Received Date : 08-Mar-2015

Revised Date : 11-Oct-2015

Accepted Date : 11-Nov-2015

Article type : Original research

Corresponding author email id: brianm@health.usyd.edu.au

Risk factors associated with incident sexually transmitted infections in HIV-positive patients in the Australian HIV Observational Database- a prospective cohort study.

Brian P Mulhall [1,2], Stephen T Wright [1], Nicole De La Mata [1], Debbie Allen [3], Katherine Brown [2,4,5], Bridget Dickson [6], Miriam Grotowski[7], Eva Jackson[8], Kathy Petoumenos[1], Rosalind Foster[1,9], Timothy Read [10], Darren Russell [11,14], David J Smith [12], David J Templeton [1,13], Christopher K Fairley [10,14] and Matthew G Law [1]

1. The Kirby Institute, University of New South Wales, Sydney, 2052, Australia
2. University of Sydney, Camperdown, NSW 2006, Australia
3. Holden Street Sexual Health Clinic, PO Box 361, Gosford, NSW 2250, Australia
4. Illawarra Sexual Health Services, PO Box 21, Warrawong, NSW 2502, Australia
5. University of Wollongong, Wollongong, NSW 2522, Australia
6. Caradata, PO Box 579, Arundel DC, Qld 4214, Australia
7. Clinic 468, Tamworth Sexual Health, HNEAHS, NSW 2340, Australia

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/hiv.12371

This article is protected by copyright. All rights reserved

Author Manuscript

8. Nepean/Blue Mountains Sexual Health, Nepean Hospital, NSW 2747, Australia
9. Sydney Sexual Health Centre, PO Box 1614, Sydney, NSW 2001, Australia
10. Melbourne Sexual Health Centre, Alfred Hospital, Prahran, Vic 3181, Australia
11. Cairns Sexual Health Service, PO Box 902, Cairns, Qld 4214, Australia
12. Lismore Sexual Health Services, 4 Shepherd Lane, Lismore 2480, Australia
13. RPA Sexual Health, 16 Marsden Street, Camperdown, NSW 2050, Australia
14. Central Clinical School Monash University, Alfred Hospital, VIC 3181, Australia.

Author Manuscript

ABSTRACT

Background

We established a sub-cohort of HIV positive individuals from ten sexual health clinics within the Australian HIV Observational Database (AHOD). The aim of this paper was to assess demographic and other factors that might be associated with an incident sexually transmitted infection (STI).

Methods

The cohort follow-up was from March 2010 to March 2013, and included patients screened at least once for an STI. We used survival methods to determine time-to first new and confirmed incident STI infection (chlamydia, gonorrhoea, syphilis or genital warts). Factors evaluated included sex, age, mode of HIV exposure, year of AHOD enrolment, hepatitis B or C coinfection, time-updated CD4 cell count, time-updated HIV RNA viral load, and prior STI diagnosis.

Results

There were 110 first incident STI diagnoses observed over 1015 person-years of follow-up, a crude rate of 10.8 (95% confidence interval [CI]:9.0-13.0) per 100

This article is protected by copyright. All rights reserved

person-years. Factors independently associated with increased risk of incident STI included younger age (≥50 vs 30-39 years old, adjusted hazards ratio, [aHR]=0.4; 95% CI:0.2-0.8, p<0.0001); prior STI infection, (aHR=2.5; 95% CI: 1.6-3.8, p<0.001); and heterosexual vs men who have sex with men (MSM) as likely exposure (aHR=0.2; 95% CI: 0.1-0.6; p<0.001).

Conclusions

In this cohort of individuals being treated with anti-retroviral drugs (ARV), who are MSM, 30-39 years old, and with a prior history of STI, are at highest risk of a further STI diagnosis

Author Manuscript

This article is protected by copyright. All rights reserved

INTRODUCTION

Over the last 20 years a wealth of evidence has accumulated to support the strong amplification effect of STI on the acquisition and infectiousness of HIV (1-3). Recently, it has been shown that treatment with anti-retroviral drugs (ARV) can reduce onward HIV transmission (5-14), but some debate exists whether this is true in the presence of an inflammatory sexually transmitted infection (STI). (15-18).Therefore, it is important to estimate the incidence and prevalence of STI in populations at potential risk of transmitting HIV.

In Australia, new HIV diagnoses occur predominantly among men who have sex with men (MSM), a population in whom STI rates have been increasing for several years (most dramatically for infectious syphilis, particularly among those who are HIV-positive) (19-23).

There is a broad consensus that the increased incidence of some STI may be due to the increased prevalence of condomless intercourse in both HIV-negative and HIV-positive MSM (23,41). By combining retrospective and prospective data we have previously shown high levels of four STI in a sub-cohort of HIV positive individuals enrolled in AHOD (24).

In the present study, we have collected additional prospective data enabling risk factors for new STI diagnoses to be assessed.

METHODS

The current study is a prospective cohort, being a subset of clinical sites of AHOD. AHOD was originally designed as a study of changes in HIV treatment patterns, and has been described in detail elsewhere (25-27). In AHOD, data are collected on a core set of variables including sex, age, HIV exposure category, hepatitis B virus surface antigen (HBV), hepatitis C antibody status (HCV), CD4 and CD8 cell

This article is protected by copyright. All rights reserved

Author Manuscript

counts, viral load, ARV history, AIDS illnesses, date and cause of death. Data variables are sent electronically to the Kirby Institute.

