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Asymptomatic Screening for *Neisseria gonorrhoeae* Among Gay and Bisexual Men Attending Public Sexual Health Services in Australia and Associations With Patterns of Ceftriaxone Consumption: A Retrospective Observational Study

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Background. *Neisseria gonorrhoeae* is a significant public health concern due to rising antimicrobial resistance. Current strategies for *N gonorrhoeae* among gay and bisexual men (GBM) include 3-month screening; however, high-frequency screening may increase ceftriaxone consumption, potentially contributing to antimicrobial resistance.

Methods. We conducted a retrospective cohort study of GBM screened for *N gonorrhoeae* at 16 Australian public sexual health services between 2016 and 2023. We classified *N gonorrhoeae* tests and ceftriaxone prescriptions as screening-related (asymptomatic screening) or nonscreening-related (testing/treatment of contacts, symptomatic testing, or empirical treatment). We explored trends in annual ceftriaxone prescription rates and used multivariable Poisson regression to examine the association between individuals' annual asymptomatic screening frequency and ceftriaxone consumption, adjusted for age, year, pre-exposure prophylaxis, HIV status, injecting drug use, and syphilis and chlamydia diagnoses.

Results. In total, 65 261 GBM contributed 133 846 person-years. From 2016 to 2023, the total ceftriaxone prescription rate rose from 2.92 defined daily doses per 100 person-years at risk to 5.25: screening-related ceftriaxone increased from 0.91 to 2.96 ($P < .001$) while nonscreening-related ceftriaxone remained stable ($P = .570$). When compared with having 1 screening test per year, having ≥4 tests was associated with a higher rate of screening-related ceftriaxone prescriptions (adjusted incident rate ratio, 5.47; 95% CI, 5.16–5.79).

Conclusions. Ceftriaxone consumption rose among GBM, largely driven by increased screening rather than nonscreening-related treatment. Our findings highlight the association between high-frequency screening and antibiotic consumption, providing real-world data to guide discussions on the benefits and risks of screening.

Keywords. antibiotic; antimicrobial resistance; asymptomatic screening; gay and bisexual men; *Neisseria gonorrhoeae*.

Neisseria gonorrhoeae, causing gonorrhea, is a common sexually transmissible infection (STI), with >80 million new cases per year globally, and it leads to sequalae such as bothersome symptoms, infertility, and other reproductive complications [1, 2]. *N gonorrhoeae* is included on the World Health Organization's (WHO's) priority pathogen list due to its propensity to develop antimicrobial resistance (AMR) to every major antibiotic [3]. The WHO has set a target to reduce new STIs by 50% between 2020 and 2030 via its global STI strategy; a key action is frequent screening to diagnose and treat asymptomatic infections and reduce onward transmission [1]. In parallel, the WHO Global Action Plan on Antimicrobial Stewardship highlights optimizing antimicrobial use through evidence-based prescribing as essential to preserving antimicrobial effectiveness [4].

Evidence-based prescribing is based on guidelines. Given rising STI rates, many countries have adopted guidelines that recommend 3-month screening for *N gonorrhoeae* at all 3 anatomic sites (pharynx, anorectum, genitals) in populations

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at increased STI risk, such as gay and bisexual men (GBM; also called "3 × 3 screening") [5, 6]. Other strategies recommended in guidelines to diagnose and treat people with gonorrhea include the following: (1) testing people who report contact with someone with *N gonorrhoeae* (contact testing), (2) testing people with symptoms that may be due to *N gonorrhoeae* (symptomatic testing), and (3) presumptive treatment among symptomatic people and/or contacts of *N gonorrhoeae* (empirical treatment). In some settings, antibiotics are administered before test results are available given the high likelihood of infection, and in other settings, antibiotics are withheld until test results are known [7]. Collectively, these screening and nonscreening strategies result in a high proportion of antibiotics consumed by GBM [8–10]. Increasing rates of treatment for gonorrhea is concerning as the infection is predominantly treated with ceftriaxone, a broad-spectrum antibiotic, with ecologic evidence showing a significant association between population-level consumption of cephalosporins and rates of gonorrhea AMR [11].

Some propose that more evidenced-based, judicious, and limited use of antibiotics is a key strategy to combat *N gonorrhoeae* AMR [12, 13]. However, more data on the patterns of antibiotic prescribing are required to inform clinical guidelines and public health responses that strike a balance between reducing the burden of gonorrhea sequelae and antibiotic overuse. Some have argued that empirical treatment leads to unnecessary ceftriaxone prescribing in resource-rich settings [9, 10]. Yet, gaps in access to appropriate testing, treatment, and contact tracing are identified as factors for the development of *N gonorrhoeae* AMR globally [14].

Australia has national guidelines on the screening and treatment of bacterial STI to which all public sexual health services (PSHSs) adhere [7]. The national recommendation for 3 × 3 *N gonorrhoeae* screening among all GBM, regardless of HIV or pre-exposure prophylaxis (PrEP) status, was introduced in 2019 [15]. This occurred following widespread implementation of HIV PrEP between 2016 and 2019 [16]. PrEP implementation was accompanied by dedicated STI/HIV screening recommendations for GBM and a longitudinal model of STI/HIV care, which saw much higher adherence to the 3-month screening recommendation among GBM [17]. Importantly, following the rollout of these recommendations, the proportion of gonorrhea isolates with decreased susceptibility to ceftriaxone (minimum inhibitory concentration ≥0.125 mg/L) increased from 0.05% in 2016 to 0.22% in 2023 [18].

