Characteristics of Individuals with Heterosexually acquired compared with Homosexually acquired HIV and Implications for Clinical Practice

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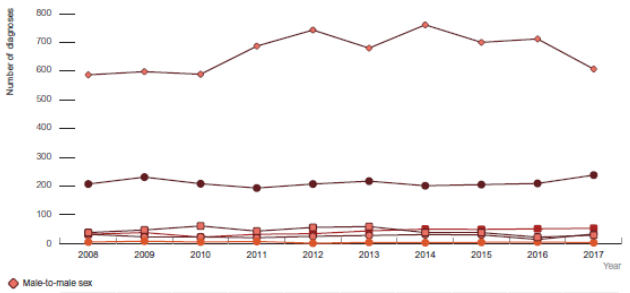
Heterosexually Acquired HIV in Australia

Figure 1.1.9 Number of new HIV diagnoses, 2008–2017, by exposure category



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Male-to-male sex	587	598	589	687	743	680	761	700	712	607
Male-to-male sex and injecting drug use	32	38	22	32	34	44	50	49	51	53
Injecting drug use	32	23	23	20	25	28	31	30	14	33
Heterosexual sex	207	231	208	193	207	217	201	205	209	238
Mother with/at risk of HIV infection	5	8	5	7	1	4	3	4	5	3
Other/undetermined	38	47	61	43	56	59	38	38	22	29

Notes: The 'male-to-male sex' category includes men who had sex with both men and women. One diagnosis was attributed to occupational exposure in healthcare or other settings in the 10 years 2008–2017 and was grouped in the 'Other' category.

Source: State and territory health authorities; see Methodology for detail.

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Heterosexually Acquired HIV in NSW

Research Aims and Methods

Aim:

To inform clinical management investigating differences in clinical characteristics between individuals reported as acquiring HIV via heterosexual contact vs homosexual contact.

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Methods: Study Design

Australian HIV Observational Database (AHOD)

Observational cohort of HIV positive individuals attending sexual health clinics, tertiary referral centres and specialised GP clinics

Patient Selection

All patients enrolled in AHOD diagnosed 1997 or later with **only** homosexual or heterosexual exposure as likely mode of HIV acquisition

(Excluded: homosexual contact + IDU, IDU, blood products or 'other'.)

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Statistical Analyses (1)

Patient characteristics were compared using χ^2 and Wilcoxon rank sum tests, as appropriate:

- Age
- Country of birth
- HBsAg
- HCV Ab (or HCV RNA if HCV Ab positive)
- CD4 count and Viral load (at diagnosis and ART initiation)
- Previous AIDS diagnosis

Characteristics were also compared between males and females within the heterosexual cohort using the same methods

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Statistical Analyses (2)

Cox proportional hazard models were used to determine time to:

- cART initiation
- first viral suppression,
- first treatment failure,
- first treatment change,
- all-cause mortality, and
- loss-to-follow-up (LTFU).

Multivariate models were adjusted *a priori* for age, sex, country of birth, HBsAg, HCV Ab +/- HCV RNA, CD4 count, Viral load, year of diagnosis or year of ART initiation, and clinical care setting.

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Results- Patient Characteristics by Exposure

	Homosexual Exposure 9457 PYFU	Heterosexual Exposure 3127 PYFU	P value
n	**1467**	**513**	
Median age at diagnosis	35.7 (29.2-43.5)	35.5 (28.9-46.2)	0.280[A]
Country of birth			
Australia	729 (60.1%)	166 (37.5%)	<.001[B]
other	484 (39.9%)	277 (62.5%)	
missing	254	70	
Most recent HBsAg			
positive	45(3.8%)	17 (3.9%)	0.937[B]
negative	1132 (96.2%)	418 (96.1%)	
missing	290	78	
Most recent HCV Ab+/-RNA			
positive	105 (7.8%)	22 (4.8%)	0.029[B]
negative	1246 (92.2%)	439 (95.2%)	
missing	116	52	

[A] Wilcoxon rank sum test
[B] χ^2 test

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Results- Patient Characteristics by Exposure (2)

	Homosexual Exposure 9457 PYFU	Heterosexual Exposure 3127 PYFU	P value
n	**1467**	**513**	
CD4 count			
at diagnosis	450 (290-635)	292 (122-574)	<.001[A]
missing	588	211	
at cART initiation	340 (220-503)	270 (156-410)	<.001[A]
missing	370	108	
Viral Load			
at diagnosis	61,075 (12,106-204,000)	63,463 (9,333-160,000)	0.276[A]
missing	597	212	
at cART initiation	65,847 (14,800-180,328)	41,200 (3,800-141,104)	<.001[A]
missing	392	116	
Previous AIDS Diagnosis			
yes	154 (10.5%)	77 (15.0%)	0.006[B]
no	1313 (89.5%)	436 (85.0%)	