AHOD data collection commenced in 1999 and currently 27 hospitals, sexual health clinics, and general medical practices throughout Australia contribute data twice annually. At March 2013, over 3000 patients had been recruited to AHOD, and 2,328 were under active follow-up, 90% of whom were receiving ARV for HIV infection.

For the current study ten sexual health clinics within AHOD were invited to provide prospective data from 2010.Besides the core AHOD data above, extra STI-specific data variables were extracted from each clinic database. They included confirmed diagnoses of STI, (infectious syphilis, chlamydia, gonorrhoea, and genital warts), site of infection, and STI treatment.

STATISTICAL METHODS

This analysis included all patients who were in active follow-up at the ten participating sites, screened at least once for an STI and had a least one CD4 and viral load test during the follow-up period. The cohort follow-up was from March 2010 to March 2013. Time-to the first incident STI infection (chlamydia, gonorrhoea, syphilis or genital warts) was summarised using Kaplan-Meier plots. The Log Rank test was used to compute p-values comparing the survival curves. Risk factors were assessed using Cox proportional hazard model (28). Covariates considered included sex, age at enrolment, mode of HIV exposure, decade of HIV diagnosis, prior STI diagnosis, hepatitis B or C coinfection, CD4 cell count and HIV RNA viral load. Co-variates that changed over time (CD4 cell count and HIV RNA viral load) were included as time-updated variables. Time to a diagnosis of an STI was the endpoint, therefore the latter co-variates were updated each time they

This article is protected by copyright. All rights reserved

Author Manuscript

were measured, and were thus used to predict the future risk of an STI. Our endpoint was time from when prospective follow-up began (March 2010) to first STI diagnosis. People who did not experience a STI diagnosis were censored at date of last follow-up.

A multivariate model including all covariates was used to assess independent associations. Sensitivity analyses were performed assessing risk factors for each individual STI. All analyses were performed using the statistical packages SAS and STATA (29,30).

Additional ethics approval was sought for the current sub-study and approved by local Human Research Ethics Committees.

RESULTS

At March 2013, there were 598 patients (that had been recruited to the parent cohort) with prospective data from the participating sites, of which 547 patients had been STI screened at least once. There were 489 remaining patients that had further CD4 and viral load test results available to be included in the analysis. All were receiving ARV. There were 110 first incident STI events observed over 1015 person-years (pys), a crude rate of 10.8 (95% CI: 9.0-13.0) per 100 pys. When considering multiple STI diagnoses during the follow up period, there were 202 incident STI events observed over 1071 pys, a crude rate of 18.9 (95% CI: 16.4-21.7) per 100 pys.

The 110 incident STI events consisted of 155 separate STI diagnoses, where 78 patients had one STI diagnosis and 32 patients had 2 or more STI diagnoses. Of the 155 STI diagnoses, there were 59 chlamydia, 29 syphilis, 39 gonorrhoea and 28 genital warts. Overall, the STI with known site diagnosis were distributed between rectal (31%), urethral (51%), pharyngeal (7%) and other (12%).

This article is protected by copyright. All rights reserved

Author Manuscript

Table 1 shows patient demographics and characteristics by presence of incident STI infection.

Table 2 shows factors associated with STI diagnosis in univariate and multivariate analysis. Factors independently associated with increased risk of incident STI included younger age (≥50 vs 30-39 years old, adjusted hazards ratio, [aHR]=0.4; 95% CI:0.2-0.8, p<0.001); prior STI infection, (aHR=2.5; 95% CI:1.6-3.8, p<0.001); and heterosexual vs MSM as likely exposure (aHR=0.2; 95% CI: 0.1-0.6; p<0.001). Figs 1-3 illustrate the associations with age, prior STI infection, and exposure to HIV by homosexual contact.

Time-updated CD4 cell count was not independently associated with incident STI (p=0.520). There was an increasing risk of STI with increasing HIV viral load, ($V_L \geq 10^5$ vs $V_L < 10^3$, aHR =1.9; 95% CI: 0.9-4.2), with a dose-response trend albeit not reaching statistical significance, (overall test for trend p=0.095). There was also a suggestion that recent recruits to AHOD (2010-2013 vs 1999-2009) were associated with increased risk (aHR=1.6; 95% CI: 1.0-2.6, p=0.074).

Sensitivity analyses assessing risk factors for the four separate STI were broadly similar for independent risk factors (namely, younger age, prior STI, and being MSM), with some differences in the trend for viral load as follows: chlamydia (aHR=1.4; 95% CI: 0.4-4.2, p=0.496), syphilis (aHR=2.6; 95% CI: 0.7-9.5, p=0.108), gonorrhoea (aHR=3.8; 95% CI: 1.0-14.4, p=0.020)and genital warts (aHR=1.8; 95% CI: 0.3-10.8, p=0.642). However, the separate numbers of incident STI were low, limiting statistical power.

