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HIV infected young people in Australia: data from the Australian HIV Observational Database (AHOD)

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Abstract

Objectives: We aimed to describe demographic factors, virologic and clinical outcomes of individuals aged 13–24 years diagnosed with HIV.

Methods: Patients diagnosed with HIV after 1997 in the Australian HIV Observational Database were divided into young adults, diagnosed at age <25 years (n=223), and older adults (n=1957). Demographic and clinical factors were compared between groups.

Results: Young adults had a median age at diagnosis of 22 years (IQR 20–24) and median age at treatment initiation of 24 years (IQR 22–26). They were more likely to be female than the older cohort (21.1% vs 10.8% $p<0.001$). Men who have sex with men was the most common exposure category in both groups. CD4 count at diagnosis was significantly higher in younger than older adults (median 460 vs 400 cells/mm³, $p=0.006$), whereas HIV viral load at diagnosis was lower (35,400 vs 61,659 copies/mL, $p=0.011$). The rate of loss to follow up (LTFU) was higher in young adults (8.0 vs 4.3 per 100PY, $p<0.001$). Young adults were more likely to have a treatment interruption compared to older adults (5.3 vs 4.0 per 100PY, $p=0.039$). Rates of treatment switch, time to treatment change, and CD4 and viral load responses to treatment were similar between groups.

Conclusions: Young adults were diagnosed with HIV at higher CD4 counts and lower viral loads than their older counterparts. LTFU and treatment interruption were more common highlighting the need for extra efforts directed towards retention in care and education regarding the risks of treatment interruptions.

Keywords

HIV; adolescent; young adult; epidemiology

Introduction

Worldwide, HIV infection in young people is common and is associated with significant morbidity and mortality. In 2015, the Centers for Disease Control and Prevention (CDC) estimated that 22% of the approximately 40,000 new HIV infections in the USA were among youth 13 to 24 years of age¹. In Australia in 2015, 2.1% of all new HIV diagnoses were among individuals 19 years of age or younger, with the majority (86.3%) of new diagnoses aged between 13 to 19 years². Globally in 2014, an estimated 4 million adolescents were living with HIV. In the preceding seven years, mortality in HIV-positive adolescents rose by 50% in stark contrast to older age groups, where worldwide mortality decreased by 30%³. In 2012, HIV/AIDS was the second leading cause of mortality in adolescents globally, whereas it was not within the top 10 causes of adolescent death a decade earlier⁴. Adolescent girls and young women are disproportionately affected, accounting for 20% of new HIV infections in 2015 worldwide⁵.

Adolescence (13–19 years) and young adulthood (20–24 years) are periods with significant physical, cognitive, social and psychological change, presenting a particular challenge in those with chronic diseases such as HIV infection. Whilst statistics regarding adolescents living with HIV worldwide are readily available, there is more limited information about

young adults (aged 20–24), despite evidence that the brain, in particular the frontal lobe, has not fully developed until after this period⁶ with consequent effects on executive and other function^{7–9} likely to influence their interaction with the health system.

Compared with older adults, both perinatally- and behaviourally-infected adolescents and young adults have been reported to have lower rates of viral suppression, higher rates of virological failure and loss to follow up (LTFU)^{10–13}. Despite the majority of new HIV infections in young adults being acquired through sexual transmission with opportunities for early ART initiation¹⁴, young adults often experience delayed ART initiation compared to older adults¹⁵.

To date, there have been no studies describing the demographics, treatment, adherence, virological control and immunological factors among Australian youths living with HIV. Our aim was to provide clinically useful information to aid physician engagement and management of young HIV-positive individuals, and highlight important areas in transition to adult HIV services with the goal of improving long term outcomes of HIV-positive Australian youth.

