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)

Two year follow-up

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EXECUTIVE SUMMARY

The Australian HIV Observational Database Temporary Residents Access Study (ATRAS) which commenced in November 2011 now has more than 2 years of follow-up data.

The main objectives of ATRAS are to provide systematically collected information on visa status and HIV related information for a subgroup of HIV positive patients who are ineligible for antiretroviral treatment via Medicare.

This report is a follow-up on the first report released in October 2013 [1] with a specific focus on the long-term outcomes of ATRAS patients in particular changes in Medicare eligibility status, HIV treatment response, and updated estimates of the current number of HIV-positive patients who are temporary residents and ineligible for Medicare supported ART in Australia. In addition this report includes mathematical modelling on HIV transmission rates and costs associated with treating all HIV-positive temporary residents ineligible for Medicare.

<u>Key findings:</u>

- After one and two years of follow-up in ATRAS:
    - The proportion with an undetectable viral load had increased to 89% (one year follow-up) and 94% (two-years of follow-up) from 47% at enrolment. *These rates are comparable to results reported in clinical studies of rates of patients achieving and sustaining an undetectable viral load on treatment*.

    - CD4 cell count increased by an average of 123 cells/μl (SD: 173) and 185 cells/μl (SD: 209) at one and two years of follow-up respectively
- By July 2014 with an average of two years of follow-up, 79 patients no longer required ART support via ATRAS, this represents a rate of 26/100 person years.
    - The majority (N=60; 76%) of these patients had become eligible for Medicare
- ATRAS supplied ART will cease in November 2015, at which time it is estimated that at least 61 of the 180 ATRAS patients will still be Medicare ineligible
    - 35 of these patients will be from NSW sites, 16 from VIC, 5 and 6 from QLD and WA respectively
- A second cross sectional survey estimated the number of HIV-positive temporary residents in Australia ineligible for Medicare and in care over the past year is 464, of whom 101 are in ATRAS
- Mathematical modelling suggests
    - Providing ART successfully to all Medicare ineligibles would avert a median of 81 new infections (IQR: 69.5 – 92.5) over 5 years.
    - The total discounted costs for treatment of all HIV 450 positive temporary residents over five years is median $26,354,092 (IQR: $21,649,876 - $31,058,309).
    - The total savings in lifetime discounted treatment costs for the 81 new HIV infections averted is median $29,411,170 (IQR: $25,002,825 - $33,819,515).

1. INTRODUCTION

ATRAS was established to collect information on HIV-positive patients who were temporary residents of Australia and consequently ineligible for PBS subsidised antiretroviral therapy. In the absence of ongoing data collection of this population an overarching aim of ATRAS was to describe a subset of this population, including determining reasons for ineligibility (ie visa status), determine the length of time these patients become eligible for Medicare, or alternatively time taken to return to their country of origin and/or permanently leave Australia.

Access to treatment for this population both for individual clinical and public health benefits derived is another important objective of ATRAS. HIV-positive temporary residents not eligible for PBS subsidised medications are required to access treatment from a variety of sources including ordering from overseas, compassionate access, clinical trials or even paying the full Australian price. This approach has several limitations in particular in terms of ordering from overseas, where supply of treatment may be interrupted due to delay in the post. There are no guarantees about the quality of medicines ordered overseas from some online suppliers. Further, ordering from overseas may limit the ART options that are available, thereby restricting patients to selecting regimens that would not reflect or equate to standard of care treatment that a HIV-positive Australian resident would receive.

The recently released 7th National HIV Strategy [2] has specific targets focusing on the reduction of sexual transmission of HIV by 50% by 2015, the virtual elimination of HIV across specific populations including sex workers, people who inject drugs and mother to child transmission, and to increase treatment uptake by people with HIV to 90%. (Similar treatment uptake targets have also been set by some Australian States).

The Strategy recognises that for these targets to be achieved a range of social, structural and individual level barriers that impact on prevention, testing, treatment and care for people

living with or at risk of HIV need to be addressed. The treatment and care component is of particular relevance to HIV positive temporary residents.

1.1 Aims of ATRAS

The three main aims of ATRAS are to:

- Describe the population of HIV-positive temporary residents including age, sex, visa status and country of origin.
- Describe the HIV disease status of these patients, and to assess the short and long-term outcomes of optimal ART.
- Model HIV transmission rates in Australia if HIV positive temporary residents do not receive optimal/effective ART; and to determine costs associated with providing treatment to this population under a similar framework to that provide to Australian residents.

The first ATRAS report released October 2013 addressed Aim1 and Aim 2 (outcomes after 1 year of follow-up). This current report we focus on Aims 2 and parts of Aim 3.

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, from tertiary referral centres, sexual health clinics and specialist general practices.

Recruitment commenced in November 2011, and ceased when a total 180 HIV positive temporary residents were enrolled.

2.1 Data collection

Core data routinely collected for AHOD include: patient demographics as well as HIV disease status and HIV treatment history. In addition visa related information is recorded for ATRAS patients only, country of birth and employment status. Visa and employment status are updated annually, including whether the patient has applied for permanent residency or if they have become eligible for Medicare.

2.2 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. Supply of ART via ATRAS will cease in November 2015.

2.3 Ethical approval

ATRAS participants were required to provide written informed consent prior to enrolment. Ethics approval was sought and provided by the UNSW 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.

2.4 MODELLING

A simple mathematical model is used to calculate the change in population size over time and the number of new infections in partners of Medicare ineligible people. Below is a brief description of the model details and assumptions (a detailed description of the model assumptions and input parameters are provided in the appendix).

2.4.1 Demographics

The model considers a population of people living with HIV (PLHIV) who are Medicare ineligible with the characteristics of people in ATRAS. The overall population is split into males who are men who have sex with men (MSM) (which, for the purposes of this analysis, we assume are exclusively homosexual) and all those who are not MSM. The proportion of people in each of these populations is based on ATRAS data and assumed to be constant over time. This compartmentalisation of the population is used to distinguish the risk of HIV infection rather than treatment coverage and adherence

It is assumed that there is only a small change in the population over time such that the population size is relatively constant.

