Supplementary table. Estimates of syphilis incidence and associated risk factors among HIV-infected patients in Singapore and other countries

Country	Study subjects	Incidence rate per 100 PYFU (95% CI)	Independent risk factors
Singapore	1,117 HIV-infected persons who had at least one visit to the national referral centre for HIV care and diagnosed with HIV infection in 2006- 2017, including 1,069 men	Men and women: 5.94 (5.24—6.69)	 Among men: Age 15-24 years compared with ≥45 years Chinese ethnicity compared with Indian and other minority ethnic groups
		Men: 6.21 (5.49–7.00)	
		MSM: 9.00 (7.86–10.27)	
		Heterosexual men: 2.22 (1.54–3.10)	 HIV exposure via MSM contact HIV diagnosis in the period after
		Women: 0.00 (0.00—1.87)	2006-2008
South Korea, Taiwan, Hong Kong ¹	657 HIV-infected persons from three participating sites of the TREAT Asia HIV Observational Database (TAHOD) that routinely tested for syphilis, September 2004 to March 2014	Men and women: 5.38 (4.52—6.41)	Among men and women:HIV exposure via MSM contact
		MSM: 7.64 (6.29—9.28)	Past diagnosis of syphilisYounger age
		Non-MSM: 2.44 (1.65–3.61)	
South Korea ²	539 HIV-infected persons aged >15 years who started highly active antiretroviral therapy (HAART) at Seoul National University Hospital in South Korea, 1998-2006	Men and women	
		Early syphilis for 4 years after the start of ART: 4.57 (3.45—5.93)	
Japan ³	671 HIV-infected MSM who visited a large HIV clinic in Tokyo for the first time in 2008-2013	MSM: 4.37 (3.65—5.23)	 Among MSM: Younger age History of syphilis at baseline Positive anti-amoeba antibody High baseline CD4 count (≥350 vs. <200)

Country	Study subjects	Incidence rate per 100 PYFU (95% CI)	Independent risk factors
China ^₄	634 HIV-infected patients who attended an outpatient clinic of a designated AIDS treatment hospital in Shenyang city between March 2009 and May 2013	Men and women: 18.7 (15.5–21.8) Men: 19.3	 Among men and women: HIV exposure via MSM contact Received ART at baseline Older age (≥40 years vs. ≤24 years)
		Women: 7.4	
		MSM: 19.5	
		Heterosexuals: 17.0	
United States⁵	6,888 HIV-infected adults who received care at an active HIV Outpatient Study (HOPS) site in the United States between 1 January 1999 and 30 June 2015	Men and women: 1.8 (1.6—1.9)	 Among men and women: HIV exposure via MSM contact Age 18-30 years compared with 31-40 years Non-Hispanic blacks Observed in later calendar years after 1999
		All men: 2.2 (2.0–2.3)	
		MSM: 2.5 (2.3–2.7)	
		Heterosexual men: 1.0 (0.8–1.3)	
United States ⁶	622 HIV-infected patients seen at 14 medical centres under an integrated health care system, Kaiser Permanente Northern California (KPNC), 1995- 2005	Men and women: 6.23	 Among men and women: Not on ART (adjusted for gender, AIDS diagnosis, age, and HIV risk behaviour)
Switzerland ⁷	3,575 HIV-infected persons enrolled in the Swiss HIV Cohort Study (SHCS) in 2004-2014, including 1,519 MSM	MSM: 2.68 (2.35—3.08)	Among MSM: • Younger age
		Heterosexuals: 0.18 (0.11-0.30)	 History of condomless sex with an occasional partner Higher frequency of syphilis testing Observed in later calendar years
		IDUs: 0.13 (0.05–0.35)	
Canada ⁸	2,271 HIV-infected MSM	MSM	Among MSM (any new syphilis
	who received specialty HIV care at one of 10 hospital- or community-based practices	New syphilis diagnosis (first documented diagnosis or subsequent diagnosis): 3.3 (2.9–3.7)	diagnosis): • Younger age • Previous syphilis diagnosis

