Monthly Public Health Webinar
(Part 2)

Gonorrhea
Chlamydia
Doxycycline PEP

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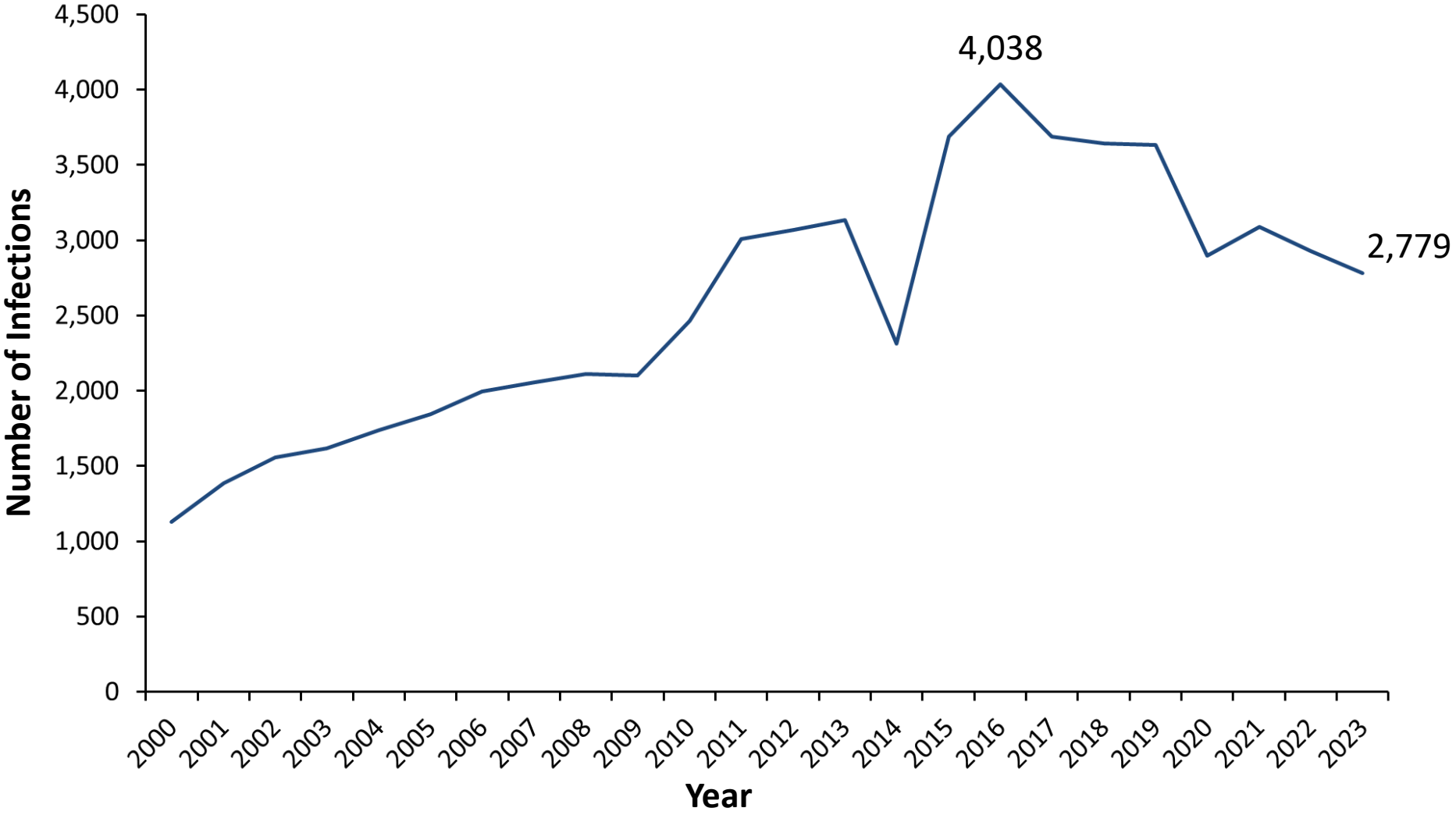
New Hampshire Division of Public Health Services

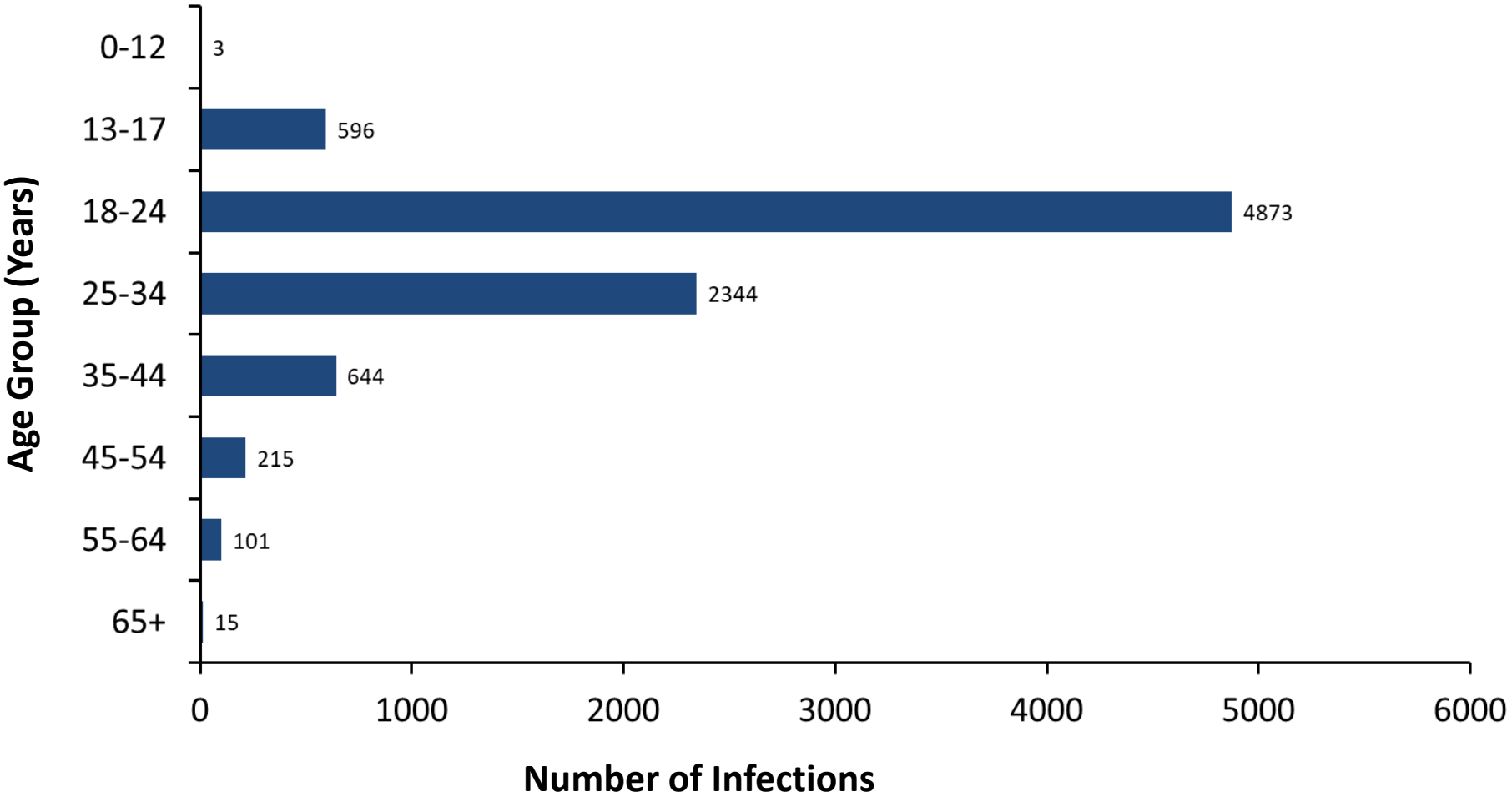
NH DIVISION OF
Public Health Services
Department of Health and Human Services