2.4.2 Clinical characteristics

For these calculations we simply considered the proportion of the population taking ART and the proportion of those on ART with viral suppression. Both of these inputs can change over time based on the ATRAS data. We do not consider different proportions for each population group. The most recent data value was used for future projections.

2.4.3 HIV transmission to partners

HIV transmission occurs through sexual intercourse between HIV-positive temporary residents and their sexual partners. We assume initiating ART does not change the risk of transmission to partners (such as through changes in behavior), and all partners are eligible for Medicare. As the sexual behaviour for the ART and non-ART population is the same, we use a simple risk equation approach with the overall annual risk of transmission calculated from national data rather than incorporating complex sexual behaviour. The key assumptions are described in the appendix.

2.4.4 Costs associated with ART provision

Our analysis includes an estimate of the annual cost of providing ART to patients ineligible for Medicare and their partners who become infected. We obtained estimates of these costs using previous work for Australian settings [3]. For sexual partners of HIV-positive temporary residents ineligible for Medicare who become infected with HIV we estimate the 'lifetime' cost of providing care and treatment. Further details are described in the appendix.

3. RESULTS

3.1 ATRAS participant characteristics

A total of 180 HIV positive temporary residents ineligible for Medicare were recruited to ATRAS from the 7th of November 2011 to the end of June 2012. The majority of participants were male (74%), and from the Asia region (46%). Most common visa type was Working (31%) and Student visa (33%). Participant Details are given in Tables 1 and 2 of this report.

3.1.1 HIV 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 2).

At enrolment median (IQR) CD4 cell count was 343 cells μ/l (222-479) overall, while 47% were undetectable (72% treated, and 2% untreated). (Table 3)

3.1.2 Antiretroviral treatment history

At enrolment, 63% of ATRAS patients were reported to have previously received ART. The majority sourced their treatment overseas (47%), via Australian compassionate access program (22%) or Australian clinical trials (11%). Prior ART source was not reported for 18% of treated participants (Table 2)

Of the previously treated population, 46% changed their treatment regimen once enrolled into ATRAS, to address issues of possible drug resistance, treatment failure and to ensure that antiretroviral regimens were consistent with those recommended under Australian antiretroviral treatment guidelines . Similar proportions were reported by Spouse (47%) and

Other visa (42%) category, while a greater proportion were reported for ATRAS patients on Student visa (60%), and lower among those on a Working visa (37%) and Bridging visa (31%).

Table 1: Patient characteristics at enrolment by sex

	Female		Male		Total	
	N	%	N	%	N	%
Total	47		133		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
Other	11	23.4	12	9.0	23	12.8
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
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	
Student	8	17.0	18	13.5	26	14.4
Unknown/other	0	0.0	4	3.0	4	
Unemployed	19	40.4	20	15.0	39	21.7

Table 2: Patient HIV characteristics at enrolment

	Female		Male		Total	
	N	%	N	%	N	%
	47		133			180
HIV exposure category						
MSM (+MSM/IDU)	0	0.0	88	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	11	23.4	41	30.8	40	22.2
>= 350	23	48.9	56	42.1	79	43.9
Missing	5	10.6	14	10.5	18	10.0
HIV RNA undetectable (<50 copies/ml)						
Yes	21	44.7	55	41.4	76	42.2
No	21	44.7	64	48.1	85	47.2
Missing	5	10.6	14	10.5	19	10.6
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

3.2 Patient Outcomes

3.2.1 Changes in immunology and virology at 12 and 24 months follow-up

Table 3 illustrates the changes in CD4 cell count (cells/μl) prior to enrolment and at 1 and 2 years of follow-up. Mean (SD) CD4 count increased from 376 (SD: 227) at baseline to 474 (SD: 198) after 1 year of follow-up to 534 (SD: 235) after 2 years of follow-up in ATRAS. Similar improvements were observed for key subcategories, including gender, visa status and region of origin.

Table 3: Patient characteristics CD4 status at enrolment, 1 and 2 years of follow-up[1]

	Baseline				Month 12				Month 24		
	N [2]	Mean	SD		N	Mean	SD		N	Mean	SD
Total	161	376	227		151	475	198		106	534	235
Female	42	350	187		37	444	190		22	524	188
Male	119	385	239		114	485	201		84	536	247
Bridging	24	436	273		24	532	216		21	554	242
Other	21	357	296		15	430	191		11	465	157
Spouse	13	391	193		12	432	184		4	435	259
Student	56	328	162		56	479	195		42	511	182
Working	47	405	238		44	464	199		28	593	311
Asia/SE Asia	76	341	214		73	458	198		56	508	208
Europe	14	422	247		13	541	234		10	702	434
North America	9	526	318		7	449	160		5	506	254
South America	18	371	149		18	556	201		13	629	197
South Pacific	14	437	164		15	512	148		9	488	88
Sub-Saharan Africa	30	371	268		25	414	199		13	461	187
High Income: OECD	24	474	291		22	509	219		18	599	373
High income: Non-OECD	6	458	215		6	567	313		4	663	297
Upper middle income	69	337	199		63	464	175		52	516	190
Lower middle income	44	394	233		42	487	194		24	528	209
Low income	18	320	184		18	409	213		8	454	115
Naïve	54	302	161		57	487	192		38	513	189
Prior ART	107	413	246		94	467	202		68	545	258
Baseline CD4 (cells/μl)											
< 200	- -	- -	- -		23	256	125		17	349	176
>= 200 & < 350	- -	- -	- -		47	440	156		36	498	175
>= 350	- -	- -	- -		68	586	180		46	634	261
Missing	- -	- -	- -		13	404	126		7	509	104

