

Real-world doxycycline post-exposure prophylaxis and bacterial STI incidence among MSM using HIV PrEP in Singapore

Ren Jie Tsai¹ MRCP (UK), Xiahong Zhao¹ PhD (Public Health), Linus Cheng¹ BSc (Information Systems), Benson Koon Wee Yeo¹ FAMS (Dermatology)

Dear Editor,

Doxycycline post-exposure prophylaxis (DoxyPEP) is an emerging strategy for preventing bacterial sexually transmitted infections (STIs). Randomised controlled trials have shown reductions of more than 70% in chlamydia and syphilis among men who have sex with men (MSM) and transgender women, with weaker and more variable effects on gonorrhoea.¹⁻³ These results have informed recent international guidance recommending targeted DoxyPEP for MSM and transgender women at increased STI risk.^{4,5} Real-world cohorts from Spain and the US have reported broadly similar findings, generally using within-person before-and-after comparisons.⁶⁻⁸ However, comparable data from Asia are lacking.

At the Department of STI Control, National Skin Centre, Singapore, DoxyPEP has been offered since mid-2025 to MSM at higher STI risk, including those on human immunodeficiency virus (HIV) pre-exposure prophylaxis (PrEP) with reduced condom use. As DoxyPEP had only recently been introduced, awareness and uptake were still developing among clinicians and patients, and it was not routinely prescribed to all PrEP users. The prescribed regimen was a single 200 mg dose of doxycycline taken as soon as possible, and within 72 hours, of sexual exposure. The authors conducted a retrospective cohort study using electronic medical records from 27 July 2024 to 31 December 2025, including MSM aged 21 years or older who were receiving HIV PrEP and subsequently initiated DoxyPEP.

Among HIV PrEP users who initiated DoxyPEP, person-time was divided into pre- and post-DoxyPEP periods. Incident chlamydia, gonorrhoea, and syphilis, including recurrent episodes, were identified from laboratory records. Incidence rates were calculated as events per 100 person-years to account for differences in follow-up duration. Incidence before and after DoxyPEP initiation was compared using Andersen–Gill recurrent-event Cox models, with DoxyPEP exposure modelled as a time-varying covariate and

robust standard errors used to account for recurrent events within individuals. Age at first visit, ethnicity, marital status, and residential status were included as covariates. Variables causing model singularity were excluded from the final Cox model. Adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were reported.

Of 735 MSM receiving HIV PrEP, 117 initiated DoxyPEP during follow-up and were included. The median age was 31 years (interquartile range 27–37). Most participants were Chinese (93/117, 79.5%), followed by Malay (11/117, 9.4%), Indian (2/117, 1.7%), and other ethnicities (11/117, 9.4%). Total pre- and post-DoxyPEP person-time was 21.259 and 14.793 person-years, respectively. Chlamydia and gonorrhoea testing frequencies were 1321.8 and 621.9 screening episodes per 100 person-years before and after DoxyPEP initiation, respectively; corresponding syphilis testing frequencies were 258.7 and 142.0 tests per 100 person-years.

In the within-person analysis, chlamydia incidence was significantly lower after DoxyPEP initiation, decreasing from 51.7 to 6.8 per 100 person-years (adjusted HR 0.059, 95% CI 0.008–0.437; $P=0.006$) (Table 1). Gonorrhoea incidence rates were similar before and after DoxyPEP initiation, at 47.0 and 47.3 per 100 person-years, respectively. No statistically significant association was observed (adjusted HR 0.490, 95% CI 0.157–1.532; $P=0.220$). Syphilis incidence was 4.7 per 100 person-years before DoxyPEP initiation and 20.3 per 100 person-years after initiation, but the number of events was small and the difference was not statistically significant (adjusted HR 3.855, 95% CI 0.407–36.555; $P=0.240$).

The reduction in chlamydia is consistent with trial and real-world evidence.⁶ The large effect size in this study should be viewed in the context of the small number of events and short post-initiation follow-up. Gonorrhoea incidence was not significantly reduced, consistent with variable trial efficacy and the high prevalence of tetracycline resistance among circulating

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¹ Department of STI Control, National Skin Centre, Singapore

Correspondence: Dr Benson Koon Wee Yeo, Department of STI Control, National Skin Centre, 31 Mandalay Road, Singapore 308205.

