The Australian HIV Observational Database Temporary Residents Access Study (ATRAS)

UNSW AUSTRALIA

Kirby Institute

napwha national association of people with HIV australia

THE AUSTRALIAN HIV OBSERVATIONAL DATABASE TEMPORARY RESIDENTS ACCESS STUDY (ATRAS)

One year follow-up

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Further copies can be obtained by contacting:

Dr Kathy Petoumenos

Email: kpetoumenos@kirby.unsw.edu.au

Phone: +612 9385 0900

The Kirby Institute

University of New South Wales

Cnr of Boundary and West Streets

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Contents

EXECUTIVE SUMMARY

The Australian HIV Observational Database Temporary Residents Access Study (ATRAS) commenced in November 2011. ATRAS provides antiretroviral treatments (ART) via a compassionate access scheme for up to 4 years to 180 HIV-positive patients who are temporary residents in Australia and ineligible for Medicare. Patients were recruited to ATRAS via the Australian HIV Observational Database (AHOD), a long-term HIV-positive observational cohort study. Recruitment via AHOD allowed for ongoing follow-up of these patients by a well-established mechanism to assess the clinical outcomes in these patients. ATRAS is the first study in Australia to systematically collect visa and HIV related information for a subgroup of HIV-positive patients who are Medicare ineligible.

All 180 HIV-positive temporary residents were recruited to ATRAS by the end of June 2012. This report describes the patient characteristics as well as outcomes one year after enrolment. In addition, two surveys of s100 (Highly Specialised Drugs program) prescribers were conducted to estimate the current numbers of HIV-positive patients who are temporary residents and ineligible for Medicare supported ART in Australia.

Key findings:

- The majority of ATRAS patients were male (N=133; 74%) and the mean (SD) age for men and women was similar (35.19 (9.40) and 34.99 (6.77) respectively).

- The most common visa types were Student visa (33%), closely followed by Working (sponsored or business) visa (31%), and then Bridging visa (14%). The remaining patients were either on Spousal (13%) or Other (13%) visa
- The majority of ATRAS patients were from Asia/South East Asia (46%), followed by Sub-Saharan Africa (19%), 11% each from South America and South Pacific, 9% from Europe and 6% North America
- Prior to enrolment:
    - 63% of ATRAS patients were already receiving ART
    - Less than half of ATRAS patients (47%) had an undetectable viral load (HIV RNA $\leq$ 50 copies/ml).
    - Median CD4 cell count was 343 cells/μl (IQR: 222-479)
- By month 12 of follow-up:
    - The proportion with an undetectable viral load had increased to 88%
    - CD4 cell count increased by an average of 118 cells/μl (SD: 165)
- In one year of follow-up 39 patients no longer required ART via ATRAS, this represents a rate of 22/100 person years.
    - The majority (N=33; 85%) of these patients had become eligible for Medicare
- The number of Medicare ineligible HIV-positive temporary residents in Australia in care over the last 2 years is estimated at 450, of whom 141 are in ATRAS.
- The reduction in detectable viral load in ATRAS from 53% at baseline to 12% at one year is estimated to correspond to approximately a 75% reduction in the risk of onward HIV transmission from ATRAS patients.

1. INTRODUCTION

The Australian Government, through the Pharmaceutical Benefits Scheme (PBS) Highly Specialised Drugs (s100) program provides fully subsidised antiretroviral (ART) treatment (Note: patients may be required to pay a pharmaceutical dispensing fee). To be eligible to receive ART under this scheme, a patient needs to be entitled to a Medicare card. Australian citizens are therefore able to access their ART equitably. However inequity in terms of treatment access exists for those living in Australia but who are ineligible for Medicare.

Persons ineligible for Medicare include temporary residents who are approved for non-permanent entry into Australia and under various visa arrangements, including student, business, and employer sponsored work visas. Their initial visa period is generally for more than three months but not more than four years [1], but visa renewals are common among those who are awaiting decisions regarding permanent residency applications. In this context, it is notable that entry to Australia on a temporary visa often leads to permanent residency, with 22,307 permanent residency visas granted to applicants who previously held 457 (working) visas in 2011-2012 [2].

Although living in Australia legally, HIV-positive temporary residents are not entitled to the same level of care as HIV-positive permanent residents. According to a 2007 survey of s100 prescribing general practitioners, of their HIV-positive temporary resident caseload, only 60% of patients who should be on ART were receiving effective ART, while 31% were said to be receiving sub-optimal treatment [1].

Further, due to their Medicare ineligibility, HIV-positive temporary residents who require ART must purchase medications at full cost, with no provision for subsidised arrangements. Cost of treatment is prohibitive for most. For example, Atripla, a co-formulated tablet containing three antiretrovirals, and currently the recommended first line regimen, is estimated to cost $12,438 per individual annually in Australia [3].

The majority of HIV-positive temporary residents are thought to source their ART from their country of origin, or overseas online, and most in generic form. A smaller proportion receive ART by participating in Australian clinical trials, while a few pay full price or receive ART via various compassionate access programs [1, 4, 5]. Accessing ART overseas poses serious issues for clinicians prescribing ART. Costs influence drug choice and subsequently may prevent appropriate treatment for the individual. Many ARTs currently considered optimal standard treatment are not available in generic form, while some are not available in countries where these patients may have to return. Ordering overseas may also result in treatment interruptions due to late ordering or stock supply issues leading to additional and frequent unscheduled treatment visits.

In 2009-2010 there were 306,030 temporary visas granted [6], and the number of 457 working visa holders in Australia has reached an all-time high of 86,050 in January 2012 [2]. As HIV testing is not required prior to entry for most (although required for an application for permanent residency), the exact number of temporary residents who were HIV-positive prior to arrival in Australia is unknown. In 2007 consultation between the National Association of People with HIV Australia (NAPWHA) and the Australasian Society of HIV Medicine (ASHM) with s100

prescribers, and with contacts from the Australian Health Protection Committee's Blood borne Virus and Sexually Transmissible Infection Standing Committee (BBVSS), had estimated numbers at around the 250 – 300 across the country.

In Australia, as in other developed countries, most treated HIV-positive patients now achieve durable HIV suppression with ART, and HIV is no longer a terminal illness, but rather a chronic illness, both treatable and manageable. HIV-positive patients have vastly improved long-term clinical outcomes, AIDS related conditions have become less common, and death rates have dramatically reduced [7-14] . Effective ART not only delays progression of HIV disease, but there is now clear evidence that ART also reduces risk of heterosexual HIV transmission by way of reduced viral load [9-15]. Yet, despite the success of ART, new HIV diagnoses in Australia remain at around 1000 per year since 2006 [15].

Reducing the rate of HIV transmission in Australia along with minimizing the personal and social impacts of HIV infection is a key focus of the current National HIV strategy (Sixth National HIV Strategy 2010-2013) [16]. Aiming for universal ART coverage, therefore, has significant public health implications, in particular, reducing risk of HIV transmission. In July 2013, all Australian Health Ministers' endorsed new national HIV prevention and treatment targets [17], which align with those agreed to by all countries under the 2011 United National Political Declaration on HIV/AIDS (UNPD). These Australian targets are:

a) Reduce sexual transmission of HIV by 50% by 2015.
b) Sustain the low general population rates of HIV in Aboriginal and Torres Strait Islander people and communities.

c) Sustain the virtual elimination of HIV amongst sex workers.
d) Sustain the virtual elimination of HIV amongst people who inject drugs.
e) Sustain the virtual elimination of mother-to-child HIV transmission.
f) Increase treatment uptake by people with HIV to 90% by 2015.
g) Maintain effective prevention programs targeting sex workers and for people who inject drugs.

Endorsement of these new prevention and treatment targets for Australia's HIV response by all Australian Health Ministers – based on scientific advances in HIV and UNPD commitments - will provide important guidance to the States/Territories and the Commonwealth Government as they move to update their HIV strategic plans and programs.

Achieving these targets will necessarily involve a policy to provide ART to all people in Australia living with HIV, including people who are Medicare ineligible.

