Funding antiretroviral treatment for HIV-positive temporary residents in Australia prevents transmission and is inexpensive

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Abstract

Background—The aim of this study is to estimate the reduction in new HIV infections and resultant cost outcomes of providing antiretroviral treatment (ART) through Australia's 'universal access' health scheme to all temporary residents with HIV infection living legally in Australia, but currently deemed ineligible to access subsidised ART via this scheme.

Methods—A mathematical model to estimate the number of new HIV infections averted and the associated lifetime costs over 5 years if all HIV-positive temporary residents in Australia had access to ART and subsidised medical care was developed. Input data came from a cohort of 180 HIV-positive temporary residents living in Australia who are receiving free ART donated by pharmaceutical companies for up to 4 years.

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Results—Expanding ART access to an estimated total 450 HIV+ temporary residents in Australia for 5 years could avert 80 new infections. The model estimated the total median discounted (5%) cost for ART and associated care to be A$36 million, while the total savings in lifetime-discounted costs for the new infections averted was A$22 million.

Conclusions—It is estimated that expanded access to ART for all HIV-positive temporary residents in Australia will substantially reduce HIV transmission to their sexual partners at little additional cost. In the context of Australia's National HIV strategy and Australia's endorsement of global goals to provide universal access to ART for all people with HIV, this is an important measure to remove inequities in the provision of HIV-related treatment and care.

Additional keywords

antiretroviral therapy; Australia; HIV prevention; mathematical modelling; migrants; treatment access

Introduction

Effective antiretroviral treatment (ART) for HIV-positive (HIV+) individuals results in viral suppression leading to long-term disease remission, prolonged survival and the prevention of HIV transmission.[1–8] Providing ART to infected individuals is a key prevention strategy and a crucial component of the HIV response internationally.[9,10] Maintaining an undetectable viral load, however, requires regular access to care and treatment, with patients adhering to their treatment regimen.

The Australian government provides fully subsidised ART to HIV+ patients eligible for a Medicare card through the Pharmaceutical Benefits Scheme (PBS).[11]. Until they apply for residency, HIV+ temporary residents living in Australia are ineligible for a Medicare card and cannot access subsidised ART. Thus, most HIV+ temporary residents have limited options for accessing treatment and must pay the full cost of ART medications (with first-line regimens costing ~A$10 500 per year[12]), source ART from their country of origin or import generic drugs from overseas suppliers. Such barriers prevent HIV+ temporary residents achieving optimal health outcomes and increase the risk of transmission to their sexual partners.[13,14]

The Australian HIV Observational Database (AHOD) Temporary Residents Access Study (ATRAS) commenced in November 2011 and followed 180 HIV+ temporary residents in clinical and financial need of subsidised ART for 4 years.[14,15] At enrolment, 63% of ATRAS patients were receiving ART from alternative sources, with only 70% having a suppressed viral load (<50 copies mL^{-1}); suggesting many were receiving suboptimal treatment. This percentage increased to 85% at 12-months follow up and to 96% at 24-months follow up. ATRAS only provided ART to the end of 2015 to a proportion of all HIV+ temporary residents who were ineligible for Medicare in Australia.[14,15] Using data from ATRAS, we estimated the effect and potential costs of providing ART to all HIV+ temporary residents in Australia.

Methods

We used a risk equation model to estimate the annual number of new infections over the next 5 years in sexual partners of the estimated 400-500 HIV+ temporary residents currently living in Australia.[14,15] The calculations used parameter values based on the characteristics of the ATRAS cohort patients at enrolment, at 12-months follow up and at 24-months follow up.[14,15] For projections beyond the years of available data, we used the most recent data value available. For each parameter, we specified a range of values and then sampled 1000 parameter sets. All model parameter values with justifications are provided in Table 1. We repeated the calculations for each parameter set 20 times to account for stochastic variations. Results were obtained using summary statistics from all simulations. Total costs are in AUD and rounded to the nearest A$10 000. We provide a detailed description of the model equations, assumptions, and input parameter values and reproducible code in an online repository.[20] All the analyses and results were generated using R version 3.1.2 and associated packages.[21]

