nature health

Article

https://doi.org/10.1038/s44360-026-00211-0

Population-level impact of doxycycline post-exposure prophylaxis on bacterial sexually transmitted infections

Received: 23 March 2026

Accepted: 30 September 2026

Published online: 21 October 2026

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Bacterial sexually transmitted infections (STIs) continue to increase in many high-income settings, disproportionately affecting gay and bisexual men (GBM). Doxycycline post-exposure prophylaxis (doxyPEP) is a highly efficacious strategy for preventing syphilis and chlamydia; however, its population-level impact following national implementation remains uncertain. Australia released an interim position statement in April 2023 and national guidance in September 2023 recommending the consideration of doxyPEP for GBM at increased risk of STIs. Here we analyse sentinel surveillance data from 29 Australian sexual health and general practice services between January 2022 and December 2025. Using interrupted time-series analyses, we examined trends in infectious syphilis, chlamydia and gonorrhoea diagnoses among 78,560 GBM before and after dissemination of doxyPEP trial evidence and national guidance. Observed cumulative STI diagnoses after September 2023 were compared with counterfactual projections based on continuation of preguidance trends. During the 27 months following release of national doxyPEP guidance, cumulative syphilis diagnoses were 55% lower than expected under the counterfactual scenario (rate ratio (RR) 0.45; 95% confidence interval (CI) 0.35 to 0.55), and chlamydia diagnoses were 36% lower (RR 0.64; 95% CI 0.45 to 0.84). No significant change was observed for gonorrhoea (RR 1.11; 95% CI 0.59 to 1.63). These findings provide the first country-level evidence that doxyPEP guidance was associated with sustained reductions in syphilis and chlamydia diagnoses among GBM.

In high-income settings globally, bacterial sexually transmitted infections (STIs) continue to rise, with priority populations such as gay and bisexual men (GBM) and other men who have sex with men disproportionately represented among diagnoses. If left untreated, syphilis can lead to serious sequalae, including neurological, cardiovascular and ophthalmic complications, as well as adverse outcomes during pregnancy. These complications highlight the need for effective prevention strategies among GBM, including those with female partners. So far, responses to bacterial STIs among GBM in Australia and other high-income settings have largely centred on test-and-treat models of care, with most countries recommending frequent screening of asymptomatic GBM, up to four times per year. Despite these efforts, STI incidence has continued to rise, and there is currently no empirical evidence that asymptomatic screening alone leads to sustained reductions in population-level prevalence among GBM[1]. Similar to other high-income settings, diagnoses of bacterial STIs in Australia have increased substantially over the past decade, with syphilis diagnoses increasing by 111% and gonorrhoea by 139% between 2015 and 2024[2].

In this context of increasing STI incidence, the advent of doxycycline post-exposure prophylaxis (doxyPEP) represents a major biomedical

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https://doi.org/10.1038/s44360-026-00211-0

Table 1 | Interrupted time-series analysis of monthly STI diagnoses among GBM attending ACCESS clinics before and after dissemination of doxyPEP evidence and national guidance

	Preguidance trend, percentage change per month	Step change at evidence dissemination, %	Trend during evidence dissemination period, percentage change per month	Step change at guideline release, %	Postguidance trend, percentage change per month	Difference between pre- and postguidance trends, percentage points per month	Model fit, R^2
Syphilis	1.78 (0.04 to 3.55) P=0.046	−18.88 (−36.96 to 4.39) P=0.101	−5.84 (−11.89 to 0.63) P=0.075	16.67 (−11.80 to 54.31) P=0.272	−1.31 (−2.02 to −0.60) P=0.001	−3.09 (−4.93 to −1.25) P=0.001	0.753
Chlamydia	0.87 (−0.58 to 2.33) P=0.235	5.19 (−15.99 to 31.71) P=0.652	−0.57 (−6.31 to 5.53) P=0.848	−1.22 (−23.00 to 26.73) P=0.921	−2.27 (−2.85 to −1.69) P<0.001	−3.14 (−4.66 to −1.61) P<0.001	0.789
Gonorrhoea	0.17 (−1.44 to 1.80) P=0.832	6.94 (−16.57 to 37.08) P=0.588	1.66 (−4.80 to 8.56) P=0.615	10.00 (−16.47 to 44.85) P=0.489	−1.01 (−1.67 to −0.35) P=0.004	−1.18 (−2.88 to 0.52) P=0.173	0.474

Values are percentage changes per month or step changes expressed as percentages, derived from exponentiated coefficients (95% CIs) from segmented linear regression models fitted to log-transformed monthly case counts. Differences between preguidance and postguidance trends represent absolute differences in monthly percentage change (percentage points). All statistical tests were two-sided and no adjustment was made for multiple comparisons. Exact P values are reported where possible. Full model coefficients and corresponding analyses using untransformed case counts are presented in Supplementary Tables 3 and 4.

innovation for bacterial STI prevention. In recent years, several large randomized controlled trials have demonstrated that a single 200-mg dose of doxycycline taken within 72 h after sex as a post-exposure prophylaxis substantially reduces the risk of syphilis and chlamydia acquisition among cisgender GBM and transgender women[3–5]. Trial data indicate relative risk reductions of approximately 73–87% for syphilis and 70–88% for chlamydia, with inconsistent evidence for efficacy against gonorrhoea[6]. Real-world observational data from a US cohort of 11,551 GBM using HIV pre-exposure prophylaxis (PrEP) similarly found that receipt of doxyPEP in routine clinical practice was associated with substantial reductions in syphilis (80%) and chlamydia (79%), and more modest reductions in gonorrhoea (12%)[7]. Recent city-level interrupted time-series analyses from San Francisco and Seattle have also demonstrated population-level reductions in bacterial STI diagnoses following the uptake of doxyPEP[8,9]. However, these studies were conducted within single jurisdictions and primarily relied on local surveillance data. National evaluations examining changes following dissemination of doxyPEP evidence and clinical guidance remain limited.

In response to increasing STI transmission and the release of clinical trial data on the efficacy and safety of doxyPEP, the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) conducted a national consultation process and released a national consensus statement in September 2023. This statement recommends that doxyPEP be considered for GBM at an increased risk of STIs[10], specifically, those with a recent bacterial STI diagnosis or those anticipating an increased period of risk, as well as those recently prescribed HIV post-exposure prophylaxis or those with sexual partners with a uterus. These recommendations provide guidance to clinicians and community members on the appropriate use and prescribing of doxyPEP. However, the population-level impact of these recommendations on bacterial STI diagnoses among GBM in Australia remains unknown. Understanding whether these developments translated into measurable population-level changes in STI diagnoses is important for informing policy and clinical practice. We therefore aimed to compare trends in STIs before and after the emergence of doxyPEP guidance, including the period of clinical trial evidence dissemination followed by the release of national doxyPEP guidance, using data from a large national STI sentinel surveillance system.

Results

Study population and STI diagnoses

We analysed routinely collected data from 29 sexual health and general practice services participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance of Sexually Transmissible Infections and Blood Borne Viruses (ACCESS) between January 2022 and December 2025. The analysis included GBM aged ≥16 years who attended a participating service during the study period. In total, 78,560 GBM received at least one test for any bacterial STI during the study period, including 68,113 with at least one syphilis test, 73,567 with at least one chlamydia test and 73,760 with at least one gonorrhoea test (see Supplementary Table 2 for the total number of tests). Of these, 27,725 GBM (35.3%) were diagnosed with at least one case of infectious syphilis, chlamydia or gonorrhoea during the study period. Overall, there were 5,198 syphilis cases, 27,190 chlamydia cases and 27,301 gonorrhoea cases during the study period. Among those diagnosed with at least one bacterial STI, the mean number of diagnoses was 2.15. Of the 27,725 GBM with at least one STI diagnosis, the mean age at first STI diagnosis during the study period was 37.0 years (s.d., 11.8 years), 13,034 (47.0%) had evidence of an HIV PrEP prescription during the study period and 3,595 (13.0%) were living with HIV by the end of the study period.

Changes in STI diagnosis trends following doxyPEP guidance

We used interrupted time-series analyses to examine monthly STI diagnoses across three periods: a preguidance period (January 2022–March 2023), an evidence dissemination period following publication and dissemination of doxyPEP trial evidence (April–September 2023) and a postguidance period following release of Australian national doxyPEP guidance (October 2023–December 2025). Results of the primary interrupted time series analyses are presented in Table 1 and Fig. 1. During the preguidance period, syphilis diagnoses increased by +1.8% per month (95% confidence interval (CI) +0.1 to +3.6), before declining by −1.3% per month (95% CI −2.0 to −0.6) following release of national doxyPEP guidance. The postguidance trend differed significantly from the preguidance trend, corresponding to an absolute reduction of −3.1 percentage points per month (95% CI −5.0 to −1.2). There was no evidence of significant immediate step changes at either interruption. The model demonstrated good fit (R^2 = 0.753).