DISCUSSION

We have previously found a high incidence of STI diagnoses in AHOD (24). Routine STI screening of HIV+ve patients is recommended (31), and pretty universally implemented over the period from 2010 onwards – especially in the

This article is protected by copyright. All rights reserved

Author Manuscript

STI clinics included in this analysis. These are HIV+ patients being seen regularly at STI clinics for their HIV treatment. So most patients also had CD4 and viral load measurements.

In the current analysis from 2010, predictive factors for an STI diagnosis included age less than 30 years, being MSM, and a prior history of STI. There was also a suggestion that recent recruits to AHOD might be at increased risk. We also found a non-significant trend towards *prior* higher viral loads being associated with an STI diagnosis.

A number of other studies, in different populations world-wide, have examined *prevalence* of STI amongst HIV-infected persons, and a recent review estimated the median point prevalence was 12% (32). However, most studies were hampered by non-standardised procedures, and were unable to examine risk factors for STI. There have been very few studies that designed to measure *incidence* of STI accurately, or that have collected data on sexual behaviours, drug use, and the use of ARV (33-38)

Overall, the available data support our conclusions that younger age and being MSM are important predictors of subsequent STI. A history of prior STI being a risk factor for future STI diagnosis has not previously been described in HIV-positive populations, although it is an intuitive finding.

Another result in our study was the trend towards association with higher *prior* HIV-1 viral loads (V_L). Although there is compelling evidence associating increased V_L at time of diagnosis of syphilis or herpes simplex infections (but not other STI), these have generally been considered concurrent measurements, and consistent with biological reactivation of HIV-1, and none were on effective ARV (39-42). The study designs have not enabled differentiation of cause from effect. However, regardless of the possible mechanisms, the association between higher

This article is protected by copyright. All rights reserved

Author Manuscript

HIV viral load and an STI diagnosis is of concern. STI are associated with unsafe sexual behaviour, and this combined with the association with higher viral load raises the possibility of an increased risk of onward transmission. The question of whether the effects of STI on viral load are mitigated by successful treatment with ARV is currently a topic of intense interest, and increased risk of STI diagnosis at times when patients have raised HIV viral loads is one possible way in which this strategy might fail. However, our findings require verification in other cohorts.

There are a number of factors that need to be considered when interpreting our results. The strength of our study is its carefully defined characteristics. The prospective data are amenable to precise calculations of STI incidence, and predictive factors. However, there are limitations to our study design. First, although our sample is representative of the parent cohort, (24), the latter may not be representative of the general population with HIV infection. Second, although the pharynx accounted for only 7% of known site diagnoses, this does not necessarily mean that oral transmission is rare. It may simply be that a sexually transmitted pathogen at other sites may be more likely to be symptomatic and/or diagnosed.

Finally, even though STI are (by definition), epidemiologic markers of sexual behaviour, we lack data on the likely most important confounders, namely, the number of sexual contacts, and specified sexual behaviours (23,43). Variations in sexual behaviour strategies in MSM such as serosorting and strategic positioning, which aim to minimise HIV transmission risk, may account for the differential effects upon HIV and STI transmission. It is quite possible that these behavioural strategies are effective at reducing HIV transmission risk but have no effect on STI transmission. In addition, we did not collect detailed information on injecting

Author Manuscript

This article is protected by copyright. All rights reserved

drug use. The increased use of recreational drugs in certain groups of MSM may be an important factor (44,45).

Our results suggest that among HIV positive patients on ARV in Australia, young MSM with a prior history of an STI are at highest risk of a further STI diagnosis.

Author Manuscript

This article is protected by copyright. All rights reserved

ACKNOWLEDGEMENTS

The Australian HIV Observational Database is funded as part of the Asia Pacific HIV Observational Database, a program of The Foundation for AIDS Research, amfAR, and is supported in part by a grant from the U.S. National Institutes of Health's National Institute of Allergy and Infectious Diseases (NIAID) (Grant No. U01-AI069907) and by unconditional grants from Merck Sharp &Dohme; Gilead Sciences; Bristol-Myers Squibb; BoehringerIngelheim; Janssen-Cilag; ViiV Healthcare. The Australian National Health and Medical Research Council also provide support by a program grant (Grant No. 568971) for sexually transmitted infection research. The views expressed in this manuscript do not necessarily represent the position of the Australian Government. The Kirby Institute **(http://www.kirby.unsw.edu.au/)** is affiliated with the Faculty of Medicine, UNSW Australia.