We aimed to examine trends in ceftriaxone prescription rates in a cohort of Australian GBM attending PSHSs for *N gonorrhoeae* screening, stratified by whether ceftriaxone was prescribed for infections diagnosed through asymptomatic screening or for nonscreening indications (contact testing, symptomatic testing, or empirical treatment). We also aimed to examine, among this screening-engaged cohort of GBM, the association between individual-level asymptomatic screening frequency and ceftriaxone consumption, as well as to identify patient characteristics that are associated with a higher likelihood of receiving screening-related ceftriaxone.

METHODS

Study Setting and Population

We conducted a retrospective cohort study using data from a network of 16 PSHSs participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Bloodborne Viruses (ACCESS; www.accessproject.org.au) [19]. The ACCESS protocol, which has previously been described [19], allows patient data to be deidentified and extracted from the electronic medical records of participating clinics via specialized data extraction software (GHRANITE). This software enables linkage within and across services using a probabilistic algorithm and nonidentifiable linkage keys generated prior to extraction [20].

Data Collection

Data extracted from electronic medical records included age, clinical consultations, electronic prescriptions for HIV PrEP, HIV status, history of injecting drug use, and ceftriaxone prescriptions, as well as chlamydia, gonorrhea, and syphilis pathology. The presence of symptoms and potential contact with a bacterial STI at the time of consultation were also extracted, as recorded in the "reason for presentation" field by coding or free text. New cases of gonorrhea or chlamydia were defined as a positive result on a nucleic acid amplification test. Individuals were classified as ever PrEP users if they had any electronic prescription for PrEP during the study period. New cases of infectious syphilis were coded by the diagnosing clinician.

Outcomes

We classified all *N gonorrhoeae* tests as 1 of the following: screening related, contact testing related, symptomatic testing related, or empirical treatment related (the last 3 indications were collectively defined as nonscreening related). We defined *N gonorrhoeae* screening-related tests as a nucleic acid amplification test for the organism from any anatomic site during a visit where the individual did not report any symptoms or recent contact with a bacterial STI. Contact testing was defined as tests where an asymptomatic individual reported recent contact with an STI; symptomatic testing was defined as tests where the individual reported any symptoms; and empirical treatment was defined as testing and antibiotic treatment undertaken during the same consultation. All *N gonorrhoeae* tests within 14 days of each other were considered part of the same episode.

Ceftriaxone prescriptions were also stratified. Ceftriaxone prescribed within 14 days of, but not on the day of, screening-related testing, contact testing, and symptomatic testing was

presumed to be for the treatment of gonorrhea diagnosed through those tests. Ceftriaxone prescribed on the same day as gonorrhea testing was presumed to be empirical treatment, regardless of reason for testing. Ceftriaxone prescriptions that did not fit into any aforementioned indications were categorized as unknown indication and grouped into nonscreening-related prescriptions. Ceftriaxone was quantified as defined daily dose (DDD) according to the WHO method [21], and the prescription rate was calculated by DDDs per 100 person-years at risk (100 PYARs). The DDD is a widely recognized unit with a predetermined conversion factor to calculate the maintenance dose per day for a medication.

Our analysis included GBM aged ≥16 years who had at least 1 *N gonorrhoeae* asymptomatic screening-related test at an included clinic during the study period (2016–2023). Included GBM each contributed 1 person-year of observation for each year that they had at least 1 screening-related test. We excluded GBM who did not attend any asymptomatic screening visits in a calendar year to reduce mixing of our cohort with patients who attended screening in other settings (eg, in general practice) but attended a sexual health clinic for treatment of positive results. GBM status was determined via patient-reported sexuality, gender of sexual partners, or history of rectal STI swab [22].

Statistical Analyses

We defined the unit of analysis as a PYAR of receiving screening-related ceftriaxone, with individuals contributing 1 year of observation for each calendar year in which they had at least 1 screening-related test. These PYARs represent periods of engagement in routine screening care and therefore reflect service utilization time rather than continuous biological time. We categorized each PYAR based on the number of screening-related tests that the individual had in the calendar year (1, 2, 3, ≥4) as a measure of screening frequency. We also measured the annual rate of ceftriaxone prescription per PYAR (defined as the total number of ceftriaxone prescriptions in each year divided by the total number of PYARs), stratified by prescription type (screening related, contact testing related, symptomatic testing related, empirical treatment related, and indication unknown).

We used multivariable Poisson regression models to examine the relationship between annual *N gonorrhoeae* screening frequency and ceftriaxone prescription. In these models, the outcome was the annual number of ceftriaxone prescriptions, and the exposure was the annual number of *N gonorrhoeae* screening tests (categorized as 1, 2, 3, or ≥4 per year). We performed separate models with the outcome as screening- and nonscreening-related prescriptions. As each individual could contribute multiple person-years of observation during the study period, we used robust standard errors to account for nonindependent clustering of observations within an individual.

