

Research Letter

AIDS 2016, 30:2251–2252

Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men

Noah Kojima^a, Dvora Joseph Davey^{a,b} and Jeffrey D. Klausner^a

We conducted a meta-analysis to summarize rates of sexually transmitted infections among men who have sex with men (MSM) on pre-exposure prophylaxis (PrEP) for HIV versus MSM not using PrEP. Incidence rate ratios showed that MSM using PrEP were 25.3 times more likely to acquire a *Neisseria gonorrhoeae* infection, 11.2 times more likely to acquire a *Chlamydia trachomatis* infection, and 44.6 times more likely to acquire a syphilis infection versus MSM not using PrEP.

The safety and effectiveness of pre-exposure prophylaxis (PrEP) to prevent HIV type 1 infection among MSM has been verified in randomized controlled trials and ‘real-world’ studies [1,2]. However, high incidence of sexually transmitted infections (STIs) among participants in PrEP trials has led clinicians and public health advocates to be concerned that PrEP use might lead to higher STI incidence because of increased sexual risk behavior [3]. We conducted a meta-analysis to evaluate differences in STI acquisition among MSM on PrEP for HIV versus MSM not using PrEP.

In March 2016, we conducted a literature review with the *MeSH* terms ‘SYPHILIS’ OR ‘GONORRHEA’ OR ‘CHLAMYDIA’ OR ‘HOMOSEXUALITY’ OR ‘MALE’ OR ‘TRANSGENDER PERSONS’ AND ‘COHORT STUDIES’ using *PubMed* as a search platform. We identified over 140 000 studies, including all five studies on PrEP (Supplemental Table; <http://links.lww.com/QAD/A944>). We restricted studies to only those with the following inclusion criteria: English language, cohort of MSM, and STI incidence rates reported with nucleic acid amplification testing. We conducted a meta-analysis of those studies to compare incidence rate ratios of STIs between MSM using PrEP versus MSM not using PrEP.

Of the studies that only reported percentages of incident infections, we estimated the number of incident infections based on the reported percentage and total number of participants in the study. In our meta-analysis of individual STIs, we included all studies that reported incidence rates of our STI of interest. The pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD)

study [2] had two study arms to compare the effectiveness of PrEP – an immediate PrEP intervention group and a deferred PrEP intervention group. We included the immediate intervention group of the PROUD study into our MSM on PrEP group and we included the deferred intervention group of the PROUD study into our MSM without PrEP group in our meta-analysis.

OpenMetaAnalyst (10.10; Medford, Massachusetts, USA) was used to calculate the overall rate of incident STIs in a meta-analysis with 95% confidence intervals. StataSE 14.1 (College Station, Texas, USA) was used to calculate incidence rate ratios with 95% confidence intervals and *P* values comparing incident STIs in studies of MSM on PrEP versus studies of MSM not on PrEP.

We identified over 70 000 person-years of follow-up in 18 cohort studies of MSM with incident STIs (Supplemental Table, <http://links.lww.com/QAD/A944>). Of the studies, five were conducted in MSM that were administered PrEP and 14 were conducted in MSM without PrEP. Incidence rate ratios showed that MSM using PrEP were 25.3 times more likely to acquire a *Neisseria gonorrhoeae* infection, 11.2 times more likely to acquire a *Chlamydia trachomatis* infection, and 44.6 times more likely to acquire a syphilis infection, when compared with MSM not using PrEP (Table 1). We repeated the meta-analysis excluding studies conducted before 1999 and found similar results.

Our analyses found that use of PrEP for HIV infection was associated with increased risk of STI acquisition among MSM. The mechanism of increased risk of STIs among PrEP users may be due to multiple factors, including increased STI detection among MSM clinically managed on PrEP [4], increased number of sex partners [5], and increased condomless sex [6]. Limitations of our analysis include utilization of studies with heterogeneous populations, different frequencies of STI screenings, and differences in diagnostic tests used. Also, PrEP studies recruited MSM with high-risk sexual behavior, whereas MSM in studies not using PrEP may have had different baseline risk behavior.

