considered for gay, bisexual, and other men who have sex with men, and for transgender women, with a history of at least one bacterial STI (i.e. gonorrhea, chlamydia or syphilis) in the last 12 months.	**AI**
• No recommendation can be given at this time on the use of doxycycline PEP for cisgender women, cisgender heterosexual men, transgender men, other queer and nonbinary individuals. If this intervention is offered, it should be implemented with considerations for ancillary services detailed below.	**There is insufficient evidence to assess the balance of benefits and harms of the use of doxycycline PEP**

How Do I Provide Doxy-PEP?

Who Should I **Offer** Doxy-PEP To?

Populations
Cis-gender MSM
Transgender women
Cis-gender MSW
~~Cis-gender women~~

Vulnerability
2 STIs in Past 12 months
1 STI in past 12 months
Persons taking PrEP
0 STIs but non-monogamous condomless sex
Presenting for Care

How Do I Counsel Patients About Doxy-PEP Risks?

Side Effects

- Photosensitivity
- Pill esophagitis
- Gastrointestinal distress

Unknowns

- Antimicrobial resistance
- Microbiome changes

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

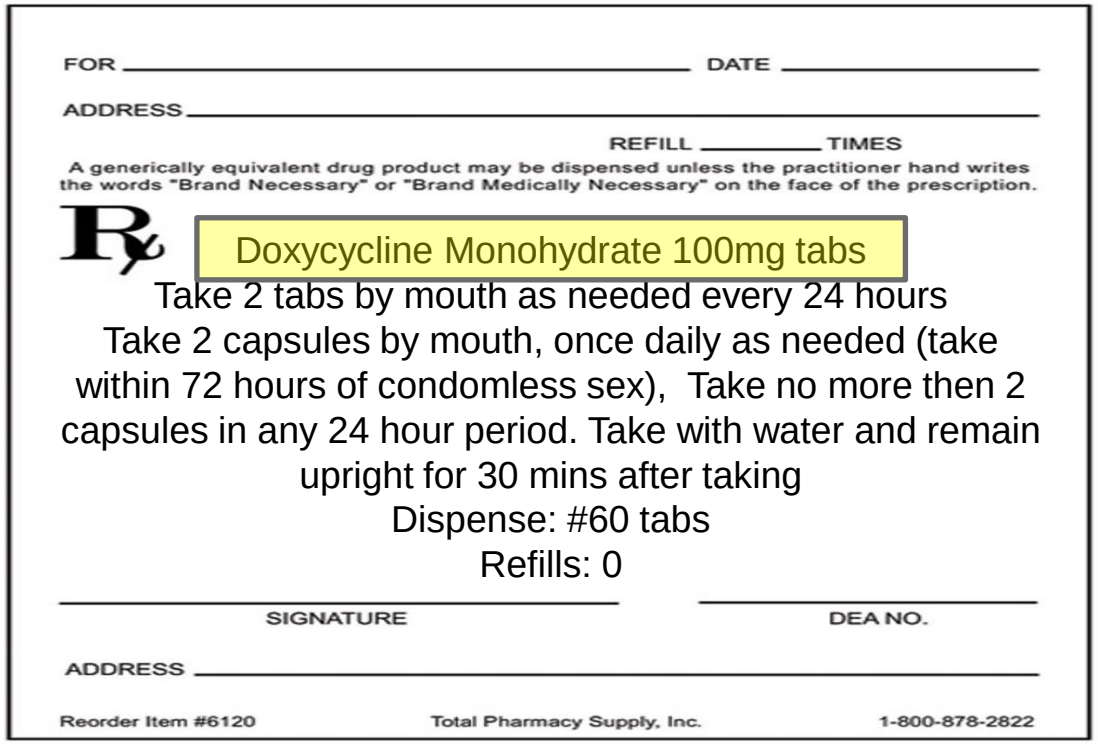
_____ _____

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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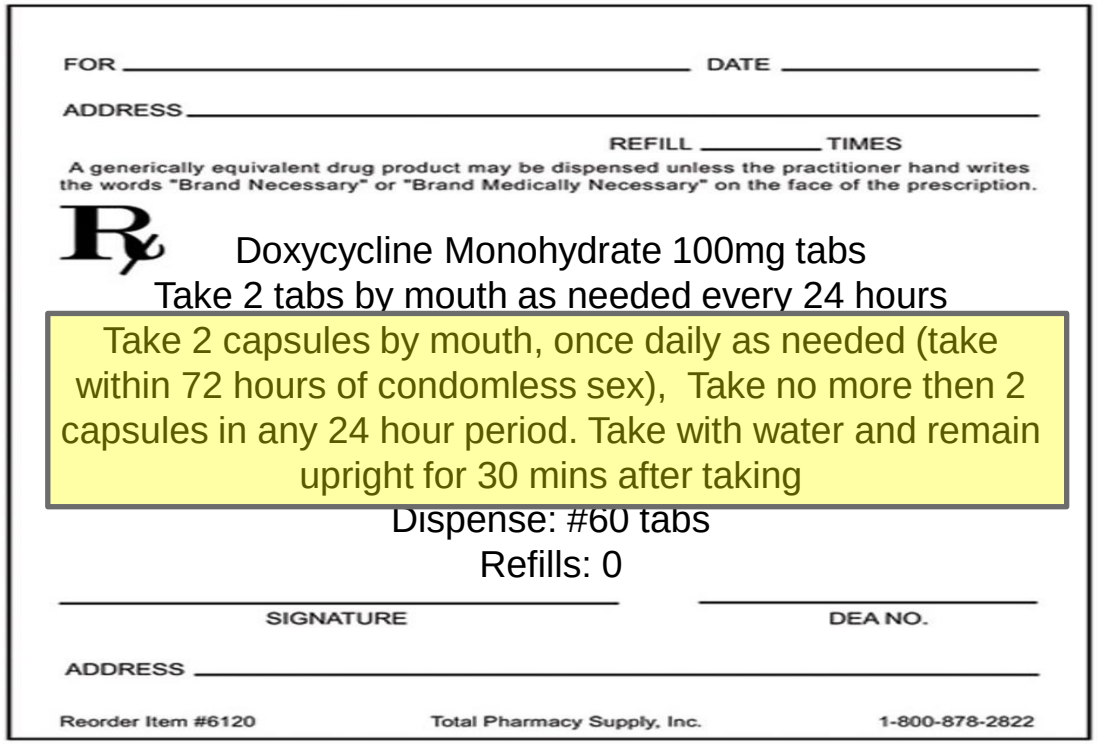
Hyclate or Monohydrate

- Hyclate – cheaper
- Monohydrate – less GI distress

How Do I Prescribe Doxy-PEP?



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- Detailed instructions

How Do I Prescribe Doxy-PEP?

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

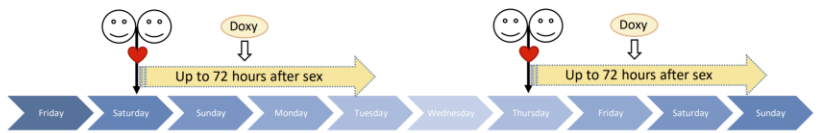
- Call us at 628-217-6692 if you run out of doxycycline, if you are having any side effects, or if you think you may have an STI.
- Please continue to get tested for STIs every 3 months and whenever you have symptoms.
- Doxy-PEP doesn't protect against MPX (monkeypox), HIV, or other viral infections

Doxy PEP – How to Take

= sex without a condom, including oral sex

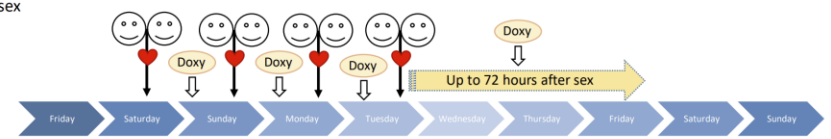
Two 100 mg pills of doxycycline ideally within 24 hours but no later than 72 hours after condomless oral, anal or vaginal sex