New Hampshire Epidemiology

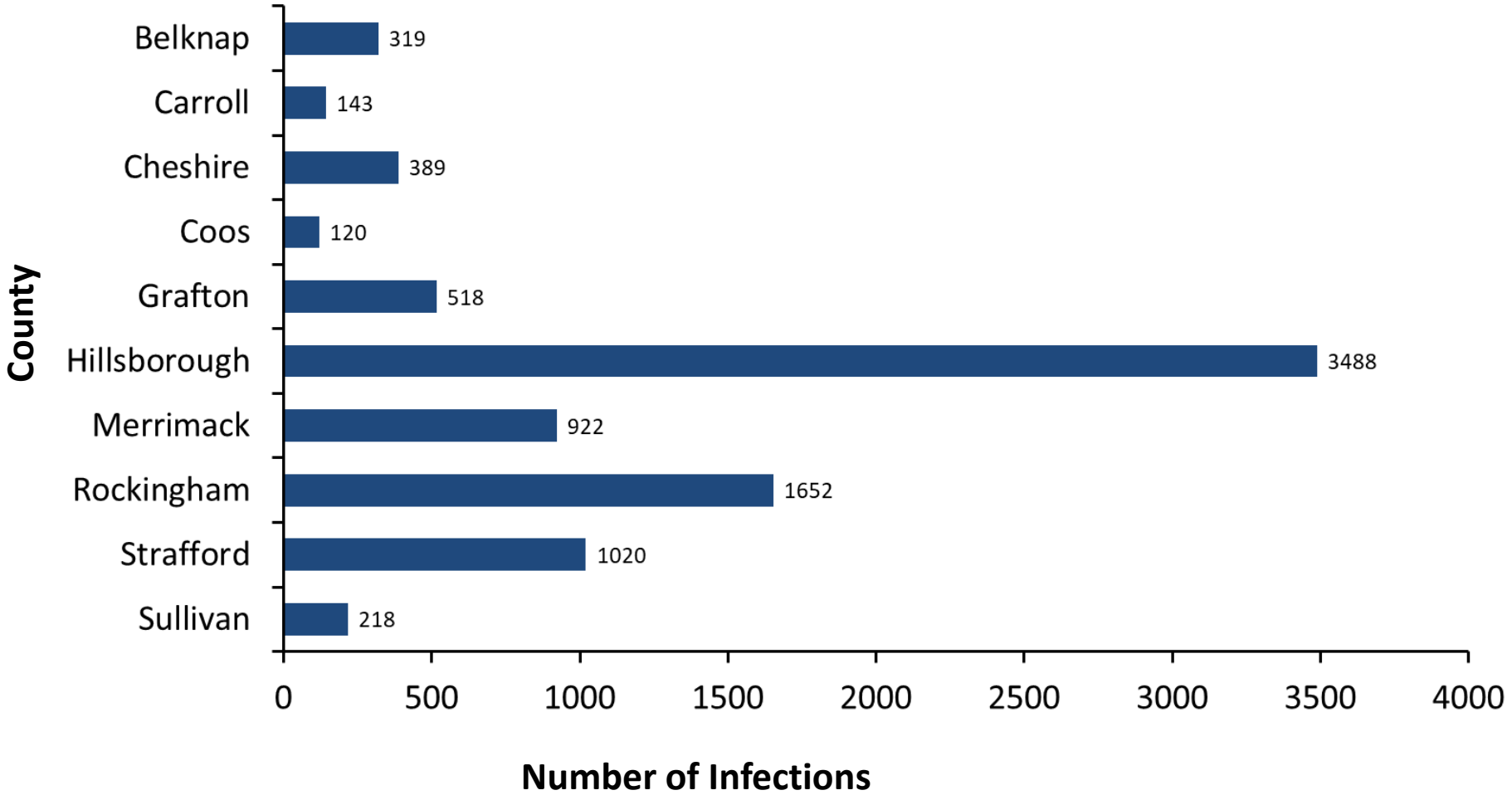
Total Number of Chlamydia Infections in NH Each Year, 2000 – 2023



