Impact of providing ART to Medicare ineligibles

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This document summarizes a simple analysis to calculate the impact of providing anti-retroviral therapy (ART) to people living with HIV (PLHIV) in Australia who are Medicare ineligible. This analysis uses data from the Australian HIV Observational Database Temporary Residents Access Study (ATRAS) [1].The R code for these calculations is available in the associated Rmarkdown file. The aim of these calculations is to estimate the number of new HIV infections that occur through transmission from Medicare ineligible people to their sexual partners, the cost of providing ART to the Medicare ineligible population, and the potential future cost of providing treatment to partners of Medicare ineligibles who become infected.

This document is written in dynamic format using R markdown v2 within R studio 0.98.1056 (using R version 3.1.2). Plots are created using the package ggplot2. Further details are available in the associated Rmarkdown file, which also contains the R code to produce all the results when the markdown is run. We have suppressed code blocks in the output document.

### Methodology

This section summarizes the methodology used for the calculations. 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. Descriptions of model details, assumptions and input parameters follow below.

#### Demographics

For this analysis, we consider a population of PLHIV who are Medicare ineligible with the characteristics of people in ATRAS [1]. 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 constant. We used this compartmentalization of the population 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. We represent this movement using a constant growth rate for the population (which is positive for a growing population and negative for a declining population). Letting equal the total population size in year , the number of medicare ineligible people in the population is then given by

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. We used the most recent data value 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 behavior for example). We also do not consider onward transmission from newly infected partners. As the sexual behavior 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 behavior.

Key assumptions:

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

#### Costs associated with ART provision

Our analysis includes an estimate of the annual cost of providing ART to Medicare ineligibles and their partners who become infected. We obtained estimates of the costs of providing treatment using previous work for Australian settings [2]. For sexual partners of Medicare ineligibles who become infected with HIV we estimate the 'lifetime' cost of providing and treatment.

#### Parameter table

Table 1 lists all input parameters and their values and ranges.

**Table 1** - Calculation input parameter ranges. Endnotes provide justifications for these parameter ranges. The simulations used for the calculations take samples from these ranges assuming a uniform distribution.

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Description | Range | Reference |
| **Demographic parameters** |  |  |  |
|  | Overall population size in initial year | [400 - 500] | 1 |
|  | Multiplicative change in annual population | [0.98 - 1.02]/yr | 1 |
|  | Proportion of Medicare-ineligible population of PLHIV who are MSM | [0.4 - 0.6] | 1 |
|  | Proportion of Medicare-ineligible population of PLHIV who are non-MSM | Given by | 1 |
| **Clinical parameters** |  |  |  |
|  | Proportion of population taking ART | 63% at enrollment and 95% after 12 months 5% | 2 |
|  | Proportion of population taking ART with undetectable viral load | 70% at enrollment, 88% after 12 months, and 96% after 24 months 5% | 2 |
| **HIV transmission parameters** |  |  |  |
|  | Annual probability an untreated non-MSM transmits HIV to another person | [0.0485 - 0.0808] | 3 |
|  | Annual probability an untreated MSM transmits HIV to another person | [0.0771 - 0.1285] | 3 |
|  | Efficacy of ART in preventing HIV transmission if virus is suppressed | [0.9 - 0.99] | 4 |
| **Treatment costs** |  |  |  |
|  | Average annual undiscounted cost of providing care and ART to Medicare ineligibles (including monitoring costs) | [$10,000 - $20,000] | 5 |
|  | Average undiscounted lifetime cost of providing care and ART post infection (including monitoring costs) | [$761,800 - $1,269,700] | 6 |
|  | Discounting rate | 5% | 7 |
|  | 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]. 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 enrollment, 89 (50%) of the males attributed their HIV infection to MSM exposure [1]. Assuming this reflects the demographic distribution over time, we assume 40-60% of the population is MSM with the remainder non-MSM.
2. At enrollment, 62.8% of ATRAS patients were already receiving ART with 71.8% having undetectable viral load [1]. After enrollment, 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 5% with the proportion with undetectable virus increasing from 70% to 96% over two years with a range of 5%.
3. These values are calculated using data for the overall population of PLHIV in Australia. Using the equation where is the overall incidence in Australian MSM and non-MSM, 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 1 we can estimate the value of for MSM and non-MSM. In 2013, there were an estimated 26,640 PLHIV in Australia and 912 new infections [3] of which around 75% are attributed to homosexual contact [4]. According to recent estimates for the HIV treatment cascade in Australia, around 75% of MSM living with HIV [4] and 55% of non-MSM living with HIV are taking ART [4], respectively. In both MSM and non-MSM taking ART, around 90% have an undetectable viral load [1,4]. Putting these values into the equation above and assuming 25% uncertainty produces the values of and .
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 [5] 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) [6].
5. At enrollment, 83% of the ATRAS cohort on ART are 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 and undertake annual monitoring of their infection. From Schneider et al., the average annual cost of first-line drugs in Australia is $10,685 ($6,945- $14,424) [2]. 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/L, CD4 350-499 cells/L, CD4 200-349 cells/L, and CD4 < 200 cells/L was estimated to equal A$3,097, $4,402, $4,762, and $7,883, respectively. In recent years, patients in the AHOD cohort have initiated ART at around 350 cells per L [1]. We therefore assume all patients have a CD4 count 200 cells/L and the associted annual monitoring costs to range from $3,000 to $5,000. Using these values, we assume a range in the annual ART cost (including monitoring) of $10,000 to $20,000.
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 [7] 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 [2], we assume the annual costs of proving each line of drugs is $10,685 for first-line drugs, $19,364 for second-line drugs, $31,411 for third-line drugs, and $28,162 for fourth and higher lines of drugs. Multiplying the values for each drug class and summing produces the undiscounted treatment cost. To account for all uncertainties in time on each treatment class and drug costs we assume a range of 25% in the overall undiscounted cost. Finally we added the annual monitoring cost ranging from $3,000 to $5,000 as described in footnote 4 to produce the undiscounted cost presented here.
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 enrollment in ATRAS for all treatment costs. For discounting purposes we include 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 around 350 cells per L [1], it is estimated it takes 4.4 years for a person to reach this CD4 count post infection [3]. 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 infected through partnerships with HIV-positive people ineligible for Medicare. The appendix provides details of the calculations.