Data suggest that in Australia approximately 13% of HIV-positive patients on effective ART still have a detectable viral load [18], and are therefore infectious and at risk of HIV transmission. If indeed only 60% of HIV-positive temporary residents are receiving effective ART [1], then it is expected that rates of detectable viral load in this population would be up to 50%, underlining the vulnerability of this group of the HIV population in Australia, and the disproportionate number expected to have poorer outcomes and disease progression rates. Such prognosis would have serious

public health implications, as well as adversely affect therapeutic options for clinical management of the HIV-positive individual. Negative outcomes may include loss of patients to follow-up clinical care, development of HIV drug resistance, and inadequate monitoring of disease progression.

It remains unclear what proportion of this population require ART, what level of ART they are currently receiving, what stage of their HIV disease they are in, their age, gender, country of origin, and length of time in the country, whether they apply for permanent residency or whether they return home. Furthermore, the impact of sub-optimal treatment and care for this group on their long-term disease outcome is not well understood or described. Doctors treating these patients are having to manage these patients on limited resources, and are often unable to adequately fulfil their duty of care. Australian government policy allows these individuals to live and work in Australia, yet there remains a disconnect between Australian government policy in terms of the extent of support for these temporary residents compared with the current National HIV strategy [16].

Finally, the potential risk of HIV transmission from this population has also not been previously investigated. In the current era of treatment as prevention, consideration of this population needs to be included in any future policy. The NSW Ministry of Health HIV strategy 2012 – 2015 has set a number of ambitious targets based on those agreed to under the 2011 UNPD, which include working towards the virtual elimination of HIV and increased ART uptake to more than 90% of the HIV infected population. Priority areas of action include the promotion of increased testing and treatment uptake and linking HIV positive people to prevention, treatment and care

services. For this 'test and treat' approach to be successful in working toward the elimination of HIV then HIV-positive temporary residents must be included. Similar goals to NSW are proposed in the QLD HIV Strategy 2013-2015 released in September 2013. It is expected that other States/Territories may also endorse new HIV prevention and treatment targets in lines with those endorsed by the Australian Health ministers [17].

The lack of data and the need to provide access to treatment to all people living in Australia lead to efforts by NAPWHA during 2010/2011 to engage all seven pharmaceutical companies with registered HIV antiretroviral drugs to commit to providing ART to 180 HIV-positive temporary residents in Australia for up to four years. By July 2011, all seven companies (AbbVie, Boehringer-Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Jannsen Pharmaceuticals, MSD, ViiV Healthcare) were committed to this scheme, and following ethics approval, the Australian HIV Observational Database Temporary Residence Access Study (ATRAS) commenced in November 2011.

1.1 Aims

The overall aims of ATRAS are as follow:

Aim 1: To describe the population of HIV-positive temporary resident patients who are currently ineligible for subsidised ART via the s100 scheme. Specifically to:

- determine reasons for ineligibility (eg visa status and type)

- determine the length of time for these patients to become eligible for Medicare; or alternatively time taken to return to country of origin (or leave Australia).

Aim 2: To describe the HIV disease status of these patients and to assess short and long-term outcomes of optimal ART, including:

- monitoring patterns of ART use, including the efficacy of different treatment regimens, related to demographic factors and markers of HIV disease stage
- monitoring how often patients are changing ART regimens, and the reasons for treatment changes
- monitoring patterns of toxicities/adverse events associated with ART use, related to demographic factors and markers of HIV disease stage
- monitoring clinical outcomes including HIV related and non-HIV related causes of death

Aim 3:

a) To model HIV transmission rates in Australia if HIV-positive temporary residents do not receive effective ART.

b) To undergo a cost-effectiveness analysis to assess the costs to government for providing subsidised treatment and medical care to HIV-positive temporary residents, and assess economic impact if these individuals do not receive ART. The intention will be to estimate the costs of providing HIV treatment services (either in full or limited to antiretroviral therapy only) to Medicare ineligible HIV-positive

temporary residents to the estimated full costs of treatment for those who could be infected if this population does not receive treatment.

This current report which is based on one year follow-up data will focus on Aim 1 and parts of Aim 2.

2. RESEARCH METHODS

HIV-positive patients who are currently under clinical care and legal residents, but are ineligible for Medicare PBS, or for any other program that can provide antiretroviral treatment access, and who satisfy an income level means test were invited to participate in ATRAS. Patients were recruited via the Australian HIV Observational Database (AHOD), a long-term prospective observational cohort study of more than 3,000 HIV-positive patients. AHOD commenced in 1999 and is a collaboration of 28 currently active tertiary referral centres, sexual health clinics and specialist general practices throughout most states and territories of Australia [19].

Recruitment via AHOD allowed a standardised patient follow-up and monitoring mechanism. The core data variables collected in AHOD include clinical and treatment information recorded in most HIV treatment clinics as part of routine clinic care. AHOD is an entirely observational study, patients therefore are not required to make any additional visits or undergo any additional tests other than those dictated by local standard of care. These data are electronically transferred to The Kirby Institute, University of New South Wales (UNSW) where AHOD is managed.

2.1 Data collection

The core HIV related variables routinely collected in AHOD include:

- patient identifiers – name code (first two letters of surname and given name), sex, date of birth, cultural/ethnic group, Aboriginal and/or Torres Strait Islander identity

- clinical history – exposure category, date of first HIV positive test, date of last HIV negative test, hepatitis B and C status
- stage of disease - CD4 and CD8 counts, HIV viral load, AIDS defining illness
- antiretroviral treatments and reasons for stopping/changing antiretroviral treatment
- cause of death (using a standardised data collection form)
- laboratory parameters: albumin, AST ALT, S-creatinine, total cholesterol, HDL, triglycerides, blood glucose, and blood pressure

In addition to the core data routinely collected in AHOD, the following data variables were collected at the time of recruitment:

- visa status and type
- country of origin
- year arrived in Australia
- employment status
- applied for permanent residency

In addition to the regular six monthly clinical data transfers, there is an annual update for ATRAS patients regarding visa status, employment status, if they have applied for permanent residency, or if they have become eligible for Medicare.

2.3 Provision of Antiretroviral treatment

Supply of ART is provided on a compassionate basis for a maximum of four years. As temporary resident visas are for a maximum of four years, it is expected that almost all recruited patients will either have applied for permanent residency (eligible

for Medicare) or returned home after this time. At the initial visit the patient is consented, an ART drug supply form is completed and sent to the relevant pharmaceutical companies. Once a patient has received a temporary Medicare card then provision of ART will no longer be supplied directly by the companies, instead will be covered by Medicare.

2.4 Ethical approval

ATRAS participants were required to provide written informed consent prior to enrolment. Ethics approval was sought and provided by the University of New South Wales Human Research Ethics Committee and from ethics committees with local jurisdiction over participating sites as required. These committees work in accordance with NHMRC guidelines. Strict procedures for maintaining patient confidentiality were adhered to at all times.

3. RESULTS

3.1 ATRAS participant characteristics

Recruitment to ATRAS commenced November 7, 2011, and was completed by end of June 2012 when a total of 180 Medicare ineligible patients were enrolled from 21 AHOD sites. Details are summarised in Table 1. The majority of ATRAS patients were male (N=133; 74%). The mean (SD) age for men and women was similar (35.19 (9.40) and 34.99 (6.77) respectively). Most of the participants were recruited via sexual health clinics (N=82, 46%) followed evenly by general practice (27%) and tertiary referral centers (27%). Most men were recruited from general practices (GP: 34%) or sexual health clinics (44%). While the majority of women were recruited via tertiary referral centres (41%) or sexual health clinics (50%), with only a few women were recruited via GPs (9%).