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

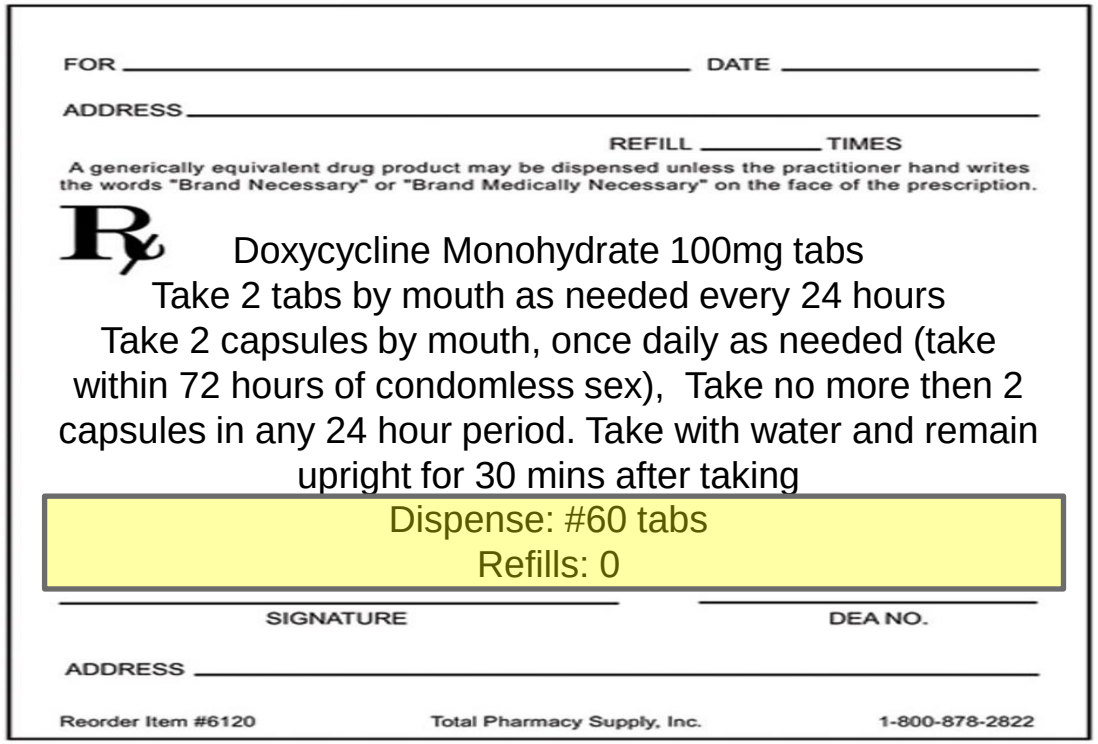


***No more than* 200 mg every 24 hours**

COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

NEW YORK CITY STD HIV PREVENTION TRAINING CENTER

How Do I Prescribe Doxy-PEP?