Chlamydia diagnoses were stable during the preguidance period (+0.9% per month; 95% CI −0.6% to +2.3%), before declining by −2.3% per month (95% CI −2.9% to −1.7%) following national doxyPEP guidance. The postguidance trend differed significantly from the preguidance trend (difference, −3.2 percentage points per month; 95% CI −4.7 to −1.6). No significant immediate step changes were observed. The model fit was good (R^2 = 0.789).

Gonorrhoea diagnoses showed no significant change during the preguidance period (+0.2% per month; 95% CI −1.4% to +1.8%). Although diagnoses declined by −1.0% per month (95% CI −1.7% to −0.4%) during the postguidance period, the overall trend did not differ significantly from the preguidance period (difference, −1.2 percentage points per month; 95% CI −2.9 to +0.6). No significant immediate step changes were observed. The model fit was moderate (R^2 = 0.474). Analyses

using untransformed case counts yielded results that were broadly consistent across all STIs (Supplementary Table 4), as did analyses of chlamydia and gonorrhoea stratified by anatomic site of infection (Supplementary Fig. 11).

Alternative model specifications, including one-interruption models and models incorporating seasonal terms, did not materially alter the estimated interruption effects. Although seasonal adjustment modestly improved the model fit for some outcomes, it did not consistently improve fit across all STIs (Supplementary Tables 6 and 7).

Trends in STI test positivity

Analyses of monthly test positivity showed stable positivity for all STIs during the pre-doxyPEP period (Supplementary Table 5). Consistent with trends in case counts, declines in positivity were observed for syphilis in the evidence dissemination and postguidance periods, and for chlamydia in the postguidance period. In contrast to analysis of case counts, gonorrhoea positivity showed a significant step increase at the second interruption. However, higher overall test positivity observed for gonorrhoea during the postguidance period was consistent with analyses of monthly case counts (Supplementary Fig. 9).

Estimated cumulative reductions in STI diagnoses after doxyPEP guidance

We compared model-predicted cumulative STI diagnoses during the postguidance period (October 2023–December 2025) under the observed trends with a counterfactual scenario estimating the number of diagnoses that would have occurred had preguidance trends continued unchanged (that is, no doxyPEP guidance). The estimated number of syphilis cases during the postguidance period was 2,430 based on the observed trend, compared with 5,403 cases under the counterfactual scenario of no doxyPEP guidance (rate ratio (RR) 0.45; 95% CI 0.35 to 0.55; $P < 0.001$), corresponding to a 55.0% relative reduction. Similarly, the estimated number of chlamydia cases during the postguidance period was 13,676 under the observed trend, compared with 21,280 under the counterfactual scenario (RR 0.64; 95% CI 0.45 to 0.84; $P < 0.001$), representing a 35.3% relative reduction. By contrast, estimated gonorrhoea cases during the postguidance period were 16,099 under the observed trend and 14,543 under the counterfactual scenario, with no evidence of a significant difference (RR 1.11; 95% CI 0.59 to 1.63; $P = 0.688$; Table 2).

Subgroup analyses among populations prioritized for doxyPEP

In subgroup analyses restricted to GBM with an STI diagnosis in the preceding 12 months, estimated reductions due to doxyPEP were greater for syphilis (RR 0.36; 95% CI 0.27 to 0.45) and similar for chlamydia (RR 0.67; 95% CI 0.44 to 0.90). Similar reductions were also observed among GBM with evidence of HIV PrEP use and among GBM using PrEP or living with HIV. Among each subgroup, the cumulative number of gonorrhoea diagnoses remained non-significantly higher than the number projected under the counterfactual scenario (Table 2 and Supplementary Fig. 10).

Trends in doxycycline prescribing

Exploratory analyses of doxycycline prescribing were restricted to 16 clinics with prescription instruction data that could be used to identify prescriptions indicative of doxyPEP use. Among 15,719 unique GBM attending these 16 clinics, 41,556 doxycycline prescriptions were issued during the study period, of which 6,917 contained instructions indicative of doxyPEP use. Across the 16-clinic prescribing subset, 4,001 unique individuals received at least one prescription containing instructions indicative of doxyPEP use during the study period. The cumulative number of unique individuals with a recorded doxyPEP-indicative prescription increased steadily over time (Fig. 1d).

DoxyPEP-indicative prescriptions accounted for 0.04% (5/13,083) of doxycycline prescriptions during the preguidance period, increasing to 1.6% (59/3,682) during evidence dissemination and 27.7% (6,853/24,791) following national guidance. By December 2025, 50.1% of all doxycycline prescriptions contained instructions indicative of doxyPEP (Supplementary Fig. 8).