Methods

Study population

The Australian HIV Observational Database (AHOD) is an observational cohort study of more than 4000 adults living with HIV in Australia under routine clinical care. Details of this cohort have been published elsewhere¹⁶. Briefly, data are transferred electronically to the Kirby Institute at the UNSW Sydney, every six months for aggregation, quality control and analysis. Core data variables include: sex; date of birth; date of most recent visit; HIV exposure; hepatitis B virus (HBV) surface antigen status; hepatitis C virus (HCV) antibody status; CD4 and CD8 counts; HIV viral load; antiretroviral treatment data; AIDS-defining illnesses; and date and cause of death. Ethics approval was obtained from the UNSW Sydney Human Research Ethics Committee and all other relevant institutional review boards, and written informed consent was obtained from all patients¹⁶.

In these analyses we included all AHOD participants who were aged less than 25 years at time of diagnosis (young adults) and compared them to those aged greater than or equal to 25 years at diagnosis (older adults). Participants diagnosed with HIV prior to 1st January 1997 were excluded to omit selection bias from the period prior to ART. All data from ART initiation until either death, most recent clinic visit, or cohort censoring date (31 March 2017) were used.

Variables considered in our comparison were: sex, patient care setting (sexual health clinic, specialist general practice, or tertiary referral centre), country of birth, mode of HIV exposure, Aboriginal/ Torres Strait Islander descent, culturally and linguistically diverse (CALD) background, smoking status, hepatitis B and C infection, time of treatment initiation, CD4 count and HIV viral load, treatment interruptions, mortality, loss to follow-up (LTFU) and ART switches. CALD was defined as those born outside of Australia/New Zealand in a non-English speaking country or born in Australia/New Zealand with ethnicity

not Caucasian; and excluded those who identify as Aboriginal, Torres Strait Islander or Maori. We defined LTFU as lost to AHOD for greater than 365 days between the last clinic visit and the censor date. ART switches were defined as the addition of at least one different antiretroviral class to the original ART regimen, the addition of two drugs of the same class, or the removal of at least two drugs and concurrent addition of at least one drug of the same class. ART regimen duration and treatment interruptions needed to be at least 14 days to be considered for the analyses. We selected the closest CD4 cell count or plasma HIV viral load to HIV diagnosis, ART initiation, and first ART switch within a window of three months prior and one month post. Similarly, CD4 cell count and plasma HIV viral load at 12 and 24 months after ART initiation were taken as the values closest within a window of ± 3 months.

Statistical analysis

We tabulated patient characteristics by age at diagnosis (aged under 25 years, 25 years and older). Differences between the two groups were assessed using Pearson's χ^2 test or Fisher's exact test for categorical variables, and the Mann–Whitney U-test for comparison of metric variables. Differences in rates were assessed by exact tests. We used Cox proportional hazards models to evaluate factors associated with time to the first ART switch. Stepwise backward selection of covariates (with a significance level of 0.05 for removal) and *a priori* inclusion of age was used to develop a multivariate model. Multivariate linear regression models *a priori* adjusted for age, gender, period of ART initiation, treatment interruptions and CD4 at treatment initiation were used to analyse the mean CD4 cell count response after 12 and 24 months of ART respectively

All statistical tests were performed two-sided and P-values below 0.05 were considered statistically significant. Analyses were conducted using R Version 3.3.2¹⁷ and SAS/STAT software, Version 9.4 of the SAS system for Windows (SAS Institute, Cary NC).

Results

Demographics and Risk Profiles

Of those 2180 patients diagnosed after 1997, there were 223 who were under 25 years of age at diagnosis. Patient characteristics are shown in Table 1. Of the young adult group, 47 (21.1%) were women compared with 211 (10.8%) in the older age group ($p < 0.001$). Median age at diagnosis was 22 years in the young adult group (IQR 20–24) versus 37 years (IQR 31–45) in the older group. In the younger cohort, 196 patients initiated ART treatment at a median age of 24 years (IQR 22–26). The median age at most recent visit was 29 years (IQR 25–34).

The most common exposure category in the young adults was men who have sex with men (MSM) (66.8%), and was no different from the older age group. Of note, the 'other' category which includes perinatal transmission accounted for only 4 patients in the younger adult group (1.8%).