We explored the associations between ceftriaxone prescription and the following covariates in bivariable Poisson models: age group (16–29, 30–39, 40–49, and ≥50 years), current HIV status, PrEP use during the study, history of injecting drug use, and diagnosis of infectious syphilis or incident chlamydia within the year. Covariates associated with increased ceftriaxone prescription ($P < .20$) in bivariable analyses were included in a multivariable model. Unadjusted and adjusted incident rate ratios (IRRs) for ceftriaxone prescriptions were computed from each multivariable model. In addition, to explore whether more frequent screening was associated with differences in symptomatic or contact-related infections, we examined the relationship between annual *N gonorrhoeae* screening frequency and the number of positive *N gonorrhoeae* test results performed for nonscreening-related indications, also using a bivariable Poisson model.

All analyses were performed in Stata version 17.0 (Stata Corp).

Ethics

Ethical approval for ACCESS was granted by the human research ethics committees of the Alfred Hospital (248/17), Northern Territory Department of Health and Menzies School of Health (08/47), University of Tasmania (H0016971), and St Vincent's Hospital (08/051).

RESULTS

Study Population

Overall, there were 237 507 person-years of GBM attending services during the study period, including 213 708 (90.0%) with any *N gonorrhoeae* testing in a calendar year. Among these, 133 846 (62.6%) person-years from 65 261 GBM had at least 1 asymptomatic screening test and were therefore considered at risk of screening-related ceftriaxone and included in the analysis. Of these, 21 641 GBM (33.2%) contributed 1 PYAR; 14 420 (22.1%), 2 PYARs; 9473 (14.5%), 3 PYARs; and 19 727 (30.23%), ≥4 PYARs. Characteristics of GBM at their first tests during the study period are reported in Table 1. The median age at the first test was 32 years (IQR, 27–40); 13 661 (10.2%) had HIV at the end of the study period; and 44 173 (33.0%) were prescribed PrEP at least once during the study period. There were 6215 (4.6%) PYARs with at least 1 gonorrhea diagnosis, 6577 (4.9%) with at least 1 chlamydia diagnosis, and 4680 (3.5%) with at least 1 infectious syphilis diagnosis (Table 2).

Asymptomatic *N gonorrhoeae* Screening Tests

For all PYARs, the number categorized as having 1, 2, 3, and ≥4 screening-related tests within the year was 84 192 (62.9%), 28 738 (21.5%), 12 474 (9.3%), and 8442 (6.3%), respectively (Table 2). The number of PYARs with at least 1 *N gonorrhoeae* screening-related test increased from 15 378 in 2016 to 19 320 in 2019. This was followed by a decrease during the period of

Table 1. Characteristics of Gay and Bisexual Men at First Test (N = 65 261)

	No.[a]	%
Age, y, median (IQR)	30 (26–38)	
Age group, y		
16–29	29 680	45.48
30–39	20 604	31.57
40–49	7959	12.20
≥50	7018	10.75
HIV status		
Negative	60 598	92.85
Positive	4663	7.15
Pre-exposure prophylaxis		
No	50 671	77.64
Yes	14 590	22.36
Year at entry into observational period		
2016	15 378	23.56
2017	9906	15.18
2018	9016	13.82
2019	8603	13.18
2020	5855	8.97
2021	4865	7.45
2022	5472	8.38
2023	6166	9.45

[a]No. is the total number of person-years in which a gay or bisexual man had at least 1 screening-related gonorrhea test.

COVID-19 restriction, down to 15 841 in 2020 and 14 678 in 2021. Among those tested, the proportion who had ≥2 screening tests per year increased from 33.6% to 38.2% (Figure 1).

Ceftriaxone Prescriptions

Ceftriaxone prescription for any indication per PYAR consistently increased during the study period from 2.92 DDDs/100 PYARs in 2016 to 5.25 in 2023 (Figure 2). The rate of screening-related ceftriaxone prescribing increased steadily over the study period from 0.91 DDDs/100 PYARs in 2016 to 2.96 in 2023 (IRR, 1.14; 95% CI, 1.13–1.15; $P < .001$). In contrast, the rate of nonscreening-related ceftriaxone prescribing remained stable over this period (IRR, 1.00; 95% CI, .99–1.01; $P = .570$). In 2016, there were 0.08 DDDs/100 PYARs of ceftriaxone related to contact testing, 0.53 related to symptomatic testing, and 1.27 related to empirical treatment. In 2023, these figures were at 0.27, 0.56, and 1.19, respectively (Figure 2).

Factors Associated With Prescription

We observed a dose-response relationship between the number of screening-related tests within a year and the rate of screening-related ceftriaxone prescribed, with the rate of prescription highest for GBM who had ≥4 asymptomatic screening tests per year (7.09 DDDs/100 PYARs), followed by those with 3 tests (4.50), 2 tests (2.67), and 1 test (1.07; Table 3). The rate of nonscreening-related ceftriaxone was highest among GBM who had 3 screening tests per year (3.04 DDDs/100 PYARs).

