The High Burden of Sexually Transmitted Infections in Persons Initiating Preexposure Prophylaxis—Challenge or Opportunity?

Roger Chou, MD

Preexposure prophylaxis (PrEP) involves the use of daily or on-demand (before and after possible HIV exposure events) antiretroviral therapy to decrease the risk of acquiring HIV infection. The World Health Organization, the US Public Health Service, the US Preventive Services Task Force, and others recommend PrEP in persons at substantial risk for HIV acquisition. Because persons at high risk for sexual HIV acquisition are also at risk for other sexually transmitted infections (STIs), guidelines recommend screening for STIs prior to PrEP initiation and regular monitoring for STIs in patients using PrEP. Understanding the burden of STIs in persons using PrEP could help inform optimal STI screening and monitoring practices and facilitate more efficient allocation of resources. A systematic review and meta-analysis by Ong and colleagues summarizes the global epidemiology of STIs in patients initiating PrEP and during the first 3 months of use. The authors found an STI (chlamydia, gonorrhea, or early syphilis) present in nearly one-quarter of patients at the time of PrEP initiation, and STI incidence during the first 3 months of PrEP use was 72.2 per 100 person-years.

The high burden of STIs in persons initiating PrEP is not surprising. Indeed, a recent STI is a factor used to identify patients eligible for PrEP, and persons at high risk for sexual acquisition of HIV may be more likely to adhere to PrEP and benefit from it. In addition to STI screening and monitoring, PrEP should be administered with counseling on STI risk reduction, including use of condoms. However, patients using PrEP may not adhere to STI risk reduction practices or may engage in behavioral risk compensation (ie, increase HIV sexual risk behaviors owing to the perception of lower risk), highlighting the need for vigilance.

The systematic review and meta-analysis by Ong and colleagues differs from previous reviews that focused on STI rates in persons using PrEP compared with those not using PrEP, which were largely based on data from high-income countries and focused on populations of men who have sex with men (MSM). Ong and colleagues limited their analysis to persons initiating PrEP, provided additional information on STI rates by anatomical site of infection, and included additional data from low- and middle-income settings and non-MSM or mixed (MSM and non-MSM) populations. However, much of the data remained derived from high-income settings and MSM populations. The prevalence of STIs was highest in the rectum but also notable in genital and oropharyngeal sites, with a higher prevalence of gonorrhea in oropharyngeal than genital sites—reinforcing the importance of testing for STIs at different anatomical sites. Because the analysis did not compare patients using PrEP with those not using PrEP, it was not designed to assess whether use of PrEP results in behavioral risk compensation.

Ong and colleagues generally adhered to published methodological standards for conducting systematic reviews, though some issues warrant consideration. Statistical heterogeneity was high in pooled estimates, but this is expected for absolute measures such as STI prevalence and incidence, which are likely to vary in different populations and settings, as opposed to relative effect measures (eg, relative risks or odds ratios), which tend to be more stable. Small study effects were observed in some pooled analyses but are difficult to interpret. Evaluations for small study effects are often unreliable when marked statistical heterogeneity is present, as in this case, and empirical evidence on the association between small study effects and publication bias in studies reporting incidence rates is lacking. Ong and colleagues used unpublished data obtained by contacting PrEP implementers and researchers. While including such data increases the precision of estimates and...
provides evidence from additional populations and settings, details about the methods used to collect and analyze these unpublished data were lacking. The review only included studies that met a methodological quality threshold based on meeting 5 or more of 9 prespecified criteria. However, using such a threshold to determine quality is discouraged, because it downplays serious limitations in 1 or a few domains and may exaggerate the importance of minor limitations in multiple domains.\(^5\) Importantly, the review was limited in its ability to control for factors associated with risk of STI, such as condom use and other sexual behaviors, as well as frequency of STI testing. Finally, patients tested for STIs at different sites could have been double-counted in some meta-analyses, which included STI data from each anatomical site. None of these factors is likely to invalidate the main findings of the review, given the robustness of findings across multiple types of STIs, anatomical sites, study types, populations, and country income levels.

The findings of the review by Ong and colleagues underscore the importance of prevention, screening, and monitoring as part of a comprehensive strategy for STI control in persons initiating PrEP. Rather than viewing PrEP as a trade-off between prevention of HIV and prevention of other STIs, initiation of PrEP should be considered a prime opportunity for reducing the burden of STIs in this high-risk population. This issue is of particular importance in the current era of drug-resistant STIs. More research is needed to define optimal STI screening and monitoring practices, including which sites to test and at what intervals, as well as effective methods for reducing sexual risk behaviors. Although current guidelines recommend STI monitoring at least every 6 months in asymptomatic persons not known to be at high risk for recurrent bacterial STIs,\(^1\) the high incidence of STIs after PrEP initiation suggests that more frequent routine testing may be indicated. In the meantime, evidence indicates poor adherence to existing recommendations on STI screening and monitoring.\(^6,7\) Scale-up and implementation of PrEP should prioritize efforts to address this important practice gap.

**ARTICLE INFORMATION**

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**Corresponding Author:** Roger Chou, MD, Department of Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, 3181 SW Sam Jackson Park Rd, Mail Code: BICC, Portland, OR 97239 (chour@ohsu.edu).

**Author Affiliation:** Department of Medical Informatics and Clinical Epidemiology, Oregon Health and Science University, Portland.

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**REFERENCES**