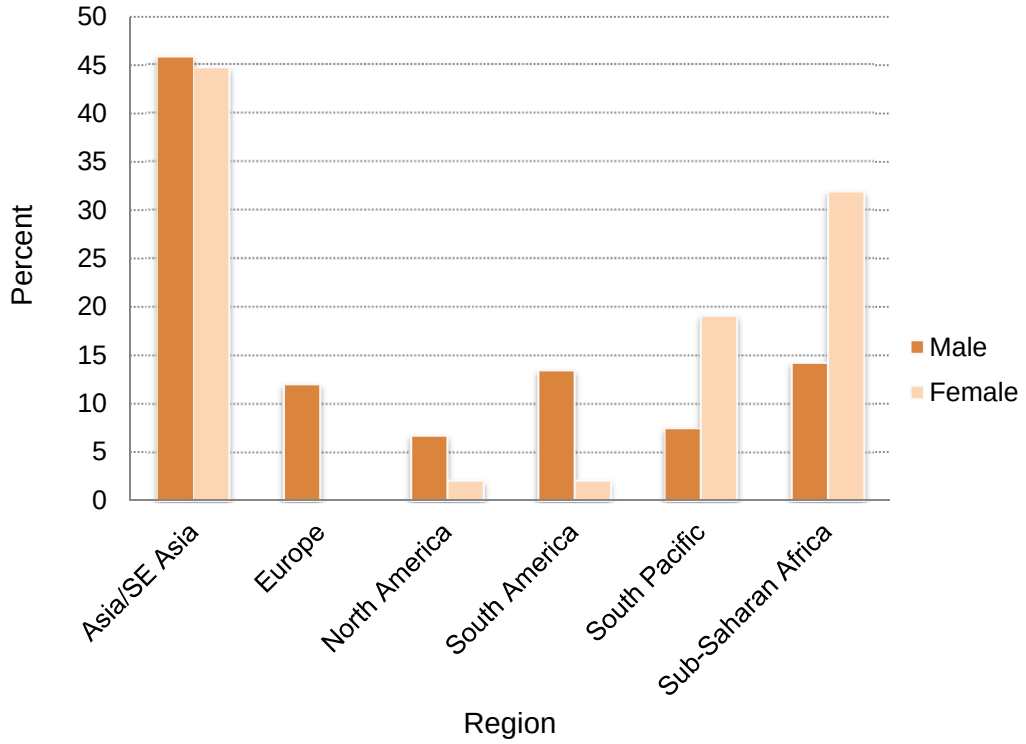
3.1.1 Region of origin

ATRAS patients were from various regions around the world (Table 1). The majority from Asia/South East Asia (46%), followed by Sub-Saharan Africa (19%), 11% each from South America and South Pacific, 9% from Europe and 6% North America. The majority of patients were from Thailand (16% of men and 26% of women). The following most common countries or origin were India and Zimbabwe for men (9% and 7% respectively), and PNG and Zimbabwe for women (13% each). Figure 1 illustrates the region of birth for men and women.

Table 1: Patient characteristics at enrolment by sex

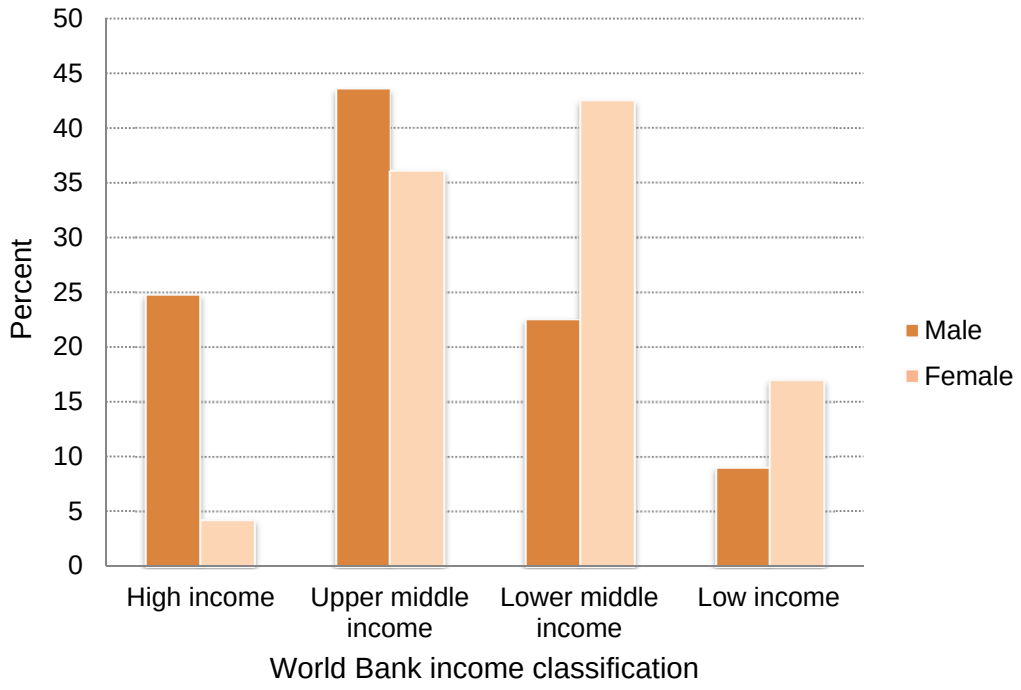
	Female		Male		Total	
	N	%	N	%	N	%
Total	47	26	133	74	180	
Mean Age (SD)	35.0	(6.77)	35.2	(9.40)	35.1	(8.77)
AHOD clinic type						
General Practice	5	10.6	44	33.1	49	27.2
Tertiary referral Centre	19	40.4	30	22.6	49	27.2
Sexual Health Clinic	23	48.9	59	44.4	82	45.6
Visa type						
Bridging	2	4.3	24	18.0	26	14.4
Spouse	10	21.3	6	4.5	16	8.9
Student	15	31.9	45	33.8	60	33.3
Working	9	19.1	46	34.6	55	30.6
Other	11	23.4	12	9.0	23	12.8
Region						
Asia/SE Asia	21	44.7	61	45.9	82	45.6
Europe	0	0.0	16	12.0	16	8.9
North America	1	2.1	9	6.8	10	5.6
South America	1	2.1	18	13.5	19	10.6
South pacific	9	19.1	10	7.5	19	10.6
Sub-Saharan Africa	15	31.9	19	14.3	34	18.9
World Bank Criteria						
High income	2	4.3	33	24.8	35	19.4
Upper middle income	17	36.2	58	43.6	75	41.7
Lower middle income	20	42.6	30	22.6	50	27.8
Low income	8	17.0	12	9.0	20	11.1
Year arrived						
<2006	12	25.5	25	18.8	37	20.6
2007	6	12.8	15	11.3	21	11.7
2008	4	8.5	21	15.8	25	13.9
2009	11	23.4	24	18.0	35	19.4
2010	4	8.5	18	13.5	22	12.2
2011	6	12.8	21	15.8	27	15.0
2012	4	8.5	8	6.0	12	6.7
Missing	0	0.0	1	0.8	1	0.6
Employment						
Full time	8	17.0	40	30.1	48	26.7
Part-time/Casual/Self	12	25.5	51	38.3	63	35.0
Student	8	17.0	18	13.5	26	14.4
Unemployed	19	40.4	20	15.0	39	21.7
Unknown/other	0	0.0	4	3.0	4	0.2

Figure 1: Region of origin by sex



Country of origin was also categorised by income according to World Bank Classification (WBC) criteria. As the WBC criteria are regularly updated, 2011-12 classification was used to reflect the period of recruitment into ATRAS. The classification groups are: High income: non OECD, High income: OECD, Upper middle income, Lower middle income and Low income. The majority of patients were from upper middle income countries (42%), 28% from lower middle income, 11% from low income, and the remaining 20% from High income (OECD plus non-OECD) countries. More men (69%) were from upper middle or high incomes countries compared to women (37%) (Figure 2).

Figure 2: Word bank classification for income by sex



3.1.2 Visa type

The most common visa types were Student visa (33%), closely followed by Working visa (31%), and then Bridging visa (14%). The remaining patients were either on Spousal (13%) or Other (13%) visa. The type of visa varied by sex (Table 1), with similar proportions of men on either Working or Student visas (35% and 34% each), and a further 18% were on Bridging visa. While only 4.5% of men are on a Spousal visa. Among females, 19%, 23% and 32% were on Working, Spousal and Student visas respectively, and only 5% on Bridging visas.