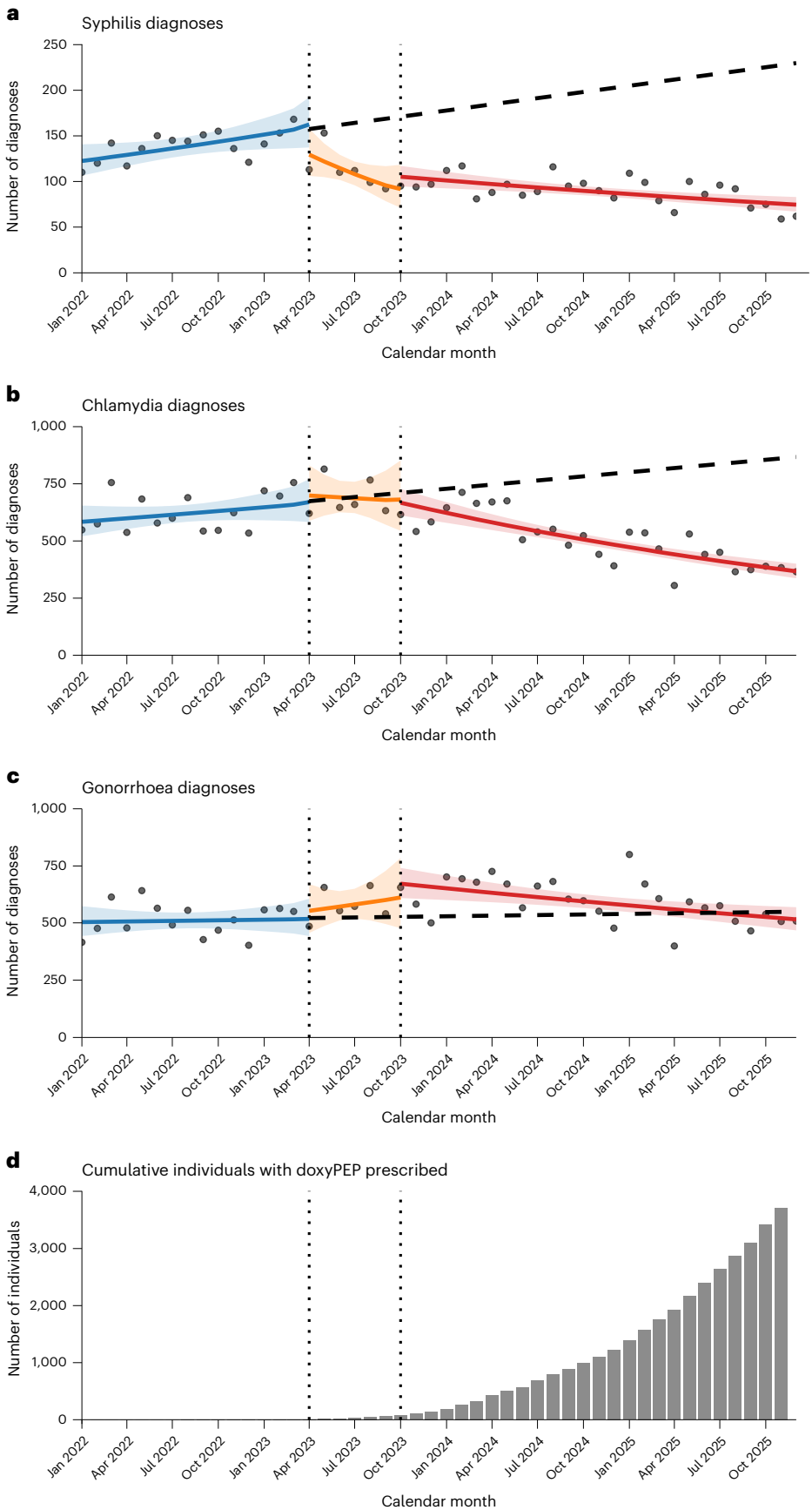
Discussion

In this interrupted time-series analysis of national sentinel surveillance data, the release of doxyPEP trial evidence and subsequent national clinical guidance was associated with substantial reductions in syphilis and chlamydia among GBM in Australia, with no corresponding reduction observed for gonorrhoea. Subgroup analyses among groups prioritized in doxyPEP guidance, including GBM using HIV PrEP, GBM living with HIV, and GBM with a recent STI, demonstrated similar reductions, consistent with the uptake of doxyPEP among individuals at the highest risk of STIs. This study provides national-level evidence of sustained reductions over more than 2 years in bacterial STI diagnoses following the release of doxyPEP guidance, extending findings from clinical trials and early local evaluations to real-world population outcomes. Consistent with this interpretation, exploratory analyses of prescription data from a subset of clinics showed temporal patterns in doxycycline prescribing indicative of increasing uptake of doxyPEP following dissemination of trial evidence and national guidance. The observed declines in syphilis and chlamydia diagnoses are consistent with the high efficacy of doxyPEP for preventing these infections reported in randomized trials[6] and suggest that these individual-level benefits probably translate into measurable population-level effects.

Multiple independent data sources suggest that awareness and use of doxyPEP increased in Australia following the dissemination of clinical trial evidence and national guidance. Before the release of doxyPEP guidance, a survey conducted in 2018 at an Australian sexual health centre found that among 1,065 GBM using HIV PrEP, 9.9% reported any use of doxycycline as STI prophylaxis in the past month[11]. In a national cross-sectional survey conducted in 2024 among 2,095 GBM and trans and gender-diverse people recruited through sexual health services and online platforms, participants reported high awareness and higher use, with more than half having heard of doxyPEP, among whom the ever use of doxyPEP was reported by 33% of PrEP users and 37% of people living with HIV, with 32% in both groups reporting use in the past 12 months[12]. Consistent with these findings, population-level behavioural surveillance surveys conducted among 2,238 GBM living in Melbourne in 2025 found that 65% had heard of doxyPEP, 13% had used it in the past 6 months and 24% of PrEP users reported doxyPEP use during this period[13]. Taken together, these data, alongside our observation of increasing doxycycline prescriptions indicative of doxyPEP use, support the interpretation that release of doxyPEP guidance was associated with increased uptake of doxyPEP among GBM in Australia,

Fig. 1 | Monthly STI diagnoses and cumulative doxyPEP prescribing among GBM attending ACCESS clinics from January 2022 to December 2025. **a**–**d**, Monthly diagnoses of syphilis (**a**), chlamydia (**b**) and gonorrhoea (**c**), and the cumulative number of individuals prescribed doxyPEP (**d**) in a subset of clinics ($N = 16$). Points represent observed monthly case counts. Solid lines show model-fitted monthly diagnosis counts from segmented Prais–Winsten interrupted time-series models for the preguidance period (blue), evidence dissemination period (orange) and postguidance period (red), with shaded areas indicating 95% CIs. Models accounted for first-order autocorrelation; fitted values and CIs were back-transformed to the original count scale. Dashed black lines show counterfactual projections from segmented linear regression models of untransformed monthly diagnosis counts, assuming continuation of the preguidance trend. Vertical dotted lines indicate April 2023 (publication of the US DoxyPEP trial and start of evidence dissemination) and October 2023 (release of Australian national doxyPEP guidance). Full model estimates, 95% CIs and *P* values are presented in Table 1.

https://doi.org/10.1038/s44360-026-00211-0



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Table 2 | Estimated cumulative STI diagnoses during the postguidance period under observed and counterfactual scenarios

	Counterfactual scenario[a]	Observed scenario	RR (95% CI)	*P* value
All GBM				
Syphilis	5,403	2,430	0.45 (0.35 to 0.55)	<0.001
Chlamydia	21,280	13,676	0.64 (0.45 to 0.84)	<0.001
Gonorrhoea	14,543	16,099	1.11 (0.59 to 1.63)	0.688
GBM with a recent STI[b]				
Syphilis	2,132	768	0.36 (0.27 to 0.45)	<0.001
Chlamydia	8,193	5,515	0.67 (0.44 to 0.90)	0.005
Gonorrhoea	5,751	7,086	1.23 (0.59 to 1.87)	0.481
GBM using PrEP				
Syphilis	2,212	1,060	0.48 (0.33 to 0.63)	<0.001
Chlamydia	10,556	7,395	0.70 (0.46 to 0.95)	0.016
Gonorrhoea	6,703	9,001	1.34 (0.50 to 2.19)	0.425
GBM using PrEP or living with HIV				
Syphilis	3,807	1,715	0.45 (0.33 to 0.57)	<0.001
Chlamydia	13,686	9,393	0.69 (0.45 to 0.92)	0.013
Gonorrhoea	8,604	11,101	1.29 (0.54 to 2.05)	0.455

RRs compare cumulative model-predicted diagnoses under observed postguidance trends with counterfactual projections assuming continuation of preguidance trends. CIs were derived from the variance–covariance matrix of the fitted segmented linear regression models using the delta method. *P* values test the null hypothesis that the RR equals 1. All tests were two-sided and no adjustment was made for multiple comparisons. Exact *P* values are reported where possible. [a]Counterfactual estimates represent projected cumulative diagnoses assuming continuation of preguidance trends in the absence of doxyPEP guidance. [b]Recent STI defined as a diagnosis of chlamydia, gonorrhoea or syphilis within the 12 months preceding diagnosis. GBM were classified as HIV PrEP users if they had an electronic prescription record for PrEP in the 12 months before diagnosis and as living with HIV if evidence of HIV was present before STI diagnosis, including laboratory or clinical records. Corresponding interrupted time-series plots for subgroup analyses are shown in Supplementary Fig. 10.

providing a plausible explanation for the observed population-level declines in syphilis and chlamydia. These observed reductions also align with recent Australian modelling demonstrating that doxyPEP is likely to be a cost-effective STI prevention strategy when targeted to GBM at the highest risk[14].

Declines in syphilis cases and test positivity were first observed during the evidence dissemination period, earlier than the observed decline in chlamydia, which began during the postguidance period. However, formal statistical comparisons between the timing of changes across outcomes were not undertaken and these temporal differences should be interpreted cautiously. Regardless of the relative timing of changes, sustained reductions in both syphilis and chlamydia diagnoses were observed following dissemination of doxyPEP evidence and national guidance, consistent with the established efficacy of doxyPEP against both infections.

The greater relative declines in syphilis compared with chlamydia may also reflect the design of Australia's national doxyPEP guidance. The ASHM DoxyPEP Consensus Statement recommends that clinicians consider doxyPEP for GBM and other men who have sex with men with a recent syphilis diagnosis, multiple bacterial STIs in the past 12 months or anticipated periods of heightened sexual risk, such as travel or attendance at sex-on-premises venues. Use is intended to be time limited, typically over 3-month periods, with regular clinical review. Importantly, the guidance emphasizes that doxyPEP should be delivered within comprehensive sexual health care, including quarterly STI screening, HIV prevention (including HIV PrEP and PEP) and vaccination. Prior modelling suggests that targeting doxyPEP use to individuals with a recent STI may yield the greatest population-level reductions in subsequent syphilis infections[15]. Framing doxyPEP as a targeted, time-limited intervention integrated with routine care may have facilitated early uptake among individuals at the highest risk of syphilis, contributing to the temporal patterns observed in this analysis.

In this analysis, trends in test positivity closely mirrored patterns observed in case counts, supporting the interpretation that observed reductions in syphilis and chlamydia were unlikely to be driven solely by changes in testing volume over time. This is particularly relevant, as the Australian DoxyPEP Consensus Statement recommends that GBM using doxyPEP follow the same standard quarterly STI screening recommendations as all sexually active GBM[16]. Concurrent declines in both diagnoses and positivity suggest a true reduction in the underlying incidence among GBM attending services within this sentinel network. These findings should be interpreted with some caution, as both STI diagnoses and testing practices may have been influenced by doxyPEP implementation. Nevertheless, the broadly similar patterns observed for diagnoses and positivity provide additional support that reductions in syphilis and chlamydia were not driven solely by changes in testing volume.