Table 2. Characteristics of Gay and Bisexual Men Undergoing Asymptomatic *Neisseria gonorrhoeae* Screening at Sexual Health Services in Australia (N = 133 846 PYARs of Screening-Related Ceftriaxone)

	Characteristics Associated With Each PYAR	
	No.[a]	%
Age, y, median (IQR)	32 (27–40)	
Age group, y		
16–29	51 329	38.35
30–39	47 537	35.52
40–49	18 824	14.06
≥50	16 156	12.07
CT/NG screening visits per year		
1	84 192	62.90
2	28 738	21.47
3	12 474	9.32
≥4	8442	6.31
Year		
2016	15 378	11.49
2017	16 681	12.46
2018	18 596	13.89
2019	19 320	14.43
2020	15 841	11.84
2021	14 678	10.97
2022	16 129	12.05
2023	17 223	12.87
HIV status		
Negative	120 185	89.79
Positive	13 661	10.21
Prescribed PrEP during study period		
No	89 673	67.00
Yes	44 173	33.00
History of injecting drug use		
No	130 171	97.25
Yes	3675	2.75
Infectious syphilis[b]		
No	129 166	96.50
Yes	4680	3.50
Incident chlamydia diagnosis[b]		
No	127 269	95.09
Yes	6577	4.91
Incident gonorrhea diagnosis[b]		
No	127 631	95.36
Yes	6215	4.64

Abbreviations: CT/NG, *Chlamydia trachomatis*/*Neisseria gonorrhoeae*; PrEP, pre-exposure prophylaxis; PYAR, person-year at risk.

[a]No. is the total number of PYARs of screening-related ceftriaxone in which a gay or bisexual man had at least 1 screening-related gonorrhea test.

[b]Incident syphilis, chlamydia, or gonorrhea diagnoses in a year.

Screening-Related Prescriptions

Unadjusted and adjusted IRRs for screening- and nonscreening-related ceftriaxone are presented in Table 4.

In bivariable analysis, the number of screening-related tests per year was significantly associated with the number of screening-related ceftriaxone prescriptions per year ($P < .001$ for all categories vs 1 test per year). When compared with