1. CD4 count at enrolment is within 6 months prior to enrolment. Month 12 is measure with 3 moths either side of 12 month time point closest to 1 year, and within 6 months either side of 2 year follow-up

2. Number with results: Baseline - 161, Month 12 - 151, Month 24 - 106

Table 4: Patient characteristics and undetectable HIV viral load (< 50 copies/mL) at enrolment, 1 and 2 years of follow-up[1]

	Baseline			Month 12			Month 24	
	N[2]	%		N	%		N	%
Total	76	47.2		126	88.7		99	94.3
Female	21	50.0		28	80.0		21	100.0
Male	55	46.2		98	91.6		78	92.9
Asia/SE Asia	32	42.7		63	91.3		52	94.5
Europe	7	50.0		12	100.0		11	100.0
North America	5	55.6		4	57.1		4	80.0
South America	5	27.8		16	100.0		12	92.3
South Pacific	8	57.1		10	76.9		8	100.0
Sub-Saharan Africa	19	61.3		21	84.0		12	92.3
Bridging	14	58.3		22	91.7		20	95.2
Other	12	60.0		13	81.3		11	100.0
Spouse	6	40.0		10	83.3		3	75.0
Student	21	38.9		45	93.8		38	95.0
Working	23	47.9		36	85.7		27	93.1
CD4 (cells/μl)								
< 200	8	28.6		17	73.9		17	89.5
200 & < 350	13	26.5		39	90.7		32	97.0
>= 350	55	68.8		58	90.6		44	93.6
Missing	0	0.0		12	100.0		6	100.0
Naïve	2	3.6		48	85.7		35	92.1
Prior ART	74	70.5		78	90.7		64	95.5

1. CD4 count at enrolment is within 6 months prior to enrolment. Month 12 is measure with 3 moths either side of 12 month time point closest to 1 year, and within 6 months either side of 2 year follow-up

2. Number with results: Baseline - 161, Month 12 - 142 , Month 24 - 105

The proportion with an undetectable viral load increased significantly from baseline (47%) to 89% and 94% after 1 and 2 years of follow-up respectively. Increases were observed across most patient characteristics.

3.2.2 Rate of patients coming off ATRAS

Table 5 shows ATRAS Medicare status by key patient subgroups. By July 2014, with approximately 300 person years of follow-up, 79 (45%) of ATRAS participants were no longer receiving ART via ATRAS. This is an overall rate of 26/100 person years. In Table 6, rates of coming off ATRAS by key patient characteristics are also reported.

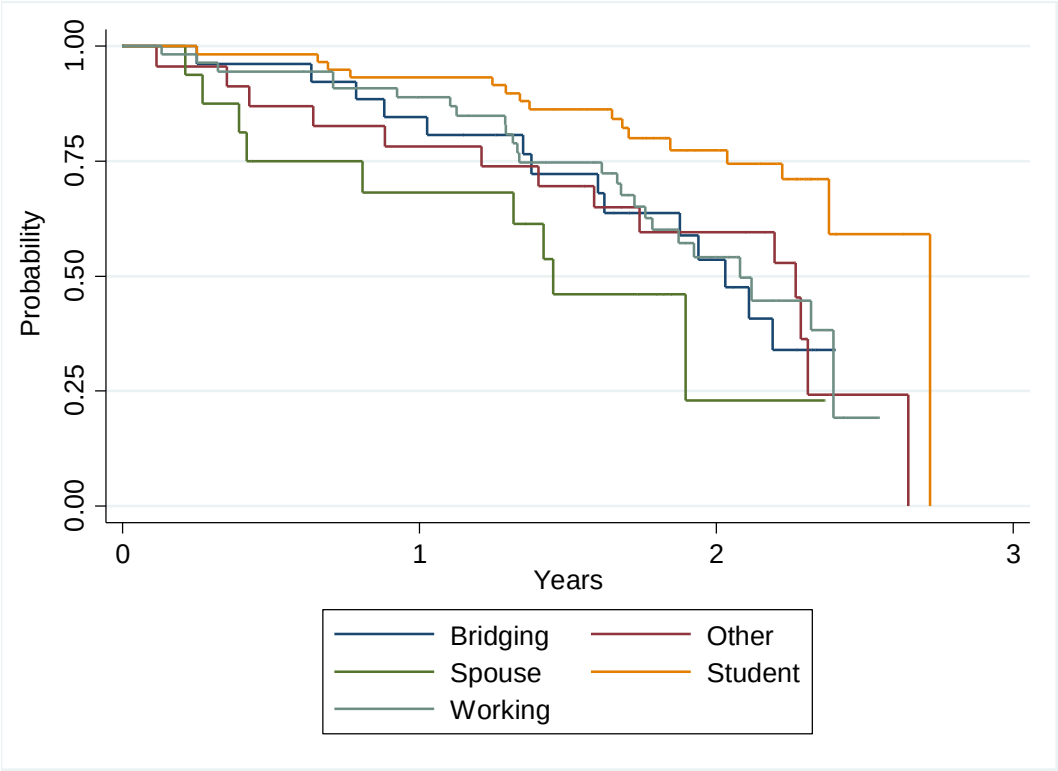
Table 5: Reasons for coming off ATRAS supplied ART by baseline characteristics