Our results, as well as prior studies, support updating Center for Disease Control and Prevention guidelines to recommend that MSM using PrEP receive quarterly STI screenings, an increase from their current guidelines that recommend biannual to quarterly screenings [7,8]. Furthermore, physicians must not only vigilantly identify patients that may benefit from PrEP but also provide their patients with a sexual health prevention package that includes quarterly STI screenings, timely treatment of

DOI:10.1097/QAD.0000000000001185

Table 1. Meta-analysis of studies of sexually transmitted infection incidence among men who have sex with men using pre-exposure prophylaxis for HIV versus MSM not using pre-exposure prophylaxis for HIV

Sexually transmitted infections	MSM using PrEP			MSM not using PrEP			Incidence rate ratio, 95% CI	P value
	Incidence per 100 person-years, 95% CI	Number of studies	Total person-years followed	Incidence per 100 person-years, 95% CI	Number of studies	Total person-years followed		
Any <i>Neisseria gonorrhoeae</i> infection	37.5 (24.3, 50.7)	4	1561	4.2 (2.7, 5.7)	5	43 294	25.3 (22.6, 28.4)	<0.001 or <0.001
Any <i>Chlamydia trachomatis</i> infection	38.0 (20.3, 55.7)	4	1561	6.6 (3.8, 9.4)	6	54 703	11.2 (10.2, 12.3)	<0.001 or <0.001
Syphilis	14.5 (3.8, 25.2)	5	4887	0.9 (0.6, 1.3)	11	50 957	44.6 (39.1, 51.1)	<0.001 or <0.001

Shown are crude incidence per 100 person-years and crude incidence rate ratios with 95% confidence intervals and *P* values. Studies included are from 2010 to 2016 for MSM using PrEP infection and from 1998 to 2016 for studies in MSM not using PrEP infection. CI, confidence interval; PrEP, pre-exposure prophylaxis.

infection, expedited partner treatment, and rescreening if positive. In addition, our results and prior reports, which not only found a higher incidence of STI among PrEP users versus nonusers [2] but also high rates of condomless anal sex among PrEP users [9], suggest that more research is needed to understand if PrEP causes a higher incidence of STIs among MSM. We must ensure that our efforts fighting one public health crisis do not lead to another.

Acknowledgements

Time for data collection, analysis, and manuscript preparation was supported in part by NIH P30MH058107 (The Center for HIV Identification, Prevention, and Treatment Services) and NIH/NIAID AI028697 (UCLA Center for AIDS Research).

Conflicts of interest

There are no conflicts of interest.

^aDavid Geffen School of Medicine at the University of California Los Angeles; and ^bFielding School of Public Health, University of California Los Angeles, Los Angeles, California, USA.

Correspondence to Noah Kojima, David Geffen School of Medicine at the University of California Los Angeles, 10833 Le Conte Ave., Los Angeles, CA 90095, USA. Tel: +1 310 825 6373; e-mail: nkojima@ucla.edu

Received: 28 May 2016; accepted: 7 June 2016.

References

- Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. **Preexposure chemoprophylaxis for HIV prevention in men who have sex with men.** *N Engl J Med* 2010; **363**:2587–2599.
- McCormack S, Dunn DT, Desai M, Dolling DI, Gafos M, Gilson R, et al. **Preexposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial.** *Lancet* 2016; **387**:53–60.
- Scott HM, Klausner JD. **Sexually transmitted infections and preexposure prophylaxis: challenges and opportunities among men who have sex with men in the US.** *AIDS Res Ther* 2016; **13**:5.
- Koester KA, Grant RM. **Editorial commentary: keeping our eyes on the prize: no new HIV infections with increased use of HIV pre-exposure prophylaxis.** *Clin Infect Dis* 2015; **61**:1604–1605.
- Volk JE, Marcus JL, Phengrasamy T, Blechinger D, Nguyen DP, Follansbee S, Hare CB. **No new HIV infections with increasing use of HIV preexposure prophylaxis in a clinical practice setting.** *Clin Infect Dis* 2015; **61**:1601–1603.
- Paz-Bailey G, Mendoza M, Finlayson T, Wejnert C, Le B, Rose C, et al. **Trends in condom use among men who have sex with men in the United States: the role of antiretroviral therapy and sero-adaptive strategies.** *AIDS* 2016.
- Centers for Disease Control and Prevention. **Preexposure prophylaxis for the prevention of HIV infection in the United States – 2014 a clinical practice guideline.** Atlanta, GA: US Department of Health and Human Services, CDC. Available at: <http://www.cdc.gov/hiv/pdf/prepguidelines2014.pdf>
- Golub SA, Boonrai K, Douglas N, Hunt M, Radix A. **STI Data From Community-Based PrEP Implementation Suggest Changes to CDC Guidelines.** Boston, MA: CROI; 2016.
- Liu AY, Cohen SE, Vittinghoff E, Anderson PL, Doblecki-Lewis S, Bacon O, et al. **Preexposure prophylaxis for HIV infection integrated with municipal- and community-based sexual health services.** *JAMA Intern Med* 2016; **176**:75–84.