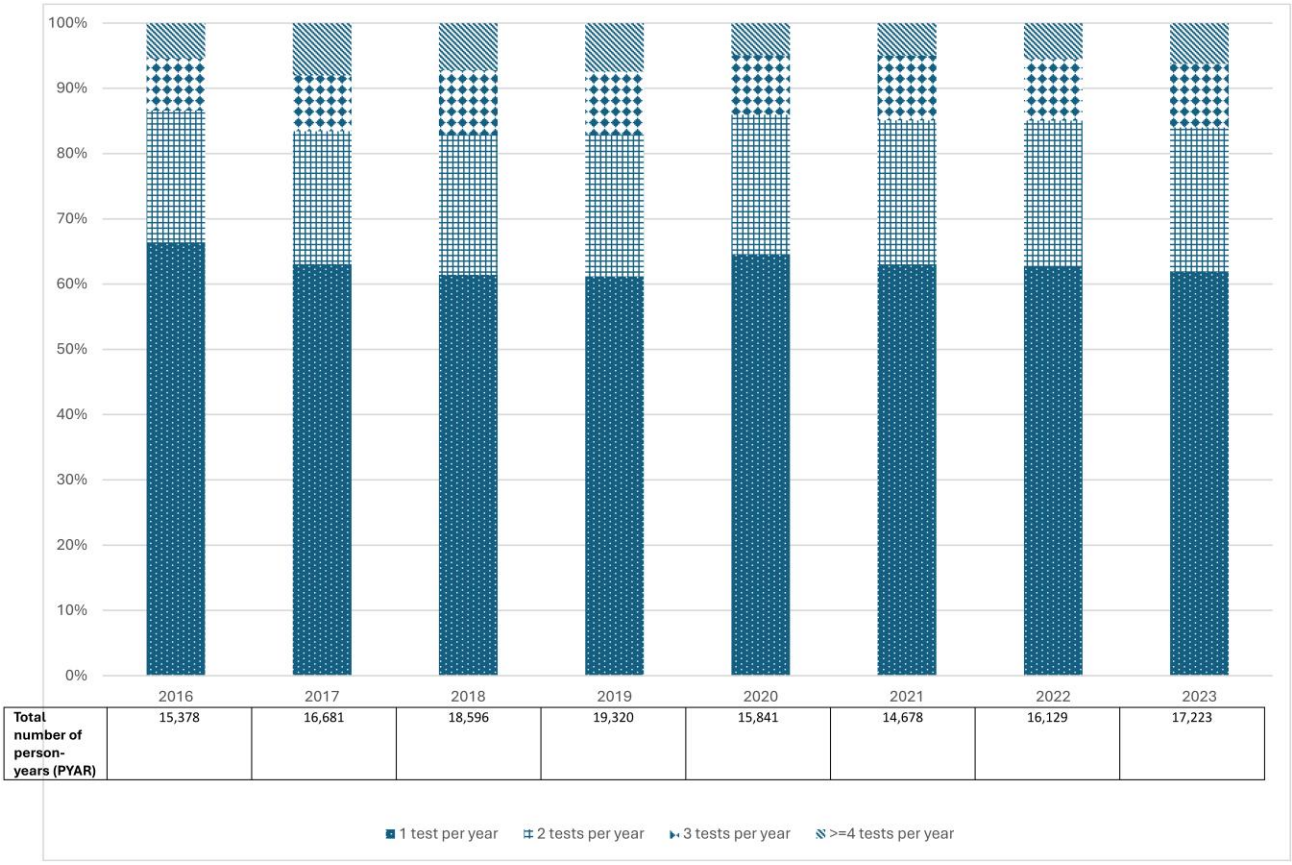

Figure 1. Proportion of person-years at risk (PYAR) of screening-related ceftriaxone among gay and bisexual men at each *Neisseria gonorrhoeae* screening frequency, stratified by calendar year.

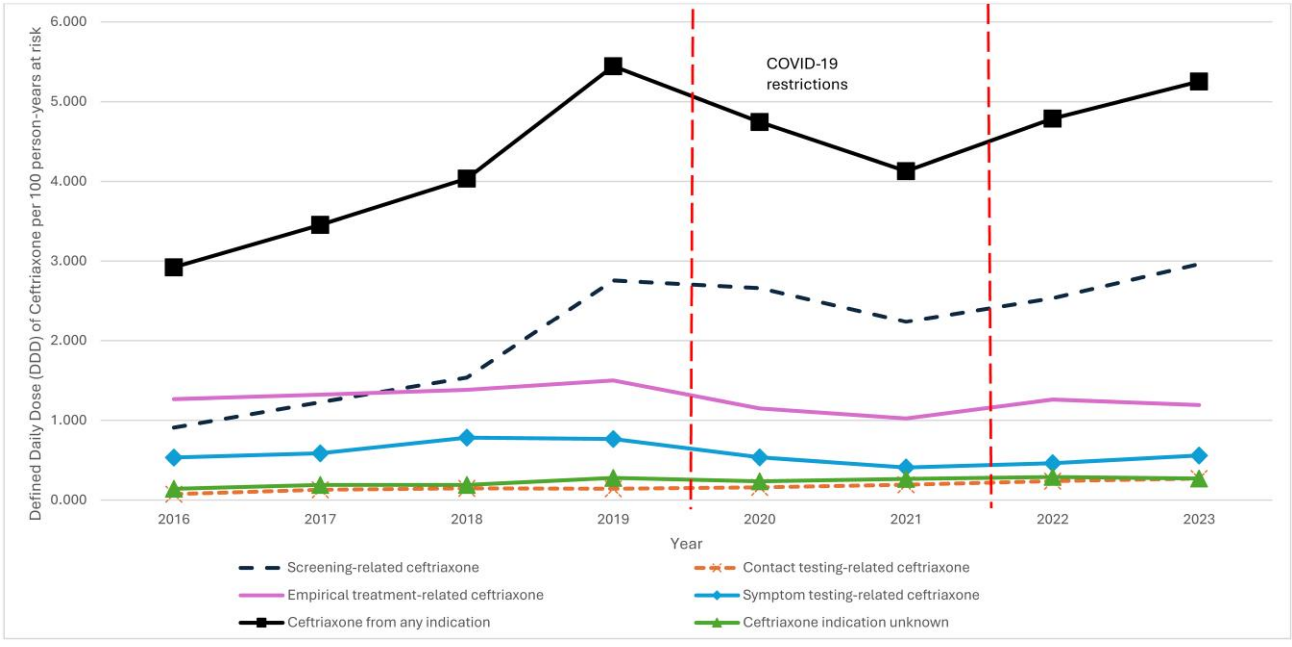

Figure 2. Defined daily dose (DDD) of ceftriaxone administered per 100 person-years at risk of screening-related ceftriaxone stratified by indication: screening related, empirical, contact testing related, symptomatic testing related, and indication unknown.

Table 3. Screening- vs Nonscreening-Related Ceftriaxone Administered per Person-Year Stratified by Characteristics of Gay and Bisexual Men

	Total PYARs of Screening-Related Ceftriaxone	DDDs of Screening-Related		DDDs of Nonscreening-Related	
		Ceftriaxone	Ceftriaxone per 100 PYARs	Ceftriaxone	Ceftriaxone per 100 PYARs
Age group, y					
16–29	51 329	1160	2.26	1245	2.43
30–39	47 537	1136	2.39	1149	2.42
40–49	18 824	349	1.85	395	2.10
≥50	16 156	188	1.16	242	1.50
Gonorrhea screening tests per year					
1	84 192	905	1.07	1644	1.95
2	28 738	768	2.67	778	2.71
3	12 474	561	4.50	379	3.04
≥4	8442	599	7.09	229	2.71
Year					
2016	15 378	140	0.91	310	2.01
2017	16 681	205	1.23	372	2.23
2018	18 596	286	1.54	465	2.50
2019	19 320	533	2.76	519	2.69
2020	15 841	422	2.66	330	2.08
2021	14 678	329	2.24	278	1.89
2022	16 129	409	2.54	363	2.25
2023	17 223	510	2.96	394	2.29
HIV status					
Negative	120 185	2402	2.00	2576	2.14
Positive	13 661	431	3.15	454	3.32
Prescribed PrEP during study period					
No	89 673	1412	1.57	1369	1.53
Yes	44 173	1421	3.22	1661	3.76
History of injecting drug use					
No	130 171	2671	2.05	2818	2.16
Yes	3675	161	4.39	212	5.78
Infectious syphilis diagnosis in the same year					
No	129 166	1170	0.91	2777	2.15
Yes	4680	244	5.21	253	5.41
New chlamydia diagnosis in the same year					
No	127 269	2477	1.95	2585	2.03
Yes	6577	355	5.40	445	6.76

