

# Letters

## COMMENT & RESPONSE

**In Reply** We appreciate the Letter by Kenyon related to our study on doxyPEP and bacterial STI incidence<sup>1</sup> and welcome the opportunity to further discuss the implications of our findings for STI control and antibiotic resistance. We share Kenyon's concern that wider doxyPEP use could lead to increases in antibiotic resistance in gonorrhea, as there is evidence that resistance to important antibiotics for gonorrhea treatment, including cephalosporins, can be co-transmitted with tetracycline resistance. Nevertheless, it is important to balance the potential risks of gonorrhea antibiotic resistance with the population-level benefits of preventing syphilis and chlamydia infections, which can have detrimental health outcomes.

New approaches to prevent syphilis, in particular, are critically needed. In the US in 2023, there were 98 791 cases of unknown duration or late syphilis, a 12.8% increase from 2022. In 2023, there were 3882 cases of congenital syphilis, a 3.0% increase from 2022 and a staggering 740.3% increase since 2014.<sup>2</sup> These trends have been observed in other high-income settings and represent a serious threat to public health globally.<sup>3</sup> In contrast, the number of primary and secondary syphilis cases among gay and bisexual men decreased in 2023 for the first time since the US Centers for Disease Control and Prevention began reporting trends in this group in the mid-2000s. This national decline, alongside findings from our study across northern California and data from San Francisco, California,<sup>4</sup> suggests that doxyPEP may reduce the incidence of syphilis and chlamydia infections at a population level.

As doxyPEP implementation continues, efforts are needed to monitor and respond to any increases in resistant gonorrhea, which were a concern even before the emergence of doxyPEP. Research is also needed to understand the impact of doxyPEP implementation on population-level antibiotic consumption, including potential offsets in the amount of antibiotics, including doxycycline, prescribed for treatment.

DoxyPEP is a new and important tool in the STI prevention toolbox, especially for syphilis and chlamydia. Given limited effectiveness of doxyPEP in preventing gonorrhea, novel prevention strategies, such as vaccines<sup>5</sup> and new antibiotics in development,<sup>6</sup> will be critical for gonorrhea control.

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