[A] Wilcoxon rank sum test
[B] χ^2 test

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Patient Characteristics **(Heterosexual Exposure only)** by Gender

	Male	Female	P value
n	**282**	**231**	
Median age at diagnosis	40.7 (31.1-51.6)	32.0 (27.6-39.7)	<.001[A]
Country of birth			
Australia	109 (45.2%)	57 (28.2%)	<.001[B]
other	132 (54.8%)	145 (71.8%)	
missing	41	29	
Most recent HBsAg			
positive	6 (2.6%)	11 (5.5%)	0.119[B]
negative	228 (97.4%)	190 (94.5%)	
missing	48	30	
Most recent HCV Ab+/-RNA			
positive	15 (6.0%)	7 (3.3%)	0.178[B]
negative	235 (94.0%)	204 (96.7%)	
missing	32	20	

[A] Wilcoxon rank sum test
[B] χ^2 test

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Patient Characteristics **(Heterosexual Exposure only)** by Gender

	Male	Female	P value
n	**282**	**231**	
CD4 count			
at diagnosis	256 (102-510)	358 (173-630)	0.009[A]
missing	104	107	
at cART initiation	250 (129-388)	280 (180-430)	0.020[A]
missing	51	57	
Viral Load			
at diagnosis	97,724 (23,800-228,544)	22,191 (4,650-100,000)	<.001[A]
missing	106	106	
at cART initiation	60,400 (10,514-190,000)	23,262 (1,548-100,000)	0.002[A]
missing	53	63	
Previous AIDS Diagnosis			
yes	49 (17.4%)	28 (12.1%)	0.097[B]
no	233 (82.6%)	203 (87.9%)	

[A] Wilcoxon rank sum test
[B] χ^2 test

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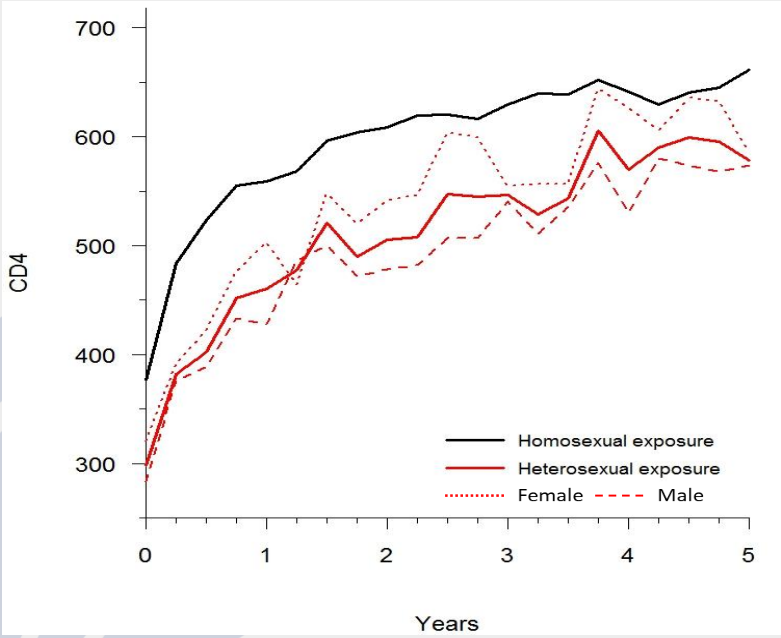
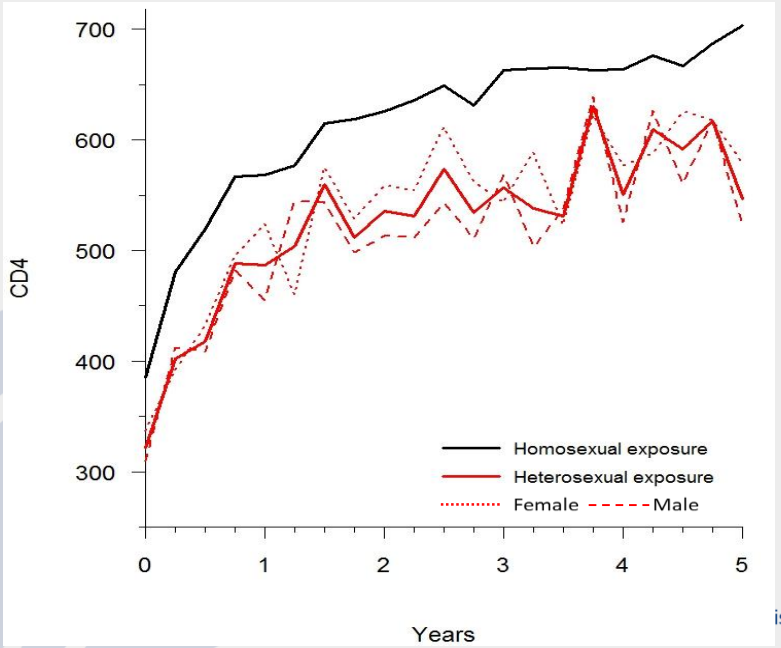
CD4 Response (entire cohort 1997 onwards)