Abbreviations: DDD, defined daily dose; PrEP, pre-exposure prophylaxis; PYAR, person-year at risk.

GBM who had only 1 screening-related test, the unadjusted IRR was 2.50 (95% CI, 2.37–2.61) for those who had 2 tests, 4.19 (95% CI, 3.35–3.74) for those who had 3 tests, and 6.60 (95% CI, 6.23–6.99) for those who had ≥4 tests.

In the multivariable analysis, after adjusting for age, calendar year, PrEP use, HIV status, history of injecting drug use, and infectious syphilis and new chlamydia diagnoses in the same year, the number of screening tests remained associated with ceftriaxone prescriptions ($P < .001$ for all categories). Older age was associated with reduced ceftriaxone prescription in the multivariable model. When compared with those aged 16 to 29 years, the adjusted IRR was 0.86 (95% CI, .82–.90) for those 30 to 39 years, 0.69 (95% CI, .65–.73) for those 40 to 49 years, and 0.452 (95% CI, .42–.49) for those ≥50 years (Table 4).

Nonscreening-Related Prescriptions

In bivariable analysis, the number of *N gonorrhoeae* screening tests was significantly associated with the number of nonscreening-related ceftriaxone prescriptions. When compared with GBM who had 1 screening test per year, the unadjusted IRR was 1.39 (95% CI, 1.32–1.46) for those who had 2 tests, 1.56 (95% CI, 1.46–1.66) for those who had 3 tests, and 1.39 (95% CI, 1.27–1.52) for those who had ≥4 tests. However, after adjusting for the covariates in the multivariable model, only those who had 2 screening tests were more likely to

Table 4. Unadjusted and Adjusted Incident Risk Ratios for Factors Associated With Ceftriaxone Consumption Among Gay and Bisexual Men Attending ACCESS Clinics Between 2016 and 2023

		Screening-Related Ceftriaxone						Nonscreening-Related Ceftriaxone					
	No.	uIRR	95% CI	*P* Value	aIRR	95% CI	*P* Value	uIRR	95% CI	*P* Value	aIRR	95% CI	*P* Value
Total PYARs	133 846												
Screening visits per year													
1	84 192	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
2	28 738	2.488	2.370–2.610	<.001	2.210	2.104–2.320	<.001	1.385	1.319–1.455	<.001	1.107	1.053–1.163	<.001
3	12 474	4.188	3.969–4.419	<.001	3.540	3.352–3.736	<.001	1.556	1.456–1.662	<.001	1.063	0.994–1.137	.074
≥4	8442	6.602	6.233–6.992	<.001	5.466	5.158–5.793	<.001	1.389	1.270–1.519	<.001	0.790	0.721–0.866	<.001
Age group, y													
16–29	51 329	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
30–39	47 537	1.058	1.009–1.109	.02	0.861	0.824–0.899	<.001	0.996	0.943–1.052	.893	0.877	0.832–0.925	<.001
40–49	18 824	0.819	0.766–0.877	<.001	0.688	0.645–0.733	<.001	0.864	0.798–0.936	<.001	0.732	0.678–0.791	<.001
≥50	16 156	0.515	0.472–0.562	<.001	0.452	0.416–0.491	<.001	0.618	0.562–0.679	<.001	0.563	0.513–0.617	<.001
Year													
2016	15 378	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
2017	16 681	1.351	1.215–1.502	<.001	1.180	1.061–1.312	.002	1.106	1.020–1.199	.015	0.967	0.892–1.049	.418
2018	18 596	1.689	1.526–1.871	<.001	1.453	1.312–1.608	<.001	1.241	1.145–1.344	<.001	0.995	0.918–1.079	.907
2019	19 320	3.056	2.760–3.340	<.001	2.528	2.300–2.780	<.001	1.334	1.231–1.444	<.001	0.994	0.917–1.078	.881
2020	15 841	2.930	2.657–3.231	<.001	2.590	2.349–2.856	<.001	1.033	0.948–1.127	.456	0.720	0.660–0.786	<.001
2021	14 678	2.463	2.226–2.725	<.001	2.084	1.884–2.306	<.001	0.939	0.857–1.028	.173	0.614	0.559–0.674	<.001
2022	16 129	2.790	2.530–3.088	<.001	2.371	2.149–2.616	<.001	1.118	1.025–1.220	.012	0.727	0.664–0.796	<.001
2023	17 223	3.260	2.962–3.588	<.001	2.716	2.466–2.991	<.001	1.136	1.043–1.237	.003	0.726	0.665–0.793	<.001
PrEP ever													
No	89 673	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
Yes	44 173	2.042	1.956–2.132	<.001	1.368	1.307–1.432	<.001	2.464	2.346–2.588	<.001	2.927	2.774–3.089	<.001
Current HIV													
No	120 185	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
Yes	13 661	1.577	1.482–1.678	<.001	1.756	1.650–1.868	<.001	1.549	1.436–1.671	<.001	2.342	2.164–2.536	<.001
History of IDU													
No	130 171	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
Yes	3675	2.138	1.957–2.336	<.001	1.744	1.607–1.892	<.001	2.668	2.432–2.927	<.001	1.941	1.768–2.130	<.001
Infectious syphilis													
No	129 166	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
Yes	4680	2.601	2.431–2.784	<.001	1.652	1.548–1.763	<.001	2.515	2.330–2.714	<.001	1.747	1.618–1.887	<.001
New chlamydia													
No	127 269	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…	1 [Ref]	…	…
Yes	6577	2.775	2.613–2.947	<.001	1.680	1.586–1.779	<.001	3.327	3.140–3.525	<.001	2.51	2.419–2.733	<.001