The total number of new infections equals the sum of 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 on ART and with suppressed virus changes over time, matching the ATRAS data in Table 1.

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 1) lifetimecost and the discounted lifetime cost.

#### Simulations

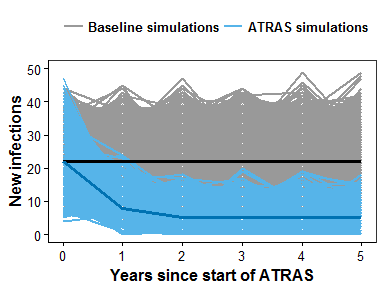
To perform this analysis, we generated 1000 input parameter sets by sampling from each of the parameter ranges in Table 1. For each of these parameter sets we then ran 20 simulations to account for stochastic variations. We ran each simulation for 5 years since the enrollment of patients into ATRAS. We then calculated summary statistics using the results from each simulation.

### Results

During the first year after enrollment for ATRAS, the number of new infections caused by Medicare ineligible people is estimated to be 22 (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 1).

The impact of expanding ATRAS to all Medicare ineligibles and achieving almost universal viral suppression is to reduce annual new infections to a median of 5 (IQR: 3 - 7) after r years (Figure 1). This corresponds to 1% of the Medicare ineligible population.

**Figure 1** - Annual number of new infections caused by HIV-positive Medicare ineligibles for each simulation. 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 ART simulations respectively.

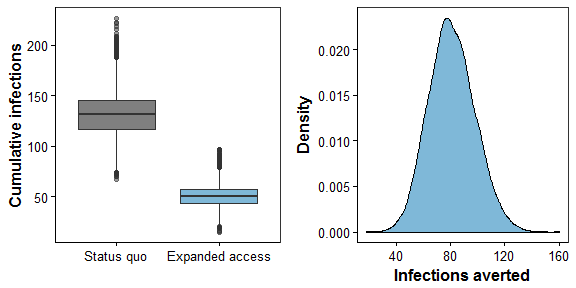


**Table 2** - Summary results for status-quo scenario and the expanded access scenario. The results show the median and inter-quartile range (IQR) of all simulations for each scenario. NA = not applicable. Costs are rounded to the nearest $10,000

|  |  |  |
| --- | --- | --- |
| Indicator | Status-quo scenario  (median, IQR) | Expanded access scenario (median, IQR) |
| Annual infections after 5 years | 22 (18 - 25) | 5 (3 - 7) |
| Cumulative infections | 131 (116 - 145) | 50 (43 - 57) |
| Infections averted | NA | 80 (68 - 91) |
| Cost providing ART (undiscounted) | NA | $40,300,000  ($33,480,000 - $47,120,000) |
| Lifetime care and ART costs (undiscounted) | $131,640,000  ($111,610,000 - $151,660,000) | $50,280,000  ($41,320,000 - $59,240,000) |
| Reduction in lifetime ART costs (undiscounted) | NA | $80,620,000  ($66,130,000 - $95,120,000) |
| Cost providing ART (discounted 5%) | NA | $35,830,000  ($29,780,000 - $41,870,000) |
| Lifetime care and ART costs (discounted 5%) | $40,300,000  ($33,480,000 - $47,120,000) | $40,300,000  ($33,480,000 - $47,120,000) |
| Reduction in lifetime ART costs (discounted 5%) | NA | $17,740,000  ($14,560,000 - $20,920,000) |

Figure 2 shows the distributions for the cumulative number of new infections in partners of Medicare ineligibles for the baseline scenario and if ART is provided to all Medicare ineligibles. Providing treatment to all Medicare ineligibles will avert a median of 80 new infections (IQR: 68.5 - 91.5) over 5 years.

