

Supplementary Material

Hepatitis C virus infection in HIV-infected men in Singapore, 2006–2018: incidence and associated factors

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Table S1. Demographic and epidemiological characteristics of HIV-infected men who were included and excluded from the study, 2006–2018

Characteristic	All men (n=3,239)	Included (n=1,348)	Excluded (n=1,891)	P value
Age at HIV diagnosis, n (%)				<0.0005
0–14	1 (0.0)	0 (0.0)	1 (0.1)	
15–24	346 (10.7)	177 (13.1)	169 (8.9)	
25–34	810 (25.0)	393 (29.2)	417 (22.1)	
35–44	872 (26.9)	376 (27.9)	496 (26.2)	
45–54	727 (22.4)	265 (19.7)	462 (24.4)	
≥55	483 (14.9)	137 (10.2)	346 (18.3)	
Ethnic group, n (%)				0.999
Chinese	2,479 (76.5)	1,032 (76.6)	1,447 (76.5)	
Malay	497 (15.3)	207 (15.4)	290 (15.3)	
Indian	156 (4.8)	64 (4.7)	92 (4.9)	
Others	107 (3.3)	45 (3.3)	62 (3.3)	
HIV transmission risk group, n (%)				0.001
Heterosexual	1,278 (39.5)	490 (36.4)	788 (41.7)	
MSM	1,723 (53.2)	776 (57.6)	947 (50.1)	
IDU	14 (0.4)	5 (0.4)	9 (0.5)	
IDU and sexual	117 (3.6)	38 (2.8)	79 (4.2)	
Others	17 (0.5)	5 (0.4)	12 (0.6)	
Unknown	90 (2.8)	34 (2.5)	56 (3.0)	
Period of HIV diagnosis, n (%)				<0.0005
2006–2009	1,200 (37.0)	521 (38.6)	679 (35.9)	
2010–2012	825 (25.5)	421 (31.2)	404 (21.4)	
2013–2015	702 (21.7)	275 (20.4)	427 (22.6)	
2016–2018	512 (15.8)	131 (9.7)	381 (20.1)	
Prior AIDS diagnosis, n (%)				0.001
No	2,065 (63.8)	904 (67.1)	1,161 (61.4)	
Yes	1,174 (36.2)	444 (32.9)	730 (38.6)	
Ever on ART, n (%)				<0.0005
No	144 (4.4)	29 (2.2)	115 (6.1)	
Yes	3,095 (95.6)	1,319 (97.8)	1,776 (93.9)	
Ever tested positive for syphilis [§] , n (%)				<0.0005
No	1,788 (55.2)	687 (51.0)	1,101 (58.2)	
Yes	1,276 (39.4)	636 (47.2)	640 (33.8)	
Not tested	175 (5.4)	25 (1.9)	150 (7.9)	
Ever used recreational or illicit drugs [†] , n (%)				0.606
No	642 (19.8)	278 (20.6)	364 (19.2)	
Yes	402 (12.4)	168 (12.5)	234 (12.4)	
Unknown	2,195 (67.8)	902 (66.9)	1,293 (68.4)	
CD4 (cells/mm ³) at HIV diagnosis [‡] , n (%)				0.005
>350	906 (28.0)	405 (30.0)	501 (26.5)	
201–350	713 (22.0)	317 (23.5)	396 (20.9)	

Characteristic	All men (n=3,239)	Included (n=1,348)	Excluded (n=1,891)	P value
≤200	1,378 (42.5)	539 (40.0)	839 (44.4)	
Not available	242 (7.5)	87 (6.5)	155 (8.2)	
Viral load (copies/mL) at diagnosis‡, n (%)				0.164
≤200	83 (2.6)	27 (2.0)	56 (3.0)	
>200	1,972 (60.9)	814 (60.4)	1,158 (61.2)	
Not available	1,184 (36.6)	507 (37.6)	677 (35.8)	

§ During the duration of follow-up.