	Medicare		**Overseas**		**LTFU**		**Total**
	N	%	N	%	N	%	
Total	60	75.9	12	15.2	7	8.9	79
Bridging	12	85.7	0	0.0	2	14.3	14
Other	12	85.7	1	7.1	1	7.1	14
Spouse	9	100.0	0	0.0	0	0.0	9
Student	8	50.0	5	31.3	3	18.8	16
Working	19	73.1	6	23.1	1	3.8	26
Female	17	89.5	0	0.0	2	10.5	19
Male	43	71.7	12	20.0	5	8.3	60
Asia/SE Asia	24	82.8	2	6.9	3	10.3	29
Europe	6	66.7	2	22.2	1	11.1	9
North America	1	33.3	2	66.7	0	0.0	3
South America	5	55.6	4	44.4	0	0.0	9
South Pacific	7	87.5	1	12.5	0	0.0	8
Sub-Saharan Africa	17	81.0	1	4.8	3	14.3	21
NSW	17	56.7	8	26.7	5	16.7	30
NT	2	100.0	0	0.0	0	0.0	2
QLD	14	93.3	1	6.7	0	0.0	15
SA	3	100.0	0	0.0	0	0.0	3
VIC	12	85.7	2	14.3	0	0.0	14
WA	12	80.0	1	6.7	2	13.3	15
Hospital	17	68.0	4	16.0	4	16.0	25
Private	3	60.0	2	40.0	0	0.0	5
SHC	40	81.6	6	12.2	3	6.1	49

Table 6: Rates of coming off ATRAS supplied ART by baseline characteristics

	No Off ATRAS	Person years	Rate/100	95%	CI
Total	79	299.74	26.36	20.848	32.819
Female	19	79.02	24.05	14.480	37.558
Male	60	220.73	27.18	20.718	34.947
Bridging	14	43.13	32.46	17.800	54.627
Other	14	38.39	36.47	19.625	60.230
Spouse	9	19.54	46.06	20.577	85.424
Student	16	110.16	14.52	8.314	23.621
Working	26	88.35	29.43	19.300	43.291
Asia/SE Asia	29	151.13	19.08	12.777	27.401
Europe	9	27.51	32.14	14.698	61.017
North America	3	15.00	20.00	4.125	5.845
South America	9	32.68	27.27	12.471	51.772
South Pacific	8	27.68	28.57	12.335	56.297
Sub-Saharan Africa	21	45.24	46.67	28.887	71.335
High Income: OECD	14	46.10	30.37	16.639	51.064
High income: Non-OECD	3	12.88	23.29	4.759	67.441
Upper middle income	32	132.46	24.24	16.582	34.223
Lower middle income	20	81.92	24.41	14.898	37.669
Low income	10	26.38	37.90	18.444	70.732
NSW	30	141.39	21.22	14.355	30.374
NT	2	3.00	66.67	8.074	240.823
QLD	15	43.00	34.88	19.524	57.535
SA	3	4.00	75.00	15.467	219.182
VIC	14	66.00	22.73	12.720	37.485
WA	15	42.00	35.71	19.989	58.905
Hospital	25	74.52	33.55	21.572	49.207
Private	5	20.22	24.73	8.12	5.834
Sexual Health Clinic	49	205.00	23.90	17.683	31.600

Figure 1 Rate of coming off ATRAS supplied ART by visa status.



By November 2015, it is estimated that 61 of the 180 ATRAS patients will still be Medicare ineligible and therefore still in need of ongoing ART supplied. It is estimated that 35 of these patients are from NSW sites, 16 from VIC, 5 and 6 from QLD and WA respectively (Table 7)

Table 7: Rate off ATRAS by State

	Rate/100 py	No. currently (July 2014) still on ATRAS	Estimated no. still on by Nov 2015
Overall	26	101	61
NSW	20	50	35
NT	67	2	0
QLD	35	10	5
SA	75	1	0
VIC	23	25	16
WA	36	13	6

4. ESTIMATES OF NEED

The number of HIV-positive temporary residents who are ineligible for Medicare in Australia at any given time is unknown. In June/July 2013 two aligned surveys conducted by the Kirby Institute and NAPWHA of 42 clinics with an HIV-caseload obtained estimates on the number of HIV-positive patients that each clinic had that were currently ineligible for Medicare. From these estimates it determined that the number of Medicare ineligible patients in Australia was approximately 450 patients [4].

The Kirby Institute and NAPWHA surveys were conducted again in October 2014. All 42 clinics surveyed were approached again plus an additional 15 sites. All responded to the survey questions, 34 (60%) SHC, 13 (23%) private clinics, and 10 (17%) tertiary referral centres.

The clinics were asked the following: how many patients did the clinic have since July 2013 that were Medicare ineligible, what proportion of these patients were currently receiving ART, and what was the estimated total HIV-patient caseload of their clinic?

Of the clinics surveyed by the Kirby (limited to AHOD sites), there was an estimated 194 patients who were Medicare ineligible (excluding ATRAS patients), of whom 78% were receiving ART. Among the NAPWHA surveyed sites, 124 patients were ineligible for Medicare, of which 104 (84%) were on ART.

4.1 Current estimate of HIV-positive temporary residents

The combined caseload of HIV positive patients estimated from the 57 clinics surveyed is 18,000, which represents approximately 90% of the entire Australian HIV-positive caseload

currently living with HIV in Australia and linked to and retained care [5], then over the last year. Of these, approximately 464 HIV-positive patients are estimated to be Medicare ineligible.

Based on snap shot estimates from the last ATRAS report which estimated approximately 450 HIV positive patients ineligible for Medicare [1] then the provision of subsidised ART for Medicare ineligible patients appears to remain consistent around 460 individuals at any given time. It is unknown how long it takes for a HIV-positive temporary resident currently in Australia to become Medicare eligible or leave the country. Determining therefore how long HIV-positive temporary residents require subsidised ART until they become eligible for Medicare or return home is also difficult. Three quarters of patients who have come off ATRAS have become Medicare eligible, if this is indicative of all HIV positive temporary residents in Australia, then we can assume that a substantial proportion of Australian temporary residents who are HIV-positive will eventually transition to being permanent residents and therefore eligible to receive ART via PBS. If we apply the rate coming off ATRAS of 26/100 person years, then the median time to becoming Medicare eligible or leaving the study is approximately 2 years. Hence, the average extra investment in treatment by funding ART for all Medicare Ineligible patients would be between 2 and 2 .5 years per patient. After this time, our data suggests that patients have either left the country or become Medicare eligible.