In the young adult group, 17 females (36.2%) were from CALD backgrounds (34% non-CALD and 29.8% missing data) and in the male group 53 (30.3%) were from CALD backgrounds (45.7% non-CALD and 24% data missing).

Treatment Setting

Patient care settings were predominantly sexual health clinics (54.3% in young adults and 48.7% in older adults, $p=0.24$), followed by general practitioner (GP) and hospital tertiary centres for both groups. Data regarding the location at initial diagnosis and treatment initiation was not recorded.

Immunological and Virological Status

Median CD4 count at diagnosis was 460 cells/mm³ (IQR 312–622) in the young adult group, and was significantly higher than that of the older cohort (median 400 cells/mm³, IQR 200–607, $p = 0.006$). However, CD4 counts at the time of treatment initiation were no different. There was no significant difference between groups in terms of CD4 count at first ART switch.

HIV viral load was significantly lower in the young adult group at diagnosis (median 35,400 copies/mL (IQR 9,240–97,099) vs 61,659 copies/mL (IQR 10,000–189,000), $p=0.011$) but there was no significant difference in viral loads at the time of treatment initiation. Viral loads were generally low at the time of first ART switch with the younger cohort median VL 49 (IQR 39–1200) at first switch compared with the older cohort median VL of 50 (IQR 39–399, $p=0.824$). The percentage of those with an undetectable viral load was also similar at time of first switch (60.5% in the younger cohort vs 62.2% in older cohort, $p=0.763$).

At the time of the current analyses, there were 142 patients (63.7%) in follow up from the young adult cohort, compared with 1385 (70.8%) from the older cohort. The most recent median CD4 count was 700 cells/mm³ (IQR 525–850) in the young adult group, compared with 689 cells/mm³ (IQR 501–888) in the older cohort ($p=0.85$). There were more than 90% with an undetectable viral load in both groups.

Treatment and Outcomes

Rates of mortality, loss to follow up, treatment switch and interruption and CD4 count/viral load testing are shown in Table 2. A time to death analysis was not performed as only two deaths occurred in the young adult cohort. Significantly more young adults were lost to follow up (incidence 8.0 vs. 4.3 per 100PY, $p<0.001$). Treatment interruption was also significantly more likely in the younger cohort (5.3 per 100PY vs 4.0, $p=0.039$). Rates of treatment switch were similar between the groups.

Factors associated with time to first treatment change are shown in Table 3 and did not significantly differ between the two groups.

Tables 4 shows the mean CD4 cell count response after 12 months and 24 months of ART initiation for young adults versus their older peers adjusted for gender, year of ART initiation, initial CD4 cell counts and treatment interruptions. After 12 months the younger age group had a significantly greater mean CD4 count recovery (+35.9 cells/mm³, $p=0.04$) although this difference disappeared at 24 months (−5.3 cells/mm³, $p=0.82$).

Discussion

This is the largest study to date of HIV infection in Australian youth, and offers insight into possible intervention targets in management of this difficult to engage and retain group. As a group, young Australians with HIV are made up of a higher proportion of women, have a lower viral load and higher CD4 count at time of diagnosis, and a higher rate of loss to follow up and treatment interruption.

Overall demographic factors were similar between the two comparator groups. Individuals diagnosed with HIV under 25 years of age in Australia were predominantly male, although a greater proportion of newly diagnosed young adults were females compared to their older counterparts. In part these figures reflect overall trends in Australia with an increasing but relatively small proportion of women diagnosed with HIV¹⁸, and they are also reflective of migration trends in Australia¹⁹. In our cohort, male-to-male sexual contact was the predominant risk factor for HIV acquisition in both groups, and most received their HIV care at publicly funded sexual health clinics. Risk factors were similar to US data in 2014, where 70% of HIV infection in adolescents and young adults was attributed to male to male sexual contact²⁰.