† Includes ecstasy, insufflated amyl nitrites or 'poppers', erectile dysfunction medications like sildenafil, amphetamines, cannabis, heroin, cocaine, barbiturates/ benzodiazepines, opium, psychedelic psilocybin mushrooms, solvents, LSD (Lysergic Acid Diethylamide).

‡ Within ±6 months of HIV diagnosis.

ART, antiretroviral therapy; IQR, interquartile range; IDU, intravenous drug use; MSM, men having sex with men.

Table S2. Estimates of incidence of hepatitis C virus infection and associated risk factors among HIV-infected patients in Singapore and other cohort studies

Location [reference]	Study population	Study period	Overall incidence per 100 PYFU (95% CI)	Incidence trend per 100 PYFU (95% CI)	Independent risk factors
Singapore	1,353 men	2006–2018	Men: 1.10 (0.87–1.37) MSM: 1.48 (95% CI 1.15–1.90) Heterosexual men: 0.43 (0.24–0.76)	<u>Men</u> 2006–2009: 0.35 (0.07–1.01) 2010–2012: 0.43 (0.19–0.85) 2013–2015: 0.99 (0.65–1.45) 2016–2018: 2.25 (1.63–3.02)	<ul style="list-style-type: none"> • HIV exposure via MSM contact or sexual and intravenous drug use • HIV diagnosis in 2016–2018 • Recent syphilis acquisition
Taiwan [1]	3,495 HIV-infected patients (3021 MSM, 295 HET and 22 IDU)	2011–2018	Overall: 1.80 MSM: 1.92	<u>Overall</u> 2011: 1.43 (0.82–2.04) 2018: 2.54 (1.91–3.17) <u>MSM</u> 2011: 1.64 (0.92–2.36) 2018: 2.81 (2.10–3.52)	<u>MSM</u> <ul style="list-style-type: none"> • Syphilis acquisition • Aspartate aminotransferase ≥ 37 U/L • Alanine aminotransferase ≥ 41 U/L
Tokyo, Japan [2]	753 HIV-infected MSM	2005–2012	MSM: 0.935	<u>MSM</u> 2005–2006: 0.00 2007–2008: 0.30 2009–2010: 0.77 2011–2012: 2.49	<ul style="list-style-type: none"> • Illicit drug use
South Korea [3]	384 HIV-infected patients	2000–2013	Overall: 0.22 (0.06–0.58) IDU: 16.49 (3.40–48.19) MSM: 0.41 (0.09–1.2.1) MSM – no drug: 0.14 (0.04–0.78)	<u>MSM</u> 2000–2009: 0.0 (0.0–1.10) 2010–2014: 0.66 (0.14–1.93) <u>MSM – no drug</u> 2000–2009: 0.0 (0.0–1.12) 2010–2014: 0.22 (0.06–1.24)	

Location [reference]	Study population	Study period	Overall incidence per 100 PYFU (95% CI)	Incidence trend per 100 PYFU (95% CI)	Independent risk factors
Melbourne, Australia [4]	620 HIV-infected men	2002–2010	Men: 0.92 MSM: 0.9 (0.6–1.2). IDU: 4.7 (2.7–7.5) non-IDU: 0.6 (0.4–0.8)		
Melbourne, Australia [5]	822 HIV positive MSM	2008–2016	MSM: 1.19 (0.99–1.38)	<u>MSM</u> 2009: 2.9 (0.9–5.0) 2014: 1.2 (0.8–1.7) 2015: 1.0 (0.6–1.5)	<ul style="list-style-type: none"> • Younger age • Peri-incident syphilis infection • Higher CD4 cell count nadir
Europe and Canada [6]	3,014 HIV-infected MSM	1990–2007	-	<u>MSM (3 estimation methods)</u> 1995: 0.55, 0.59 (0.27–1.30) and 0.81 (0.37–1.90) 2000: 0.80, 1.06 (0.60–1.88), and 1.37 (0.80–2.37) 2005: 1.68 (1.03–2.74), 2.12, and 3.00 (1.86–4.83) 2007: 2.34 (0.82–6.69), 4.19, and 5.11 (1.95–13.40)	
Europe, Canada and Australia [7]	5,941 HIV-infected MSM	1990–2014	-	<u>MSM (2 estimation methods)</u> 1990: 0.07 (0.01–0.5), 0.3 (0.04–1.8) 2014: 1.8 (0.9–3.7). 2.1 (1.0–4.2)	
France [8]	402 HIV-infected patients (327 men and 75 women)	1996–July 2005	Overall: 0.43 Men: 0.35 Women: 0.78	<u>Overall</u> <2003: 0.12 ≥2003: 0.83	