Visa type also varied by region of birth. The majority of patients from North America, Europe and Sub-Saharan Africa were on Working visas (80%, 56% and 56%

respectively). While the majority of patients for Asia/South East Asia were on Student visas (47%). Most of the participants from the South Pacific were Other (42%). Among ATRAS patients already receiving ART prior to enrolment, the reported source of ART was broadly similar for all visa types apart from Other, where more than 70% of this group sourced their ART from overseas, compared to between 35% and 49% for all other visas types (Table 2).

Table 2: Visa characteristics by Region of birth and prior ART source

	Bridging		Spouse		Student		Working		Other		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
Total	26	14.4	16	8.9	60	33.3	55	30.6	23	12.8	180	
Region of origin												
Asia/SE Asia	11	13.4	10	0.1	39	47.6	14	17.1	8	9.8	82	45.6
Europe	6	37.5	0	0.0	1	6.3	9	56.3	0	0.0	16	8.9
North America	1	10.0	0	0.0	0	0.0	8	80.0	1	10.0	10	5.6
South America	2	10.5	0	0.0	13	68.4	3	15.8	1	5.3	19	10.6
South Pacific	1	5.3	4	0.2	4	21.1	2	10.5	8	42.1	19	10.6
Sub-Saharan Africa	5	14.7	2	0.1	3	8.8	19	55.9	5	14.7	34	18.9
Total on ART	*18*		*9*		*34*		*34*		*18*		*113*	*62.8*
Prior ART source												
Compassionate access	2	11.1	5	55.6	12	35.3	3	8.6	3	16.7	25	21.9
Country	8	44.4	4	44.4	12	35.3	16	47.1	13	72.2	53	46.9
Full paying	0	0.0	0	0.0	0	0.0	0	0.0	1	5.6	1	0.9
Trial	2	11.1	0	0.0	5	14.7	6	17.1	0	0.0	13	11.4
Unknown	6	33.3	0	0.0	5	14.7	9	25.7	1	5.6	21	18.4

3.1.3 HIV related characteristics

The main mode of reported HIV exposure among men was men who have sex with men (66%) followed by heterosexual contact (23%). Among women, the majority reported heterosexual contact (85%). Less than 2% of the ATRAS patients reported injecting drug use as mode of HIV exposure (Table 3).

At the time of enrolment, 63% of patients were already receiving ART, slightly greater proportions of women (74%) compared to men (59%). The main source of

ART was from overseas (47%), compassionate access (22%), or clinical trial (11%). Of those who received prior ART, twice as many women (34%) compared with men (17%) received ART via compassionate access.

Table 3: HIV related characteristics at enrolment by sex

	Female		Male		Total	
	N	%	N	%	N	%
	47		133		180	
HIV exposure category						
MSM (+MSM/IDU)	0	0.0	89	66.9	89	49.4
Heterosexual	40	85.1	30	22.6	70	38.9
Other/missing	7	14.9	14	10.5	21	11.7
Baseline CD4 (cells/μl)						
< 200	8	17.0	22	16.5	30	16.7
≥ 200 & < 350	12	25.5	41	30.8	53	29.4
≥ 350	23	48.9	56	42.1	79	43.9
Missing	4	8.5	14	10.5	18	10.0
Mean (SD)	349	(185)	378	(238)	370	(225)
Median (IQR)	360	(238 - 470)	340	(220 - 480)	343	(222 - 479)
HIV Viral load						
Undetectable (≤50 copies/ml)	21	44.7	54	40.6	75	41.7
Detectable	21	44.7	63	47.4	84	46.7
Missing	5	10.6	16	12.0	21	11.7
Mean (SD)	122043	(600178)	57357	(135360)	74444	(328243)
Median (IQR)	60	(40 - 2607)	150	(40 - 67353)	85	(40 - 4290)
No Prior ART	12	25.5	55	41.4	67	37.2
Prior ART	35	74.5	78	58.6	113	62.8
ART Source						
Compassionate access	12	34.3	13	16.7	25	22.1
Country	17	48.6	36	46.2	53	46.9
Full paying	1	2.9	0	0.0	1	0.9
Trial	2	5.7	11	14.1	13	11.5
Other/Unknown	3	14.3	18	35.9	21	29.2

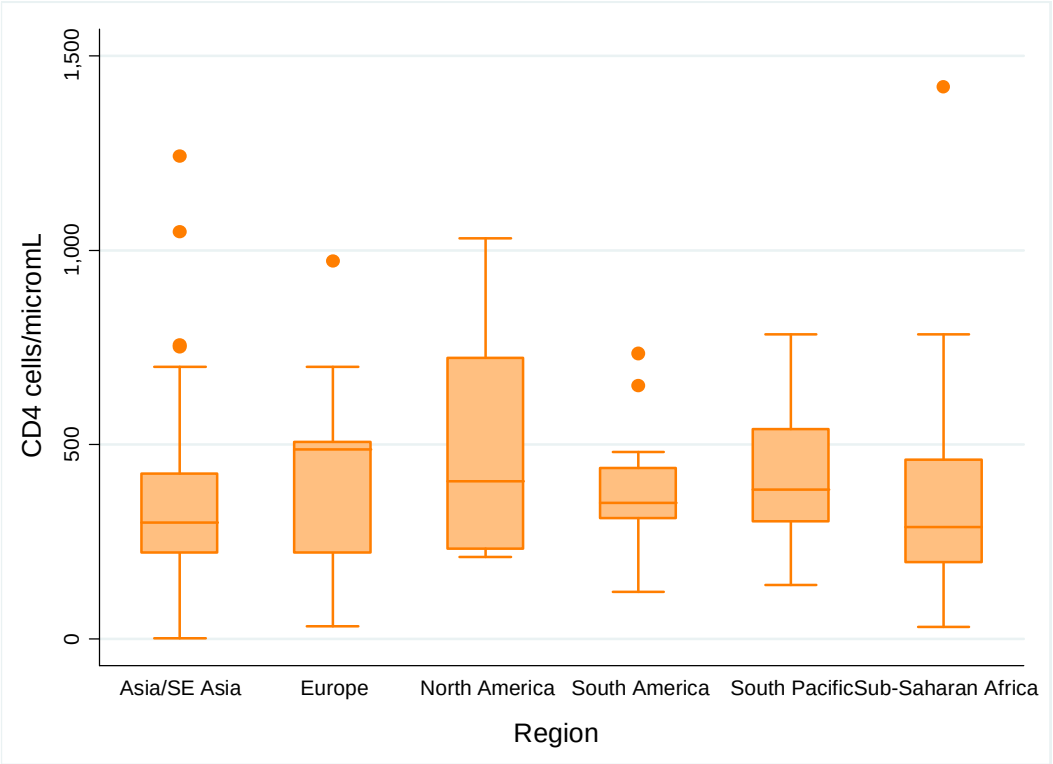
Tenofovir/Emtricitabine (Truvada) was the most common backbone (83%) prescribed at the time of enrolment, and the single most common treatment regimen prescribed was Truvada/Efavirenz (42%; 45% among males, and 34% females).

3.1.4 Immunology and virology

Among patients with a CD4 cell count measure recorded within one year prior to enrolment (N=162), the median (IQR) CD4 count was 343 cells/μl (222-479). Median CD4 count was similar for men and women, but somewhat lower among participants not previously receiving ART (285 cells/μl (IQR: 216 – 350) compared to those receiving ART (384 cells/μl (IQR: 238 – 520).