5. MODELLING RATES OF HIV TRANSMISSION

Applying data from the first year after enrolment for ATRAS to all HIV-positive temporary residents in Australia (approximately 450), and assuming that sexual behaviour in this group is similar to the Australian general population, the number of new infections that are transmitted from this population is estimated to be 22 per year (IQR:–18.5 – 25.5). As a percentage of the infected Medicare ineligible population this number of new infections equates to 4.9% of the population (Figure 2). This compares with around 1000 new HIV

infections per year from an estimated total of 26,800 living with HIV infection in Australia (~4%) [6].

Expanding access to ART to all HIV-positive temporary residents who are ineligible for Medicare and achieving almost universal HIV viral load suppression is estimated to reduce annual new infections to a median of 5 per year (IQR:–3 - 7) after 5 years (Figure 2), corresponding to 1% of the estimated Medicare ineligible population living in Australia. Providing ART successfully to all Medicare ineligibles is estimated would avert a median of 81 new infections (IQR: 69.5 – 92.5) over 5 years (Figure 3).

Figure 2: Simulated annual new infections in partners of Medicare ineligible

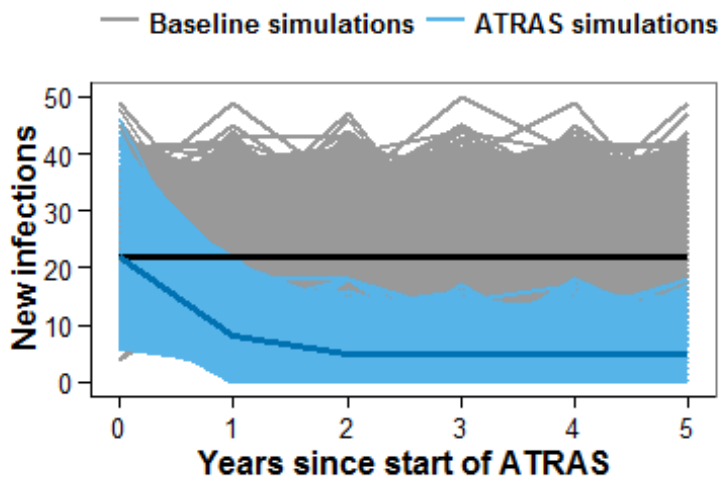
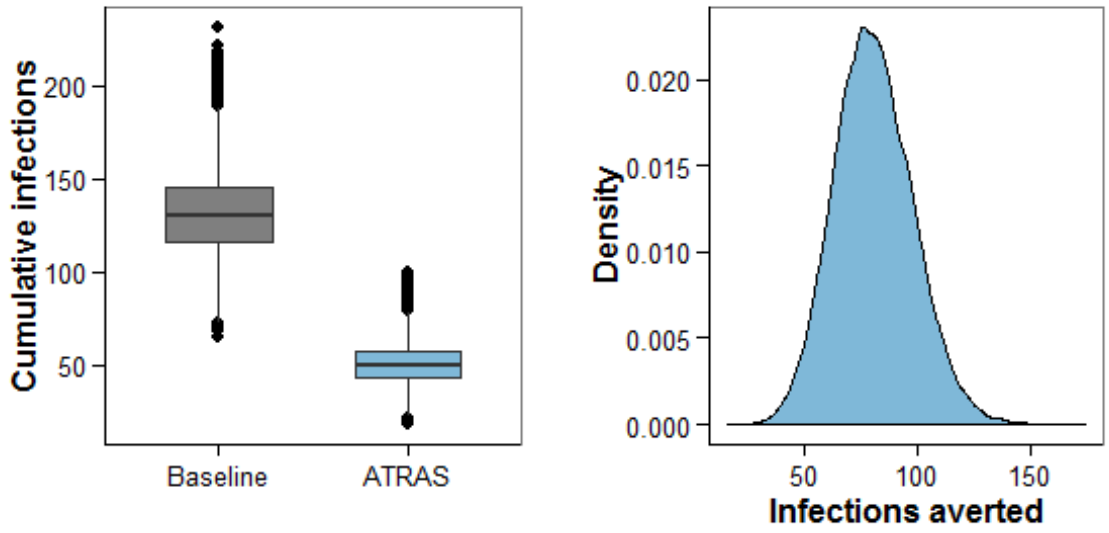


Figure description: The grey lines represent the baseline simulations while the blue lines are for the expansion of ART to all Medicare ineligibles. The black and dark blue lines show the median number of new infections for the Baseline and expanded ATRAS simulations respectively

Figure 3: Estimated total number of number of new infections (left) and the distribution in infections averted (right) over 5 years since if ART access was expanded to all Medicare ineligibles.



6. COST OF TREATMENT

Providing ART to HIV-positive temporary residents over 5 years is estimated to have a median undiscounted cost of $29,642,230 (IQR: $24,342,841 - $34,941,619) and a median discounted cost of $26,354,092 (IQR: $21,649,876 - $31,058,309). This corresponds to a median cost per infection averted of $320,000 (IQR: $258,174 - $391,334) (with 5% discounting), which may be considered a conservative estimate as it only includes ART costs and not the costs of ongoing monitoring and care as well as costs associated with illnesses associated with long-term living with HIV infection.