Model population

For this analysis, we assumed the population of HIV+ temporary residents in Australia have the characteristics of people in ATRAS.[14,15] We split the overall population into a male group of men who have sex with men (MSM) (which, for the purposes of this analysis, we assume are exclusively homosexual) and into a non-MSM group consisting of females and heterosexual males. We assumed the MSM population made up 40-60% of the overall HIV+ temporary resident population, as reported in ATRAS.[14,15] We used this compartmentalisation of the population because partners of MSM are likely to be at higher risk of infection (we did not consider population differences in treatment coverage and adherence).

Number of new infections caused byto HIV+ temporary residents

To estimate new infections due to HIV+ temporary residents, we first calculated the probability of HIV transmission over time.[20] Our calculation incorporates the annual probability for an untreated HIV+ person to transmit HIV to another person (β), the proportion of the population taking ART (θ), the proportion taking ART with an undetectable viral load (ψ), and the efficacy of viral suppression on HIV transmission (ε_{ART}; assumed to be 90–99% [6–8]); this is given by the equation:

$$\beta' = (1 - \theta \psi \varepsilon_{ART})\beta. \quad (1)$$

We used 2011-15 ATRAS data for the proportion of HIV+ temporary residents taking ART and the corresponding proportion with an undetectable viral load. By using the calculated probability for each year (Equation 1), we then estimated the number of new infections each year (I) using a binomial distribution and the estimated population size for HIV+ temporary residents (N); that is, $I \sim binom(N, \beta')$. From Equation 1, for large N and small β', this is approximately equal to:

$$I = N(1 - \theta \psi \varepsilon_{\mathrm{ART}}) \beta. \quad (2)$$

We estimated the annual probability that an untreated HIV+ person transmits HIV to another person (β) using a weighted average of the separate probabilities for HIV+ temporary resident MSM and non-MSM. As the number of new infections for temporary residents is unknown, we assumed the transmission probability for untreated HIV+ temporary residents equals the transmission probability for the overall untreated HIV+ population in Australia. Substituting estimates for the overall Australian population obtained from the 2014 HIV care and diagnosis cascade (with a 25% uncertainty range)[22,16] into Equation 2, and using annual notifications in the overall population in place of new infections (this assumption has been validated in previous modelling studies),[23], we obtained a range in the transmission risk for non-MSM of 0.049–0.081 per year and 0.077–0.128 per year for MSM (Table 1). This estimate for β implicitly includes behaviour affecting HIV transmission and the impact of current prevention programs. Our analysis then assessed the impact of ART and viral suppression, in addition to this background transmission.

The ATRAS cohort only provides clinical data and does not report behavioural data or sexual partner characteristics relevant to HIV transmission. Due to this lack of data, we were unable to develop a more detailed model of HIV transmission for HIV+ temporary residents. Thus, our analysis did not include additional infections due to transmission from newly infected partners (unless they are also temporary residents in which case they would become part of the HIV+ temporary resident population). Only infections directly attributed to HIV+ temporary residents were included. We also assumed HIV+ temporary residents on ART, but with unsuppressed virus, had the same annual transmission probability as untreated HIV+ temporary residents.

Model scenarios

To assess the impact of expanding ART access to all HIV+ temporary residents, we considered two modelling scenarios. First, we ran a 'status quo' scenario, where the proportion of HIV+ temporary residents virally suppressed remained constant and equalled the proportion at the start of ATRAS (58–68% on ART with 65–75% suppressed). We then ran an 'expanded access' scenario, where the proportion of the population taking ART and with suppressed virus changed over time to reach 90–100% of HIV+ temporary residents by 24 months, matching ATRAS data.[14,15] For both scenarios, the annual probability an untreated HIV+ person transmits HIV to another person (β) retained the same value. This means the sexual behaviour of temporary residents and the effects of current prevention strategies are maintained for both scenarios. Any change in new infections is then due to the change in treatment coverage and the level of viral suppression.