AHOD-STI participating sites:

New South Wales: Holden Street Sexual Health Clinic, Gosford; Lismore Sexual Health & AIDS Services, Lismore; RPA Sexual Health, Camperdown; Blue Mountains Sexual Health and HIV Clinic, Katoomba; Tamworth Sexual Health Service, Tamworth; Nepean Sexual Health and HIV Clinic, Penrith; Illawarra Sexual Health Service, Warrawong; Sydney Sexual Health Centre, Sydney;

Queensland: Cairns Sexual Health Service, Cairns;

Victoria: Melbourne Sexual Health Centre, Melbourne

REFERENCES

1. Wasserheit JN. Epidemiological synergy: interrelationships between HIV and other sexually transmitted diseases. *Sex Transm Dis* 1992; 19: 61–77. doi:10.1097/00007435-199219020-00001

This article is protected by copyright. All rights reserved

Author Manuscript

2. Røttingen JA, Cameron W, Garnett GP. A systematic review of the epidemiological interactions between classic sexually transmitted diseases and HIV. How much really is known? *Sex Transm Dis* 2001; 28: 579–97. doi:10.1097/00007435-200110000-00005
3. Johnson LF, Lewis DA. The effect of genital tract infections on HIV-1 shedding in the genital tract: a systematic review and meta-analysis. *Sex Transm Dis* 2008; 35: 946–59. doi:10.1097/OLQ.0b013e318 1812d15
4. Hayes R, Watson-Jones D, Celum C, van de Wijgert J, Wasserheit J. Treatment of sexually transmitted infections for HIV infection: end of the road or new beginning? *AIDS* 2010; 24: S15–26. doi:10.1097/01. aids.0000390704.35642.47
5. AbdoolKarim Q, AbdoolKarim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, *et al*. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science* 2010; 329: 1168–74. doi:10.1126/science.1193748
6. Grant RM, Lama JR, Anderson PL. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010; 363: 2587–99. doi:10.1056/NEJMoa1011205
7. Baetan D, Donnell , Ndase P, Mugo NR, Campbell JD, Wangisi J, *et al*. Antiretroviral prophylaxis for HIV protection in heterosexual men and women. *N Engl J Med* 2012; 367: 399–410.
8. EDas M, Chu PL, Santos GM. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS ONE* 2010; 5: e11068. doi:10.1371/journal.pone.0011068
9. Montaner JS, Lima VD, Barrios R. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet* 2010; 376: 532–9. doi:10.1016/S0140-6736 (10)60936-1
10. Del Romero J, Castilla J, Hernando V, Rodriguez C, Garcia S. Combined antiretroviral treatment and heterosexual transmission of HIV-1: cross sectional and prospective cohort study. *BMJ* 2010; 340: c2205. doi:10.1136/bmj.c2205

Author Manuscript

This article is protected by copyright. All rights reserved

11. Reynolds SJ, Makumbi F, Nakigozi G. HIV-1 transmission among HIV-1 discordant couples before and after the introduction of antiretroviral therapy. *AIDS* 2011; 25: 473–7. doi:10.1097/ QAD.0b013e3283437c2b
12. Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, *et al*. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 2010; 375: 2092–8. doi:10.1016/S0140-6736(10)60705-2
13. Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 2009; 23: 1397–404. doi:10.1097/ QAD.0b013e32832b7dca
14. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al*. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365: 493–505. doi:10.1056/NEJMoa1105243
15. Lambert-Niclot S, Tubiana R, Beaudoux C, Lefebvre G, et al. Detection of HIV-1 RNA in seminal plasma samples from treated patients with undetectable HIV-1 RNA in blood plasma on a 2002-2011 survey. *AIDS* 2012; 26:971-975
16. Butler DM, Smith DM, Cachay ER, Hightower GK, et al. Herpes simplex virus 2 serostatus and viral loads of HIV-1 in blood and semen as risk factors for HIV transmission among men who have sex with men. *AIDS* 2008; 222:1667-1671
17. Fisher M, Pao D, Brown AE, Sudarshi D, Gill OE, et al. Determinants of HIV-1 transmission in men who have sex with men: a combined clinical, epidemiological and phylogenetic approach. *AIDS* 2010; 24:1739-1747
18. Politch JA, Mayer KH, Welles SL, O'Brien WX, Xu C, Bowman DJ. Highly active antiretroviral therapy does not completely suppress HIV in semen of sexually active HIV-infected men who have sex with men. *AIDS* DOI:10.1097/QAD.0b013e328353b.2012
19. Jin F, Prestage GP, Zablotska I, Rawstorne P, Kippax SC, Donovan B*, et al.* High rates of sexually transmitted infections in HIV positive homosexual men: data from two community based cohorts. *Sex Transm Infect* 2007,83:397-399.