In contrast to syphilis and chlamydia, we observed no cumulative reduction in population-level gonorrhoea diagnoses following the release of doxyPEP guidance. Although a modest decline in monthly gonorrhoea cases was detected during the postguidance period, this followed an increase at the second interruption, and the postguidance trend did not differ significantly from the pre-doxyPEP trend. Further, no declining trend was observed in gonorrhoea test positivity during the postguidance period. In addition, the overall model fit was the lowest for gonorrhoea ($R^2 = 0.63$), suggesting that variation in gonorrhoea diagnoses over the study period was less well explained by the timing of doxyPEP guidance. These findings are consistent with trial and observational evidence indicating that doxyPEP effectiveness against gonorrhoea is weaker and less consistent than for syphilis and chlamydia, probably reflecting substantial geographic variation in tetracycline susceptibility among gonococcal isolates. In Australia, tetracycline resistance among isolates has been reported to reach up to 60% in some jurisdictions[17]. A recent systematic review reported increasing global tetracycline resistance in gonorrhoea, with the median resistance in the East Asia and Pacific region estimated at 82.1%[18]. Notably, observed gonorrhoea case counts at the end of the follow-up were similar to counterfactual predictions, indicating no measurable impact on gonorrhoea diagnoses following doxyPEP guidance and providing no evidence of

behavioural change that would be expected to increase gonorrhoea transmission. Ongoing surveillance of gonorrhoea incidence and associated antimicrobial resistance will be particularly important as doxyPEP implementation expands and as asymptomatic screening recommendations potentially evolve[19], alongside continued research into emerging biomedical prevention strategies for gonorrhoea, including potential vaccine candidates[4,20].

These findings have implications for ongoing policy discussions regarding the optimal role of asymptomatic screening for chlamydia and gonorrhoea, particularly among GBM using doxyPEP. There is growing debate regarding the benefits and potential harms of routine asymptomatic screening for chlamydia and gonorrhoea among gay men, particularly considering the generally low risk of severe health sequelae for these infections in men without female partners and concerns about overtreatment and antimicrobial resistance[19,21,22]. In settings where biomedical prevention strategies such as doxyPEP are widely implemented, it may be appropriate to reassess the balance between screening intensity and clinical benefit. Future STI control strategies and clinical guidelines should consider how biomedical prevention and screening interact, with an emphasis on ongoing monitoring and adaptive approaches that maximize public health impact while minimizing unintended consequences. In addition to reducing infection risk, patient-centred approaches should also consider the potential broader individual-level benefits of doxyPEP use, including increased pleasure and reduced anxiety, stigma and symptom- or treatment-related discomfort associated with recurrent bacterial STIs[23], which may further support its acceptability and uptake among priority populations for STIs.

Our findings are also consistent with a recent study from San Francisco that explored city-level notifications of bacterial STIs among GBM and transgender women and compared trends in notifications before and after the San Francisco Department of Health released doxyPEP guidelines in October 2022, one of the first jurisdictions globally to do so, in which researchers also observed a decline in chlamydia and early syphilis notifications, but no decline in gonorrhoea[8]. With a longer period of follow-up after guideline release, our findings build on this early evidence and suggest that the population-level impact of doxyPEP on syphilis and chlamydia is consistent across different high-income settings and can be sustained following broader guideline implementation.

Key strengths of this study include its national scope, large sample size and linkage of individuals across clinics, allowing evaluation of population-level trends following dissemination of doxyPEP guidance. Probabilistic linkage enabled subgroup analyses based on individual-level characteristics, including HIV status, HIV PrEP use and recent STI history, allowing us to examine patterns relevant to populations prioritized for doxyPEP and the potential impact on recurrent STIs, an advantage over prior population-level analyses. The availability of prescribing data from a subset of clinics also provided supporting evidence that increasing doxyPEP uptake occurred contemporaneously with the observed reductions in STI diagnoses.

This analysis also has several limitations. First, although ACCESS captures a large and geographically diverse population of GBM, it is a sentinel surveillance system and may over-represent individuals more engaged with sexual health services. As such, the magnitude of the observed reductions may not be fully generalizable to GBM who do not access regular sexual health care. Second, transgender status was not consistently captured across participating services. Consequently, we were unable to stratify analyses by cisgender and transgender individuals or assess whether the impact of doxyPEP differed between these groups. Future studies should evaluate doxyPEP among transgender populations using dedicated study designs developed in partnership with transgender communities, as more complete gender identity data become available within surveillance systems. Third, we were unable to reliably identify individuals prescribed doxyPEP across the full dataset given unreliable prescription data in some clinics. In addition, some individuals may obtain doxyPEP without a prescription, including through online sources or from partners or friends[24], further limiting ascertainment of individual-level doxyPEP exposure. Consequently, we could not directly attribute changes in STI diagnoses to individual doxyPEP use or evaluate dose–response relationships, adherence or effectiveness at the individual level. Our findings therefore reflect population-level associations following dissemination of doxyPEP guidance rather than the causal effect of doxyPEP use in individual participants. Fourth, as with all observational time-series analyses, residual confounding or unmeasured factors may have contributed to observed trends. Also, changes in sexual practices unrelated to doxyPEP use could not be measured. However, the divergent patterns observed across STIs (declines in syphilis and chlamydia alongside stable or increasing gonorrhoea diagnoses) are consistent with trial evidence on doxyPEP efficacy and reduce the likelihood that the findings are explained solely by unmeasured behavioural factors or secular trends. Fifth, some STI diagnoses may have occurred outside the sentinel surveillance network and therefore not been captured in our analysis. However, this is unlikely to impact the observed trends in test positivity, which are less sensitive to changes in testing or to attendance for testing outside of the network. Sixth, ACCESS primarily captures laboratory and prescribing data and does not consistently record clinical information such as symptoms, reason for testing or treatment uptake. Consequently, we were unable to distinguish symptomatic from asymptomatic infections, assess treatment uptake following diagnosis or determine whether a small number of empirically treated infections may not have been captured by laboratory-based outcome definitions. Finally, despite exclusion of tests conducted within 14 days of a prior positive result, some misclassification of new versus persistent infections may have occurred, although this would be unlikely to differentially affect trends across study periods. Further, services participating in ACCESS have extensive experience in delivering STI care in accordance with national treatment guidelines, making it unlikely that diagnosed infections were left untreated.

National dissemination of doxyPEP evidence and clinical guidance in Australia was associated with significant population-level reductions in syphilis and chlamydia diagnoses among GBM over more than 2 years following release but not in gonorrhoea diagnoses. These data support doxyPEP as an effective population-level STI prevention strategy when integrated with comprehensive sexual health services. Together, these findings highlight doxyPEP as a promising complement to existing test-and-treat strategies and suggest that biomedical STI prevention interventions may play an important role in addressing rising STI trends in high-income settings. The lack of a corresponding decline in gonorrhoea highlights the importance of pairing doxyPEP implementation with enhanced gonorrhoea-specific prevention and control efforts.

Methods

This study complied with all relevant ethical regulations. ACCESS was approved by the Alfred Hospital Human Research Ethics Committee (248/17), Central Australian Human Research Ethics Committee (CA-19-3355), Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (08/47), and Aboriginal Health and Medical Research Council Human Research Ethics Committee (1099/15). It was also reviewed by community research panels specializing in LGBTQ+ research, the ACON Research Ethics Review Committee (2015/14) and Community Research Endorsement Panel of Thorne Harbour Health (VAC REP 15/003). As ACCESS analyses de-identified data collected for public health surveillance, the requirement for individual participant consent was waived. Individuals could opt out of having their data included in ACCESS. Participants were not recruited or directly contacted for this study and received no compensation.

Data source and study population

Data were extracted from a network of sexual health services and general practice clinics participating in ACCESS (www.accessproject.org.au). ACCESS is a sentinel surveillance network that monitors Australia's progress in controlling STIs and blood-borne viruses. The ACCESS protocol has been previously published[25]. The ACCESS network aims to include health services that are representative of the prevention and management of blood-borne viruses and STIs in Australia. For bacterial STIs, this includes sexual health services and high-caseload general practice clinics, defined as clinics that see at least 50 individuals per year from one or more of Australia's priority populations for STIs, or services specifically established to provide STI care and management, such as clinics offering rapid STI testing or general practices specializing in sexual health. While national estimates of STI notifications among GBM are not available, ACCESS is estimated to capture approximately 29% of syphilis notifications, 22% of chlamydia notifications and 31% of gonorrhoea notifications among men nationally during the study period. Previous analyses have also estimated that ACCESS captures more than 70% of GBM receiving publicly subsidized HIV PrEP in Australia[26].

