

## Reply to Boyd et al

TO THE EDITOR—We welcome with great interest a randomized controlled trial to evaluate the efficacy of doxycycline prophylaxis for sexually transmitted infections (STIs) as proposed by Boyd et al [1,2], although we offer several concerns:

Syphilis is readily treatable and curable; doxycycline prophylaxis, therefore, would be considered an alternative to guideline-recommended quarterly testing and treatment [3], which alone may be sufficient. Although we agree that a fully powered clinical trial would determine if a daily pill for prophylaxis could add value over quarterly testing and treatment, the resources might be better spent on improving compliance with existing recommendations for frequent testing.

A clinical trial could evaluate whether STI prophylaxis would impair, or enhance, adherence to human immunodeficiency virus (HIV) preexposure prophylaxis (PrEP). This consideration would not apply to men who have sex with men (MSM) at high risk for certain STIs but at low risk for HIV (eg, MSM engaging only in condomless oral sex). Among MSM at high risk for HIV acquisition, pill-taking receptiveness might be best prioritized for HIV prevention efforts, as HIV remains without a cure and is responsible for worse outcomes; adherence to just 1 pill a day can prove challenging, as we observed in iPrEx. Alternatively, uptake of sexual health services may increase by offering a variety of prophylactic combinations, which might include HIV prophylaxis, STI prophylaxis, and contraception, depending on individual needs and desires.

Importantly, offering doxycycline as prophylaxis will increase antibiotic pressure and may lead to increased drug resistance, especially within communities and sexual networks where multidrug-resistant bacterial infections, such as gonorrhea, have already emerged.

Although doxycycline is typically well tolerated and there is extensive experience with its chronic use in acne or for long-

term (including life-long) suppressive therapy, side effects such as sun sensitivity, esophagitis, and diarrhea are common.

Despite these cautions, we agree that STI prophylaxis or a combined approach (ie, PrEP plus) would be worthwhile to examine in trials.

## Note

**Potential conflicts of interest.** All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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