Author Manuscript

This article is protected by copyright. All rights reserved

20. Jin F, Prestage GP, Mao L, Kippax SC, Pell CM, Donovan B*, et al.*Incidence and risk factors for urethral and anal gonorrhoea and chlamydia in a cohort of HIV-negative homosexual men: the Health in Men Study. *Sex Transm Infect* 2007,83:113-119.
21. Middleton MG, Guy RJ, Grulich AE, Donovan BJ, McDonald AM, Kaldor JM. Recent trends in infectious syphilis in men who have sex with men. (Oral Abstract), Australasian Sexual Health Conference, 15-17 Sept 2008, Perth, Australia. *Sexual Health* 2008; 5:389
22. Jin F, Prestage GP, Zablotska I, et al. High incidence of syphilis in HIV-positive homosexual men: data from two community-based cohort studies. *Sexual Health* 2009; 6: 281-284.
23. The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia. Annual Surveillance Report 2014. *The Kirby Institute.* The University of New South Wales, Sydney, NSW 2052, Australia
24. Mulhall BP, Wright S, Allen D, Brown K, Dickson D, Grotowski M, Jackson E, Petoumenos K, Read P, Read T, Russell D, Smith DJ, Templeton DJ, Fairley CK and Law MG. High rates of sexually transmissible infections in HIV-positive patients in the Australian HIV Observational Database: a prospective cohort study. *Sexual Health 2014, 11, 291-297.*http://dx.doi.org/10.1071/SH13074
25. Law MG, Anderson J, Cui J, et al. Trends in antiretroviral treatment for people with HIV in Australia: an observational data base pilot study. *Venereology* 1999:12:97-103
26. The Australian HIV Observational Database. Rates of combination antiretroviral treatment change in Australia, 1997-2000. *HIV Medicine* 2002;3:28-36.
27. Petoumenos K, on behalf of the Australian HIV Observational Database. The role of observational data in monitoring trends in antiretroviral treatment and disease stage. Results from the Australian HIV Observational Database. *J ClinVirol* 2003; 26: 209-22.
28. Cox DR, Oakes D. Analysis of survival data*. London: Chapman and Hall, 1984*
29. SAS. *SAS version 8.02. Cary, NC, USA:SAS Institute 8.02:2001)*
30. STATA *Stata Statistical Software, Release 8.0, College Station, TX:Stata Corporation, 2003)*

Author Manuscript

This article is protected by copyright. All rights reserved

31. *NSW Ministry of Health. Australian Sexually Transmitted Infection and HIV testing guidelines for asymptomatic MSM 2014. Available online at : http://stipu.nsw.gov.au/wp-contents/uploads/STIGMA.Testing guidelines_Final_v5.pdf (verified 8 July 2014)*
32. Kalichman SC, Pellowski J, Turner C. Prevalence of sexually transmitted co-infections in people living with HIV/AIDS: systematic review with implications for using HIV treatments for prevention. Sex Transm Infect 2011; 87: 183–
33. Erbelding EJ, Chung SE, Kamb ML, Irwin KL, Rompalo AM. New sexually transmitted diseases in HIV-infected patients. Markers for ongoing HIV transmission behaviour. J Acquir Immune Defic Syndr 2003; 33: 247–52.
34. Manning SE, Pfeiffer MR, Nash D, Blank S, Sackoff J. Newly diagnosed HIV/AIDS in New York City, 2001–2002: a population based assessment. *Sex Transm Dis* 2007; 34: 1008–11
35. Scheer S, Lee Chu P, Klausner JD, Katz MH, Schwarz SK. Effect of highly active antiretroviral therapy on diagnoses of sexually transmitted diseases in people with AIDS. *Lancet* 2001;357:432-35
36. Manavi K, Luo PL, McMillan A. The three-year positivity rate of ions among persons living with sexually transmitted infections among a group of HIV-infected men attending the Department of Genitourinary Medicine, Edinburgh, UK. *Intl Journal of STD&AIDS* 2005; 16 (11): 730-73
37. Dang T, Jaton-Ogay K, Flepp M, Kovari H, Evison JM, Fehr J, Schmid P, El Amari EB, Cavassini M, Odorico M, Tarr PE, Greub G, and the Swiss Cohort Study. High Prevalence of Anorectal Chlamydial Infection in HIV-Infected Men Who Have Sex with Men in Switzerland. *Clin Infect Dis* 2009; 49:1532-5.
38. Guy R, Wand H, Franklin N, Fairley CK, Chen MY, O'Connor CC, Marshall L, Grulich AE, Kaldor JM, Hellard ME, Donovan B. Chlamydia trends in men who have sex with men attending sexual health services in Australia, 2004-2008. *Sex Transm Dis* 2011;38(4):339-346

Author Manuscript

This article is protected by copyright. All rights reserved

39. Buchacz K, Patel P, Taylor M, Kerndt PR, Byers RH, Holmberg SD, Klausner JD. Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. AIDS 2004; 18: 2075-2079

40. Schacker T, Zeh J, Hu H, Shaughnessy M, Corey L. Changes in Plasma Human Immunodeficiency Virus Type 1 RNA Associated with Herpes Simplex Virus Reactivation and Suppression. JID 2002; 186: 1718-25.

41. Cohen MS, Hoffman IF, Royce RA, Kazembe P, Dyer JR, Daly CC, et al. Reduction of concentration of HIV-1 in semen after treatment of urethritis: implications for prevention of sexual transmission of HIV-1. AIDSCAP Malawi Research Group. Lancet 1997; 349:1868-1873

42. Jarzebowski W, Caumes E, Dupin N, Farhi D, Lascaux AS, et al, for the FHDH-ANRS CO4 Study Team. Effect of early syphilis infection on plasma viral load and CD4 count in Human Immunodeficiency Virus-infected men. *Arch Intern Med* 2012; 172 (16):1237-1243.

43. Holt M, Lee E, Prestage GP, Zablotska I, de Wit J, Mao L. The converging and diverging characteristics of HIV-positive and HIVnegative gay men in the Gay Community Periodic Surveys, 2000–2009.*AIDSCare*2013; 25: 28–37.

44. Gilbart VI, Simms I, Gabin M, Oliver I, Hughes G. High risk drug practices in men who have sex with men. *Lancet* 2013; 381: 1385–9.