There was a statistically significant lower viral load at time of diagnosis in the younger adult group compared to older adults, which is in contrast to a number of other studies^{21, 22} showing youth had a higher VL at diagnosis. The reason for this difference is not clear but is unlikely to represent earlier diagnosis in Australian youths compared with other developed countries. In a 2014 survey of 200 Australian youth aged 16–20 who identified as same sex attracted, 70% reported being previously tested for sexually transmitted infections²³. This is comparable to the United States where in men who have sex with men aged 18–24 surveyed in 2008, 66.8% reported having a HIV test in last 12 months²⁴. In another 2014 study, from Zhejiang province in China, 61.9% of youths less than 25 years who identified as having had male partners had had a HIV test previously²⁵. In our young cohort, there was also a significantly higher CD4 count at diagnosis which may be explained by higher CD4 counts seen in healthy, HIV-uninfected, children and young adolescents^{26, 27}. The median age of our older adult cohort was 37 years, therefore immunosenescence and weaker immunological response in that group seems unlikely. Our findings contradict what has been suggested in the literature: that HIV infected youth have higher levels of CD4+ and CD8+ T-cell immune activation and exhaustion compared with matched controls²⁸, and that they are less likely to experience immunological recovery compared with older adults²⁹.

This difference between the groups in terms of VL and CD4 count at diagnosis was no longer seen at treatment initiation, suggesting a delay in the commencement of ART in the young adult group, which may be less likely to occur in the current era with guidelines recommending treatment initiation at diagnosis. This is supported by historical US data where only 62% of adolescents diagnosed with HIV engage with medical care in the year following HIV diagnosis¹². Reassuringly in our cohort of those engaged in care, there was no significant difference between the younger and older adults in terms of current viral suppression.

There was a significantly higher loss to follow up rate to AHOD in the younger cohort compared with older adults, consistent with findings from other studies^{12, 30}. Zandoni et al report that by combining data from published US studies only 43% of adolescents and young adults are retained in care over a 1–3 year period¹². In a previous analysis of loss to follow up rates from the entire AHOD cohort³¹, multivariate predictors of LTFU were heterosexual exposure, higher VL, time under follow up and prior LTFU; and each additional year of age was associated with decreased risk of LTFU. However, that particular study showed no significant increase in mortality, thought to be consistent with timely reengagement with treatment, possibly via linkage with other healthcare providers not included in the AHOD study.

Rates of treatment interruption were also significantly higher in the younger cohort. Mao et al found in a self-reported survey of HIV positive gay men in Australia, younger age was one factor associated with non-use of ART (along with recent HIV diagnosis, lack of welfare support and lack of annual sexually transmissible infection screening)³². Possible explanations for the higher rate of treatment interruption in young people include “treatment holidays”, or non-adherence due to medication related reasons (such as complexity or side effects) as well as patient related issues (such as mental health problems, financial reasons, substance abuse or other psychosocial issues)^{33–35}. However, this has potentially detrimental implications, given previous studies have shown that with treatment interruption immunologic decline may be substantial and difficult to reverse³⁶.

AHOD is a large, prospective, curated database and by only looking at those diagnosed after the introduction of triple therapy ART we have omitted selection bias. However, there remain some limitations to this study. Firstly, there were very few perinatally infected participants captured in our study. This reflects excellent perinatal HIV management in Australia, which has avoided any perinatal HIV transmission in recent years⁷. Also, participants in the AHOD database are recruited in adult settings (tertiary hospital clinics, sexual health clinics etc) and thus perinatally infected children cared for by paediatric services may be missed if not referred later to these services. Therefore we are unable to extrapolate the above findings to the perinatally infected group, who are more likely to be treatment experienced and have less favourable resistance profiles. Secondly, there were very few deaths amongst participants, preventing us from determining factors associated with mortality or performing a time to death analysis. Thirdly there is some selection bias related to enrolment onto the AHOD database, and may underestimate the true prevalence of adolescent/young adult group living with HIV in the community, including those yet to be diagnosed, with the CDC estimating that as high as 60% of adolescents infected with HIV in the US are undiagnosed³⁷.