Email: bensonyeo@nhghealth.com.sg

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Table 1. Bacterial STI incidence before and after DoxyPEP initiation among HIV PrEP users (within-person comparison).

Outcome	Pre-DoxyPEP events (per 100 person-years)	Post-DoxyPEP events (per 100 person-years)	Adjusted HR (95% CI)	P
Chlamydia	51.7	6.8	0.059 (0.008–0.437)	0.006
Gonorrhoea	47.0	47.3	0.490 (0.157–1.532)	0.220
Syphilis	4.7	20.3	3.855 (0.407–36.555)	0.240

CI: confidence interval; DoxyPEP: doxycycline post-exposure prophylaxis; HIV PrEP: human immunodeficiency virus pre-exposure prophylaxis; HR: hazard ratio; STI: sexually transmitted infections

Neisseria gonorrhoeae strains in the Western Pacific region.⁹ In addition to the small number of syphilis events, the numerical increase may partly reflect delayed detection of infections acquired before or around DoxyPEP initiation, given the interval between infection, seroconversion, and diagnosis. The wide confidence interval also indicates substantial uncertainty around this estimate. Several limitations should be noted. As this was a retrospective study using routinely collected clinical data, information on sexual behaviour, condom use, number of partners, and DoxyPEP adherence was unavailable. Incident infections were detected only when patients attended for testing, and differences in testing frequency before and after DoxyPEP initiation could have affected the observed incidence. However, the large reduction in chlamydia incidence, with no comparable reduction in co-tested gonorrhoea, suggests that the finding is unlikely to be explained solely by reduced testing frequency. DoxyPEP was also introduced only in mid-2025, resulting in a relatively short post-initiation follow-up and few incident events. This limited the precision of the chlamydia estimate and the power to detect changes in gonorrhoea and syphilis. Finally, this was a single-centre study, and antimicrobial resistance outcomes were not assessed.

To the authors' knowledge, this is among the first real-world evaluations of DoxyPEP outcomes among MSM in Asia. Among MSM receiving HIV PrEP, DoxyPEP initiation was associated with a significant reduction in chlamydia incidence, supporting a potential role for targeted DoxyPEP in chlamydia prevention among MSM already identified as benefiting from biomedical STI/HIV prevention. No significant reduction was observed for gonorrhoea or syphilis in this early cohort. Larger prospective studies with standardised STI testing intervals, assessment of DoxyPEP adherence, sexual behaviour data, and a contemporaneous PrEP-only comparison group would help validate these findings and provide more precise estimates of effectiveness. Replication across other centres and Asian settings would determine

reproducibility and generalisability and inform targeted DoxyPEP implementation in the region. Integration of gonococcal antimicrobial susceptibility and molecular resistance surveillance will also be important in interpreting the absence of an observed reduction in gonorrhoea. A recent longer-term study¹⁰ reported declining DoxyPEP effectiveness against gonorrhoea in association with the expansion of high-level tetracycline-resistant *N. gonorrhoeae*. Although the present study did not assess whether DoxyPEP use was associated with the emergence or increased prevalence of tetracycline-resistant *N. gonorrhoeae*, antimicrobial resistance remains an important consideration with wider implementation. DoxyPEP may nevertheless retain substantial value for the prevention of other bacterial STIs, particularly chlamydia. Wider implementation should therefore be accompanied by antimicrobial resistance surveillance and periodic reassessment of clinical effectiveness. Future Singapore-based studies could compare tetracycline susceptibility and resistance determinants in *N. gonorrhoeae* isolates from DoxyPEP users and non-users.

Ethics statement

The study was approved by the National Healthcare Group Domain Specific Review Board (2025-2028).

Declaration

The authors declare that they have no affiliations or financial involvement with any commercial organisation with a direct financial interest in the subject or materials discussed in the manuscript.

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