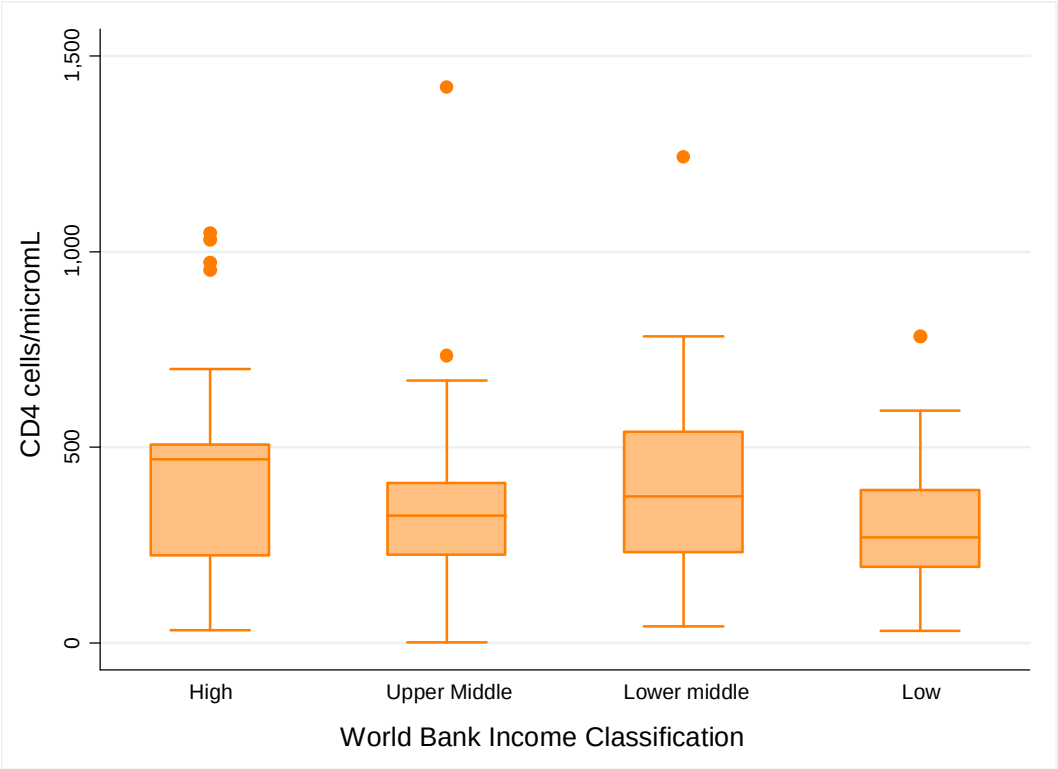
There were differences in CD4 count at baseline by region. Patients from Europe and North America had considerably higher CD4 counts (487 cells/μl (IQR: 20 – 507) and 405 cells/μl (IQR: 233 – 723) respectively) compared to the other regions. CD4 count at enrolment were lowest for patients from Sub-Sahara Africa and Asia (288 (IQR: 196 – 461) and 299 cells/μl (IQR: 425) respectively) (Figure 3).

Figure 3: Baseline CD4 cell count by region of birth



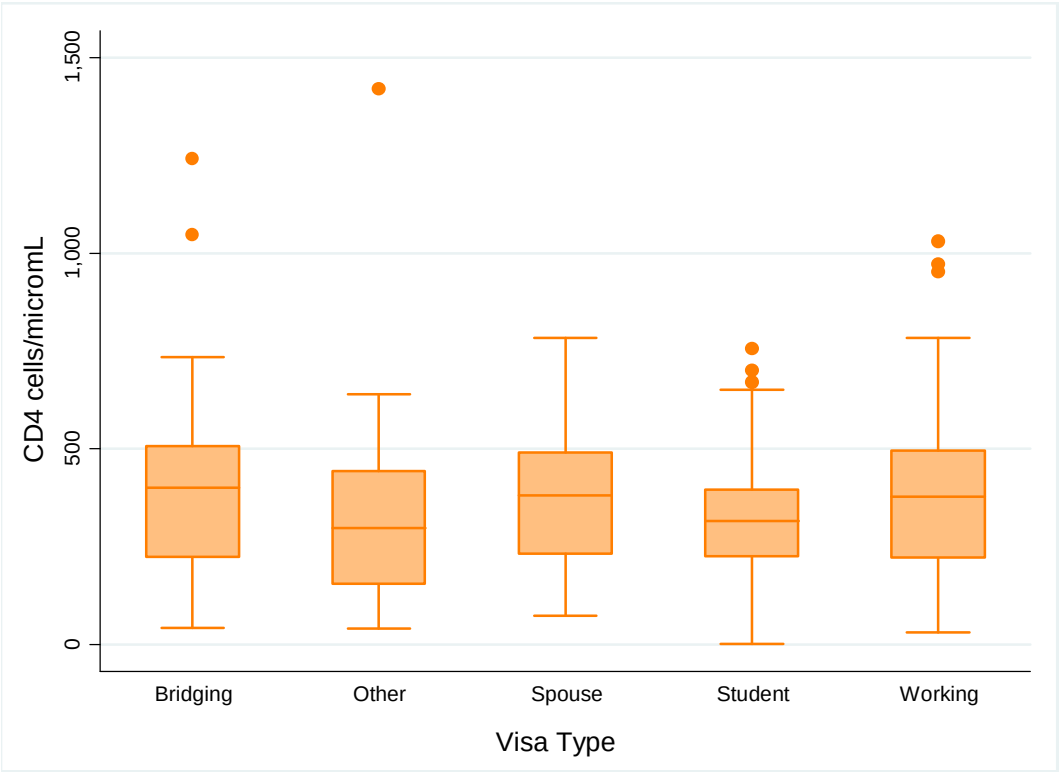
Most patients from low income countries had baseline CD4 counts below 300 cells/μl, compared to High income countries with CD4 counts above 400 cells/μl at baseline (Figure 4).

Figure 4: Baseline CD4 cell count by World Bank Classification for Income



Lower median CD4 counts were observed for patients on Other (298 cells/μl IQR: 153 – 443) and Student visas (2315 cells/μl IQR: 223 – 395), compared to the remaining visa types: Bridging (400 cells/μl IQR: 222 – 507), Spouse (380 cells/μl IQR: 232 – 490) and Working (377 cells/μl IQR: 220 – 495) (Figure 5).

Figure 5: Baseline CD4 count by Visa type



Among ATRAS patients with a HIV viral load measure available within one year prior to enrolment into ATRAS (N=159), the mean (SD) viral load was 74,444 (328243), and 47% were undetectable (≤ 50 copies/ml). Of patients receiving ART prior to enrolment 72% were undetectable compared to almost all patients not on treatment (98%) having a detectable viral load. Approximately 70% of patients who had a baseline CD4 count above 350 cells/μl were undetectable, compared to 25% or less for the lower CD4 categories. Some regional differences were observed, with lower proportions of patients with undetectable HIV viral load from South America (28%) and 42% from Asia, compared to 50% or more for the other regions. More than 60% of patients on Bridging and Other visas respectively were undetectable, compared to 47% or less for all other visa types (Table 4).

Table 4: Patient characteristics by HIV viral load at baseline

		HIV viral load				
	Detectable[1]		Undetectable		Missing	Total[3]
	N	%[2]	N	%[2]	N	N
Total	84	52.8	75	47.2	21	159
Female	21	50.0	21	50.0	5	42
Male	63	53.8	54	46.2	16	117
Region						
Asia/SE Asia	43	58.1	31	41.9	8	74
Europe	7	50.0	7	50.0	2	14
North America	3	37.5	5	62.5	2	8
South America	13	72.2	5	27.8	1	18
South Pacific	6	42.9	8	57.1	5	14
Sub-Saharan Africa	12	38.7	19	61.3	3	31
Visa category						
Bridging	9	39.1	14	60.9	3	23
Other	8	40.0	12	60.0	3	20
Spouse	9	60.0	6	40.0	1	15
Student	33	61.1	21	38.9	6	54
Working	25	53.2	22	46.8	8	47
World Bank Classification						
High income	11	37.9	18	62.1	6	29
Upper middle income	39	59.1	27	40.9	9	66
Lower middle income	26	57.8	19	42.2	5	45
Low income	8	42.1	11	57.9	1	19
Prior ART	29	28.2	74	71.8	10	103
Prior ART Source						
Compassionate access	11	44.0	14	56.0	0	25
Country	11	21.2	41	78.8	2	52
Full paying	0	0.0	0	0.0	1	0
Trial	3	25.0	9	75.0	1	12
Other/unknown	5	33.3	10	66.7	6	15
Baseline CD4 (cells/μl)						
< 200	22	75.9	7	24.1	1	29
≥ 200 & < 350	38	74.5	13	25.5	2	51
≥ 350	23	29.5	55	70.5	1	78
Missing	1	100.0	0	0.0	17	1