Results from this study could lead to better targeted interventions for HIV positive youth in Australia. This may include more effort and resources directed toward retention of adolescents and young adults in medical care, paired with increased education about importance of follow up and continuation of treatment. Use of sexual health services may be problematic for paediatric populations, and increased focus on transition from paediatric to adult care with innovative, youth friendly services may benefit retention in care and decrease treatment interruption.

Directions for future research may include ongoing longitudinal studies of the AHOD cohort to follow this adolescent/young adult population over a longer period of time, along with increased participant numbers to gain further information about long term outcomes, particularly mortality. It would also be worthwhile enrolling children and adolescents cared for by paediatric services, and longitudinally following their clinical progress into adulthood. Comparison of our young adults with those from other populations with varying demographics may also be helpful in ascertaining differences in outcomes and possible reasons for those differences.

Conclusion

This is the first large prospective study of Australian youth living with HIV. Adolescents and young adults diagnosed with HIV were mostly male, with the predominant risk exposure of male-to-male sexual contact, and were most commonly seen in sexual health clinics. Young adults in our cohort were diagnosed with HIV at higher CD4 counts and lower viral loads than their older counterparts, though this difference was no longer apparent at treatment initiation. LTFU and treatment interruptions were both significantly more common among young adults highlighting the need for extra efforts and funding directed towards retention in care, improved education regarding the risks of treatment interruptions and further support for young people attending HIV services.

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Table 1.

Patient characteristics.

	Under 25 years at diagnosis	25 years or older at diagnosis	p Value
Total patients	223	1957	
Gender			
male	175 (78.5%)	1744 (89.1%)	<.001 *
female	47 (21.1%)	211 (10.8%)	
transgender	1 (0.5%)	2 (0.1%)	
Age at diagnosis (years)			
median (IQR)	22 (20–24)	37 (31–45)	-
Age at treatment initiation (years)			
n	196	1787	
median	24 (22–26)	39 (33–48)	-
Age at most recent visit/ DOD (years)			
median (IQR)	29 (25–34)	47 (40–55)	-
Patient care setting			
General practitioner	63 (28.3%)	587 (30.0%)	0.240
Hospital tertiary centre	39 (17.5%)	417 (21.3%)	
Sexual health clinic	121 (54.3%)	953 (48.7%)	
Country of birth			
Australia/New Zealand	99 (44.4%)	1012 (51.7%)	0.078
other	78 (35.0%)	594 (30.6%)	
missing	46 (20.6%)	351 (17.9%)	
Exposure category			
MSM	149 (66.8%)	1323 (67.6%)	0.140 *
MSM/injecting drug use	1 (0.5%)	46 (2.4%)	
heterosexual	57 (25.6%)	443 (22.6%)	
injecting drug use	7 (3.1%)	39 (2.0%)	
other	4 (1.8%)	62 (3.2%)	
missing	5 (2.2%)	44 (2.2%)	
Aboriginal/Torres Strait Islander			
no	143 (64.1%)	1332 (68.1%)	0.193 *
yes	7 (3.1%)	37 (1.9%)	
missing	73 (32.7%)	588 (30.1%)	
Smoking			
no	64 (28.7%)	439 (22.4%)	0.022
yes	32 (14.4%)	377 (19.3%)	
missing	127 (57.0%)	1141 (58.3%)	
Hepatitis B infection			
no	166 (74.4%)	1544 (78.9%)	0.612
yes	5 (2.2%)	65 (3.3%)	
missing	52 (23.3%)	348 (17.8%)	