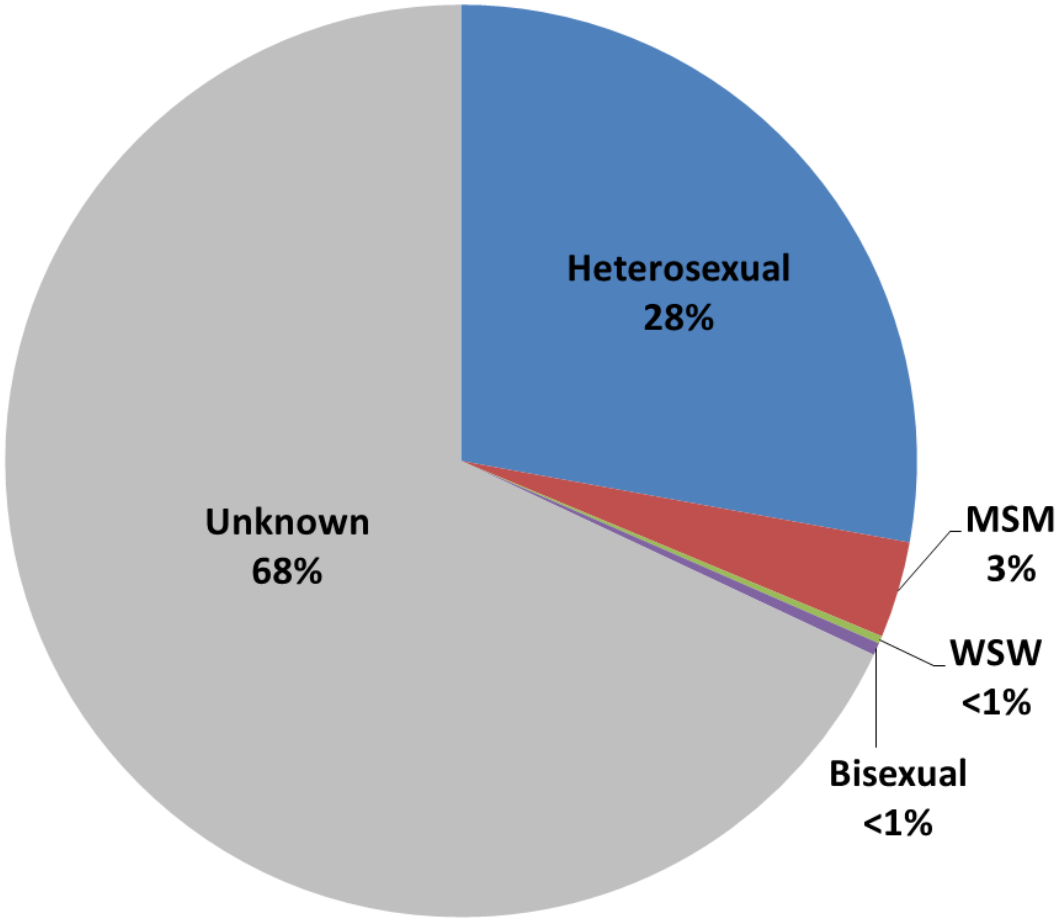
Total Number of Chlamydia Infections in NH by Age, 2021 – 2023 Combined



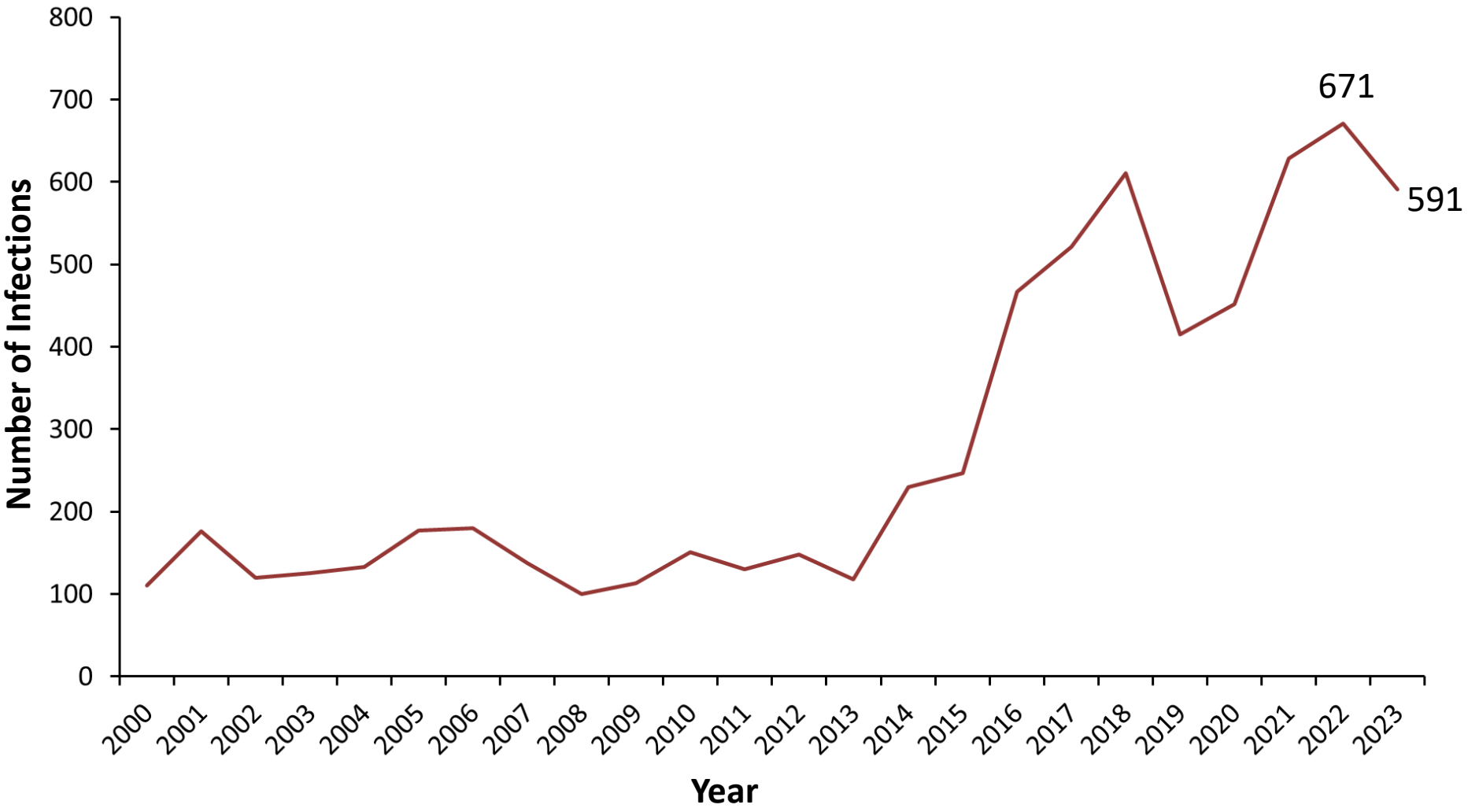
Total Number of Chlamydia Infections in NH by County, 2021 – 2023 Combined