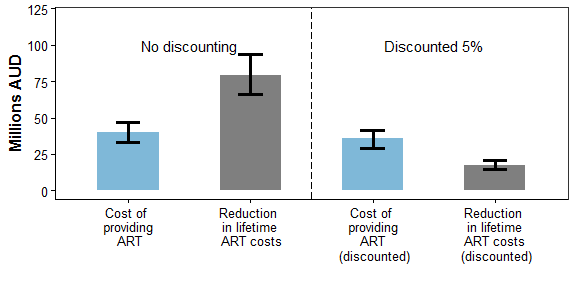
**Figure 2** - Total number of number of new infections (left) and the distribution in infections averted (right) over 5 years after all HIV-positive people ineligible for Medicare are provided ART.



Providing ART to Medicare ineligibles over 5 years is estimated to have a median undiscounted cost of $40,300,000 (IQR: $33,480,000 - $47,120,000) and a median discounted cost of $35,830,000 (IQR: $29,780,000 - $41,870,000). This corresponds to a cost per infection averted of $440,000 (IQR: $350,000 - $530,000) (with 5% discounting).

Figure 3 shows the cumulative costs for providing ART to Medicare ineligible people for the next 5 years and the savings due to the reduction in infections during this period. The median undiscounted cumulative cost when ART is expanded to all Medicare ineligible PLHIV is $40,300,000 (IQR: $33,480,000 - $47,120,000) (taking the median of the sum for each simulation). The resulting reduction in infections gives a median saving of $80,620,000 (IQR: $66,130,000 - $95,120,000); Figure 3) in the lifetime treatment costs for newly infected people. When discounting is taken into account, the costs of providing ART reduce to a median $35,830,000 (IQR: $29,780,000 - $41,870,000) and the resulting saving in treatment costs reduces to a median of $17,740,000 (IQR: $14,560,000 - $20,920,000).

**Figure 3** - Median total costs for providing all Medicare ineligibles with ART and the reduction in lifetime treatment costs for partners of Medicare Ineligibles who acquire infection over 5 years. The bars show the interquartile range in total costs across all simulations.



### Appendix: Details of calculations

The overall number of new infections per year is calculated by summing the number of new infections caused by MSM and non-MSM population group; i.e.

where is the given year.

Letting the index represent one of the populations groups (and dropping for the time being), the probability of HIV transmission to a HIV-negative sexual partner is given by

as ineffective treatment (resulting in unsuppressed virus) has the same transmission probability as no treatment. After some algebra this gives

Using this probability, the number of new infections each year is given by a binomial distribution

For large N and small this is approximately equal to

and the number of new infections is given by a risk equation. Given the relatively small population size and the high levels of ART coverage and viral suppression, likely resulting in a small number of infections, we use the stochastic approach in this analysis.

Adding the population terms together gives the overall number of new infections in a given year . The cumulative number of new infections in partners of medicare ineligibles over years is then equal to

and the total cost of providing ART to Medicare ineligibles is

(undiscounted costs are calculated by setting the discount rate to ). The total future costs of providing treatment to newly infected partners of Medicare ineligibles is given by

where is the number of years infected people will be on ART, is the annual cost of ART years from initiation, and is the time between infection initiating ART (undiscounted costs are calculated by setting the discount rate to ).

### References

1. Petoumenos K (2013) THE australian hiv observational database temporary residents access study (atras) one year follow-up.

2. Schneider K, Gray RT, Wilson DP (2014) A cost-effectiveness analysis of hiv pre-exposure prophylaxis for men who have sex with men in australia. Clinical infectious diseases 58: 1027–1034.

3. Jansson J, Kerr CC, Mallitt K-A, Wu J, Gray RT, et al. (2015) Inferring hiv incidence from case surveillance with cd4+ cell counts. AIDS (London, England).

4. Institute TK (2014) HIV in australia annual surveillance report 2014 supplement. Report. The Kirby Institute, UNSW Australia, Sydney NSW 2052.

5. Cohen M, Chen Y, McCauley M, Gamble T, Hosseinipour M, et al. (2011) Prevention of hiv-1 infection with early antiretroviral therapy. New England Journal of Medicine.

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7. Jansson J, Wilson DP, Carr A, Petoumenos K, Boyd MA (2013) Currently available medications in resource-rich settings may not be sufficient for lifelong treatment of hiv. AIDS (London, England) 27: 1245.