Importance of promoting HIV testing for preventing secondary transmissions: modelling the Australian HIV epidemic among men who have sex with men

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Abstract. Background: We address the research questions: (i) what proportion of new HIV infections is transmitted from people who are (a) undiagnosed, (b) in primary HIV infection (PHI), (c) on antiretroviral therapy?; and (ii) what is the expected epidemiological impact of (a) increasing the proportion of newly acquired HIV infections receiving early treatment, and (b) increasing HIV testing rates? Methods: We used a mathematical model to simulate HIV transmission in the population of men who have sex with men (MSM) in Australia. We calibrated the model using established biological and clinical data and a wide range of Australian MSM epidemiological and behavioural data sources. Results: We estimate that ~19% of all new HIV infections are transmitted from the ~3% of Australian HIV-infected MSM who are in PHI; ~31% of new HIV infections are estimated to be transmitted from the ~9% of MSM with undiagnosed HIV. We estimate that the average number of infections caused per HIV-infected MSM through the duration of PHI is ~0.14–0.28. Conclusions: The epidemiological impact of increasing treatment in PHI would be modest due to insufficient detection of newly-infected individuals. In contrast, increases in HIV testing rates could have substantial epidemiological consequences. The benefit of testing will also increase over time. Promoting increases in the coverage and frequency of testing for HIV could be a highly-effective public health intervention, but the population-level impact of interventions based on promoting early treatment of patients diagnosed in PHI is likely to be small. Treating PHI requires further evaluation of its long-term effects on HIV-infected individuals.

Additional keywords: Australia, early treatment, HIV/AIDS, men who have sex with men, testing.

Introduction

The total number of HIV notifications in Australia has steadily increased in recent years to ~1000 per year, after a nadir of 720 HIV diagnoses in 1999. The majority of the rise in diagnosed HIV infections in Australia has occurred in men who have sex with men (MSM). Similar trends have also been observed in the USA, UK, the Netherlands, and other developed countries. Understanding the preventative benefit of changes in implementation of current biomedical and behavioural interventions is important for planning public health campaigns to mitigate the current rises in HIV. One of the cornerstones of effective prevention programs is the promotion of HIV testing. Therefore, we investigate the relationship between expected HIV incidence and diagnoses and the proportion of MSM who are tested for HIV each year. We also investigate the population-level effectiveness of increasing the proportion of newly diagnosed people who receive early antiretroviral therapy to reduce their infectiousness.

Newly infected people enter the stage of primary HIV infection (PHI). In this stage viral loads are higher than at any other time during the course of infection. Consequently, people in PHI have the greatest infectiousness per sexual encounter. Newly-infected people are generally unaware of their new serostatus and their potential to cause secondary HIV transmissions. However, PHI typically lasts for only 3–6 months, after which viral levels stabilise to considerably lower levels for the long chronic/asymptomatic stage of infection. Because of its short duration, the importance of PHI in contributing to secondary HIV transmissions relative to the longer chronic and AIDS stages of HIV infection is unclear. It is also unclear how reliably one can determine the presence of a PHI case and the duration of time since seroconversion. The short duration of PHI also makes it difficult to capture cases in this stage of infection.

Approximately 5 years ago, if a person in Australia was diagnosed in PHI s/he would have a large likelihood of commencing combination antiretroviral therapy (cART) at diagnosis. The trend has moved away from this, towards delaying therapy, but the best clinical practice is still being debated. Effective suppression of HIV using cART has remarkably altered the clinical outcomes of HIV-infected individuals. cART first became widely available in Australia during 1996 and was rapidly and widely taken up among HIV-infected patients, leading to rapid improvements...
in morbidity and mortality. Despite the trend away from early treatment, the proportion of diagnosed HIV-infected MSM in Australia that are treated is high (70–90% are on cART). By decreasing HIV viral load in treated individuals, it is thought that cART also reduces infectiousness of treated individuals, but empirical studies to confirm this are yet to be completed. Treating patients who are diagnosed in PHI might have public health benefits for reducing HIV transmission.

Detecting newly infected people in PHI for initiating treatment can only occur if there are high rates of testing for HIV (in terms of coverage, i.e. the proportion of people who are tested, and the frequency of testing, i.e. number of times people are tested per year). High testing rates can also have additional epidemiological benefits. One benefit is that individuals who are diagnosed as HIV-positive typically change their behaviour in order to reduce onward transmission to others. Although some individuals might increase sexual activity and/or the acquisition of new sexual partners, most individuals diagnosed with HIV significantly decrease sexual partner acquisition by as much as 50% on average. In Australian MSM, if a regular partnership is known to be serodiscordant, condoms are used ~75–80% of the time compared with less than 10% of the time in relationships thought to be seroconcordant. In casual partnerships, serological disclosure is not as common as in regular relationships, but condoms are used in ~60–70% of all casual sexual encounters; presumably if the casual partnership was known to be serodiscordant then the proportion of acts in which condoms are used would increase considerably or alternatively the partnership may not form at all. Knowledge of true serostatus is very important. Therefore, increasing the proportion of men who test for HIV each year could have large preventative benefits, from changing behaviour to reducing infectiousness, if the diagnosis leads to treatment.