CD4 Response (patients starting ART 2007 or later)



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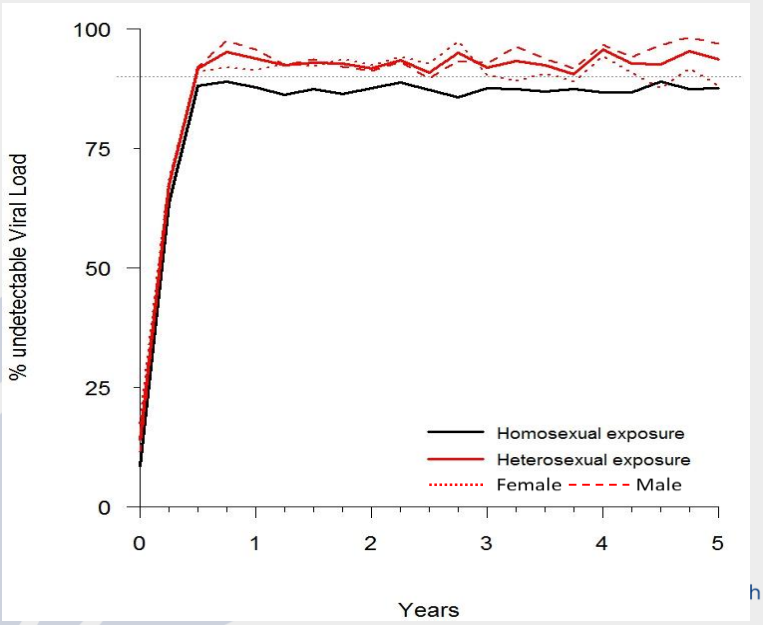
Viral Load Response, % undetectable (<400 copies/ml)
(entire cohort 1997 onwards)



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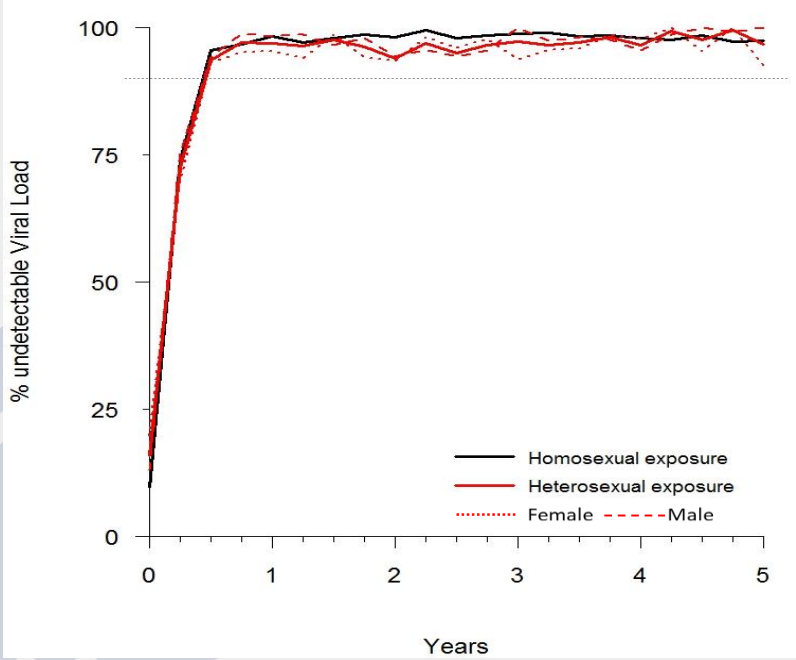
VL Response, % undetectable (starting ART 2007 or later)



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Clinical end-point univariate and covariate-adjusted Cox proportional hazard ratios

End-Point	Hazard ratio (homosexual exposure referent)	95% CI	P- value
Viral Suppression			
univariate	1.02	0.90-1.16	0.721
multivariate[A]	1.06	0.90-1.24	0.470
Virological Failure			
univariate	0.87	0.67-1.13	0.298
multivariate[A]	0.97	0.69-1.37	0.861
1st Treatment Change			
univariate	1.01	0.89-1.16	0.849
multivariate[A]	0.88	0.72-1.07	0.210

[A]Adjusted for sex, age at ART initiation, country of birth, HCV Ab +/- HCV RNA, HBsAg, CD4 count at ART initiation, HIV viral load at ART initiation, year of ART initiation and clinical care setting.