Location [reference]	Study population	Study period	Overall incidence per 100 PYFU (95% CI)	Incidence trend per 100 PYFU (95% CI)	Independent risk factors
France [9]	21,519 HIV-infected patients	2012–2016	0.35	<u>MSM</u> 2012: 0.35 2016: 0.92	
Amsterdam, the Netherlands [10]	504 HIV infected MSM	1984–2003	MSM: 0.18 (0.08–0.36)	<u>MSM</u> 1984–1999: 0.08 (0.02–0.23) 2000–2003: 0.87 (0.28–2.03)	
Switzerland [11]	6,534 HIV-infected patients (3,333 MSM, 3,078 HET and 123 IDU)	1998–2011	MSM: 0.43	<u>MSM</u> 1998: 0.23 (0.08–0.54) 2011: 4.09 (2.57–6.18)	<u>MSM</u> <ul style="list-style-type: none"> • history of inconsistent condom use • past syphilis
United Kingdom [12]	308 HIV-infected MSM attending a London outpatient clinic	1999–2005	Overall: 0.92	-	
United States [13]	1,941 HIV-infected patients (including 1,184 MSM, 584 heterosexuals, 52 IDU)	2000–2013	Overall: 1.07 (0.87–1.30) MSM: 1.04 (0.80–1.34)	<u>Overall</u> 2000–2003: 1.83 (1.20–2.66) 2004–2007: 0.94 (0.64–1.33) 2008–2010: 0.95 (0.63–1.37) 2011–2013: 0.88 (0.50–1.42) <u>MSM</u> 2000–2003: 1.33 (0.69–2.32) 2004–2007: 0.87 (0.51–1.39) 2008–2010: 0.96 (0.56–1.54) 2011–2013: 1.26 (0.69–2.12)	<ul style="list-style-type: none"> • Male gender • Having no/other/unknown insurance (compared with private insurance)

HET, heterosexual; IDU, injecting drug user; MSM, men having sex with men; PYFU, person-years of follow-up.

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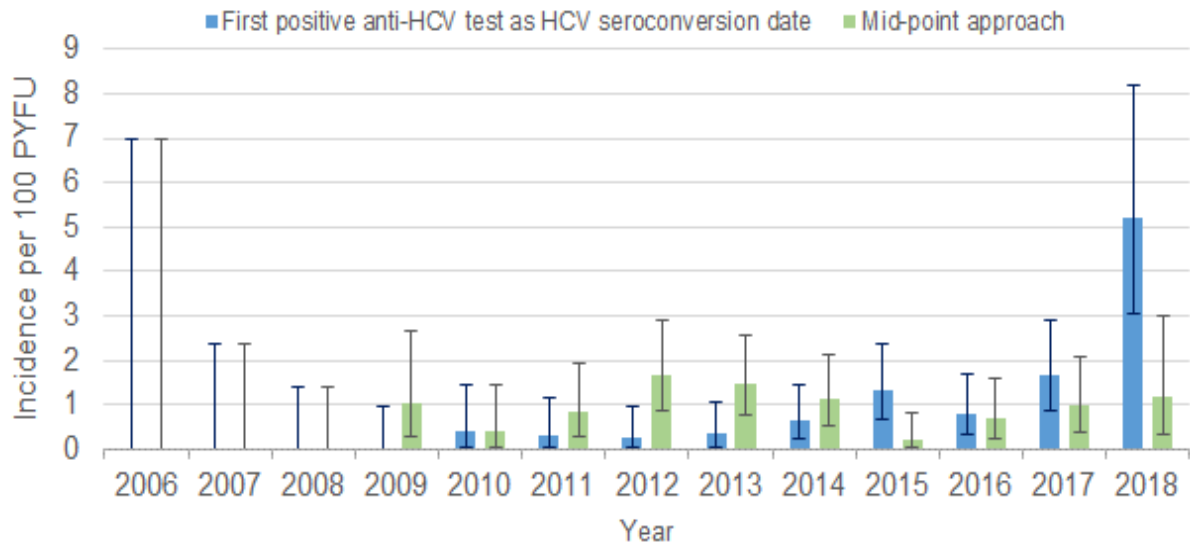