Chlamydia Cases with Reported Sexual Risk Factor in NH, 2021 – 2023 Combined



Total Number of Gonorrhea Infections in NH Each Year, 2000 – 2023



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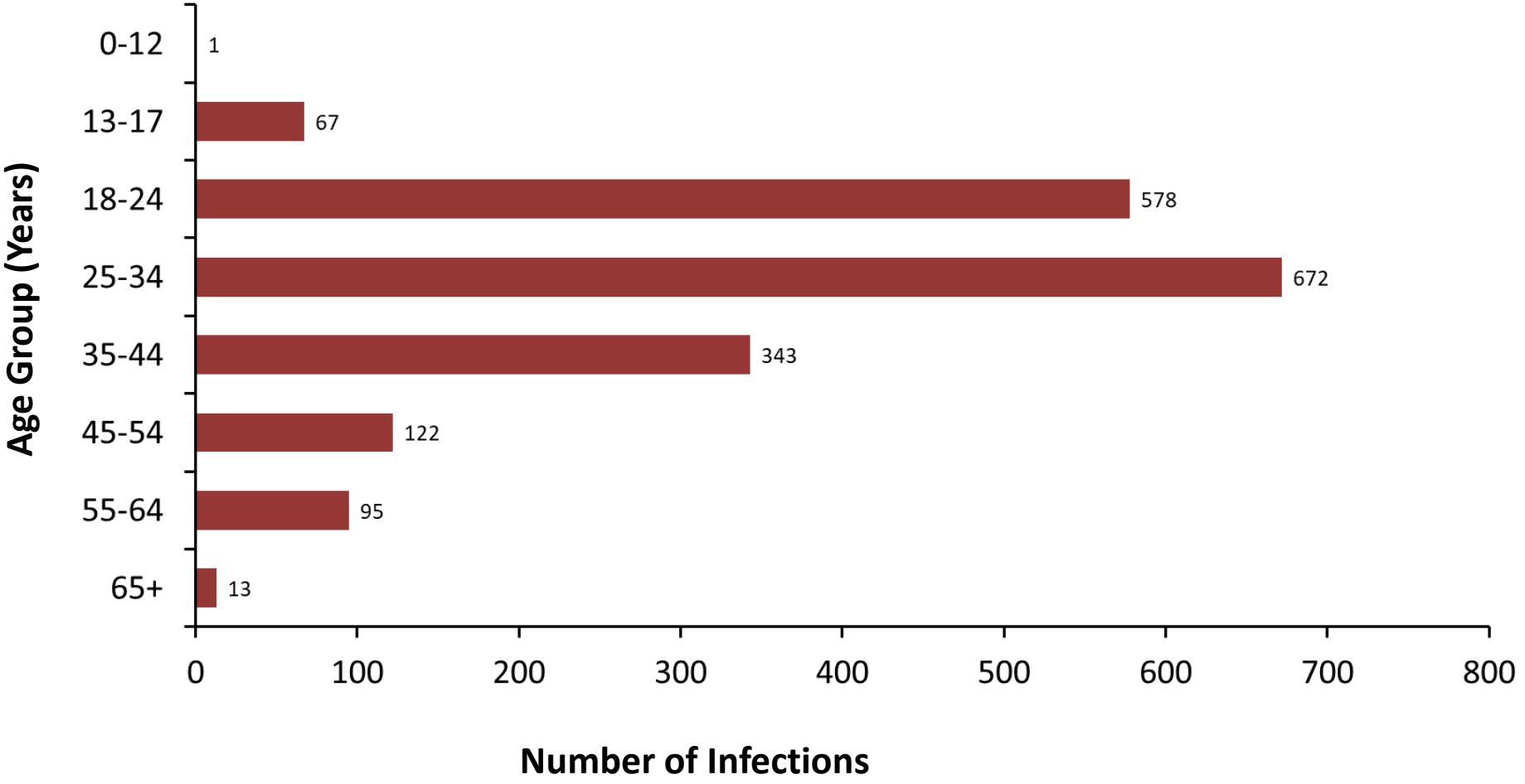
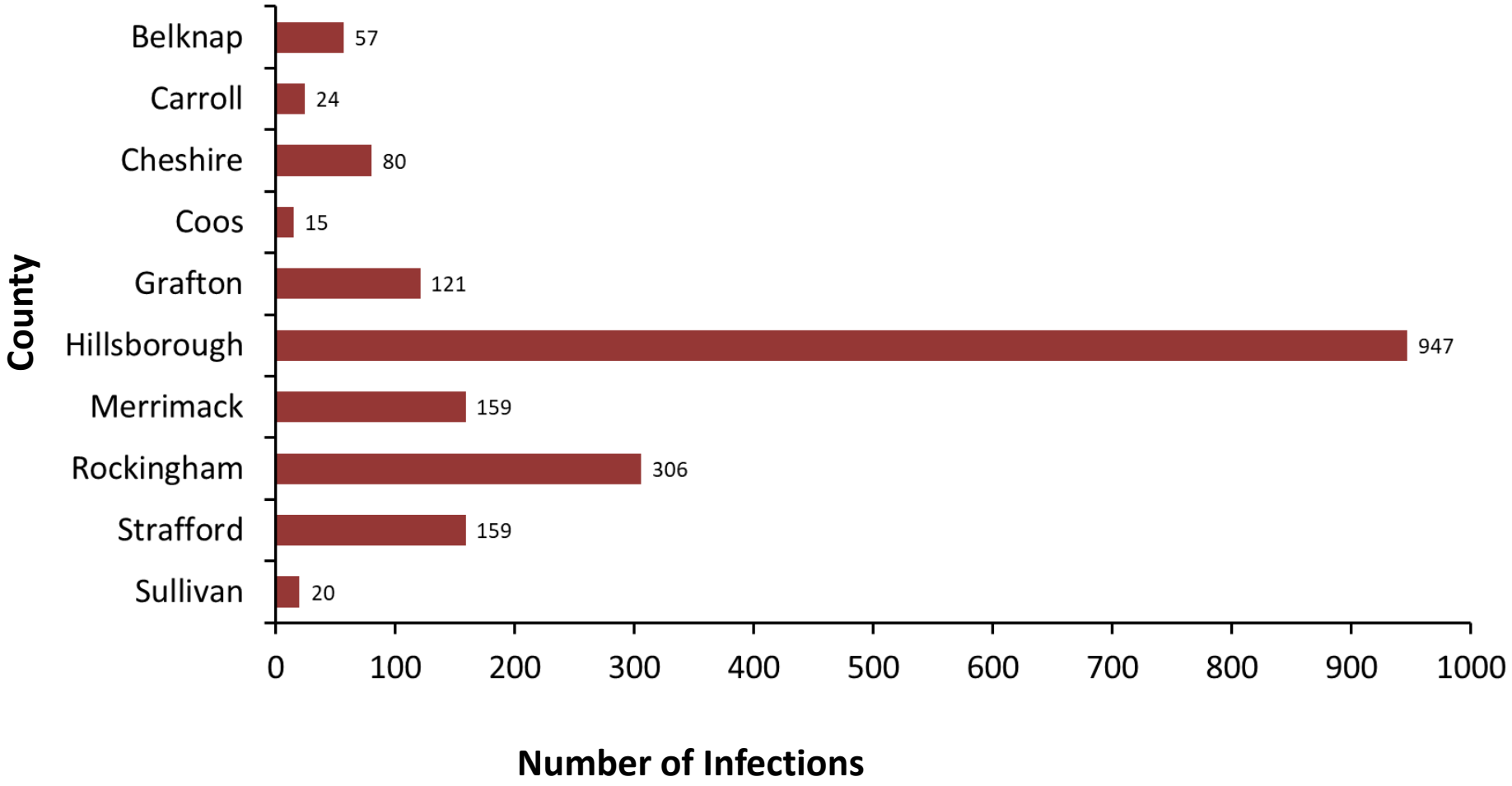
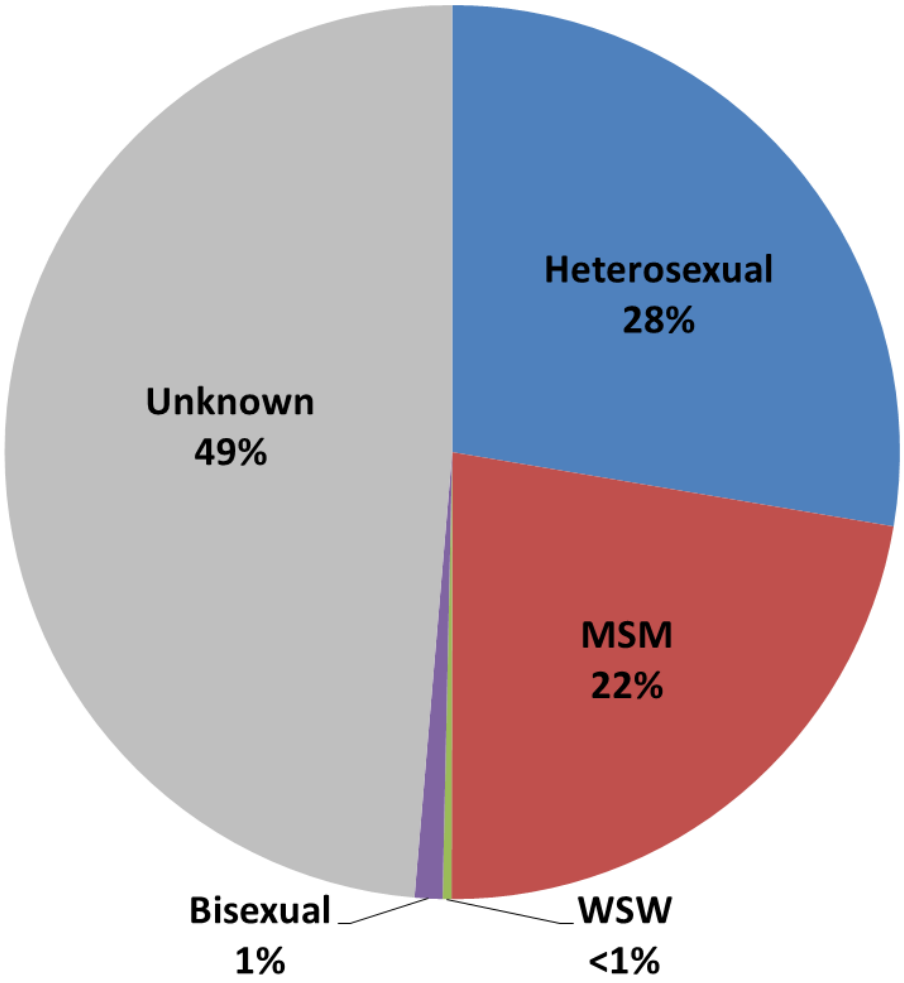