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Clinical end-point univariate and covariate-adjusted Cox proportional hazard ratios

End-Point	Hazard ratio (homosexual exposure referent)	95% CI	P- value
ART Initiation			
univariate	1.17	1.06-1.30	0.003
multivariate[B]	1.04	0.90-1.19	0.591
All cause mortality			
univariate	0.79	0.43-1.45	0.447
multivariate[C]	0.58	0.27-1.25	0.161
Loss-to-follow-up			
univariate	0.80	0.66-0.97	0.024
multivariate[B]	0.75	0.58-0.98	0.034

[B]Adjusted for sex, age at diagnosis, country of birth, HCV Ab +/- HCV RNA, HBsAg, CD4 count at diagnosis, HIV viral load at diagnosis, year of diagnosis and clinical care setting.
[C]Adjusted for sex, age at cohort enrolment, country of birth, HCV Ab+/-HCV RNA, HBsAg, CD4 cell count cohort enrolment, HIV viral load at cohort enrolment, year of ART initiation and clinical care setting.

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Results Summary

- Compared to homosexuals, heterosexuals in AHOD:
  - less likely to be Australian-born
  - less likely to have current Hepatitis C infection
  - lower CD4 counts at diagnosis and cART initiation
  - don't reconstitute their CD4 counts to similar levels, despite similar viral suppression on cART
  - no difference in all-cause-mortality
  - less likely to be lost-to-follow-up
- Compared to female heterosexuals, male heterosexuals in AHOD:
  - older at HIV diagnosis
  - more likely to be Australian-born
  - lower CD4 counts at diagnosis and cART initiation
  - higher viral loads at diagnosis and cART initiation

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Discussion

- Limitations:
  - Size of heterosexual group
  - Generalisability to other populations
  - Limited by scope of AHOD data
    - Missing data
    - lack of specific pregnancy data available in AHOD
    - Adherence to therapy not measured
    - 'heterosexual' - self reported

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Implications for Clinical Practice

- Identifies at risk groups for heterosexually acquired HIV (young overseas-born females, older Australian men)
- More likely to be overseas born:
  - Issues including lack of Medicare, compassionate access for ART more likely to affect heterosexuals
  - Language and cultural barriers
  - Greater role for involvement of multicultural health services and support workers
- Late diagnoses:
  - Role for greater health promotion and increased screening (little perceived risk, esp heterosexual men)
  - Low CD4 counts may mean a greater risk of HIV related complications
- Less risk of loss to follow up than MSM.

Mortality

- No difference in all-cause Mortality between groups in our study
- However:
  - Several studies have shown increased risk of mortality when ART commenced at lower CD4 counts[1,2].
  - Heterosexual men mostly diagnosed >50yo. Older age has been associated with poorer outcomes (delayed start ART, more frequent treatment changes, impaired immune reconstitution[3])
  - Australian study found no difference in mortality between men and women living with HIV in Australia[4].
  - ?limited by numbers and scope for further research

[1] Kitahata Mari M *Effect of Early versus Deferred Antiretroviral Therapy for HIV on Survival,* N Engl J Med 2009;360:1815-26
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[4] M. L. Giles *et al. How do outcomes compare between women and men living with HIV in Australia? An observational cohort study.* Sexual Health, *2016(13);155-161*

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Conclusion

- Largely consistent with known Australian surveillance data
- Builds on existing data
  - Heterosexuals have lower rates of current Hepatitis C infection
  - Heterosexuals have lower CD4 counts at ART initiation
  - After 5y of treatment CD4 counts remain below those of homosexually acquired HIV
  - Clinical endpoints- no difference between groups
  - Lower rates of loss-to-follow-up
- Ongoing research will further help to characterise this cohort.

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Definitions

- ART Initiation:
  - Time from diagnosis to cART initiation
- Viral suppression:
  - Time to VL<400copies/ml from cART start
- Virological Failure:
  - Time to VL>1000 copies/ml after reaching suppression.
- LTFU:
  - No data for that participant uploaded from any site in >12months since last visit.
- Treatment Change: A change from the initial treatment regimen that involves either
  - At least 2 drugs added, or
  - At least one drug of a different class added, or
  - At least two drugs dropped and one added.

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Time Windows

- Time windows for CD4 and VL measurements at time points (dates prior always prioritised)
  - At diagnosis: 90 days prior to 30 days after
  - At ART initiation: 180 days prior to 14 days after.

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