Abbreviations: ACCESS, Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Bloodborne Viruses; aIRR, adjusted incident risk ratio; IDU, injecting drug use; PrEP, pre-exposure prophylaxis; PYAR, person-year at risk; Ref, reference; uIRR, unadjusted incident risk ratio.

receive more nonscreening-related ceftriaxone (adjusted IRR 1.11; 95% CI, 1.05–1.16; Table 4).

Association With Positive *N gonorrhoeae* Test Results for Nonscreening-Related Indications

In bivariable analysis, the number of *N gonorrhoeae* screening tests per year was positively associated with the number of positive *N gonorrhoeae* tests performed for nonscreening indications (ie, for symptom- and contact-related testing). See Supplementary Table 1 for regression outputs.

DISCUSSION

In this cohort of 65 261 GBM engaging in asymptomatic *N gonorrhoeae* screening (133 846 person-years of data), we examined cohort- and individual-level ceftriaxone prescribing within a large national network of PSHSs during the period of widespread PrEP implementation and associated increases in 3 × 3 *N gonorrhoeae* screening. To our knowledge, this is the first large national study to demonstrate the association between screening and ceftriaxone consumption on an individual level and a cohort level. Over the 8-year study period, the rise in *N gonorrhoeae* screening among GBM was followed by a sustained increase in ceftriaxone use, mostly driven by an increase in screening-related prescribing. Yet, the rate of ceftriaxone prescribed for nonscreening indications combined (ie, contact testing, symptomatic testing, and empirical treatment related) has remained stable and, in the second half of the study period, was lower than screening-related prescribing. At the individual level, we found that an increase in the number of annual asymptomatic screening tests had a dose-response relationship with ceftriaxone prescribing for screening-related indications.

It has been proposed that asymptomatic screening for *N gonorrhoeae* in GBM should be significantly reduced due to the ecologic association between population-level ceftriaxone use and the likelihood of emergent gonococcal resistance [11, 13, 23]. Coinciding with the introduction of 3 × 3 *N gonorrhoeae* screening, the proportion of isolates from the Australian Gonococcal Surveillance Program with reduced susceptibility to ceftriaxone increased from 0.05% in 2016 to 0.51% in 2024 [24]. Based on our 2023 estimates, cessation of asymptomatic screening could result in a reduction of up to 510 DDDs in cohort-level ceftriaxone prescribing among screening-engaged GBM. However, it is unclear to what extent a reduction in screening may translate into the slowing of gonorrhea AMR given other contributing factors. For instance, high rates of gonococcal AMR are also seen in settings where regular gonorrhea screening is unavailable, and such rates are instead due to the lack of access to testing and appropriate treatment [14, 25].

Proponents for 3 × 3 *N gonorrhoeae* screening among GBM argue that early diagnosis interrupts onward transmission. However, in our analysis, intensification of screening was not associated with a commensurate decrease in the use of ceftriaxone or in positive *N gonorrhoeae* tests detected through nonscreening-related indications, such as symptomatic presentation or contact testing. Nevertheless, there are other potential benefits to frequent *N gonorrhoeae* screening beyond avoidance of antibiotic use that require careful consideration. For example, 3 × 3 *N gonorrhoeae* screening may prevent bridging transmission into sexual networks with cisgender women and transgender men who are at higher risk of serious sequalae from gonorrhea [17, 26]. Our analysis also showed that up to a third of ceftriaxone prescriptions were for nonscreening indications, which would still contribute to a significant amount of cohort-level ceftriaxone use even without regular asymptomatic screening [27, 28]. Our analysis provides real-world data on antibiotic exposure associated with intensive screening strategies and may help inform ongoing discussions about the value of frequent asymptomatic screening and its potential impact on *N gonorrhoeae* transmission, community prevalence, and AMR.