Total Number of Gonorrhea Infections in NH by County, 2021 – 2023 Combined



Gonorrhea Cases with Reported Sexual Risk Factor in NH, 2021 – 2023 Combined



Strategies to Prevent the Spread of Chlamydia and Gonorrhea

- Primary Prevention (prevent infection)
  - Behavior modification and risk-reduction strategies (e.g., reducing number of partners, wearing condoms, etc.)
- Secondary Prevention (early detection of infection)
  - Screening/testing for early diagnosis
  - Appropriate treatment
  - Re-testing (if appropriate)
  - Contact tracing to identify exposed/susceptible persons
  - Expedited Partner Therapy (EPT)

Doxycycline Post-Exposure Prophylaxis (PEP)

CDC's *Draft* Doxycycline PEP Guidelines

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**

https://www.cidrap.umn.edu/sites/default/files/CDC-2023-0080-0002_content.pdf

THE LANCET
Infectious Diseases

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

- Amended study of high-risk MSM originally conducted to study the efficacy of HIV PrEP with tenofovir/emtricitabine (Truvada®)
- Studied the efficacy of doxycycline PEP in France at preventing bacterial STIs (open-label study – participants knew if they received doxycycline)
- Participants:
  - Adults 18+ years of age
  - MSM or transgender women having sex with men
  - HIV-negative
  - High-risk for HIV
- Doxycycline PEP group: instructed to take doxycycline 200 mg PO x1 ideally within 24 hrs, but no later than 72 hrs, after each high-risk sex event (maximum of 3 doses/week)

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30725-9/fulltext

Additional Study Methodology

- Primary outcome: occurrence of a first bacterial STI (chlamydia, gonorrhea, or syphilis)
- Clinic follow-up every 2 months with testing for chlamydia and gonorrhea (throat and rectal swabs, and urine), and syphilis
- Assessed doxycycline adherence (pill count, plasma levels, interviews)

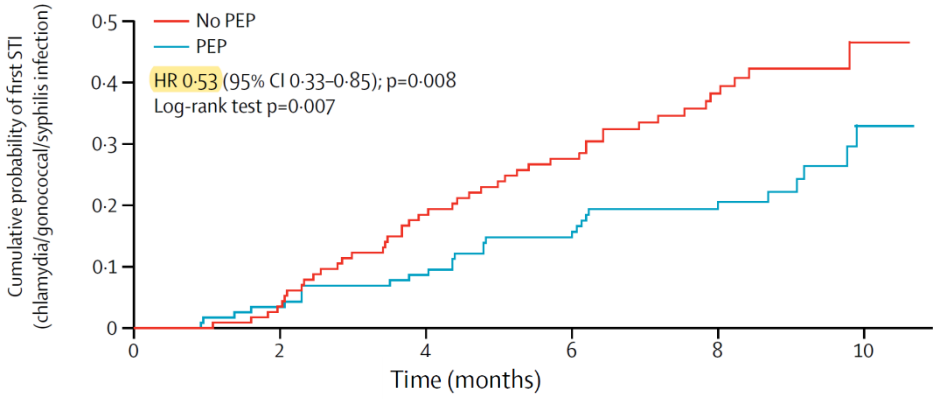
	Doxycycline PEP	No PEP
2 months	111/116 (96%)	107/114 (94%)
4 months	112/116 (97%)	109/114 (96%)
6 months	106/114 (93%)	105/111 (95%)
8 months	99/101 (98%)	91/97 (94%)
10 months	45/46 (98%)	42/42 (100%)

PEP=post-exposure prophylaxis.