For this analysis, high-caseload general practice clinics and sexual health services participating in ACCESS were included if their most recent data extraction extended to 31 December 2025. Of the 48 eligible general practice and sexual health services, 2 were excluded because they commenced during the study period and a further 17 were excluded because their most recent data extraction occurred before 31 December 2025, leaving 29 services for analysis. Routinely collected patient data including demographics (age, gender, HIV status and sexual orientation), pathology reports (test results for chlamydia, gonorrhoea and syphilis) and electronic prescriptions (for HIV PrEP, HIV antiretroviral treatment and doxycycline) were de-identified and extracted from electronic health records from participating services using specialized data extraction software called GHRANITE. Using GHRANITE, individuals' data were linked within and across participating services using a linkage algorithm, which utilizes probabilistic and de-identifying linkage keys generated from patient identifiers (for example, first and last name, date of birth, phone number and Medicare number) before data were extracted[27].

We included GBM aged 16 years and older who attended a participating service during the observation period. The study was restricted to GBM because this is the population for whom doxyPEP has been primarily recommended, prescribed and studied in Australia during the observation period. Gay or bisexual status among men was determined from routinely collected demographic and behavioural information, including self-reported sexual orientation and gender of sexual partners or, where sexual orientation data were unavailable, inferred from a previously validated algorithm based on history of a rectal swab for chlamydia or gonorrhoea as an indicator of male-to-male sex[28]. Sex recorded at birth and transgender status were not consistently available across all participating services. The study population therefore includes both cisgender and transgender men classified as gay or bisexual using the criteria described above; however, analyses could not be disaggregated by cisgender/transgender status because these data were incomplete.

New diagnoses of chlamydia and gonorrhoea were defined as positive nucleic acid amplifications tests or, for gonorrhoea, a positive culture result. Repeat positive tests for the same infection at the same anatomical site within 14 days of a previous positive result were excluded to minimize duplicate counting of the same infectious episode. Positive results from different anatomical sites were treated as separate site-specific infections; however, concurrent positive results for the same infection across multiple anatomical sites within a single testing episode were counted as one diagnosis in the primary analysis. New cases of syphilis were identified using a pathology-based algorithm aligned with the national case definition of laboratory-confirmed infectious syphilis[29]. See Supplementary Methods 1 for further information on syphilis algorithm.

Study design and periods

We conducted a retrospective interrupted time-series analysis of STI diagnoses among GBM attending ACCESS services. Three periods were defined to reflect the emergence and dissemination of doxyPEP evidence and subsequent national clinical guidance.

The preguidance period was defined as January 2022 to March 2023. January 2022 was selected as the start of the observation period because many Australian jurisdictions experienced prolonged coronavirus disease 2019-related lockdowns and service disruptions during 2020–2021, with final lockdowns being lifted in October 2021[30].

An evidence dissemination period was included as a 6-month lead-in phase preceding the release of formal national guidance, defined as April 2023 to September 2023. This period began with the publication of an Australian interim position statement on doxyPEP on 17 March 2023[31], followed by the release of the US DoxyPEP Trial results on 5 April 2023[3]. From April to September 2023, clinical trial evidence was actively disseminated through national clinician resources[32], online media[33] and community-led health promotion in Australia and internationally[34]. This period concluded with the publication of the Australian DoxyPEP Consensus Statement on 20 September 2023.

The postguidance period was defined as October 2023 to December 2025, during which nationally endorsed guidance on doxyPEP prescribing and use was widely available. In Australia, doxycycline can be prescribed off label for doxyPEP, which means that clinicians were able to prescribe it before the publication of the national guidelines. The evidence dissemination period was included because doxyPEP awareness and use probably began following dissemination of trial evidence and interim guidance, before the publication of formal national guidance. The postguidance period therefore reflects the availability of nationally endorsed prescribing recommendations rather than the onset of doxyPEP use.

Outcomes

The primary outcomes were the monthly number of diagnoses of chlamydia, gonorrhoea and infectious syphilis among GBM attending ACCESS sexual health services and general practice clinics over the study period. For chlamydia and gonorrhoea, individuals with concurrent positive results for the same infection at multiple anatomical sites within a single testing episode were counted as a single diagnosis. Secondary outcomes were monthly test positivity for syphilis, chlamydia and gonorrhoea, defined as the proportion of test events in a calendar month that were positive, to assess whether changes in testing may have influenced observed trends.

Primary, secondary and exploratory analyses

The primary analysis consisted of interrupted time-series analyses of monthly diagnoses of infectious syphilis, chlamydia and gonorrhoea. As a secondary analysis, we estimated the cumulative number of STI diagnoses averted following the release of doxyPEP guidance by comparing model-predicted counts under observed postguidance trends with counterfactual projections assuming continuation of preguidance trends. Additional secondary analyses included interrupted time-series analyses of monthly test positivity, subgroup analyses among populations prioritized in doxyPEP guidance (including GBM with a recent STI, using HIV PrEP and living with HIV) and, for chlamydia and gonorrhoea, analyses stratified by anatomical site of infection (anorectal, oropharyngeal and urethral). Positivity analyses were included as a supplementary assessment to explore whether changes in testing volume might plausibly explain observed trends in diagnoses and were not intended to estimate the effect of doxyPEP implementation. Exploratory analyses examined temporal trends in doxycycline prescribing using prescription instruction data from a subset of clinics to assess whether observed prescribing patterns were consistent with uptake of doxyPEP over the study period.

Statistical analysis

For the primary analysis, we used segmented linear regression models estimated using Prais–Winsten regression to account for first-order autocorrelation in residuals[35]. Two interruption points were specified: April 2023, corresponding to the publication of the US DoxyPEP Trial and the start of the evidence dissemination period, and October 2023, corresponding to the release of the ASHM DoxyPEP Consensus Statement and the start of the post-doxyPEP guidance period.

Models were fitted to log-transformed monthly case counts so that regression coefficients could be exponentiated and interpreted as relative (percentage) changes in STI diagnoses per 1-month increase in time, rather than absolute change in case counts per month, to facilitate comparability across STIs with different baseline incidence (that is, a higher incidence of chlamydia and gonorrhoea compared with syphilis). For visualization, fitted values from these log-transformed models were back-transformed and presented on the original count scale, together with the observed monthly case counts, to facilitate interpretation of absolute changes in diagnoses over time. The model estimated the effect of each interruption on both the level and slope of the monthly case trend, using the following specification:

$$\ln(Y_t) = \beta_0 + \beta_1 T + \beta_2 X_1 + \beta_3 (T - T_1) X_1 + \beta_4 X_2 + \beta_5 (T - T_2) X_2 + \varepsilon_t,$$

where Y_t represents the observed number of monthly STI diagnoses, T is a continuous time variable indicating number of months passed since the start of the study period, X_1 is an indicator variable for the first interruption (0 before first interruption and 1 after), X_2 is an indicator variable for the second interruption (0 before second interruption and 1 after), and T_1 and T_2 are the time of the first and second interruption, respectively.

For each outcome (syphilis, chlamydia and gonorrhoea), the segmented regression models estimated six coefficients: β_0, the predicted logarithm of monthly diagnoses at time zero (intercept); β_1, the slope of the logarithm of monthly diagnoses during the pre-doxyPEP period; β_2, the immediate step change in the logarithm of monthly diagnoses at the first interruption (publication of the US DoxyPEP Trial and release of interim position statement); β_3, the change in slope of the logarithm of monthly diagnoses following the first interruption; β_4, the immediate step change in the logarithm of monthly diagnoses at the second interruption (release of the ASHM doxyPEP Consensus Statement); and β_5, the change in slope of the logarithm of monthly diagnoses following the second interruption. ε_t is the error term, with first-order autocorrelation permitted in the error structure.

Trends in monthly STI diagnoses (slopes) during the evidence-dissemination and postguidance periods were derived analytically from the model coefficients by summing the baseline time coefficient with the estimated changes in trend at each interruption. As outcomes were log transformed, slopes were expressed as relative changes in the number of diagnoses per month by exponentiating coefficients (and corresponding linear combinations), with percentage changes calculated as $(e^{\beta} - 1) \times 100$. The overall difference in slope between the preguidance and postguidance periods was reported as an absolute difference in monthly percentage change (percentage points), derived from exponentiated slopes.

Sensitivity analyses examined alternative model specifications, including comparison of one- and two-interruption models using the Akaike information criterion and Bayesian information criterion, and assessment of seasonality through inclusion of sine and cosine terms representing a 12-month cycle.