Figure 4 shows the cumulative costs for providing ART to HIV-positive temporary residents for the next 5 years and the savings due to the reduction in infections during this period. The median undiscounted cumulative cost of providing ART to all 450 people living with HIV (PLHIV) who are ineligible for Medicare for five years is $29,642,230 (IQR: $24,342,841 -

$34,941,619). Under this scenario we estimate a median of 81 infections would be averted, resulting in a median saving in the lifetime treatment costs for these newly infected people of $69,412,098 (IQR: $59,000,616 - $79,823,580). When discounting is taken into account, the long term costs are reduced. The discounted cost of providing ART to 450 Medicare ineligible patients for five years, reduces to $26,354,092 (IQR: $21,649,876 - $31,058,309) and the resulting savings in the treatment costs of the 81 infections averted reduces to a median of $17,982,044 (IQR: $14,766,353 - $21,197,735). This much larger discounting for this scenario is due to the much longer time horizon for discounting for ART treatment of new infections compared with ART treatment of PLHIV temporary residents ineligible for Medicare for five years.

Figure 4: Median total costs for providing all HIV temporary residents ineligible for Medicare with ART and the reduction in lifetime treatment costs for partners of HIV positive temporary residents who acquire infection over 5 years.

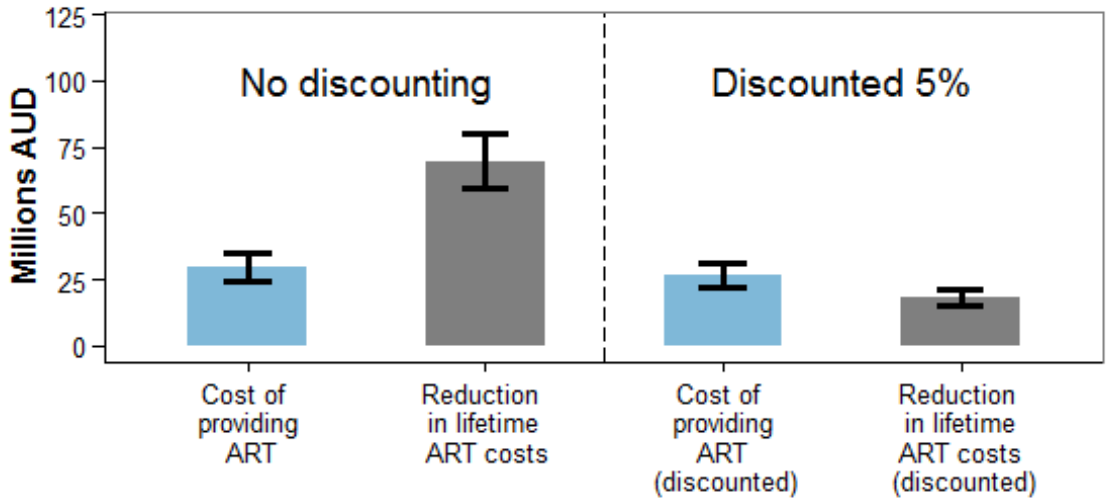


Figure description. The bars show the interquartile range in total costs across all simulations

In summary the mathematical modelling and costing suggest that expanding treatment to all HIV-positive temporary residents would avert 81 new infections over 5 years. Without

discounting, providing ART to the entire temporary resident population would reduce costs by approximately $40 million. With discounting (5% per year) providing ART has a modest increased cost of $10 million compared with the denying access to ART.

7. CURRENT JURISDICTIONAL ARRANGEMENTS FOR MANAGING MEDICARE INELIGIBLE HIV POSITIVE PATIENTS

The current arrangements for managing HIV positive patients ineligible for Medicare vary by jurisdiction. Formal arrangements are reported by SA, where all treatment and medication costs for Medicare ineligible HIV positive people who are seen within major public hospital treatment centres are met by SA Health. In WA, there is an operational directive in place whereby funds must be recouped by health insurance companies, and in the instances where this is not possible then approval must be provided by the director of an area health service for treatment costs in excess of $10,000 (http://www.health.wa.gov.au/CircularsNew/circular.cfm?Circ_ID=12895). Less formal arrangements exist in NSW, where clinicians of patients with financial barriers to treatment, are advised to approach HIV/Sexual Health Services as some Clinic Directors have the discretion to approve the purchase of treatments for patients in need. In QLD, there are varying arrangements across services and regions due to the decentralised health system where decisions are made locally. This ranges from full support to applying for welfare grants. In the Northern Territory access to treatment is obtained under “compassionate access” arrangements. Formal arrangements are reported by ACT, where treatment and medication costs for Medicare ineligible HIV positive people are met by ACT Health. In VIC there is currently no formal system wide approach. The treating medical practitioner of patients ineligible for Medicare can apply for compassionate access through pharmaceutical companies (who provide free treatment on an individual level). Patients can also purchase treatments over the internet. There are no arrangements at the national health level.

The disparity in arrangements across jurisdictions represent significant inequity of in care and access to treatment for these individual. Their short term visa status denies them access to the Medicare system which includes the 100% subsidy of expensive medications (excluding any co-payment fee), such as antiretrovirals. Although many patients have private health insurance as part of their visa requirements, health insurance companies in Australia do not cover the costs of antiretroviral drugs. Because of global patent protection laws, generic antiretrovirals have limited penetration in the Australian market. Many non-Medicare patients are therefore disadvantaged by a range of national and commercial restrictions on drug availability.

7. CONCLUSION

This is the second report from the Australian HIV Observational Database Temporary Resident's Access Study (ATRAS). One hundred and eighty HIV-positive patients were recruited to ATRAS between November 2011 and June 2012. As previously described the majority of ATRAS patients were male, though just over one quarter (26%) are female, and the majority of patient are from the Asia Pacific Region and the most common visa type was student or working visa.

By June 2014 there were 79 of the 180 ATRAS patients who were no longer receiving ART via the ATRAS scheme. This represents an overall rate of 26/100 person years coming off ART. Rates varied by visa status with a slower rates coming off ATRAS demonstrated for patients on student and working visas.

In this report we demonstrated a continued long-term positive effect of receiving optimal and uninterrupted ART, with 94% of patients with two years of follow-up with having an undetectable HIV viral load (an increase from 89% after one year of follow-up). This is comparable to results on rates of achieving and sustaining undetectable viral loads demonstrated in many clinical studies. CD4 cell count also continued to rise during the second year of follow-up.