Costs associated with ART provision

At enrolment, nearly all ATRAS patients already on ART were taking ART drug combinations recommended in current ART treatment guidelines.[23] We assumed all patients were on and continued to take recommended ART drug combinations over the analysis

period and assumed a range in the annual cost of providing ART (including the cost of medical care) of A $10000-A$20 000 based on previous work,[12] as described in Table 1.

We estimated the 'lifetime' cost of providing care and treatment to sexual partners of temporary residents who become infected; this was based on the number of years a patient takes first, second, third and higher classes of drugs if they begin ART in their twenties.[19] Using the cost estimates for each drug class in Australia[12] with an assumed uncertainty of ±25% and adding annual medical care costs, gives a range in the undiscounted lifetime cost of providing ART post infection of $761 800-$1 269700 (Table 1). We applied a discount rate of 5% to all treatment costs. For discounting purposes, we assumed a conservative time between infection and initiating ART of 4–5 years.[16] Note that this time between becoming infected with HIV and initiating ART reflects the estimated time to reach the average CD4 count at which HIV+ temporary residents in ATRAS started treatment, and does not include the effect of changing guidelines for initiating ART (see footnote 7, Table 1). To assess the sensitivity to this assumption, we also ran our analysis with a 2- to 4-year range in time between infection and initiating ART. This change produced only a minor increase (<10%) to our discounted cost estimates presented here, and did not affect the conclusions (the results of this analysis are available in the online repository).[20]

Results

During the first year after providing ART to all HIV+ temporary residents, there were 22 (interquartile range (IQR) :18–26) new infections caused by HIV+ temporary residents (Fig. 1). Expanding ATRAS to all HIV+ temporary residents and achieving almost universal viral suppression reduced annual new infections to a median of 5 (IQR: 3–7) after 5 years (Table 2; Fig. 1). Providing treatment and care to all HIV+ temporary residents averted a median of 80 new infections (IQR: 68.5–91.5) over 5 years (Table 2; Fig. 2a), at a median undiscounted cost of A$4 0820 000 (IQR: A$34 110 000–A $47 530 000) and a median discounted cost of A$36 240 000 (IQR: A$30 280 000–A$42 200 000) (taking the median of the sum for each simulation). This corresponds to a cost per infection averted of A$450 000 (IQR: A$360 000–A$540 000) (with 5% discounting).

Figure 2b shows the cumulative costs for providing ART and subsidised care to this population for the next 5 years compared with the savings due to the reduction in infections during this period. The resulting reduction in infections gives a median saving of A$80 570 000 (IQR: A$6 5840 000–A$95 310 000); Fig. 2b) in the lifetime treatment and care costs for newly infected people. When discounting is considered, the resulting savings in treatment and care costs reduces substantially (as lifetime costs are considered for infected partners) to a median of A$21730000 (IQR: A$17930 000–A$25530000).

Discussion

Our analysis showed that providing ART to HIV+ temporary residents within Australia will substantially reduce new infections and is unlikely to place a significant financial burden on the Australian Government — providing strong justifications for the provision of ART to temporary Australian residents. In our view, the only sustainable way to support optimal