1. detectable HIV viral load >50 copies/ml
2. denominator for all proportions is number of patients with an HIV viral load measure at baseline (N=159)
3. excludes missing

3.2 Patient Outcomes

3.2.1 Changes in immunology and virology at 6 and 12 months follow-up

Among patients with a baseline CD4 measure and a follow-up CD4 measure at 6 months (N=133) the mean increase in CD4 was 87 cells/μl (SD: 138). Greater mean increases were observed among men (99 cells/μl (SD: 139)) compared to women (54 cells/μl (SD: 132)), and among patients with lower baseline CD4 counts (CD4 < 200: 103 cells/μl (SD: 90); and CD4 200 - < 350: 118 cells/μl SD: 147) compared to higher baseline CD4 counts above 350 cells/μl (56 cells/μl SD: 143) (Table 5). Greater mean increases were also observed among patients who were not on ART at enrolment into ATRAS (119 cells/μl SD: 112) compared to patients already receiving ART (68 cells/μl SD: 149). Considerably smaller mean increases were observed among patients from North America (15 cells/μl SD: 189) and the South Pacific (36 cells/μl SD: 106) compared to the other regions.

Table 5: Increases in CD4 counts (cells/μl) from baseline to 6 months

	Mean	SD	Median	LQ[1]	UQ
Total	87	138	84	8	150
Female	54	132	61	-40	120
Male	99	139	92.5	10	168
Baseline CD4 (cells/μl)					
< 200	103	90	95	40	150
≥ 200 & < 350	118	147	100	30	170
≥ 350	58	143	59	-33	133
Visa type					
Bridging	79	200	76	-60	130
Other	49	74	30	-2.5	125
Spouse	58	107	51	3	102
Student	115	134	92	40	170
Working	85	136	90	-10	168
Region					
Asia/SE Asia	90	150	81	-1	150
Europe	104	99	95	52	133
North America	15	189	75	-37	150
South America	160	143	102	72	250
South Pacific	36	107	45	-50	120
Sub-Saharan Africa	71	104	62	-1	127.5
World Bank Criteria					
High income	81	193	90	-10	150
Upper middle income	104	125	99	11	170
Lower middle income	62	115	80	-10	120
Low income	98	131	72	30	168
No Prior ART	120	112	100	59	170
Prior ART	68	149	71	-15	134

1. LQ: lower quartile; UQ: upper quartile

At 12 months follow-up similar mean increases were observed for men and women (123 cells/μl SD: 167 and 110 cells/μl SD: 160 respectively), and greater increases among the lower baseline CD4 cell strata (Table 6). By month 12 the South Pacific region and North America demonstrated larger mean increases in CD4 change approaching that of the other regions.

Table 6: Increases in CD4 counts (cells/μl) from baseline to 12 months

	Mean	SD	Median	LQ	UQ
Total	119	165	120	18	224
Female	110	160	110.5	14	182
Male	123	167	120	39	230
Baseline CD4 (cells/μl)					
< 200	143	105	133	60	213
≥ 200 & < 350	171	157	149.5	65	268
≥ 350	78	177	70	-20	181
Visa					
Bridging	84	227	70	16	140
Other	158	104	176	50	243
Spouse	93	132	121.5	-18	184
Student	142	150	120	60	230
Working	106	167	101.5	7.5	225
Region					
Asia/SE Asia	122	176	121	50	199
Europe	138	170	120.5	-37	315.5
North America	99	133	67	39	200
South America	174	131	174	69	270
South Pacific	119	131	140	80	181
Sub-Saharan Africa	76	177	60	14	216
World Bank Classification					
High income	125	204	70	-37	265.5
Upper middle income	142	124	129	60	230
Lower middle income	110	165	140	60	182
Low income	63	206	54	-36	249
No Prior ART	187	115	169.5	100.5	284
Prior ART	87	176	70	-10	181

At month 6 and 12 there was a marked increase in the proportion of patients with a viral load measure available who had an undetectable (≤ 50 copies/ml) result, 87% and 88% at 6 and 12 months respectively. For almost all patient characteristics, gender, region, baseline CD4 category, region, prior ART therapy and visa type, more than 75% were undetectable (Table 7 and 8). The mean (SD) viral load at 6 and 12 months was 1578 (11954) and 2066 (12533)/copies respectively.

Table 7: Patient characteristics by HIV viral load at 6 months

	HIV viral load					
	Detectable[1]		Undetectable		Missing	Total[3]
	N	%[2]	N	%[2]	N	N
Total	18	13.0	120	87.0	42	138
Female	7	19.4	29	80.6	11	36
Male	11	10.8	91	89.2	31	102
Visa type						
Bridging	1	5.9	16	94.1	9	17
Other	2	11.1	16	88.9	5	18
Spouse	4	28.6	10	71.4	2	14
Student	6	13.3	39	86.7	15	45
Working	5	11.4	39	88.6	11	44
Region						
Asia/SE Asia	10	14.9	57	85.1	15	67
Europe	0	0.0	13	100.0	3	13
North America	1	14.3	6	85.7	3	7
South America	0	0.0	13	100.0	6	13
South Pacific	3	27.3	8	72.7	8	11
Sub-Saharan Africa	4	14.8	23	85.2	7	27
World Bank Classification						
High income	2	7.4	25	92.6	8	27
Upper middle income	4	7.1	52	92.9	19	56
Lower middle income	9	23.7	29	76.3	12	38
Low income	3	17.6	14	82.4	3	17
Prior ART	5	6.0	79	94.0	29	84
Baseline CD4 (cells/μl)						
< 200	6	24.0	19	76.0	5	25
≥ 200 & < 350	6	12.8	41	87.2	6	47
≥ 350	5	8.6	53	91.4	21	58
Missing	1	12.5	7	87.5	10	8

1. detectable HIV viral load >50 copies/ml
2. denominator for all proportions is number of patients with an HIV viral load measure
3. excludes missing