Table 1: **Bi-monthly visit attendance in both groups**

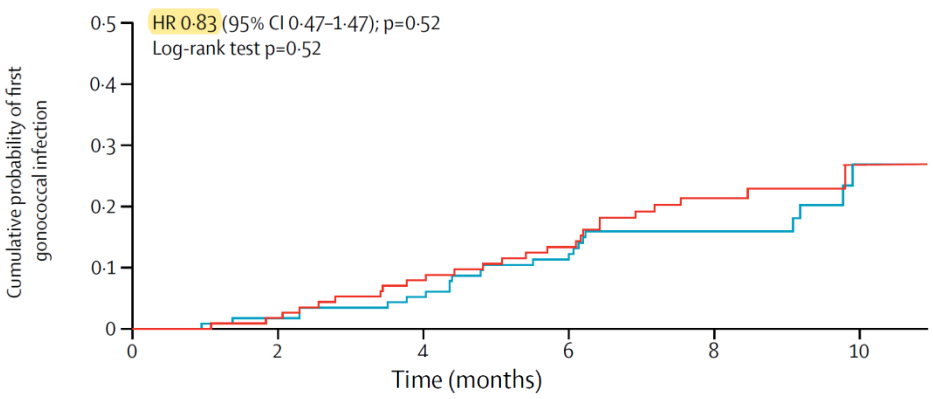
https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30725-9/fulltext

Chlamydia, Gonorrhea, or Syphilis



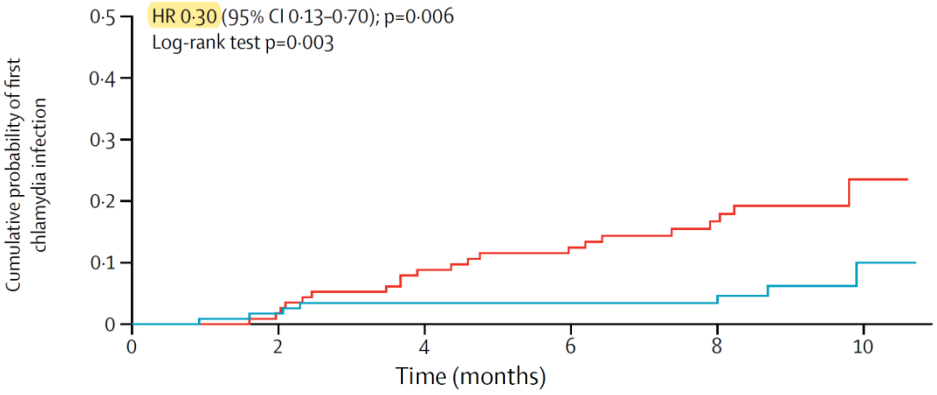
47% reduced risk of a new bacterial STI

Gonorrhea



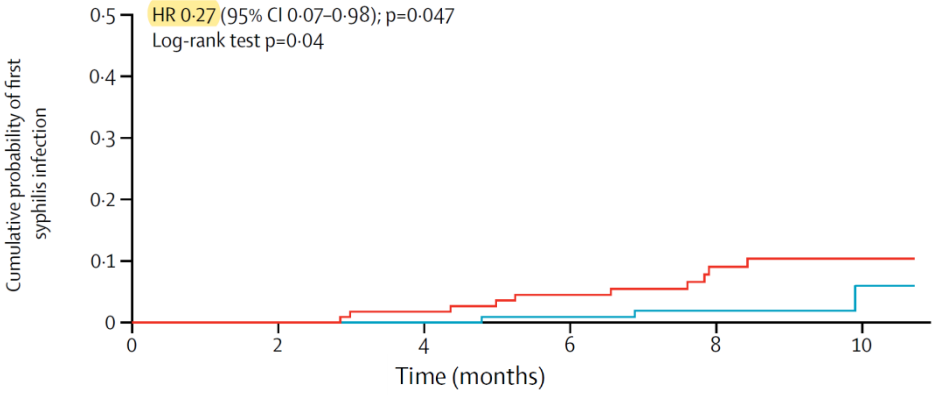
No reduced risk of gonorrhea

Chlamydia



70% reduced risk of chlamydia

Syphilis



73% reduced risk of syphilis

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30725-9/fulltext

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Additional Study Findings

- Majority of gonorrhea and chlamydia was detected from rectal and throat swabs (highlights the importance of testing at sites of sexual contact)
- 71% of STIs were asymptomatic (highlights the importance of screening)
- Doxycycline adherence:
  - 83% reported taking doxycycline within 24 hours of sex encounters
  - Plasma concentrations detected doxycycline in 30% of doxy-PEP group (testing only detected doxycycline use in the previous 48 hours)
  - 63% of participants in doxy-PEP group vs. 25% in no-PEP group had at least one plasma sample with doxycycline detected
- The study did not assess the impact of doxy-PEP on antibiotic resistance

https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30725-9/fulltext

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Postexposure Doxycycline to Prevent Bacterial Sexually Transmitted Infections

- Randomized (2:1), open label clinical trial, conducted at HIV and sexual health clinics in San Francisco and Seattle
- Participants:
  - Adults 18+ years of age
  - MSM or transgender women having sex with men
  - HIV-positive, or were taking or planning to start HIV PrEP (2 different cohorts)
  - High-risk for HIV
  - High-risk for STIs (diagnosed with a bacterial STI in the previous 12 months)
- Doxycycline PEP group: instructed to take doxycycline 200 mg PO x1 ideally within 24 hrs, but no later than 72 hrs, after each high-risk sex contact (maximum of once every 24 hrs)

https://www.nejm.org/doi/full/10.1056/NEJMoa2211934

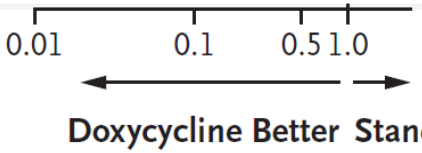
Additional Study Methodology

- Primary outcomes:
  - occurrence of at least one bacterial STI (gonorrhea, chlamydia, or syphilis) each quarter – a person with multiple STIs in a quarter contributed to the analysis once per quarter
  - Tetracycline resistance in *N. gonorrhoeae* and *S. aureus* isolates
- Followed for a total of 12 months with quarterly scheduled clinic visits and testing for chlamydia and gonorrhea (throat and rectal swabs, and urine), and syphilis
- Assessed doxycycline adherence quarterly
- Swabs of the nares and oropharynx were obtained for *S. aureus* culture with doxycycline-resistance testing
- Study was stopped early because of effectiveness of doxy-PEP