antiretroviral treatment for HIV+ temporary residents and achieve the resulting patient and population benefits over the long-term is through government subsidised ART. At the cessation of ATRAS in November 2015, 66 ATRAS patients and 400–500 HIV+ temporary residents nationally required an alternative mechanism for accessing ART. Pharmaceutical companies are currently providing access to antiretroviral treatment for Medicare ineligible patients on a compassionate basis in Australia. This is neither ideal nor sustainable. Applying for compassionate access is inefficient, time consuming for clinical staff, and delays treatment initiation. Numerous administrative barriers for specific treatments exist and not all antiretroviral drugs are available through compassionate access; this results in the use of suboptimal regimens instead of drugs, which are clinically indicated and medically appropriate. Furthermore, patients are often required to initially attempt sourcing ART from overseas, which leads to stress and further delays to achieving viral suppression. Overseas supplies of drugs are also often less safe and of lower quality. Finally, basing this important public health measure on the goodwill of commercial companies is subject to change, especially as generic antiretrovirals enter the Australian market from 2017. While the majority of HIV+ temporary residents within Australia eventually become permanent residents and eligible for ART under Medicare,[15] results from the START trial[24] and ATRAS[14] show that any barriers and delays in treatment are detrimental to their health and are contrary to public health considerations.

Australia's current National HIV Strategy aims to have 90% of all HIV+ people on ART and to virtually eliminate transmission by 2020.[25] To achieve ambitious HIV and ART targets across Australia will require a maximum focus on vulnerable and marginalised populations like HIV+ temporary residents, and must ensure they have access to quality information, support, testing and ART.

Several analysis limitations affect the results. Most importantly, due to data for sexual and injecting behaviour, sexual partner characteristics and prevention practices being unavailable, we were unable to develop a more detailed model of HIV transmission among temporary residents in Australia. The only data source providing data for HIV+ temporary residents is the ATRAS study, which is a clinical cohort with no associated behavioural- or transmission-related data. This meant our calculations required several simplifying assumptions to estimate the risk of transmission. We assumed transmission parameters for treated and untreated patients are constant over time, whereas there is evidence the risk of transmission has been decreasing over the last 10 years.[22] We also assumed, due to limited data for temporary residents, HIV transmission from untreated HIV+ temporary residents is the same as for the overall Australian population of people living with HIV. Temporary resident populations are often culturally and linguistically diverse, with less engagement with care and lower knowledge of HIV and prevention methods — suggesting they may have a higher risk of transmission to their partners.[26–28] Due to a lack of data on the partners of temporary residents, we were unable to consider onward transmission from newly infected partners of temporary residents. These assumptions may result in an underestimate for the number of new infections prevented. Counteracting this, however, is the assumption those with unsuppressed virus have the same transmission risk as those not taking ART, whereas treatment is likely to still have some efficacy even if it does not completely suppress a patient's viral load. In addition, the rate of partner change is constant due to an implicit

homogenous mixing assumption, whereas many temporary residents could be in monogamous partnerships (and hence can only transmit HIV once) or have no sexual partners in Australia. Overestimating the number of new infections increases the cost-effectiveness of providing ART to the temporary resident population, while underestimating new infections decreases it. Finally, we also assumed partners of HIV+ temporary residents are Medicare eligible. This assumption likely lowers the cost of providing ART to HIV+ temporary residents, as some of their sexual partners may also be ineligible for Medicare.

By denying ART access to HIV+ temporary residents via Medicare, the Australian Government increases the risk of HIV transmission and the future long-term costs of providing HIV care and treatment, eroding any savings gained by denying HIV+ temporary residents access to subsidised treatment. The Australian Government already allows HIV+ temporary residents to live and work in Australia, and contribute economically through taxation. Providing these individuals with subsidised ART will cost little overall and help Australia achieve its National HIV Strategy targets.