Mathematical modelling demonstrated that providing treatment to all PLHIV who are temporary residents and ineligible for Medicare will avert a median of 81 new infections over 5 years, indicating a significant public health benefit. Providing ART to this population over 5 years is estimated at a median discounted cost of $26,354,092 (rounded), corresponding to a median cost per infection averted of approximately $320,000.

Estimates showed that providing ART to this population over 5 years would avert 81 new infections, this results in a median saving of $69,412,098 (undiscounted) in the lifetime treatment costs of providing treatment to people that would have been otherwise infected. After discounting the cost of expanding access to ART to all PLHIV temporary residents who are ineligible for Medicare is reduced to a median $26,354,092, and the resulting savings in treatment costs is also reduced to a median of $17,982,044.

ART supplied via ATRAS will cease by November 2015, at which time and estimated 61 ATRAS patients along with a further estimated 450 HIV positive individuals throughout Australia are expected to remain ineligible for Medicare requiring provision of ART via an alternate scheme. As the current 7th National HIV Strategy has an overarching goal of working toward virtual elimination of HIV by 2020, this group of patients cannot be ignored. How these patients are currently managed and cared for varies considerably across States/Territories. More formal and transparent arrangements across the State/Territory and Commonwealth health departments on the management of these patients are urgently required. These patients are living and working legally within Australia under a number of short term visas, with the majority seeking to become permanent residents. The modelling performed in this report and the expected costs of providing ART to this population provide convincing evidence and justification to provide ART to not only permanent but also temporary Australian residents.

APPENDIX – Mathematical Modelling methodology

This methodology is written in dynamic format using R markdown v2 within R studio 0.98.1056 (using R version 3.1.0). Further details are available in the associated R markdown file which also contains the R code to produce all the results when the markdown is run. Code blocks have been supressed in the output document.

Demographics

For this analysis we consider a population of PLHIV who are medicare ineligible with the characteristics of people in ATRAS [4]. The overall population is split into males who are men who have sex with men (MSM) (which, for the purposes of this analysis, we assume are exclusively homosexual) and all those who are not MSM. The proportion of people in each of these populations is based on ATRAS data and assumed to be constant over time. This comparmentalisation of the population is used to distinguish the risk of HIV infection rather than treatment coverage and adherence.

The number of medicare ineligibles can change over time with people becoming eligible for medicare provided ART and new temporary residents entering the population. This movement is represented by a constant growth rate for the population π (which is positive for a growing population and negative for a declining population). Letting $N(y)$ equal the total population size in year y, the number of medicare ineligible people in the population is then given by

$$N(y) = N(0)\pi^y.$$

For this analysis we assume only a small change in the population over time so the overall population size is relatively constant.

Clinical characteristics

The main aim of this analysis is to investigate the effect of providing all Medicare ineligible people in ATRAS with ART on HIV transmission. For the calculations we simply consider the proportion of the population taking ART and the proportion of those on ART with viral suppression. Both of these inputs can change over time based on the ATRAS data. We do not consider different proportions for each population group. The most recent data value is used for projections beyond the years of available data.

HIV transmission to partners

HIV transmission occurs through sexual intercourse between medicare ineligibles and their sexual partners. We assume all partners are Medicare eligible and initiating ART does not change the risk of transmission to partners (through changes in behaviour for example). We

also do not consider onward transmission from newly infected partners. As the sexual behaviour for the ART and non-ART population is the same, we use a simple risk equation approach with the overall annual risk of transmission calculated from national data rather than incorporating complex sexual behaviour.

Key assumptions:

- HIV transmission from Medicare ineligibles who are not on ART is the same as for the Australian population of PLHIV not on ART.
- Partners of HIV positive people who are ineligible for Medicare are assumed to be Medicare eligible.
- Those with unsuppressed virus have the same transmission risk as those not taking ART.
- Transmission parameters are assumed constant over time.

Costs associated with ART provision

Our analysis includes an estimate of the annual cost of providing ART to PLHIV temporary residents ineligible for Medicare and their partners who become infected. We obtained estimates of the costs of providing treatment using previous work for Australian settings [3]. For sexual partners of PLHIV temporary residents who become infected with HIV we estimate the 'lifetime' cost of providing and treatment.

Parameter table

Table A1 lists all input parameters and their values and ranges.

Table A1 - Calculation input parameter ranges. Justifications for these parameter ranges are provided in endnotes. The simulations used for the calculations take samples from these ranges assuming a uniform distribution.

Parameter	Description	Range	Reference
Demographic parameters			
$N(0)$	Overall population size in initial year	[400 - 500]	1
π	Multiplicative change in annual population	[0.98 - 1.02]/yr	1
p_m	Proportion of Medicare-ineligible population of PLHIV who are MSM	[0.4 - 0.6]	1
p_n	Proportion of Medicare-ineligible population of PLHIV who are non-MSM	Given by $1 - p_m$	1

Clinical parameters			
θ	Proportion of population taking ART	63% at enrolment and 95% after 12 months $\pm$ 5%	2
ψ	Proportion of population taking ART with undetectable viral load	70% at enrolment, 88% after 12 months, and 96% after 24 months $\pm$ 5%	2
HIV transmission parameters			
β_n	Annual probability an untreated non-MSM transmits HIV to another person	[0.0485 - 0.0808]	3
β_m	Annual probability an untreated MSM transmits HIV to another person	[0.0771 - 0.0808]	3
ε_{ART}	Efficacy of ART in preventing HIV transmission if virus is suppressed	[0.9 - 0.99]	4
Treatment costs			
c_{ART}	Average annual undiscounted cost of providing ART to PLHIV temporary residents who are ineligible for Medicare	[$7,000 - $15,000]	5
c_{life}	Average undiscounted lifetime cost of providing ART post infection	[$641,821 - $1,069,702]	6
r_{disc}	Discounting rate	5%	7
t_{ART}	Average time between infection and initiating ART	[4 - 5] years	7

1. The 2013 ATRAS report estimates there are 450 Medicare ineligible PLHIV in Australia [1, 4]. We assume a range in the population between 400 and 500 PLHIV with the potential for only a small change in population size over time. In the population of 180 at enrolment 89 (50%) of the males attributing their HIV infection to MSM exposure [1, 4]. Assuming this reflects the demographic distribution over time, we assume 40-60% of the population is MSM with the remainder non-MSM.