Table 8: Patient characteristics by HIV viral load at 12 months

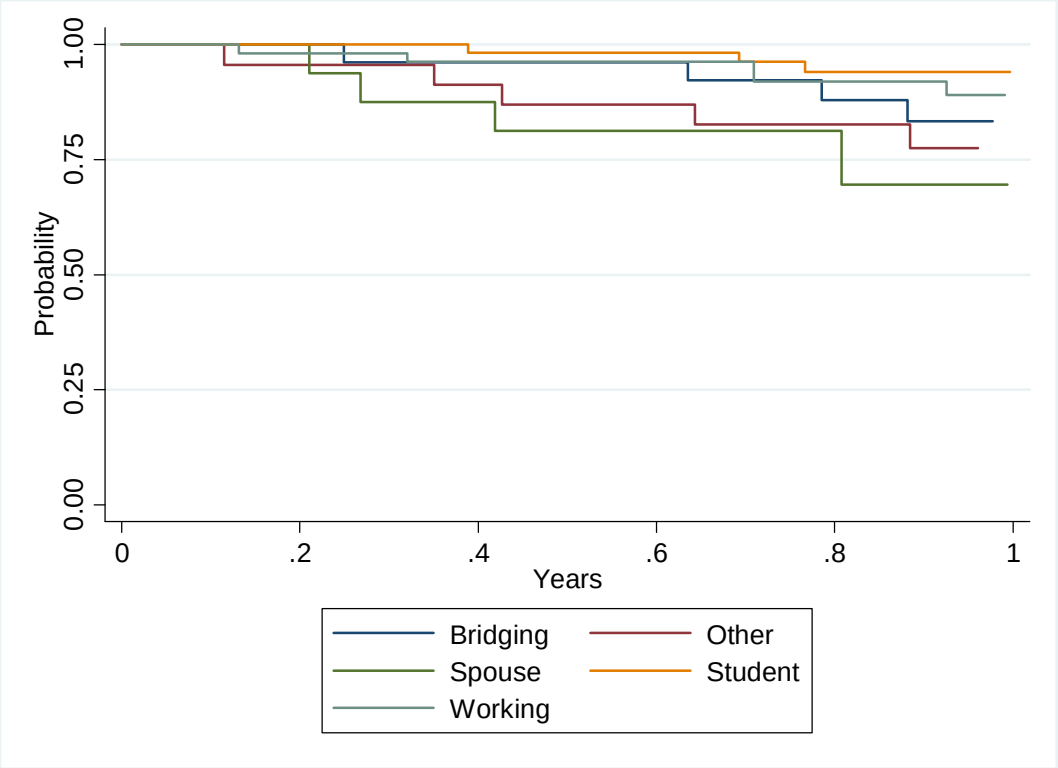
		HIV viral load				
	Detectable[1]		Undetectable		Missing	Total[3]
	N	%[2]	N	%[2]	N	N
Total	14	13.2	106	88.3		120
Female	6	18.8	26	81.3	15	32
Male	8	9.1	80	90.9	45	88
Visa						
Bridging	3	13.6	19	86.4	4	22
Other	3	18.8	13	81.3	7	16
Spouse	2	22.2	7	77.8	7	9
Student	1	2.9	33	97.1	26	34
Working	5	12.8	34	87.2	16	39
Region						
Asia/SE Asia	5	9.6	47	90.4	30	52
Europe	0	0.0	13	100.0	3	13
North America	2	33.3	4	66.7	4	6
South America	0	0.0	13	100.0	6	13
South Pacific	3	23.1	10	76.9	6	13
Sub-Saharan Africa	4	17.4	19	82.6	11	23
World Bank Classification						
High income	2	8.0	23	92.0	10	25
Upper middle income	3	6.5	43	93.5	29	46
Lower middle income	6	17.6	28	82.4	16	34
Low income	3	20.0	12	80.0	5	15
Prior ART	7	9.0	71	91.0	35	78
Baseline CD4 (cells/μl)						
< 200	4	20.0	16	80.0	10	20
≥ 200 & < 350	4	11.4	31	88.6	18	35
≥ 350	6	10.5	51	89.5	22	57
Missing	0	0.0	8	100.0	10	8

1. detectable HIV viral load >50 copies/ml
2. denominator for all proportions is number of patients with an HIV viral load measure
3. excludes missing

3.2.2 Rate of patients coming off ATRAS

An important outcome of ATRAS is to determine the rate at which patients may become eligible for Medicare or alternatively no longer reside in the country. Since enrolment up to the time of these data analyses (July 2013), 39 patients (31 (23% of males) and 8 (17% of females)) were no longer receiving ART via ATRAS, over a total of 179 person years of follow-up. The majority (N=33, 85%) had become eligible for Medicare, 4 have left the country, and 2 were lost to follow-up.

Figure 6: Time to coming off ATRAS supplied ART



The rate per 100 person years (py) of coming off ATRAS is 21.8 (95% Confidence Interval (CI): 15.9–0.30). A slightly lower rate per 100 py was observed among women (17.3, 95% CI: 8.6–34.6) compared to men (23.4, 95% CI: 16.4–33.3). More marked differences were observed by visa type. More than 30% of patients on Bridging, Spouse or Other visas are no longer receiving ATRAS supplied ART, compared to 12% and 20% of patients on Student and Working visas respectively. Consistent with this, the overall rate of coming off ATRAS-supplied ART per 100 py is greatest among patients on Spousal visa (40.1, 95%CI: 16.7–96.4), followed by Bridging (30.8, 95% CI: 16–59.1), and Other (29.7, 95% CI: 14.2–62.4) respectively. Lower rates per 100 py were observed among patients on Working (20.0, 95% CI:

11.1–36.22) and Student visas (11.9, 95% CI: 5.7–25.0). Some of the variability may be explained by small sample size among certain groups (Table 9).

A larger proportion of patients from Sub-Saharan Africa (38%), Europe (31%) and North America (30%) have already come off ATRAS, with overall rates per 100 py of: 43.2 (95%CI: 25.1-74.4), 27.5 (95% CI: 11.4–66.1) and 28.8 (95%CI: 9.3–89.2).

Table 9: Rate of coming off ATRAS supplied ART by baseline characteristics

	Off ATRAS	Person years	Rate/ 100	Lower CI[1]	Upper CI
Female	8	46.3	17.3	8.6	34.6
Male	31	132.5	23.4	16.5	33.3
Baseline CD4 (cells/μl)					
< 200	6	29.3	20.5	9.2	45.6
>= 200 & < 350	9	55.5	16.2	8.4	31.2
>= 350	20	77.1	25.9	16.7	40.2
Missing	4	16.9	23.7	8.9	63.2
Visa type					
Bridging	9	29.2	30.8	16.0	59.2
Other	7	23.5	29.8	14.2	62.4
Spouse	5	12.5	40.1	16.7	96.4
Student	7	58.7	11.9	5.7	25.0
Working	11	54.8	20.1	11.1	36.2
Region					
Asia/SE Asia	10	82.8	12.1	6.5	22.4
Europe	5	18.2	27.5	11.4	66.1
North America	3	10.4	28.8	9.3	89.2
South America	4	19.4	20.6	7.7	54.8
South pacific	4	17.9	22.4	8.4	59.6
Sub-Saharan Africa	13	30.1	43.2	25.1	74.5
World Bank Classification					
High income	10	39.2	25.5	13.7	47.4
Upper middle income	13	73.1	17.8	10.3	30.6
Lower middle income	8	48.6	16.5	8.2	32.9
Low income	8	17.8	44.9	22.4	89.7
No Prior ART	10	59.6	16.8	9.0	31.2
Prior ART	29	119.2	24.3	16.9	35.0

1. CI=confidence interval

4. ESTIMATES OF NEED

The number of HIV-positive temporary residents who are ineligible for Medicare in Australia at any given time is unknown. Estimates from a survey of s100 prescribers in 2007 indicated approximately 300 HIV-positive temporary resident patients were in need of ART.

In June 2013, two independent yet aligned surveys of HIV prescribing clinics were undertaken. The first was coordinated and conducted by staff at the Kirby Institute. All AHOD sites (of which 21 are ATRAS sites) were contacted via email and asked what their current Medicare ineligible caseload was, and what proportion of these patients were currently receiving ART. All the 28 active AHOD sites responded to the survey. The second, a phone survey, was conducted by staff at NAPWHA. They contacted a number of non AHOD s100 HIV-positive prescribing clinics, mainly HIV/sexual health clinics (N=14). Sites were also asked what were the estimated number of patients currently Medicare ineligible, what proportion were on treatment, and what proportion were in need of ART but currently not receiving ART.

From the two surveys, a total 42 clinics were contacted (and responded) from all 7 states and territories. The majority of sites contacted were sexual health or public clinics (N=28, 67%), followed by private clinics (N=8, 19%) and tertiary referral centres (N=6, 14%).

Both surveys obtained estimates on how many HIV-positive patients each site currently had that were ineligible for Medicare. From AHOD, excluding patients in

ATRAS, there was an estimated 113 HIV-positive patients who were ineligible for Medicare in July 2013, of these 74 (65%) were already receiving ART. Among the sites surveyed by NAPWHA, 61 patients were currently ineligible for Medicare, of which, 48 (79%) were receiving ART. Among the NAPWHA surveyed sites, it was also estimated that a further 10% of the ineligible patients were in need of ART according to current treatment guidelines but not on treatment.

In the NAPWHA survey, the majority of treated patients sourced their ART from either overseas (37%) or via compassionate access (53%). While among a subset of the AHOD sites surveyed and who provided these data, the majority sourced their ART either from overseas (50%), followed by compassionate access (18%) and clinical trials (32%), similar to the proportions reported among the ATRAS patients.