In secondary analyses estimating STIs averted after doxyPEP guidance, we estimated the cumulative number of diagnoses averted during the postguidance period (October 2023 to December 2025) due to doxyPEP guidance. In this secondary analysis, we ran models fitted to the untransformed case counts (number of diagnoses per month; Supplementary Table 4) to generate predicted values under both the observed postguidance conditions and a counterfactual 'no guidance' scenario in which all postinterruption terms were set to zero, effectively projecting the pre-doxyPEP period trend forwards through the study period. We calculated RRs defined as the ratio of cumulative predicted diagnoses during the postguidance period under the observed and counterfactual scenarios. CIs for RRs were derived analytically using the variance–covariance matrix of the fitted linear model coefficients.

Subgroup analyses were conducted among (1) GBM with a recent prior STI, defined as individuals with a diagnosis of syphilis, chlamydia or gonorrhoea in the 12 months preceding the outcome of interest; (2) GBM using HIV PrEP, defined as having an electronic prescription for PrEP in the 12 months before diagnosis; and (3) GBM using HIV PrEP or living with HIV. A separate analysis restricted to people living with HIV was not undertaken because the substantially smaller number of syphilis diagnoses in this subgroup was expected to provide limited statistical power and imprecise estimates. For each subgroup, cumulative diagnoses averted during the postguidance period were estimated using the same observed-versus-counterfactual approach.

Regression analyses were conducted in Stata (version 15.1; StataCorp) and plots were generated in R (version 4.5.0). Interrupted time-series models were fitted using the user-written 'itsa' command (version 2.0.7; Ariel Linden) in Stata with the 'prais' option[36]. Linear combinations of estimated parameters and corresponding exponentiated estimates were obtained using the 'lincom' command. Figure 1 and Supplementary Figs. 8–11 were generated in R using the 'tidyverse', 'haven', 'lubridate', 'scales' and 'patchwork' packages. Analysis and figure-generation code, including software requirements, is publicly available in the Zenodo repository[37].

Exploratory analysis of doxycycline prescriptions

Exploratory analyses examined temporal trends in doxycycline prescriptions with instructions indicative of doxyPEP use to assess whether changes in recorded prescribing patterns were broadly contemporaneous with dissemination of doxyPEP evidence and subsequent national guidance. This analysis was restricted to 16 clinics that used patient management systems containing prescription instruction fields that could be systematically extracted and analysed. These instruction fields were required to identify prescriptions with instructions indicative of doxyPEP use and were not available in a format suitable for analysis across all participating clinics. The monthly numbers of prescriptions indicative of doxyPEP use were examined over time. As prescription instructions may not have been recorded consistently across all clinicians and services, these analyses were considered exploratory and intended to provide contextual information regarding prescribing patterns rather than a definitive measure of doxyPEP uptake.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

The aggregate monthly analytical dataset used to reproduce the interrupted time-series analyses and Fig. 1 and Supplementary Figs. 8–11 is publicly available via Zenodo at https://doi.org/10.5281/zenodo.22978063 (ref. 37). The underlying individual-level ACCESS data cannot be made publicly available because they contain sensitive health information routinely collected from patients attending participating clinical services. Access to de-identified individual-level data may be requested by researchers for bona fide research purposes by contacting the ACCESS study team at the Burnet Institute (jason.asselin@burnet.edu.au). Access is subject to approval by the Alfred Hospital Human Research Ethics Committee and the Burnet Institute (Melbourne, Australia), and execution of appropriate data access and confidentiality agreements. Requests will be assessed against these requirements and responded to within 60 days.

Code availability

Code used to conduct the statistical analyses and generate Fig. 1 and Supplementary Figs. 8–11 from the publicly available aggregate analytical dataset is publicly available via Zenodo at https://doi.org/10.5281/zenodo.22978063 (ref. 37). Code used to extract and prepare aggregate data from the underlying individual-level ACCESS database is not publicly available because it operates on restricted individual-level health data and ACCESS-specific data infrastructure.

References

1. Kenyon, C., Herrmann, B., Hughes, G. & de Vries, H. J. C. Management of asymptomatic sexually transmitted infections in Europe: towards a differentiated, evidence-based approach. *Lancet Reg. Health Eur.* **34**, 100743 https://doi.org/10.1016/j.lanepe.2023.100743 (2023).
2. King, J., Kwon, J., Gray, R., McManus, H. & McGregor, S. *HIV, Viral Hepatitis and Sexually Transmissible Infections in Australia: Annual Surveillance Report 2025* (The Kirby Institute, UNSW Sydney, 2025).
3. Luetkemeyer, A. F. et al. Postexposure doxycycline to prevent bacterial sexually transmitted infections. *N. Engl. J. Med.* **388**, 1296–1306 https://doi.org/10.1056/NEJMoa2211934 (2023).
4. Molina, J. M. et al. Doxycycline prophylaxis and meningococcal group B vaccine to prevent bacterial sexually transmitted infections in France (ANRS 174 DOXYVAC): a multicentre, open-label, randomised trial with a 2 × 2 factorial design. *Lancet Infect. Dis.* **24**, 1093–1104 https://doi.org/10.1016/S1473-3099(24)00236-6 (2024).
5. Molina, J. M. et al. 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. *Lancet Infect. Dis.* **18**, 308–317 https://doi.org/10.1016/S1473-3099(17)30725-9 (2018).
6. Mayer, K. H., Traeger, M. & Marcus, J. L. Doxycycline postexposure prophylaxis and sexually transmitted infections. *J. Am. Med. Assoc.* **330**, 1381–1382 https://doi.org/10.1001/jama.2023.16416 (2023).
7. Traeger, M. W. et al. Doxycycline postexposure prophylaxis and bacterial sexually transmitted infections among individuals using HIV preexposure prophylaxis. *JAMA Intern. Med.* **185**, 273–281 https://doi.org/10.1001/jamainternmed.2024.7186 (2025).
8. Sankaran, M. et al. Doxycycline postexposure prophylaxis and sexually transmitted infection trends. *JAMA Intern. Med.* **185**, 266–272 https://doi.org/10.1001/jamainternmed.2024.7178 (2025).
9. Menza, T. W. et al. The population-level impact of doxycycline post-exposure prophylaxis on syphilis in King County, WA: an interrupted time series analysis. *Clin. Infect. Dis.* **83**, 267–273 https://doi.org/10.1093/cid/ciag209 (2026).
10. Cornelisse, V. J., Riley, B. & Medland, N. A. Australian consensus statement on doxycycline post-exposure prophylaxis (doxy-PEP) for the prevention of syphilis, chlamydia and gonorrhoea among gay, bisexual and other men who have sex with men. *Med. J. Aust.* **220**, 381–386 https://doi.org/10.5694/mja2.52258 (2024).
11. Chow, E. P. F. & Fairley, C. K. Use of doxycycline prophylaxis among gay and bisexual men in Melbourne. *Lancet HIV* **6**, e568–e569 https://doi.org/10.1016/S2352-3018(19)30186-9 (2019).
12. Latt, P. M. et al. Awareness, usage and perceptions of doxycycline post-exposure prophylaxis (doxyPEP) for prevention of sexually transmitted infections in Australia: insights from a national cross-sectional survey. *Med. J. Aust.* **224**, e70180 https://doi.org/10.5694/mja2.70180 (2026).
13. Broady, T. et al. *GBQ+ Community Periodic Survey: Melbourne 2025* (Centre for Social Research in Health, 2025).
14. Lai, H. et al. Impact and cost-effectiveness of doxycycline post-exposure prophylaxis in Australian men who have sex with men. *Nat. Commun.* **17**, 1846 https://doi.org/10.1038/s41467-026-68561-7 (2026).
15. Traeger, M. W. et al. Potential impact of doxycycline post-exposure prophylaxis prescribing strategies on incidence of bacterial sexually transmitted infections. *Clin. Infect. Dis.* **82**, 304–311 https://doi.org/10.1093/cid/ciad488 (2023).
16. The ASHM Australian STI management guidelines. *ASHM Health* https://sti.guidelines.org.au (accessed 1 February 2026).
17. Lahra, M. M., van Hal, S. & Hogan, T. R. Australian Gonococcal Surveillance Programme Annual Report, 2022. *Commun. Dis. Intell.* **47** https://doi.org/10.33321/cdi.2023.47.45 (2023).
18. Do, K., Unemo, M., Kenyon, C., Hocking, J. S. & Kong, F. Y. S. Tetracycline-resistant *Neisseria gonorrhoeae* global estimates—impacts on doxycycline post-exposure prophylaxis implementation and monitoring: a systematic review. *JAC Antimicrob. Resist.* **7**, dlaf120 https://doi.org/10.1093/jacamr/dlaf120 (2025).
19. Williams, E., Williamson, D. A. & Hocking, J. S. Frequent screening for asymptomatic chlamydia and gonorrhoea infections in men who have sex with men: time to re-evaluate? *Lancet Infect. Dis.* **23**, e558–e566 https://doi.org/10.1016/S1473-3099(23)00356-0 (2023).
20. Gottlieb, S. L., Rees, H. & Peters, R. P. H. Vaccines to prevent bacterial sexually transmitted infections: promise, progress, and public health potential. *PLoS Med.* **22**, e1004849 https://doi.org/10.1371/journal.pmed.1004849 (2025).
21. Kenyon, C. We need to consider collateral damage to resistomes when we decide how frequently to screen for chlamydia/gonorrhoea in preexposure prophylaxis cohorts. *AIDS* **33**, 155–157 https://doi.org/10.1097/QAD.0000000000002020 (2019).
22. Ludwick, T. et al. Are clinicians open to less asymptomatic STI screening for chlamydia and gonorrhea in gay, bisexual, and other men who have sex with men and the possibility of not treating positive diagnoses? A qualitative study from Australia. *AIDS Patient Care STDS* **40**, 31–37 https://doi.org/10.1177/10872914251399618 (2026).
23. Fredericksen, R. J. et al. Doxycycline as postsexual exposure prophylaxis: use, acceptability, and associated sexual health behaviors among a multi-site sample of clinical trial participants. *AIDS Patient Care STDS* **38**, 155–167 https://doi.org/10.1089/apc.2023.0289 (2024).
24. Traeger, M. W., Krakower, D. S., Mayer, K. H., Jenness, S. M. & Marcus, J. L. Use of doxycycline and other antibiotics as bacterial sexually transmitted infection prophylaxis in a US sample of primarily gay and bisexual men. *Sex. Transm. Dis.* **51**, 763–771 https://doi.org/10.1097/OLQ.0000000000002061 (2024).
25. Callander, D. et al. Monitoring the control of sexually transmissible infections and blood-borne viruses: protocol for the Australian collaboration for coordinated enhanced sentinel surveillance (ACCESS). *JMIR Res. Protoc.* **7**, e11028 https://doi.org/10.2196/11028 (2018).
26. Traeger, M. W. et al. Real-world trends in incidence of bacterial sexually transmissible infections among gay and bisexual men using HIV pre-exposure prophylaxis (PrEP) in Australia following nationwide PrEP implementation: an analysis of sentinel surveillance data. *Lancet Infect. Dis.* **22**, 1231–1241 https://doi.org/10.1016/S1473-3099(22)00175-X (2022).
27. Nguyen, L. et al. Privacy-preserving record linkage of deidentified records within a public health surveillance system: evaluation study. *J. Med. Internet Res.* **22**, e16757 https://doi.org/10.2196/16757 (2020).
28. Ampt, F. H. et al. Anorectal swabs as a marker of male-to-male sexual exposure in STI surveillance systems. *Epidemiol. Infect.* **145**, 2530–2535 https://doi.org/10.1017/s095026881700098x (2017).

