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Correspondence

Is It Time to Rethink Syphilis Control?

TO THE EDITOR—We read with interest the iPrEx substudy by Solomon et al electronically published in the journal on 13 June [1]. This demonstrated a strikingly increased human immunodeficiency virus (HIV) incidence associated with incident syphilis infection (2.8 cases per 100 person-years for no syphilis vs 8 cases per 100 person-years for incident syphilis (hazard ratio, 2.6; 95% confidence interval [CI], 1.2–4.1; $P < .001$). These data add substantial weight to the evidence base demonstrating the strong link between incident syphilis infection and HIV acquisition risk among gay and other men who have sex with men (GMSM) and raise the importance of prevention strategies focusing on all sexually transmitted infections (STIs) including HIV.

Since the arrival of effective combination antiretroviral therapy (ART) in the mid-1990s, GMSM across the world have experienced growing epidemics of

bacterial (STIs) including syphilis, chlamydia, and gonorrhea (Figure 1). The basis for these epidemics is related to engagement in sexual practices thought unlikely to transmit HIV infection (eg, oral sex) but through which other STIs may be readily transmitted. HIV “transmission optimism” regarding the impact of ART on the likelihood of HIV transmission, and increased sexual risk behavior in the context of “serosorting” among GMSM (ie, GMSM permitting unprotected anal intercourse with sexual partners of the same HIV infection status) [2–4]. It has been estimated that the rate of syphilis infections in GMSM in most high- and middle-income countries is >1000 times the notification rate in the general community. In Australia in 2012, there were >9500 gonorrhea notifications in men, a 68% increase since 2008. Considerable public health efforts in Australia have been undertaken to control those STIs, including the promotion of screening, timely treatment, and condom use,

but with little apparent impact on STI incidence [5].

We have previously examined the potential use of a chemoprophylactic approach to syphilis control in a mathematical model. The model indicated that chemoprophylaxis given to 50% of GMSM with >10 partners in 6 months could prevent up to 85% of new syphilis infections among all GMSM over 10 years with a use-effectiveness of as low as 50%. At 90% use-effectiveness, chemoprophylaxis could prevent a similar proportion of infections in just 5 years [6]. A recent pilot study of 30 high-risk HIV-positive GMSM in Los Angeles, California (15 subjects randomized to doxycycline 100 mg daily vs 15 control subjects receiving standard management) reported promising results: STI incidence over 9 months of follow-up was 2 vs 6 cases for syphilis, 1 vs 2 cases for gonorrhea, and 1 vs 3 cases in the doxycycline prophylaxis and standard management arms, respectively. Control subjects had a 3.5 greater odds

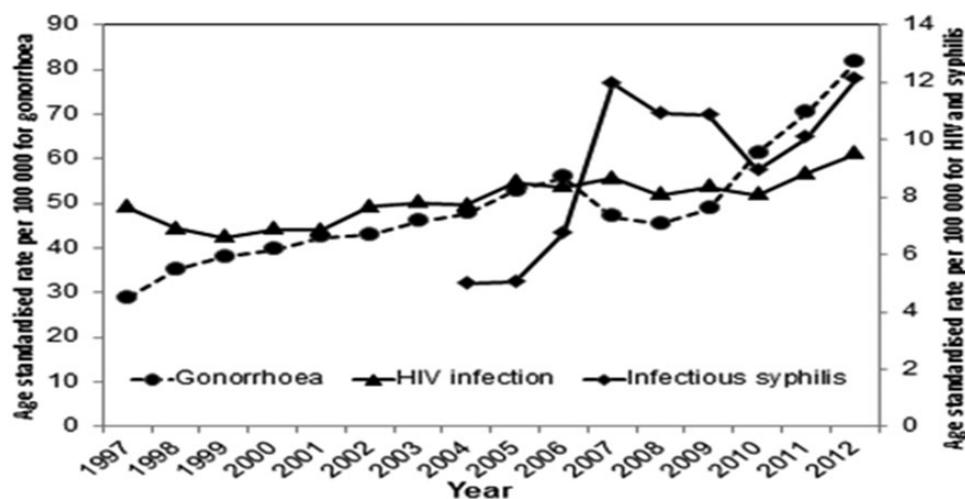


Figure 1. Notifications of infectious syphilis, gonorrhoea, and human immunodeficiency virus (HIV) infection in men, Australia 1997–2012.

(95% CI, 1.1–11; $P = .04$) for a new STI compared with those randomized to doxycycline. Behavioral outcomes for drug use, anonymous partners, and number of regular partners were not different and no safety concerns emerged [7].

There now exists a compelling case for the conduct of a sufficiently powered randomized controlled trial to determine if low-dose daily prophylactic doxycycline might effectively reduce STI rates in GMSM. In the absence of a protective vaccine and an ongoing STI epidemic, the evaluation of simple and inexpensive interventions such as chemoprophylaxis should be a public health priority.

Note

Potential conflicts of interest. All authors: No potential conflicts of interest.

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