Results in Participants on HIV-PrEP

A PrEP Cohort

Analyses	Doxycycline	Standard Care	Relative Risk (95% CI)	P Value
	no. of quarterly visits with event /total no. of visits (%)			
Primary analysis				<0.001
Any STI	61/570 (10.7)	82/257 (31.9)	0.34 (0.24–0.46)	
Secondary analysis				
Any gonorrhea	52/570 (9.1)	52/257 (20.2)	0.45 (0.32–0.65)	
Urethral	5/570 (0.9)	12/257 (4.7)	0.19 (0.06–0.55)	
Pharyngeal	38/570 (6.7)	34/257 (13.2)	0.50 (0.32–0.78)	
Rectal	25/570 (4.4)	29/257 (11.3)	0.40 (0.23–0.69)	
Any chlamydia	8/570 (1.4)	31/257 (12.1)	0.12 (0.05–0.25)	
Urethral	1/570 (0.2)	6/257 (2.3)	0.07 (0.01–0.59)	
Pharyngeal	2/570 (0.4)	4/257 (1.6)	0.22 (0.04–1.14)	
Rectal	7/570 (1.2)	23/257 (8.9)	0.14 (0.06–0.32)	
Any early syphilis	2/570 (0.4)	7/257 (2.7)	0.13 (0.03–0.59)	



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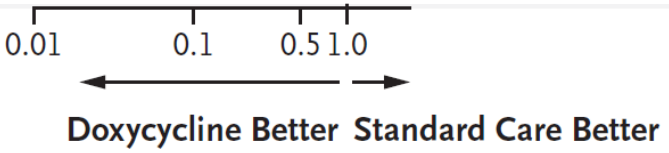
Results in Participants Living With HIV (PLWH)

B PLWH Cohort

Analyses	Doxycycline (no. of quarterly visits with event /total no. of visits (%))	Standard Care (no. of quarterly visits with event /total no. of visits (%))	Relative Risk (95% CI)	P Value
Primary analysis				<0.001
Any STI	36/305 (11.8)	39/128 (30.5)	0.38 (0.24–0.60)	
Secondary analysis				
Any gonorrhea	27/305 (8.9)	26/128 (20.3)	0.43 (0.26–0.71)	
Urethral	3/305 (1.0)	5/128 (3.9)	0.23 (0.05–1.02)	
Pharyngeal	15/305 (4.9)	13/128 (10.2)	0.49 (0.23–1.03)	
Rectal	16/305 (5.2)	20/128 (15.6)	0.33 (0.17–0.63)	
Any chlamydia	12/305 (3.9)	19/128 (14.8)	0.26 (0.12–0.57)	
Urethral	2/305 (0.7)	2/128 (1.6)	0.36 (0.06–2.27)	
Pharyngeal	1/305 (0.3)	2/128 (1.6)	0.22 (0.03–1.86)	
Rectal	9/305 (3.0)	17/128 (13.3)	0.23 (0.10–0.54)	
Any early syphilis	2/305 (0.7)	3/128 (2.3)	0.23 (0.04–1.29)	



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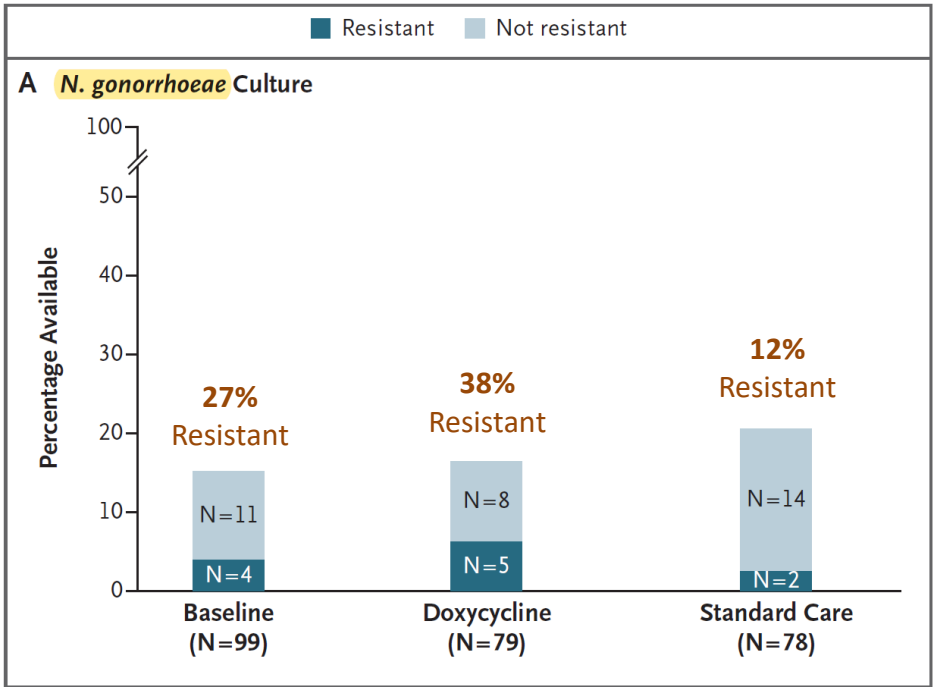
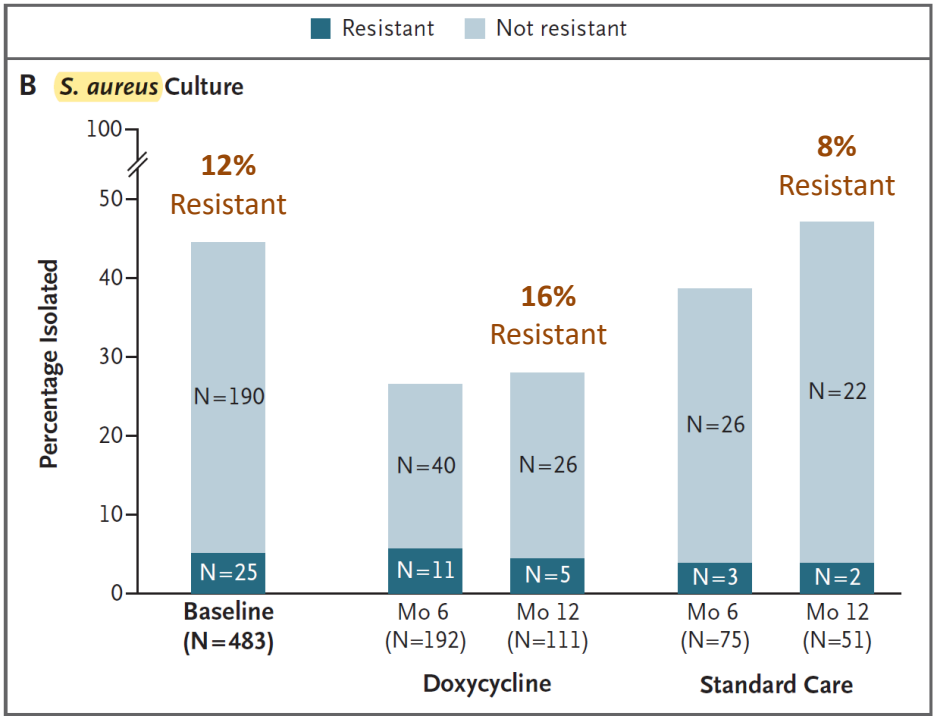
Tetracycline Resistance in *N. gonorrhoeae* and *S. aureus* Cultures