Country	Study subjects	Incidence rate per 100 PYFU (95% CI)	Independent risk factors
	enrolled in the Ontario HIV Treatment Network Cohort Study (OCS) in 2006-2010.	First syphilis diagnoses: 2.0 (1.7—2.4)	Lower CD4 cell countsObserved in later calendar years
		Re-diagnoses: 7.5 (6.3—8.8)	
Canada ⁹	2,448 HIV-infected patients on follow-up at the Calgary STI Program and the Southern Alberta Clinic with at least one regular visit in 2006-2016	Men and women: 1.29 (0.96—1.61)	
The Netherlands ¹⁰	HIV-infected patients who attended a HIV-outpatient clinic at a university hospital in Amsterdam from March to June 2003, and September through December 2003. Study subjects comprised 1,105 including 630 MSM for retrospective analysis from January 2000 through June 2003, and 1,010 including 571 MSM for prospective analysis from September through December 2003.	Metrospective analysis <u>Men and women</u> Total incidence: 2.7 Incidence of asymptomatic infection: 0.9 <u>MSM</u> Total incidence: 4.6 Incidence of asymptomatic infection: 1.5 Prospective analysis <u>Men and women</u> Total incidence: 3.5 Incidence of asymptomatic infection: 0.8 <u>MSM</u> Total incidence: 6.2 Incidence of asymptomatic infection: 1.4	

PYFU: Person-years of follow-up

References

- 1. Ahn JY, Boettiger D, Kiertiburanakul S, *et al*; Treat Asia HIV Observational Database. Incidence of syphilis seroconversion among HIV-infected persons in Asia: results from the TREAT Asia HIV Observational Database. *J Int AIDS Soc* 2016;19:20965.
- 2. Park WB, Jang HC, Kim SH, *et al.* Effect of highly active antiretroviral therapy on incidence of early syphilis in HIVinfected patients. *Sex Transm Dis* 2008;35:304-6.
- 3. Nishijima T, Teruya K, Shibata S, *et al.* Incidence and risk factors for incident syphilis among HIV-1-Infected men who have sex with men in a large urban HIV clinic in Tokyo, 2008-2015. *PLoS One* 2016;11:e0168642.
- 4. Hu QH, Xu JJ, Zou HC, *et al.* Risk factors associated with prevalent and incident syphilis among an HIV-infected cohort in Northeast China. *BMC Infect Dis* 2014;14:658.
- 5. Novak RM, Ghanem A, Hart R, *et al*; HIV Outpatient Study Investigators. Risk Factors and Incidence of Syphilis in Human Immunodeficiency Virus (HIV)-Infected Persons: The HIV Outpatient Study, 1999-2015. *Clin Infect Dis* 2018;67:1750-9.
- 6. Horberg MA, Ranatunga DK, Quesenberry CP, *et al.* Syphilis epidemiology and clinical outcomes in HIV-infected and HIV-uninfected patients in Kaiser Permanente Northern California. *Sex Transm Dis* 2010;37:53-8.
- 7. Shilaih M, Marzel A, Braun DL, *et al*; the Swiss HIV Cohort Study. Factors associated with syphilis incidence in the HIV-infected in the era of highly active antiretrovirals. *Medicine (Baltimore)* 2017;96:e5849.
- 8. Burchell AN, Allen VG, Gardner SL, *et al*; OHTN Cohort Study Team. High incidence of diagnosis with syphilis coinfection among men who have sex with men in an HIV cohort in Ontario, Canada. *BMC Infect Dis* 2015;15:356..
- 9. Lang R, Read R, Krentz HB, *et al.* Increasing incidence of syphilis among patients engaged in HIV care in Alberta, Canada: a retrospective clinic-based cohort study. *BMC Infect Dis* 2018;18:125.
- 10. Branger J, van der Meer JT, van Ketel RJ, et al. High incidence of asymptomatic syphilis in HIV-infected MSM justifies routine screening. *Sex Transm Dis.* 2009;36(2):84-85.