Acknowledgments

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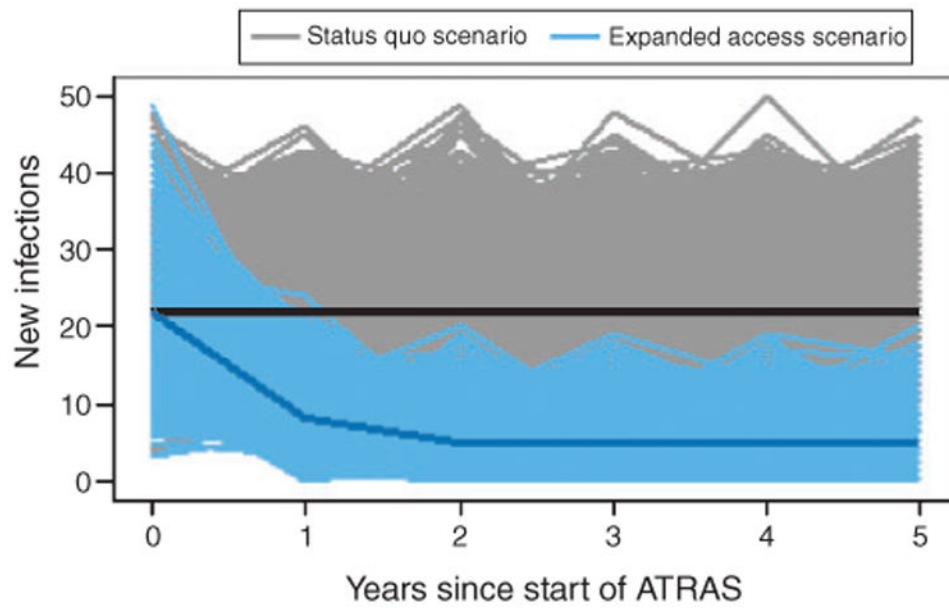
Fig. 1.
Annual number of new infections caused by HIV-positive (HIV+) temporary residents for each simulation. The grey lines represent the status quo scenario simulations, while the blue lines are for the expanded access scenario simulations (expansion of medical care and antiretroviral treatment (ART) to all temporary residents). The black and dark blue lines show the median number of new infections for the status quo and expanded access simulations respectively.
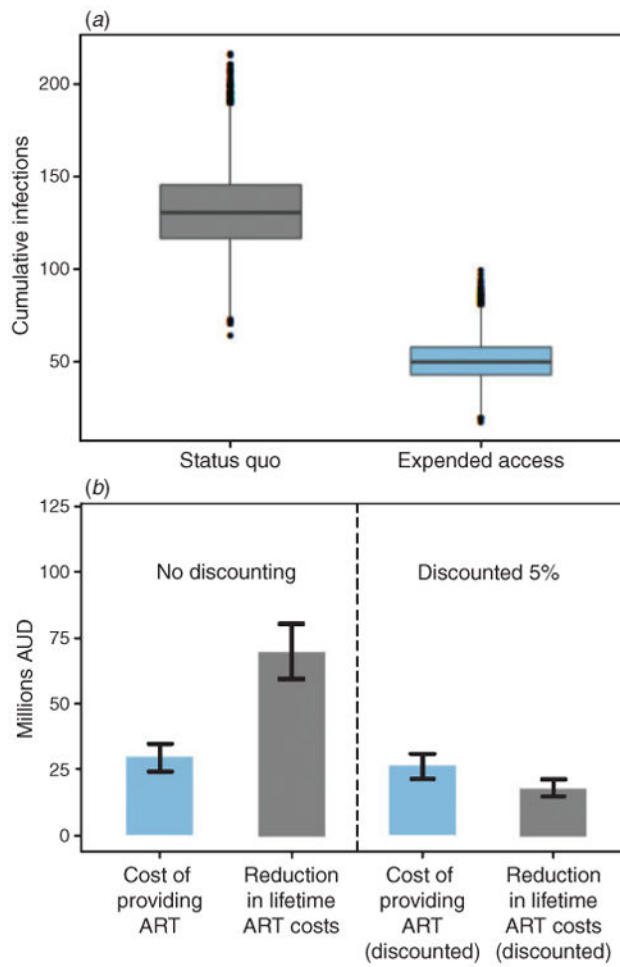
Fig. 2.
(*a*) Total number of new infections over 5 years for the expanded access scenario, where all HIV-positive (HIV+) temporary residents receive medical care and antiretroviral treatment (ART), compared with the status quo scenario, where ART coverage remains at current levels. (*b*) Median total costs for providing all HIV+ temporary residents with medical care and ART, and the reduction in lifetime treatment and care costs for partners of HIV+ temporary residents who acquire infection over 5 years. The bars show the interquartile range in total costs across all simulations.