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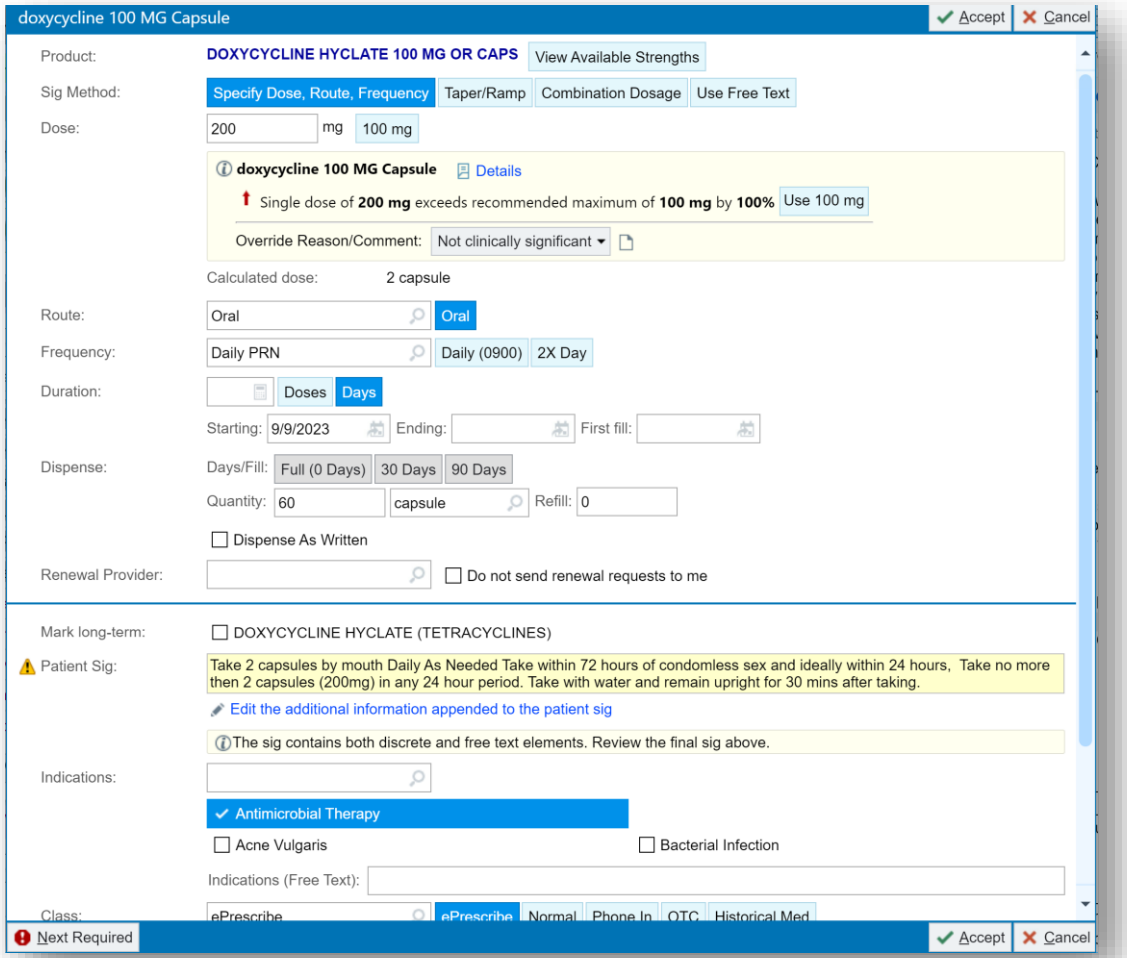
- Dispense and Refills
- 25% of patients used >= 10 doses per month

How Do I Prescribe Doxy-PEP?



How Do I Follow Patients on Doxy-PEP?

Labs

- Prior to initiation: None
  - Would not start on symptomatic patients
- ***Quarterly – STI testing***
- Annually: CBC, LFTs, Creatinine

Treatment

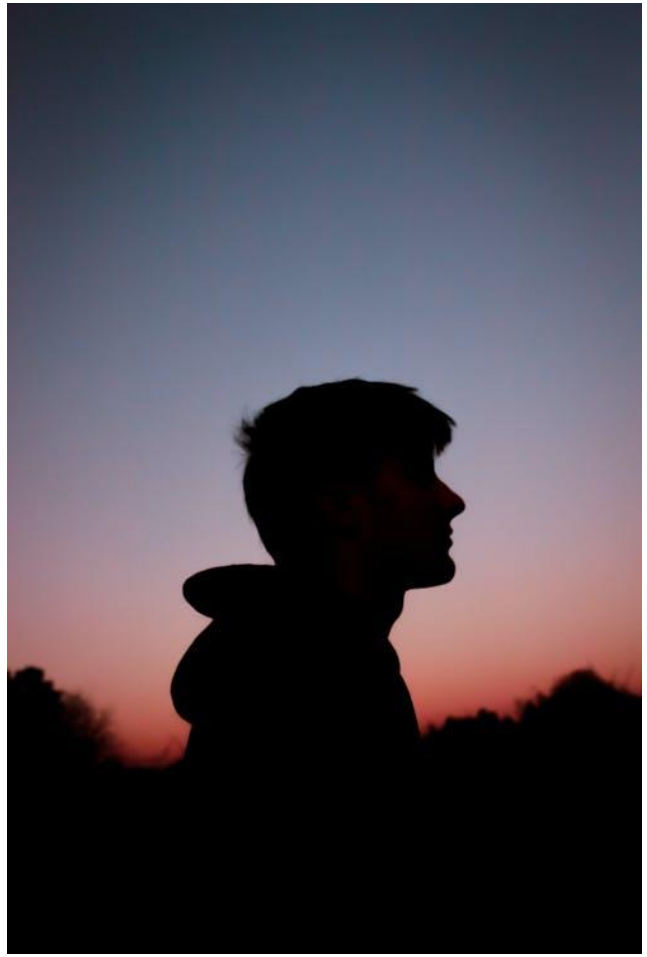
- Treat as per the 2021 STI Guidelines
  - ***Consider deferring treatment for "exposure"***