Figure S1. Annual incidence of hepatitis C virus infection among HIV-infected men who attended the national referral centre for HIV in Singapore based on two approaches for estimation of date of hepatitis C virus seroconversion, 2006–2018.

Error bars indicate 95% confidence interval. HCV, hepatitis C virus; PYFU, person-years of follow-up.

Computation of testing rates for hepatitis C virus

Hepatitis C virus (HCV) testing rates per 100 person-years of follow-up (PYFU) were determined based on the presence of any HCV test in each given calendar year when a HIV-infected patient was under observation. The start of observation for each patient was the later of either 1 January 2006 or date of first visit to the national referral centre for HIV, and the end of observation was the earliest of either the date of last visit, death or 31 December 2018.

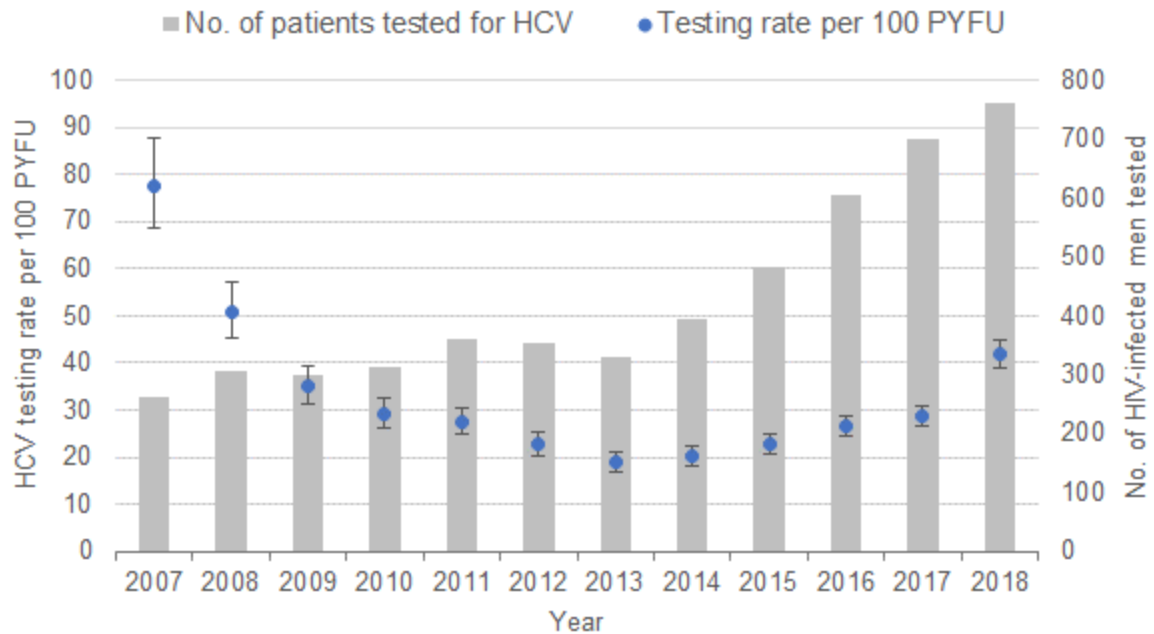


Figure S2. Annual testing rate per 100 person-years of follow-up and number of HIV-infected men tested for hepatitis C virus who attended the national referral centre for HIV, Singapore, 2007–2018.

Error bars indicate 95% confidence interval. PYFU, person-years of follow-up.