2. At enrolment 62.8% of ATRAS patients were already receiving ART with 71.8% having undetectable viral load [1]. After enrolment all patients were put onto ART resulting in 87% having undetectable viral load at 12 months and 96% having undetectable viral load at 24 months [1]. Based on the ATRAS data we assume the percentage of Medicare ineligibles on ART increases from 70% to 95% with a range of $\pm$ 5% with the

proportion with undetecvtable virus increasing from 70% to 96% over two years with a range of $\pm$ 5%.

3. These values are calculated using data for the overall population of PLHIV in Australia. Using the equation $I = N(1-\theta)\beta + N\theta(1-\psi)\beta + N\theta\psi(1-\varepsilon_{ART})\beta = N\beta(1-\theta\psi\varepsilon_{ART})$ where I is the overall incidence in Australian MSM and non-MSM, N is the overall number of PLHIV in Australia who are MSM and non-MSM, and the remaining parameters have the same meaning as in Table A1 we can estimate the value of β for MSM and non-MSM. In 2013 there were an estimated 26,640 PLHIV in Australia and 912 new infections [7] of which around 75% are attributed to homosexual contact [6]. According to recent estimates for the HIV treatment cascade in Australia around 75% of MSM living with HIV [8] and 55% of non-MSM living with HIV are taking ART [7], respectively. In both MSM and non-MSM taking ART, around 90% have an undetectable viral load [8, 9]. Putting these values into the equation above and assuming $\pm$ 25% uncertainty produces the values of β_n and β_m.

4. We assume those with viral suppression have a 96% reduction in transmission to their sexual partners in line with the results from the HPTN-052 trial for those with detectable drug [10].

5. At enrolment 83% of the ATRAS cohort on ART were taking Tenofovir/Emtrcitabine (Truvada) as the 'backbone' of their regime. This means the vast majority of those on treatment are taking first-line drugs. For this analysis we assume all patients are on and remain on first-line ART over the period of analysis. From Schneider et. al. the average annual cost of first-line drugs is $10,685 ($6,945-$14,424) [3]. Using this value we assume a range in the annual ART cost of $7,000 to $15,000.

6. If a partner of a Medicare ineligible becomes infected with HIV then they will eventually require care and treatment while they are living in Australia. As we are not tracking their infection progression in this analysis we use an estimate for the lifetime cost of providing ART. An analysis of the life expectancy of PLHIV in Australia given currently available antiretroviral treatments suggests someone starting treatment in their twenties will be taking ART for around 40 years [11] spending ~9 years on first-line drugs, ~14 years on second-line drugs, ~3 years on third-line drugs, and the reminder of the time on higher classes of drug. Using the cost estimates from [3], we assume the annual costs of proving each line of drugs is: $10685 for first-line drugs, $10685 for second-line drugs, $10685 for third-line drugs, and $10685 for fourth and higher lines of drugs. Mutiplying the values for each drug class and summing produces the undiscounted cost

presented here. To account for all uncertainties in time on each treatment class and drug costs we assume a range of $\pm$ 25% in the overall undiscounted cost.

7. To discount future costs of providing ART to people ineligible for Medicare and those who become infected we apply a discount rate of 5% from the year of enrolment in ATRAS for all treatment costs. For discounting purposes we include the time between infection and initiating ART, this is estimated from data on the CD4 count at initiating therapy and estimates for the rate of CD4 decline. In recent years participants in the AHOD cohort have initiated ART at around 350 cells/μL[9], it is estimated it takes 4.4 years for a person to reach this CD4 count post infection [7]. We therefore assume a range of 4 to 5 years for the time between infection and ART initiation.

Calculations for number of new infections caused by people ineligible for Medicare

We use simple risk-equation calculations to estimate the number of people who become infected through partnerships with HIV-positive people ineligible for Medicare. Details of the calculations are provided in the appendix.

The total number of new infections is given by the sum of the infections caused by Medicare-ineligible MSM and non-MSM each year. For each population, we first calculate the probability of infecting another person using an equation incorporating the level of ART use and viral suppression. The proportion of the population taking ART and with suppressed virus changes overtime matching the ATRAS data in Table 3.

Using this probability, we estimate the number of new infections caused by MSM and non-MSM Medicare-ineligibles each year through sampling from a binomial distribution. Adding the population terms together gives the overall number of new infections caused by Medicare-ineligibles in a given year and cumulatively over time.

Cost calculations

The total cost of providing ART to people ineligible for Medicare ineligibles is calculated by multiplying the annual number of people ineligible for Medicare infected with HIV by the annual cost of providing ART and summing over the period of analysis. For sexual partners of Medicare-ineligibles who become infected with HIV we calculate the cost per infection averted and overall future lifetime cost of providing care and treatment to these people by multiplying the cumulative number of people who acquire infection by the undiscounted (reported in Table A1) lifetime cost and the discounted lifetime cost.

Simulations

To perform this analysis, we generated 1000 input parameter sets by sampling from each of the parameter ranges in Table A1. For each of these parameter sets we then ran 20 simulations to account for stochastic variations. Each simulation was run for 6 years since the enrolment of patients into ATRAS. We then calculated summary statistics using the results from each simulation.

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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

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