	Under 25 years at diagnosis	25 years or older at diagnosis	p Value
Hepatitis C Antibody			
no	187 (83.9%)	1625 (83.0%)	0.231
yes	12 (5.4%)	157 (8.0%)	
missing	24 (10.8%)	175 (8.9%)	
Treatment initiation			
<2001	27 (12.1%)	328 (16.8%)	<.001
2001–2004	18 (8.1%)	246 (12.6%)	
2005–2007	11 (4.9%)	212 (10.8%)	
>2007	140 (62.8%)	1001 (51.2%)	
never started treatment	27 (12.1%)	170 (8.7%)	
Time off treatment (days)			
n	39	402	
median (IQR)	1063 (166–1999)	428 (116–1304)	0.071
CD4 at diagnosis (cells/mm ³)			
n	141	1363	
median (IQR)	460 (312–622)	400 (200–607)	0.006
CD4 at treatment initiation (cells/mm ³)			
n	153	1477	
median (IQR)	350 (250–515)	324 (193–500)	0.088
CD4 at first ART switch (cells/mm ³)			
n	77	891	
median (IQR)	524 (306–702)	480 (306–680)	0.699
CD4 nadir (cells/mm ³)			
n	216	1900	
median (IQR)	311 (229–422)	270 (152–400)	<.001
CD4 recent (cells/mm ³)			
n	135	1323	
median (IQR)	700 (525–850)	689 (501–888)	0.848
HIV viral load at diagnosis (copies/ml)			
n	137	1357	
median (IQR)	35,400 (9,240–97,099)	61,659 (10,000–189,000)	0.011
HIV viral load at treatment initiation (copies/ml)			
n	156	1510	
median (IQR)	12,428 (389–71,300)	22,382 (399–105,000)	0.065
HIV viral load at first ART switch (copies/ml)			
n	81	902	
undetectable (<50 copies/ml)	49 (60.5%)	561 (62.2%)	0.763
median (IQR)	49 (39–1200)	50 (39–399)	0.824
HIV viral load recent (copies/ml)			
n	131	1289	
undetectable (<50 copies)	120 (91.6%)	1211 (94.0%)	0.291
median (IQR)	20 (19–40)	20 (19–40)	0.491

	Under 25 years at diagnosis	25 years or older at diagnosis	p Value
Patients in follow-up			
n	142 (63.7%)	1385 (70.8%)	

Abbreviations: IQR, inter quartile range; DOD, date of death; MSM, men who have sex with men

p values calculated excluding missing values

* Fisher exact test

Table 2.

Comparison of Outcomes

	U25 at diagnosis	25 or older at diagnosis	p Value
Total patients	223	1957	
Mortality			
deaths	2 (0.9%)	66 (3.4%)	
incidence rate per 100 PY	0.22 (0.05–0.87)	0.57 (0.45–0.72)	0.176
LTFU to AHOD			
LTFU	74 (33.2%)	503 (25.7%)	
incidence rate per 100 PY	8.01 (6.37–10.05)	4.32 (3.96–4.72)	<.001
Treatment switch			
switches	167	2006	
incident rate per 100 PY	14.75 (12.68–17.07)	14.74 (14.11–15.39)	0.984
Treatment interruption			
interruptions	60	540	
incidence rate per 100 PY	5.30 (4.12–6.72)	3.97 (3.65–4.31)	0.039
Length of treatment interruption (days)			
Median (IQR)	409 (125–1084)	228 (70–789)	0.046
CD4 testing			
total visits median (IQR)	9 (4–15)	12 (5–24)	
rate per PY	2.45 (2.35–2.55)	2.54 (2.51–2.57)	0.074
VL testing			
total visits median (IQR)	9 (4–17)	13 (6–26)	
rate per PY	2.48 (2.39–2.59)	2.66 (2.63–2.69)	0.001

Abbreviations: IQR, inter quartile range; LTFU, loss to follow-up; PY, person-year; VL, viral load.

Table 3.

Factors associated with time to first treatment change.