Table 1

Calculation input parameter ranges

Footnotes provide justifications for these parameter ranges. The simulations used for the calculations take samples from these ranges assuming a uniform distribution. PLWHIV, people living with HIV; MSM, men who have sex with men; ART, antiretroviral treatment

Parameter	Description	Range	Footnote
Demographic			
$N(0)$	Overall population size in initial year	[400–500]	1
p	Multiplicative change in annual population	[0.98–1.02] per year	1
p_m	Proportion of Medicare-ineligible population of PLWHIV who are MSM	[0.4–0.6]	1
p_n	Proportion of Medicare-ineligible population of PLWHIV who are non-MSM	Given by $1-p_m$	1
Clinical			
θ	Proportion of population taking ART	63% at enrolment and 95% after 12 months ±5%	2
ψ	Proportion of population taking ART with undetectable viral load	70% at enrolment, 88% after 12 months, and 96% after 24 months ±5%	2
HIV transmission			
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	[0.0771–0.1285]	3
e_{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 care and ART to Medicare ineligibles (including medical care costs)	[A\$10 000–A\$20 000]	5
c_{life}	Average undiscounted lifetime cost of providing care and ART post infection (including medical care costs)	[A\$761 800–A\$1 269 700]	6
r_{disc}	Discounting rate	5%	7
t_{ART}	Average time between infection and initiating ART	[4–5] years	7

[1] The 2013 Australian HIV Observational Database (AHOD) Temporary Residents Access Study (ATRAS) report estimates there are 450 Medicare ineligible people living with HIV (PLWHIV) in Australia.[15] We assume a range in the population between 400 and 500 PLWHIV, with the potential for only a small change in population size over time. In the population of 180 at enrolment, 89 (49.4%) males attributed their HIV infection to MSM exposure.[15] Assuming this reflects the demographic distribution over time, we assume 40–60% of the population consists of MSM with the remainder being non-MSM.

[2] At enrolment, 62.8% of ATRAS patients were already receiving antiretroviral treatment (ART), with 71.8% having an undetectable viral load.[15] After enrolment, all patients were put onto ART, resulting in 87% having an undetectable viral load at 12 months and 96% having an undetectable viral load at 24 months. Based on the ATRAS data, we assume the percentage of temporary residents on ART increases from 70% to 95%, with a range of ±5%, with the proportion with undetectable virus increasing from 70% to 96% over 2 years, with a range of ±5%.

[3] These values were calculated using data for the overall population of PLWHIV in Australia and Equation 2 in the main text. In 2013, there were an estimated 26 640 PLWHIV in Australia, and 912 new infections[16] of which ~75% are attributed to homosexual contact.[17] According to the 2013 estimates for the HIV treatment cascade in Australia, ~75% of MSM living with HIV[17] and 55% of non-MSM living with HIV are taking ART[17] respectively. In both MSM and non-MSM taking ART, ~90% have an undetectable viral load.[15,17] Putting these values into Equation 2 in the main text and assuming ±25% uncertainty produces the values of β_n and β_m.