29. Traeger, M. W. et al. Syphilis testing, incidence, and reinfection among gay and bisexual men in Australia over a decade spanning HIV PrEP implementation: an analysis of surveillance data from 2012 to 2022. *Lancet Reg. Health West. Pac.* **51**, 101175 https://doi.org/10.1016/j.lanwpc.2024.101175 (2024).
30. Phillips, T. R. et al. Sexual health service adaptations to the coronavirus disease 2019 (COVID-19) pandemic in Australia: a nationwide online survey. *Aust. N. Z. J. Public Health* **45**, 622–627 https://doi.org/10.1111/1753-6405.13158 (2021).
31. Cornelisse, V. J. et al. Interim position statement on doxycycline post-exposure prophylaxis (doxy-PEP) for the prevention of bacterial sexually transmissible infections in Australia and Aotearoa New Zealand - The Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM). *Sex Health* **20**, 99–104 https://doi.org/10.1071/sh23011 (2023).
32. Simpkins, S. Is doxycycline PEP the new morning after pill for STIs? *AusDoc* https://www.ausdoc.com.au/news/is-doxycycline-pep-the-new-morning-after-pill-for-stis/ (2023).
33. Howard, J. STIs are on the rise in the US. A pill taken after sex could help slow them down. *CNN* https://edition.cnn.com/2023/08/11/health/doxypep-sti-prevention-pill (2023).
34. Hudson, D. What is doxyPEP and should more queer men use it to protect their health? *Queerty* https://www.queerty.com/doxypep-queer-men-use-protect-health-20230223/ (2023).
35. Bernal, J. L., Cummins, S. & Gasparrini, A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. *Int. J. Epidemiol.* **46**, 348–355 https://doi.org/10.1093/ije/dyw098 (2017).
36. Linden, A. Conducting interrupted time-series analysis for single- and multiple-group comparisons. *Stata J.* **15**, 480–500 https://doi.org/10.1177/1536867x1501500208 (2015).
37. Traeger, M. et al. Population-level impact of doxycycline post-exposure prophylaxis on bacterial sexually transmitted infections: data and analysis code. *Zenodo* https://doi.org/10.5281/zenodo.22978063 (2026).

Acknowledgements

We acknowledge the contribution of the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS) and thank members of the ACCESS Research Team and Steering Committee who are not co-authors of this article. A full list of acknowledged ACCESS team members is provided in Supplementary Information. We also acknowledge all clinics participating in ACCESS. ACCESS is a partnership between the Burnet Institute, Kirby Institute and NRL Quality.

Author contributions

M.W.T., R.G. and M.A.S. conceived of and designed the study. J.A., H.L.A. and A.C. comanage the ACCESS project and curated the data. M.W.T. led the formal statistical analysis with input from A.L.W. E.P.F.C., J.J.O., D.V., C.T. and J.M. are ACCESS site investigators and contributed to data acquisition. V.J.C., D.H.-P., J.J.O., T.R. and B.Q. are on the ACCESS advisory committee and contributed to interpretation of the findings. M.W.T. drafted the paper. R.G. and M.A.S. lead the ACCESS project and provided academic supervision as cosenior authors. All authors contributed to data interpretation, critically reviewed the paper for intellectual content and approved the final version for submission.

Funding

The Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS) is supported by core funding from the Australian Department of Health to monitor national progress in the control of blood-borne viruses and sexually transmissible infections. Additional funding for state-level outcomes is provided by the Governments of Victoria and Western Australia. Funding for specific components of ACCESS is provided by the Blood Borne Viruses and Sexually Transmitted Infections Research, Intervention and Strategic Evaluation (BRISE) Program; a National Health and Medical Research Council (NHMRC) project grant (APP1082336); an NHMRC partnership grant (GNT1092852); and the Prevention Research Support Program funded by the New South Wales Ministry of Health. M.W.T. is supported by an NHMRC Investigator Grant (GNT2027235). E.P.F.C. is supported by an NHMRC Investigator Grant (GNT2033299). A.C. is supported by an Investigator Grant (GNT2034148).

Competing interests

M.W.T. has received consulting fees from Gilead Sciences Ltd. E.P.F.C. has received speakers' honoraria from Gilead Sciences, MSD and CSL Seqirus. R.G. has received research support funding from Cepheid and SpeeDx. M.A.S. has received investigator-initiated grants from AbbVie and Gilead and consultancy from Gilead. V.J.C. has received consulting fees from ViiV Healthcare and speakers' honoraria from Gilead Sciences. J.J.O. has received research support from Gilead Sciences Ltd, Roche and Viiv Health. The other authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s44360-026-00211-0.

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Peer review information *Nature Health* thanks Christian Bottomley, Angelo Raccagni and the other, anonymous, reviewer(s) for their contribution to the peer review of this work. Peer reviewer reports are available. Primary Handling Editor: Lorenzo Righetto, in collaboration with the *Nature Health* team.