Igor

- 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



Igor'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

Igor's Gonorrhea Culture

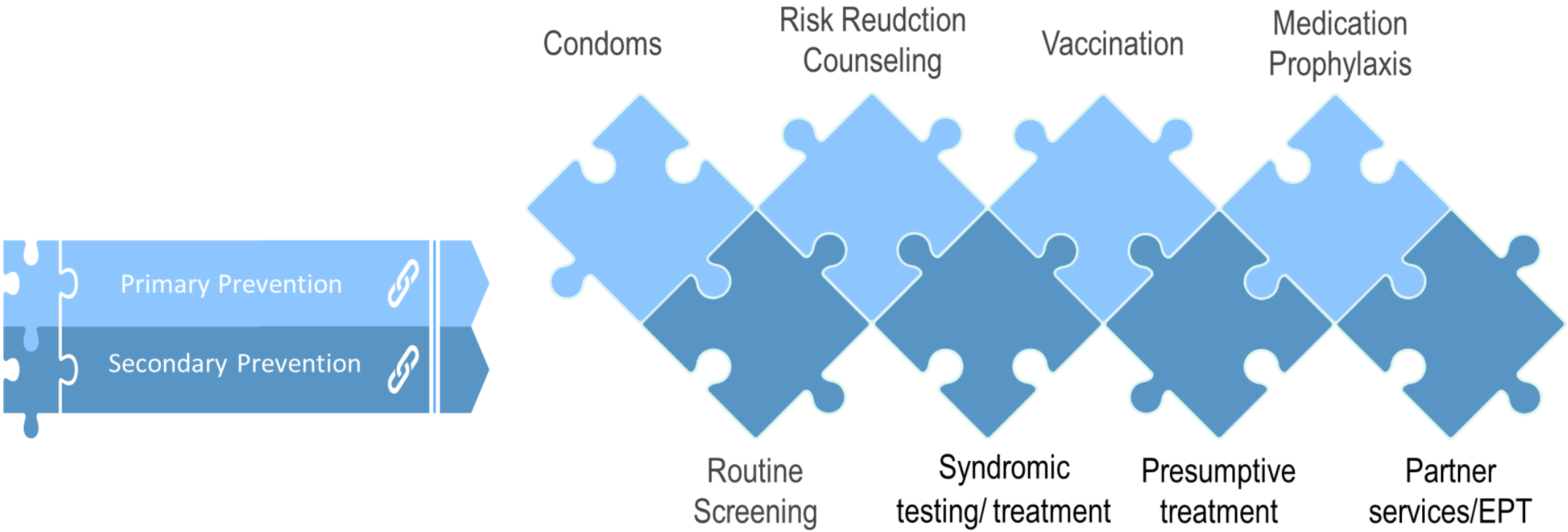
Lab results:
Azithromycin – susceptible (MIC 0.125)
Ciprofloxacin – resistant (MIC 1)
Ceftriaxone – susceptible (MIC 0.016)
Cefixime – Susceptible (48mm)
Tetracycline – resistant (MIC 12)

Doxy-PEP For 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 men who have sex with men and transgender women living with and without HIV
    - It is not 100%
  - Doxy-PEP **data does NOT support efficacy** to prevent STIs in persons born female
  - There remain unknowns about the overall impact, risks, and unintended consequences of Doxy-PEP that potential users should be aware of (**Shared Decision Making**)
  - Flexibility is key, management will change as we learn more

Questions


Primary Prevention
Secondary Prevention
Condoms
Risk Reudction Counseling
Vaccination
Medication Prophylaxis
Routine Screening
Syndromic testing/ treatment
Presumptive treatment
Partner services/EPT