

# Correspondence

## Is It Time to Rethink Syphilis Control?

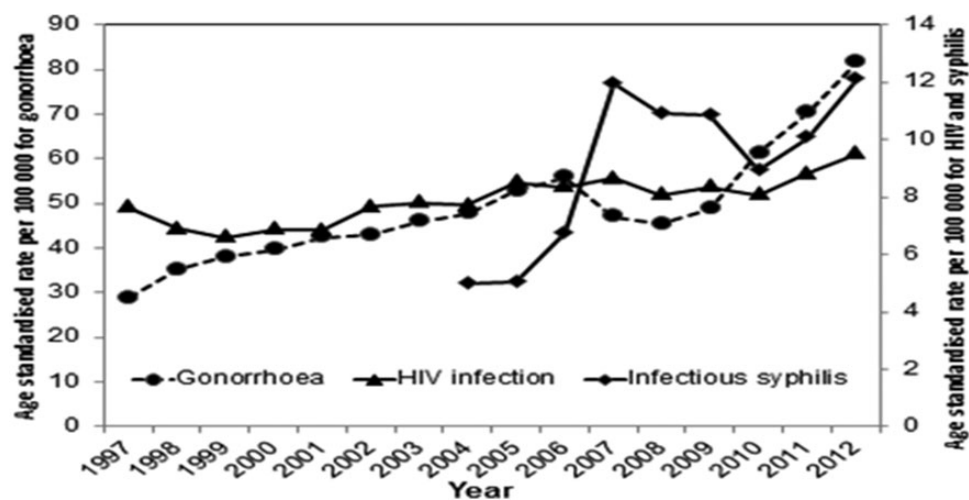
TO THE EDITOR—We read with interest the iPrEx substudy by Solomon et al electronically published in the journal on 13 June [1]. This demonstrated a strikingly increased human immunodeficiency virus (HIV) incidence associated with incident syphilis infection (2.8 cases per 100 person-years for no syphilis 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, GSM 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 GSM (ie, GSM 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 GSM 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 GSM with >10 partners in 6 months could prevent up to 85% of new syphilis infections among all GSM 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 GSM 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 GSM. 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.

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.

**M. A. Boyd,<sup>1</sup> B. Donovan,<sup>1</sup> G. Prestage,<sup>1</sup> M. Chen,<sup>2</sup> K. Petoumenos,<sup>1</sup> R. Gray,<sup>1</sup> R. Guy,<sup>1</sup> G. B. Rogers,<sup>3</sup> C. Bourne,<sup>4</sup> and J. D. Klausner<sup>5</sup>**

<sup>1</sup>The Kirby Institute, University of New South Wales, Sydney, <sup>2</sup>Melbourne Sexual Health Centre, Carlton, Victoria, <sup>3</sup>South Australian Health and Medical Research Institute, North Terrace, and <sup>4</sup>Sydney Sexual Health Centre, New South Wales, Australia; and <sup>5</sup>Division of Infectious Diseases and the Program in Global Health David Geffen School of Medicine and Fielding School of Public Health at University of California, Los Angeles

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Correspondence: Mark Boyd, MD, University of New South Wales, The Kirby Institute, Sydney, NSW 2052, Australia (mboyd@kirby.unsw.edu.au).

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