S. aureus carriage was 40% lower in the doxy-PEP vs. standard care group at 12 months



https://www.nejm.org/doi/full/10.1056/NEJMoa2211934

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Additional Study Findings

- 30% of participants had an STI diagnosed at enrollment
- 86% of participants in the doxy-PEP group reported taking doxycycline consistently within 72 hours of condomless sex
- Number needed to treat (NNT) to prevent a quarter with an STI was 4.7 in the PrEP cohort and 5.3 in the PLWH cohort (NNT = ~5)

Study Conclusions

- Doxycycline PEP taken within 72 hours after condomless sex decreased gonorrhea, chlamydia, and early syphilis by two-thirds among MSM and transgender women
- Doxycycline PEP also substantially reduced the occurrence of each bacterial STI individually, including gonorrhea
  - Syphilis: 77-87% reduced risk with doxycycline PEP
  - Chlamydia: 74-88% reduced risk with doxycycline PEP
  - Gonorrhea: 55-57% reduced risk with doxycycline PEP
- Tetracycline-resistant gonorrhea was more prevalent in France when the IPERGAY study was conducted (see prior Lancet article) compared to this U.S. based study (56% vs. 20% resistant gonorrhea), which may partially explain the different gonorrhea findings in the two studies

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Doxycycline Prophylaxis to Prevent Sexually Transmitted Infections in Women

- Randomized, open-label, clinical trial of women aged 18-30 years in Kenya who were not pregnant and were receiving HIV PrEP (with tenofovir/emtricitabine)
- Randomized 1:1 to receive doxycycline PEP or standard care
- Doxycycline PEP group: instructed to take doxycycline 200 mg PO x1 within 72 hrs after each condomless sexual encounter (maximum of 200 mg daily)

https://www.nejm.org/doi/full/10.1056/NEJMoa2304007

Additional Study Methodology

- Primary outcome: Occurrence of any bacterial STI (gonorrhea, chlamydia, or syphilis) each quarter – a person with multiple STIs in a quarter contributed to the analysis once per quarter
- Followed for 12 months with quarterly clinic visits with testing for chlamydia and gonorrhea (endocervical swabs), and syphilis
- Assessed doxycycline adherence quarterly at visits and by weekly text messages; also collected hair samples for doxycycline testing (representing ~1 month of exposure)
- Molecular resistance testing conducted to detect the tetracycline resistance gene *tet(M)* in gonorrhea and chlamydia isolates

Study Results

Table 2. Intention-to-Treat and Subgroup Analyses of Incident STIs.

Analysis and End Point	Doxycycline PEP (N = 224)	Standard Care (N = 225)	Relative Risk (95% CI)*
	no. of events/no. of trial visits		
Intention to treat			
Any STI (primary end point)	50/854	59/886	0.88 (0.60–1.29)†
Chlamydia	35/854	50/886	0.73 (0.47–1.13)
Gonorrhea	19/854	12/886	1.64 (0.78–3.47)

† P = 0.51, as calculated with the generalized-estimating-equation test.

- Incidence of bacterial STIs was NOT significantly lower in the doxy-PEP compared to standard of care group
- Only 1 syphilis infection identified, prevented separate analysis
- 100% of gonorrhea isolates showed tetracycline resistance (No chlamydia isolates had tetracycline resistance gene detected)

https://www.nejm.org/doi/full/10.1056/NEJMoa2304007

Additional Study Findings

- Quarterly visits: 80% of participants in doxy-PEP group reported taking doxycycline after condomless sex in the previous 2 weeks
- Weekly text messages: 55% of participants in the doxy-PEP group reported taking doxycycline “at least as many days as they had sex”
- Hair sample testing:
  - Doxycycline was detected in at least one visit: 56%
  - When excluding visits when doxycycline was on-hold, doxycycline was detected in 33% of visits

Study Conclusions

- Incidence of bacterial STIs was NOT significantly lower with doxycycline PEP compared with standard care in women receiving HIV PrEP in Kenya
- Hair sample testing to assess doxycycline use suggested that doxycycline was not taken during the majority of months
- Doxycycline-resistant gonorrhea (100% of isolates showed resistance) likely impacted ability to show efficacy

https://www.nejm.org/doi/full/10.1056/NEJMoa2304007

CDC's *Draft* Doxycycline PEP Guidelines

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**

- Additional Recommendations and Ancillary Services:
  - Screening and testing for STIs, HIV, hepatitis B and C
  - Risk-reduction counseling
  - Risk/benefit discussion of doxy-PEP
  - Assess for HIV PrEP
  - Vaccination (hepatitis B, hepatitis A, Mpox, HPV, etc.)

https://www.cidrap.umn.edu/sites/default/files/CDC-2023-0080-0002_content.pdf

Q&A

Webinar Slides Will Be Posted to our Healthcare Provider Resources Website

https://www.dhhs.nh.gov/programs-services/disease-prevention/infectious-disease-control/bidc-resources-healthcare-providers

Watch the webinar on Syphilis

Healthcare Provider Webinar, 12/14/2023: Syphilis & Congenital Syphilis