	Treatment change		Univariate analysis		Multivariable analysis		
	No	Yes	HR (CI)	P	aHR (CI)	P	P overall
Overall	795	1188					
Age group							
diagnosed at 25 or older	702	1085	1		1		
diagnosed U25	93	103	0.97 (0.78–1.17)	0.729	1.00 (0.78–1.25)	0.986	
Sex							
male	710	1036	1				
female	84	151	1.04 (0.87–1.23)	0.666			0.710
transgender	1	1	0.50 (0.03–2.19)	0.483			
Patient care setting							
Sexual health clinic	396	551	1				
General practitioner	234	361	1.03 (0.90–1.18)	0.636			0.325
Hospital tertiary centre	165	276	1.12 (0.97–1.29)	0.134			
Country of birth							
Australia/New Zealand	398	629	1				
other	264	351	1.07 (0.94–1.22)	0.304			0.212
missing	133	208	1.14 (0.98–1.34)	0.094			
Aboriginal/Torres Strait Islander							
no	532	827	1				
yes	15	27	0.85 (0.56–1.22)	0.401			0.452
missing	248	334	1.06 (0.93–1.20)	0.392			
HIV exposure category							
MSM	541	792	1				
MSM/IDU	15	25	1.31 (0.86–1.91)	0.182			0.565
heterosexual contact	184	277	1.02 (0.89–1.17)	0.736			
IDU	17	27	0.97 (0.64–1.39)	0.874			
other	24	38	0.83 (0.59–1.13)	0.263			
missing	14	29	1.16 (0.78–1.65)	0.428			

	Treatment change		Univariate analysis			Multivariable analysis		
	No	Yes	HR (CI)	P	P overall	aHR (CI)	P	P overall
ever smoking								
no	188	274	1					
yes	130	250	1.00 (0.84–1.18)	0.981	0.989			
missing	477	664	1.01 (0.88–1.16)	0.915				
ever HBV								
no	595	981	1					
yes	31	35	0.82 (0.58–1.14)	0.260	0.492			
missing	169	172	0.96 (0.82–1.13)	0.638				
ever HCV								
no	664	997	1			1		
yes	49	105	1.23 (1.00–1.50)	0.045	0.017	1.28 (1.02–1.59)	0.026	0.017
missing	82	86	1.28 (1.02–1.59)	0.027		1.29 (0.99–1.64)	0.050	
Period of ART initiation								
<2001	59	296	1					
2001–2004	45	219	1.07 (0.89–1.27)	0.471	0.442			
2005–2007	67	156	0.90 (0.74–1.10)	0.302				
>2007	624	517	1.02 (0.88–1.19)	0.819				
CD4+ at ART initiation								
Per 10 cells/mm ³	651	979	1.00 (1.00–1.00)	0.668				
Per 100 cells/mm ³			0.99 (0.97–1.02)	0.668				
CD4+ nadir								
Per 10 cells/mm ³	785	1143	1.00 (1.00–1.00)	0.504				
Per 100 cells/mm ³			0.99 (0.96–1.02)	0.504				
log HIV viral load at ART initiation								
Per 1 log ₁₀ (copy/ml)	664	993	1.04 (0.99–1.09)	0.108				

Abbreviations: ART, antiretroviral therapy; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; HR, hazard ratio; IDU, injecting drug use;

Table 4.

Adjusted mean CD4 response after 12 and 24 months of ART initiation.

Variable	After 12 months of ART		After 24 months of ART	
	Coefficient (β)	P-Value	Coefficient (β)	P-Value
Age group				
25 years and older	ref		ref	
U25	35.9	0.038	-5.3	0.816
Gender				
male	ref		ref	
female	-5.7	0.712	10.4	0.592
transgender	45.3	0.807	353.2	0.103
Period of ART initiation				
>2007	ref		ref	
<2001	-11.8	0.373	-4.6	0.776
2001–2004	-19.1	0.214	-28.5	0.138
2005–2007	4.2	0.798	-4.2	0.829
Treatment interruptions				
per interruption	-95.7	<0.001	-130.8	<.001
CD4 at treatment initiation				
500+	ref		ref	
<200	102.5	<0.001	138.1	<.001
200–349	86.3	<0.001	135.1	<.001
350–499	74.1	<0.001	90.4	<.001

For 12 month calculations n=1413, nU25=130, for 24 month calculations n=1212, nU25=99

Abbreviations: ART, antiretroviral therapy;