45. Kirby T, Thornber-Dunwell M. High risk drug practices tighten grip on London gay scene. *Lancet* 2013; 381: 101–2.

Author Manuscript

This article is protected by copyright. All rights reserved

This article is protected by copyright. All rights reserved

Author Manuscript

Table 1. Patient demographics and characteristics by incident STI.

Factor		STI N (%)	No STI N (%)
Total		*110*	*379*
Sex	Male	106 (96)	352 (93)
	Female	4 (4)	27 (7)
Age (years) at study enrolment (2010)	<30	24 (22)	23 (6)
	30-39	46 (42)	119 (31)
	40-49	30 (27)	128 (34)
	>50	10 (9)	109 (29)
Mode of HIV exposure	MSM[a]	97 (88)	271 (72)
	Heterosexual	4 (4)	55 (15)
	PWID[b]	8 (7)	26 (7)
	Other	1 (1)	27 (7)
Year of cohort enrolment	1999-2009	71 (65)	295 (78)
	2010-2013	39 (35)	84 (22)
Hepatitis B Coinfection (ever)	Yes	3 (3)	14 (4)
	No	69 (63)	299 (79)
	Not Tested	38 (35)	66 (17)
Hepatitis C Coinfection (ever)	Yes	11 (10)	38 (10)
	No	94 (85)	325 (86)
	Not Tested	5 (5)	16 (4)
STI[c] prior to study enrolment (2010)	No	48 (44)	302 (80)
	Yes	62 (56)	77 (20)
CD4 cell count (cells/μL) at study enrolment (2010)	0-349	18 (16)	68 (18)
	350-499	31 (28)	92 (24)

[a] MSM: Men who have sex with men.
[b] PWID: People who inject drugs.
[c] STI: Sexually Transmitted Infection.

This article is protected by copyright. All rights reserved

Author Manuscript

	≥500	61 (55)	217 (57)
	Not tested	0 (-)	2 (1)
HIV viral load (copies/mL) at study enrolment (2010)	<399	68 (62)	308 (81)
	400-9999	18 (16)	25 (7)
	≥10000	24 (22)	42 (11)
	Not tested	0 (-)	4 (1)

Author Manuscript

This article is protected by copyright. All rights reserved

Table 2. Risk factors associated with incident STI.

Factor	Level	events / pys[a]	Rate per 100 pys[a] (95% CI[c])	Univariate Analysis Hazard Ratio (95% CI[C])	Univariate Analysis p-value[b]	Multivariate Analysis Hazard Ratio (95% CI[C])	Multivariate Analysis p-value[b]
Year of cohort enrolment	1999-2009	71 / 829	8.6 (6.8, 10.8)	1.0 (ref)	<0.001	1.0 (ref)	0.074
	2010-2013	39 / 187	20.9 (15.3, 28.6)	2.4 (1.6, 3.6)		1.6 (1.0, 2.6)	
Age (years) at study enrolment (2010)	<30	24 / 76	31.7 (21.3, 47.4)	2.2 (1.3, 3.6)	<0.001	1.5 (0.9, 2.6)	<0.001
	30-39	46 / 341	13.5 (10.1, 18.0)	1.0 (ref)		1.0 (ref)	
	40-49	30 / 326	9.2 (6.4, 13.2)	0.7 (0.4, 1.1)		0.8 (0.5, 1.3)	
	≥50	10 / 273	3.7 (2.0, 6.8)	0.3 (0.1, 0.6)		0.4 (0.2, 0.8)	
Sex	Male	106 / 941	11.3 (9.3, 13.6)	1.0 (ref)	0.090	1.0 (ref)	0.479
	Female	4 / 75	5.4 (2.0, 14.3)	0.4 (0.2, 1.1)		1.4 (0.5, 4.0)	
Mode of HIV exposure	MSM[d]	97 / 748	13.0 (10.6, 15.8)	1.0 (ref)	0.005	1.0 (ref)	0.008
	Heterosexual	4 / 139	2.9 (1.1, 7.7)	0.2 (0.1, 0.6)		0.2 (0.1, 0.6)	
	PWID[e]	8 / 65	12.3 (6.1, 24.6)	0.9 (0.4, 1.9)		1.1 (0.5, 2.5)	
	Other	1 / 63	1.6 (0.2, 11.2)	0.1 (0.1, 0.9)		0.2 (0.1, 1.4)	
STI[f] prior to study enrolment (2010)	Yes	62 / 241	25.8 (20.1, 33.0)	3.9 (2.7, 5.8)	<0.001	2.5 (1.6, 3.8)	<0.001
	No	48 / 775	6.2 (4.7, 8.2)	1.0 (ref)		1.0 (ref)	
Hepatitis B coinfection	Yes	3 / 36	8.3 (2.7, 25.6)	0.9 (0.3, 2.9)	0.001	1.2 (0.4, 4.2)	0.061

[a] pys: Person-years
[b] Global p-values for year of cohort enrolment, age, CD4 cell count and HIV viral load are test for trend. Other global p-values are test for heterogeneity.
[c] CI: Confidence interval.
[d] MSM: Men who have sex with men.
[e] PWID: People who inject drugs.
[f] STI: Sexually transmitted infection.