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Last updated by author(s): Sep 27, 2026

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☐	☒ A description of all covariates tested
☐	☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒ A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☐	☒ For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☒	☐ Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated

Our web collection on statistics for biologists contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection	Data were extracted from electronic health records using GHRANITE (University of Melbourne), a privacy-preserving data extraction and linkage software used within the ACCESS surveillance network.
Data analysis	Interrupted time-series models were fitted using the user-written itsa command (version 2.0.7; Ariel Linden) in Stata with the prais option. Linear combinations of estimated parameters and corresponding exponentiated estimates were obtained using the lincom command. Figures were generated in R using the tidyverse, haven, lubridate, scales and patchwork packages. Analysis and figure-generation code, including software requirements, is publicly available in the Zenodo repository (https://doi.org/10.5281/zenodo.22978063). No custom or proprietary algorithms were developed for this study.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The aggregate monthly analytical dataset used to reproduce the interrupted time-series analyses and figures in this study is publicly available in the Zenodo repository at https://doi.org/10.5281/zenodo.22978063. The underlying individual-level ACCESS data cannot be made publicly available because they contain sensitive health information routinely collected from patients attending participating clinical services. Access to de-identified individual-level data may be requested by researchers for bona fide research purposes by contacting the ACCESS study team at the Burnet Institute (jason.asselin@burnet.edu.au). Access is subject to approval by the Alfred Hospital Human Research Ethics Committee and the Burnet Institute (Melbourne, Australia), and execution of appropriate data access and confidentiality agreements. Requests will be assessed against these requirements and responded to within 60 days.

Research involving human participants, their data, or biological material

Policy information about studies with human participants or human data. See also policy information about sex, gender (identity/presentation), and sexual orientation and race, ethnicity and racism.

Reporting on sex and gender	The study population was restricted to gay and bisexual men aged ≥16 years and included both cisgender and transgender men. Gay or bisexual status among males was determined from routinely collected demographic and behavioural information, including self-reported sexual orientation and gender of sexual partners or, where sexual orientation data were unavailable, inferred using a previously validated algorithm based on a history of rectal testing for chlamydia or gonorrhoea as an indicator of male-to-male sex. Sex recorded at birth and transgender status were not consistently available across participating services. Analyses were therefore not disaggregated by cisgender/transgender status because these data were incomplete.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, and other socially constructed groupings were not included in the analysis. These variables are not routinely or consistently collected across all participating services within the ACCESS surveillance network and were therefore not available for reliable inclusion.
Population characteristics	The study population comprised gay and bisexual men aged ≥16 years attending participating sexual health and general practice services. Demographic and clinical characteristics available for analysis included age, HIV status, HIV pre-exposure prophylaxis (PrEP) use, and prior sexually transmitted infection history, as recorded in routinely collected electronic health records.
Recruitment	No participants were actively recruited. This study used de-identified electronic health record data collected as part of routine clinical care within the ACCESS sentinel surveillance network. The study population reflects individuals attending participating services for STI testing and care and may over-represent those more engaged with healthcare. The ACCESS network is designed to capture a large and geographically diverse sample of the target population. Individual informed consent was not required because the study analysed de-identified data collected under public health surveillance; individuals could opt out of inclusion in ACCESS. No compensation was provided because participants were not recruited or directly contacted for this study.
Ethics oversight	This study complied with all relevant ethical regulations. ACCESS was approved by the Alfred Hospital Human Research Ethics Committee (248/17), Central Australian Human Research Ethics Committee (CA-19-3355), Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research (08/47), and Aboriginal Health and Medical Research Council Human Research Ethics Committee (1099/15). It was also reviewed by community research panels specialising in LGBTQ+ research, the ACON Research Ethics Review Committee (2015/14) and Community Research Endorsement Panel of Thorne Harbour Health (VAC REP 15/003). As ACCESS analyses de-identified data collected for public health surveillance, the requirement for individual participant consent was waived. Individuals could opt out of having their data included in ACCESS. Participants were not recruited or directly contacted for this study and received no compensation.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☐ Life sciences ☒ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/documents/nr-reporting-summary-flat.pdf

Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description	This study is a quantitative, observational epidemiological analysis using a retrospective interrupted time-series design. Routinely collected longitudinal surveillance data were analysed to evaluate changes in monthly diagnoses of bacterial sexually transmitted infections before and after dissemination of doxycycline post-exposure prophylaxis (doxyPEP) evidence and national clinical guidance in Australia.
Research sample	The analytical dataset comprised 78,560 gay and bisexual men (GBM) aged ≥16 years who received STI testing at 29 sexual health services and general practice clinics participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS) between January 2022 and December 2025. The analytical extract provided for this study was restricted to GBM aged ≥16 years. The study population included cisgender and transgender men who identified as gay or bisexual. Gender was obtained from routinely collected electronic medical records, where it is recorded during clinical care. Demographic and clinical characteristics, including age, HIV status and PrEP use, were derived from routinely collected electronic health records. ACCESS aims to include services representative of STI and blood-borne virus prevention and management in Australia, including sexual health services and high-caseload general practices. However, the analytical sample should not be considered representative of all GBM in Australia because it comprises individuals accessing STI testing at participating services and may over-represent people more engaged with testing and clinical care.
Sampling strategy	The analytical dataset provided for this study was restricted to GBM aged ≥16 years. This population was selected because doxyPEP evidence and Australian clinical guidance during the study period primarily concerned STI prevention among GBM. ACCESS aims to include services representative of the prevention and management of blood-borne viruses and STIs in Australia, including sexual health services and high-caseload general practices. For this analysis, services were required to have complete data throughout the study period to support longitudinal interrupted time-series analyses. All eligible individuals within the included services were analysed; no further participant sampling was undertaken and no formal sample-size calculation was performed.
Data collection	Data were derived from routinely collected electronic health records at participating ACCESS services and extracted using GRHANITE software, which performs privacy-preserving extraction and linkage of de-identified data. The analytical extract provided for this study was restricted to GBM aged ≥16 years and included demographic characteristics, laboratory test results for chlamydia, gonorrhoea and syphilis, and prescription records. No direct participant interaction occurred and researchers were not involved in primary data collection. As this was a secondary analysis of routinely collected, de-identified surveillance data, blinding to study hypotheses during data collection was not applicable.
Timing	Data were collected continuously from 1 January 2022 to 31 December 2025. Three periods were prespecified for the interrupted time-series analysis: pre-guidance (January 2022–March 2023), evidence dissemination (April 2023–September 2023), and post-guidance (October 2023–December 2025). There were no gaps in data collection across the study period among included services.
Data exclusions	Service-level eligibility criteria were prespecified. Of 48 eligible ACCESS services, 2 were excluded because they commenced during the study period and 17 were excluded because their most recent data extraction occurred before 31 December 2025, leaving 29 services for analysis. The analytical dataset provided for this study was already restricted to GBM aged ≥16 years; therefore, no additional exclusions based on age or population eligibility were made by the study investigators. For chlamydia and gonorrhoea, tests conducted within 14 days of a previous positive result were excluded to avoid duplicate counting of the same infection episode. No other exclusions were applied.
Non-participation	Individual informed consent was waived because the study used de-identified data collected through public health surveillance. Individuals attending participating services could opt out of having their data included in ACCESS. There was no active recruitment or study-specific participation and therefore no study-specific non-participation or dropout. All individuals meeting the prespecified eligibility criteria were included in the analytical dataset.
Randomization	This was an observational study using routinely collected surveillance data; participants were not allocated to experimental groups and no randomization was performed. Outcomes were evaluated over time using an interrupted time-series design with prespecified interruption points. Segmented regression accounted for underlying temporal trends and estimated changes in level and trend associated with each interruption.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJE guidelines for publication of clinical research and a completed CONSORT checklist must be included with all submissions.

Clinical trial registration	This study is an observational analysis of routinely collected surveillance data and was not a clinical trial. Trial registration was therefore not required.
Study protocol	No formal trial protocol was registered, as this was a retrospective observational study. The study design, inclusion criteria, outcomes, and statistical analysis plan were prespecified and are described in the Methods section of the manuscript.
Data collection	Data were collected from 29 sexual health services and general practice clinics participating in the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance (ACCESS) network. Routinely collected electronic health record data, including demographic characteristics, laboratory test results, and prescription records, were extracted using GHRANITE software, which performs de-identified, privacy-preserving data linkage across sites. The study period spanned 1 January 2022 to 31 December 2025, with continuous data collection across all sites.
Outcomes	The primary outcomes were monthly counts of diagnoses of infectious syphilis, chlamydia, and gonorrhoea among gay and bisexual men attending participating services. Diagnoses were defined using laboratory-confirmed test results (nucleic acid amplification tests or culture for gonorrhoea, and a pathology-based algorithm for infectious syphilis aligned with national case definitions). Secondary outcomes included monthly test positivity for each infection, defined as the proportion of test events in a calendar month that were positive. Outcomes were prespecified and assessed using routinely collected pathology data.

Plants

Seed stocks	*Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.*
Novel plant genotypes	*Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.*
Authentication	*Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosiacism, off-target gene editing) were examined.*