4.1 Current estimate of HIV-positive temporary residents

Combining the reported number of HIV-positive patients ineligible for Medicare in July 2013 from the Kirby/AHOD and NAPWHA surveys, with the number of patients still on ATRAS in July 2013, there was an estimated 315 HIV-positive Medicare ineligible patients in care in July 2013 from 42 s100 prescribing clinics from various parts of the country.

The combined HIV-positive caseload of AHOD sites is approximately 15,000 patients (based on clinic self-report). If we assume that AHOD sites include an estimated 70% of the entire Australia HIV-positive caseload (an estimated 22,500 linked to care) [20], and that the NAPWHA survey captured a further 10%, then over the last

two years there are approximately 450 HIV-positive Medicare ineligible patients in care of whom 141 are currently in ATRAS.

Based on the estimates from the NAPWHA and AHOD surveys, as well as the ATRAS baseline data, the proportion of these patients currently on ART ranges somewhere between 60% (n=270) to 80% (n=360). From the NAPWHA survey, approximately a further 45 patients (10%) are in need of ART, yet currently not receiving ART.

Provision of subsidised ART for Medicare ineligible patients would therefore most likely not exceed 450 individuals at any given time. The estimated duration for which these individuals would require subsidised treatment up until they either become eligible for Medicare or return to their home is difficult to determine. However, data from ATRAS indicate that the rate of either becoming Medicare eligible or leaving the country is 22/100 person years. As indicated earlier in this report, most (85%) of the patients who no longer required subsidised treatment via ATRAS became eligible for Medicare. Becoming eligible for subsidised ART via the PBS will eventuate for the majority of currently ineligible patients. If the rate at which patients become eligible for Medicare or return home remains at 22/100 person years, then the median time to becoming eligible is approximately 2.5 years. This period reflects the amount of support required before the process of becoming eligible for Medicare is finalized.

4.2 HIV Transmission

Baseline data from the ATRAS report indicates that 53% of patients had a detectable HIV viral load (98% of those not on treatment), and were therefore at appreciable risk of transmitting HIV. Follow-up data from ATRAS at 12 months demonstrate a decrease in detectable HIV viral load to 12%. It is generally accepted that patients with undetectable viral load have minimal risk of onward HIV transmission. If we assume that ART does not affect sexual or other HIV-transmission risk behaviors, this represents a 77.4% reduction in the number of patients who have detectable viral load and who have a substantial risk of onward transmission.

A more quantitative estimate of the reduction in risk of transmission is possible by using the method published by Wilson et al (2008) [21]. This method is based on the Rakai study of HIV transmission in heterosexual couples, in which each ten-fold reduction in HIV viral load was associated with a 2.45-fold reduction in the risk of transmission. In ATRAS, the mean HIV viral load at baseline was 74,444 copies/ml, and the mean HIV viral load at 12 months follow-up was 2,060 copies/ml. Assuming again that ART does not affect sexual or other HIV-transmission risk behaviours, these reductions in mean viral load due to expanded and improved ART are estimated to reduce the risk of onwards transmission by 75.2%.

Although the absolute risk of transmission remains uncertain, further modeling with greater follow-up data, and including cost effectiveness data, will be conducted in future ATRAS reports.

5. CONCLUSION

This is the first comprehensive report of HIV-positive Medicare ineligibles in Australia. Recruited to ATRAS were a total of 180 patients, a little under half of the estimated 450 HIV-positive patients currently Medicare ineligible in Australia. Although the majority of ATRAS patients were male, 26% were female, a larger proportion than the overall Australian HIV epidemic.

Most ATRAS patients were from the Asia Pacific region (46%) followed by Sub-Saharan Africa (19%). The most common visa types were Student or Working visa. At the time of enrolment 63% were receiving ART, but less than 50% of patients had an undetectable viral load (HIV viral load $\leq$ 50 copies/ml). These patients mainly sourced the ART from overseas or via compassionate access, while only one patient reportedly paid for the ART at full cost.

Within one year of follow-up in ATRAS and with continued optimal ART supply, the proportion of ATRAS patients with undetectable viral load had increased substantially to 88%, and CD4 cell count increased on average by 118 cells/μl. During this period 39 ATRAS patients no longer required ART via ATRAS, of whom 33 had become eligible for Medicare. The overall rate of coming off ATRAS-supplied ART was 22/100 person years. By these estimates, 50% of the ATRAS patients will no longer require ATRAS-supplied ART within 2.5 years of commencing ATRAS.

This report demonstrates a significant improvement in the clinical status of ATRAS patients within 6 months of commencing effective ART. The immunological and virological improvements highlight the importance of supplying ART to this

population in need. The increase in the proportion with undetectable HIV viral load as early as 6 months demonstrates a potentially significant impact on the risk of onward HIV transmission. This report also highlights that among these temporary residents a large proportion of patients will eventually become eligible for Medicare or leave the country. The median time to this outcome is estimated to be 2.5 years.

This is the first the first of several projected ATRAS reports. Further reports addressing in particular Aims 2 and 3 of the study will follow. The ATRAS Reference group will continue to evaluate this process. Reports will be provided to the BBVSS Committee.

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ATRAS REFERENCE GROUP

Chair: Bill Whittaker
Special Representative, NAPWHA
National Association of People with HIV Australia (NAPWHA)
PO Box 917
Newtown NSW 2042

Professor Jennifer Hoy
The Alfred Hospital
Infectious Diseases Unit
2nd Floor, Burnet Institute
85 Commercial Road
Melbourne VIC 3004

Professor Don Smith
Albion Street Centre
150-154 Albion Street
Surrey Hills NSW 2010

Dr Robert Finlayson
Taylor Square Private Clinic
393 Bourke Street
Darlinghurst NSW 2010

Dr Andrew Sloane
AbbVie Pty Ltd
32-34 Lord Street
Botany NSW 2019

Lisa Bastian
Sexual Health and Blood Borne Virus Program
Department of Health, Western Australia
PO Box 8172
Perth Business Centre
Perth WA 6849

Jo Watson
National Association of People with HIV Australia (NAPWHA)
PO Box 917
Newtown NSW 2042

Professor Matthew Law
Head, Biostatistics and Databases Program
The Kirby Institute
University of New South Wales
Cnr Boundary and West Streets
Darlinghurst NSW 2035

Dr Kathy Petoumenos
Senior Lecturer, Biostatistics and Databases Program
The Kirby Institute
University of New South Wales

Cnr Boundary and West Streets
Darlinghurst NSW 2035

AHOD/ATRAS coordinators:
Hamish McManus
Statistician
Biostatistics and Databases Program
The Kirby Institute
University of New South Wales

Stephen Wright
Statistician
Biostatistics and Databases Program
The Kirby Institute
University of New South Wales

Report survey data collection:
Courtney Bendall,
The Kirby Institute
University of New South Wales

Adrian Ogier
National Association of People with HIV Australia (NAPWHA)
PO Box 917
Newtown NSW 2042

Lance Feeney
Positive Life NSW
PO Box 831
Darlinghurst NSW 1300

Jae Comden
National Association of People with HIV Australia (NAPWHA)
PO Box 917
Newtown NSW 2042

ATRAS Participating Sites

New South Wales
Albion Street Centre
Clinic 16, Royal North Shore
Holdsworth House Medical Practice, Darlinghurst
Nepean Sexual Health Clinic
Parramatta Sexual Health Clinic
RPA Sexual Health
St Vincent's Hospital
Sydney Sexual Health Clinic
Taylor Square Private Clinic
Northern Territory
Clinic 34

Queensland
Brisbane Sexual Health and HIV Service
Cairns Sexual Health Clinic
Clinic 87
South Australia
O'Brien Street Practice

Victoria
Melbourne Sexual Health Clinic
Monash Medical Centre
Northside Clinic
Prahran Market Clinic
The Alfred Hospital

Western Australia
Royal Perth Hospital

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