This article is protected by copyright. All rights reserved

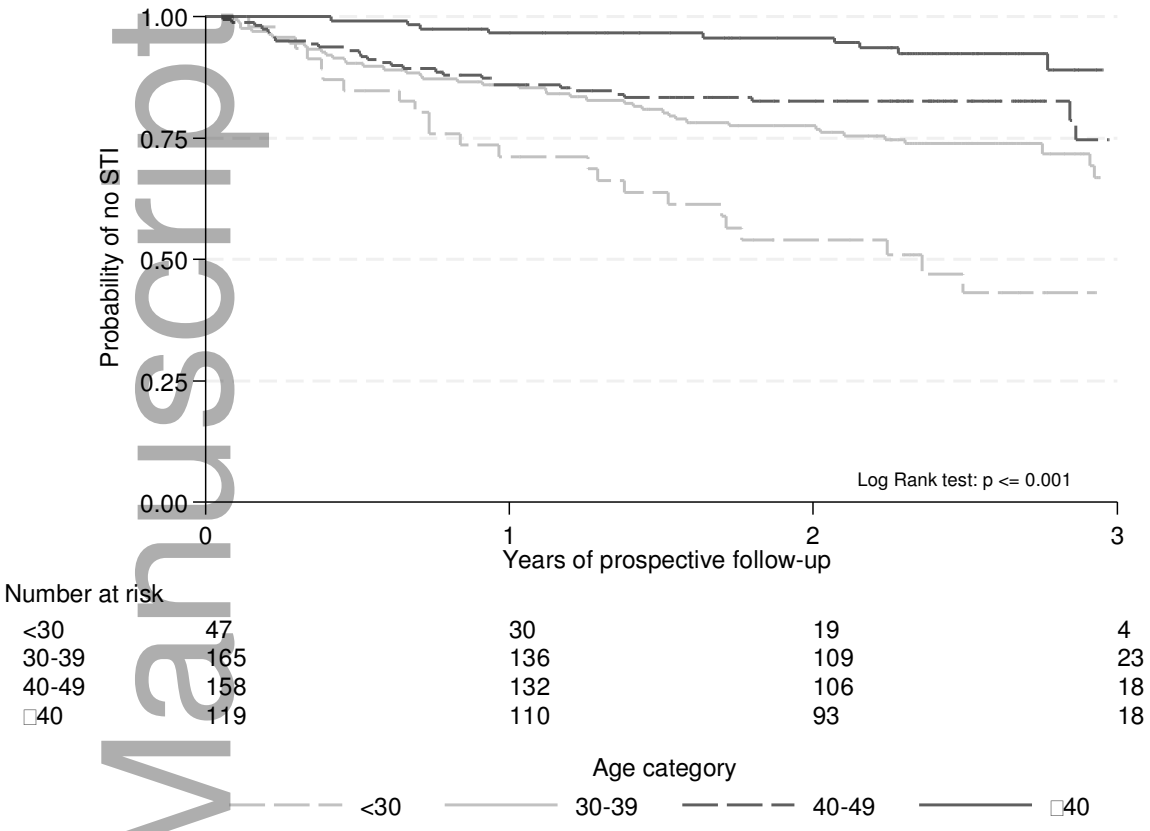
Author Manuscript

(ever)	No	69 / 786	8.8 (6.9, 11.1)	1.0 (ref)		1.0 (ref)	
	Not reported	38 / 193	19.7 (14.3, 27.1)	2.1 (1.4, 3.2)		1.7 (1.1, 2.6)	
Hepatitis C coinfection	Yes	11 / 104	10.5 (5.8, 19.0)	0.9 (0.5, 1.7)	0.923	0.8 (0.4, 1.7)	0.400
(ever)	No	94 / 869	10.8 (8.8, 13.2)	1.0 (ref)		1.0 (ref)	
	Not reported	5 / 42	11.8 (4.9, 28.3)	1.1 (0.5, 2.8)		1.7 (0.7, 3.8)	
CD4 cell count (cells/µL)	0-349	14 / 150	9.3 (5.5, 15.8)	1.0 (0.6, 1.8)	0.418	1.1 (0.6, 2.0)	0.520
(time-updated)	350-499	34 / 214	15.9 (11.3, 22.2)	1.6 (1.0, 2.4)		1.3 (0.9, 2.0)	
	≥500	62 / 651	9.5 (7.4, 12.2)	1.0 (ref)		1.0 (ref)	
HIV viral load (copies/mL)	$<10^3$	79 / 882	9.0 (7.2, 11.2)	1.0 (ref)	<0.001	1.0 (ref)	0.095
(time updated)	10^3-10^4	8 / 45	18.0 (9.0, 35.9)	1.6 (0.8, 3.4)		1.3 (0.7, 2.6)	
	10^4-10^5	15 / 64	23.4 (14.1, 38.7)	2.6 (1.5, 4.5)		1.5 (0.8, 2.9)	
	$\geq 10^5$	8 / 25	31.8 (15.9, 63.6)	3.4 (1.6, 7.1)		1.9 (0.9, 4.2)	

Author Manuscript

This article is protected by copyright. All rights reserved

Figure 1. Kaplan-Meier estimates of the probability of remaining STI free by age category.