Notification rates of *N gonorrhoeae* in Australia rose over the study period and were disproportionately concentrated among GBM prescribed PrEP and GBM with HIV [28]. One possible explanation for the rise in the ceftriaxone prescription rate is the increase in adherence to 3 × 3 screening recommendations [16]. This is supported by our observation that the increase in ceftriaxone prescribing is driven by screening-related indications while nonscreening-related ceftriaxone prescribing has remained stable. Furthermore, in 2019, Australian guidelines changed from recommending empirical antibiotics for all gonorrhea contacts to recommending testing in asymptomatic contacts and treatment only if gonorrhea is detected [29], potentially confounding the amount of contact testing–related ceftriaxone prescribed in the subsequent period.

Our finding that higher rates of asymptomatic screening are associated with more antibiotic consumption is consistent with recent data from a randomized controlled trial on the impact of 3 × 3 screening on the incidence of STI diagnoses [30]. In this study, the difference in antibiotic consumption was driven by lower consumption among those who were not told of their gonorrhea diagnoses given their randomization to less frequent screening [17]. Similarly, our findings are likely explained by the fact that those who are attending PSHSs for more screening tests are more likely to have asymptomatic gonorrhea infections diagnosed and therefore be prescribed ceftriaxone—rather than any true difference in incidence among GBM being screened at different frequencies.

The finding that the likelihood of receiving screening-related ceftriaxone is highest among the youngest GBM (16–29 years), even after adjustment for other factors associated with STI risk, is notable. Previous epidemiologic evidence among Australian GBM attending PSHSs highlights that *N gonorrhoeae* incidence remains high until the fourth decade of life [31]. Therefore, younger GBM who commence asymptomatic *N gonorrhoeae*

screening early in adulthood and continue screening over subsequent decades may experience high cumulative exposure to broad-spectrum antibiotics such as ceftriaxone. Emerging evidence also suggests that exposure to cephalosporins during early adulthood may be associated with enduring alterations to the human microbiome [32, 33] and long-term metabolic outcomes such as diabetes mellitus [34] and obesity [35]. These considerations highlight the importance of carefully evaluating the long-term risk-benefit profile of intensive 3 × 3 screening strategies in this population.

There are several important limitations. Our cohort included only PYARs in which an individual had undergone asymptomatic screening in a calendar year; therefore, our finding of increased ceftriaxone consumption applies specifically to GBM engaged in routine screening. As we relied on data from electronic medical records from PSHSs, screening tests that occurred outside of these services were not captured. Sexual health care in Australia is provided by PSHSs and general practitioners in the community, meaning that we may have missed tests that occurred outside of the PSHS network. We excluded GBM who did not attend any asymptomatic screening at PSHSs in a calendar year to avoid misclassification of those who were undergoing regular asymptomatic screening via general practitioners but attended a sexual health service for treatment based on positive results or symptoms. This may have led to an underestimation of the prescription rate of screening- and nonscreening-related ceftriaxone. Also, we were not able to extract patient notes; as such, there may be some missing data on patient symptoms or STI contact if there was incomplete coding. However, we endeavored to address this by conducting a free-text search in the "reason for presentation" field. Ceftriaxone prescriptions with unknown indication represented only 5.3% of total prescriptions.

CONCLUSIONS

Our large cohort study based on surveillance data from GBM undergoing *N gonorrhoeae* screening in Australian PSHSs showed a significant and sustained increase in ceftriaxone prescribing since widespread rollout of HIV PrEP and 3 × 3 screening recommendations. We observed a dose-response relationship between frequent screening and increases in ceftriaxone consumption and that ceftriaxone prescribing due to screening-related testing rose while prescribing due to other indications remained stable. Our findings contribute to current global discussions to understand the benefits and harms of intensive *N gonorrhoeae* screening in GBM and to reduce antibiotic consumption.

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (http://jid.oxfordjournals.org/). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Author contributions. A. W. and M. W. T. conceived the study. M. W. T., R. G., E. P. F. C., C. K. F. contributed substantially to interpretation of the data. A. W. and M. W. T. undertook the formal data analysis. A. W., M. W. T., and H. L. A. curated the data. R. G., H. L. A., and M. S. coordinate the ACCESS study and were responsible for funding acquisition. R. V., D. J. T., A. N., S. M., L. O., A. M., C. K. F., C. S. B., E. P. F. C., and J. J. O. are ACCESS clinic investigators and contributed to data acquisition. A. W. and M. W. T. had full access to all the data in the study and verified the data. M. W. T. and R. G. provided academic supervision. A. W. led the manuscript preparation. All authors read and revised the manuscript critically for important intellectual content and approved the final version of the manuscript for publication.

Data sharing. Deidentified individual participant data in this study cannot be shared publicly because of the sensitive nature of participant data anonymously extracted from participating clinical services. Access to deidentified data is available via the Burnet Institute with approval from the Alfred Hospital Human Research Ethics Committee for researchers who meet the criteria for access to confidential data. The ACCESS study protocol has been published previously (accessproject.org.au).

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