[4] We assume those with viral suppression have a 90–99% reduction in transmission to their sexual partners. This assumption is in line with the results from the HPTN-052 trial for those with detectable drug levels[7] and the recent PARTNER study, which recorded zero HIV transmissions

from 1166 HIV+ people to their sexual partners (though the upper 95% confidence interval was 0.84, 0.88, and 0.97 per 100 couple-years for MSM, heterosexual males and heterosexual females respectively).[18]

[5]At enrolment, 83% of the ATRAS cohort on ART are taking Tenofovir/Emtrcitabine (Truvada) as the 'backbone' of their regime. This means most 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 and undertake annual monitoring of their infection. From Schneider *et al*, the average annual cost of first-line drugs in Australia is A$10685 (A$6945-A$14 424).[12] Estimated annual medical costs for people living with HIV were also estimated in Schneider *et al* by CD4 count. Annual medical care and infection monitoring for HIV+ people with CD4 >500 cells μL^{-1}, CD4 350–499 cells μL^{-1}, CD4 >200-349 cells μL^{-1} and CD4 <200 cells μL^{-1} was estimated to cost A$3097, A$4402, A$4762 and A$7883 respectively. In recent years, patients in the Australian HIV Observational Database (AHOD) cohort have initiated ART at ~350 cells μL^{-1}. We therefore assumed all patients have a CD4 count >200 cells/μL and the associated annual monitoring costs to range from A$3000 to A$5000. Using these values, we assumed a range in the annual ART cost (including medical care) of A$10 000 to A$20 000.

[6]If a partner of a temporary resident 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 used an estimate for the lifetime cost of providing ART. An analysis of the life expectancy of PLWHIV in Australia, given currently available antiretroviral treatments, suggests someone starting treatment in their twenties will be taking ART for ~40 years,[19] spending ~9 years on first-line drugs, ~14 years on second-line drugs, ~3 years on third-line drugs, and the remainder of the time on higher classes of drug. Using the cost estimates from the study by Schneider *et al*,[12] we assume the annual costs of proving each line of drugs is A$10 685 for first-line drugs, A$19 364 for second-line drugs, A$31411 for third-line drugs and A$28 162 for fourth and higher lines of drugs. Multiplying the values for each drug class and summing the resulting values produces the undiscounted treatment cost. To account for all uncertainties in the time patients are on each treatment class and drug costs, we assumed a range of ±25% in the overall undiscounted cost. Finally, we added the annual monitoring cost ranging from A$3000 to A$5000, as described in footnote 5 to produce the undiscounted cost presented here.

[7]To discount future costs of providing ART to temporary residents and to those who become infected, we applied a discount rate of 5% from the year of enrolment in ATRAS for all treatment costs. For discounting purposes, we included the time between infection and initiating ART; we estimated this 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 ~350 cells μL^{-1};[15] it is estimated that it takes 4.4 years for a person to reach this CD4 count post infection.[16] We therefore assume a range of 4–5 years for the time between infection and ART initiation.

Table 2

Summary results for status quo scenario and the expanded access scenario

Results show the median and interquartile range (IQR) of all simulations for each scenario. ART, antiretroviral treatment; NA, not applicable. Costs are, rounded to the nearest A$10 000

Indicator	Status quo scenario (median, IQR)	Expanded access scenario (median, IQR)
Annual infections after 5 years	22 (18–26)	5 (3–7)
Cumulative infections	131 (116–145)	50 (42–57)
Infections averted	NA	80 (68–91)
Cost of providing care and ART (undiscounted)	NA	A$40 820 000 (A$34 110 000-A$47 530 000)
Lifetime care and ART costs (undiscounted)	A$131 620 000 (A$111 230 000–A$152020 000)	A$50 570 000 (A$41450 000-A$59 700 000)
Reduction in lifetime care and ART costs (undiscounted)	NA	A$80 570 000(A$65 840 000-A$95 310 000)
Cost of providing care and ART (discounted 5%)	NA	A$36 240 000(A$30 280 000-A$42 200 000)
Lifetime care and ART costs (discounted 5%)	A$36640000 ($A31 490 000–A$41780000)	A$14 720 000 (A$12 300 000-A$17 140 000)
Reduction in lifetime care and ART costs (discounted 5%)	NA	A$21 730 000 (A$17 930 000-A$25 530 000)