Author Manuscript

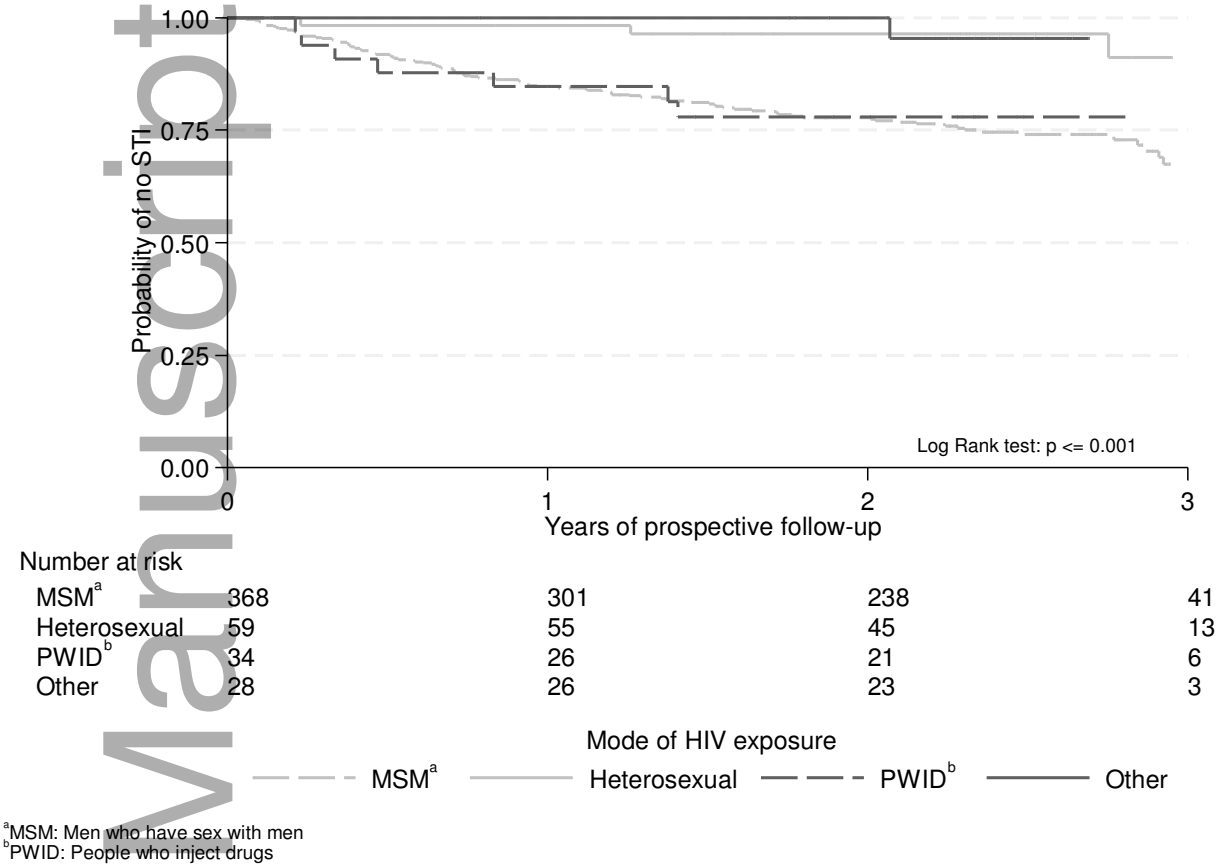
This article is protected by copyright. All rights reserved

Figure 2. Kaplan-Meier estimates of the probability of STI diagnosis by prior STI status.

Author Manuscript

This article is protected by copyright. All rights reserved

Figure 3. Kaplan-Meier estimates of the probability of STI diagnosis by HIV exposure category.



[a]MSM: Men who have sex with men
[b]PWID: People who inject drugs

Author Manuscript

This article is protected by copyright. All rights reserved

University Library

MINERVA ACCESS

A gateway to Melbourne's research publications

Minerva Access is the Institutional Repository of The University of Melbourne

Author/s:
Mulhall, BP; Wright, ST; De La Mata, N; Allen, D; Brown, K; Dickson, B; Grotowski, M; Jackson, E; Petoumenos, K; Foster, R; Read, T; Russell, D; Smith, DJ; Templeton, DJ; Fairley, CK; Law, MG

Title:
Risk factors associated with incident sexually transmitted infections in HIV-positive patients in the Australian HIV Observational Database: a prospective cohort study

Date:
2016-09-01

Citation:
Mulhall, B. P., Wright, S. T., De La Mata, N., Allen, D., Brown, K., Dickson, B., Grotowski, M., Jackson, E., Petoumenos, K., Foster, R., Read, T., Russell, D., Smith, D. J., Templeton, D. J., Fairley, C. K. & Law, M. G. (2016). Risk factors associated with incident sexually transmitted infections in HIV-positive patients in the Australian HIV Observational Database: a prospective cohort study. HIV MEDICINE, 17 (8), pp.623-630. https://doi.org/10.1111/hiv.12371.

Persistent Link:
http://hdl.handle.net/11343/291099

File Description:
Accepted version