In the present study we attempt to address the following research questions: (i) what proportion of new HIV infections in Australia is transmitted from people who are (a) undiagnosed, (b) in PHI, (c) on antiretroviral therapy?; and (ii) what is the expected epidemiological impact of (a) increasing the proportion of those diagnosed in PHI that commence early treatment, and (b) increasing the proportion of MSM tested for HIV each year? To answer these questions we use a mathematical model to simulate HIV transmission in the population of MSM in Australia. We calibrate the model using established biological and clinical data from the published literature and a wide range of Australian MSM epidemiological and behavioural data sources (Table 1).

Methods

We use a previously published mathematical model to address the research questions. Our dynamic transmission model simulates the HIV epidemic among the population of MSM in Australia. The model tracks the incidence of new HIV infections and the numbers of HIV-infected MSM as they progress in disease from PHI, to chronic infection, to the AIDS stage disease. The ‘force of infection’ depends on the number of people in each HIV-infected stage, the average number of casual and regular partnerships per MSM, the average number of penile-anal acts per partnership, the proportion of these acts in which condoms are used, and the efficacy of condoms. We also include the proportion of sexual partnerships in which HIV serostatus is disclosed and the effect of disclosure on condom usage. The model distinguishes undiagnosed HIV-infected MSM from those who become diagnosed through testing. In the model, MSM who are diagnosed with HIV might change their behaviour and could commence antiretroviral therapies, and MSM in AIDS stage have reduced sexual activity. For those on cART, a proportion is assumed to have undetectable viral load and thus, they are less likely to transmit infection. Although this is dependent on the level of adherence to therapy, we do not model adherence and its impact on suppression. Rather, we directly use data from the Australian HIV Observational Database on the proportion of people on cART who attain viral suppression. The flows in the number of people between these compartments are presented schematically in Fig. 1 and are determined by biological, behavioural, clinical, and epidemiological parameters (Table 1).

For each model parameter we explored a range of input values to account for the intrinsic heterogeneity and for the uncertainty in the parameter. We sampled over the entire parameter space and conducted detailed uncertainty and sensitivity analyses from 10 000 simulations using the SaSAT software package (NCHERC, University of New South Wales, Sydney, Australia). Results presented in the present paper are based on median outcome variables obtained from running the 10 000 simulations. In each stage of infection we model different viral load levels, which influence differential transmission probabilities. Treated MSM have substantially lower viral loads, which also significantly slows disease progression rates; we also account for the effectiveness of cART in achieving viral suppression. We also include HIV-related death rates. The dynamic transmission model is mathematically represented by 10 ordinary differential equations, one equation for each compartment/state (uninfected MSM and HIV-infected MSM in either primary, chronic, or AIDS stage, and for each of the three HIV-infected groups we distinguish between undiagnosed, diagnosed and untreated, or on treatment). See Fig. 1 for a schematic diagram of the model, and Hoare et al. and Table 1 for detailed mathematical description of the model and data sources.

Results

Our simulations yielded 12 000–18 000 MSM living with HIV in Australia in 1999, the starting point of our simulations. This is consistent with other independent estimates of prevalence of ~5% in Australian MSM. Of the HIV-infected MSM, we estimated the percentage in each disease stage as well as the percentage undiagnosed, diagnosed and untreated, and treated (Table 2). We also estimated the proportion of all new infections that are transmitted from MSM in each of these compartments (Table 2). Our simulations suggest that although ~9% of HIV-infected MSM are undiagnosed, they are responsible for ~31% of the new HIV infections, and although only ~3% of MSM are in primary infection, they are responsible for ~19% of all new HIV infections. It is not surprising that treated individuals contribute lower proportions of new infections because viral load is suppressed in a large number of treated patients. Thus, we
Table 1. Model parameter definitions, ranges and references. For all time-dependent parameters (*) the value used in our mathematical model is the linear interpolation of the weighted average across each Australian state, as weighted by the population size.

See Appendix 1 for explanation of how values were obtained for parameters associated with reference (a)–(k); ART, antiretroviral therapy; MSM, men who have sex with men; STI, sexually transmissible infection.

<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average number of sexual partnerships per year (undiagnosed MSM)</td>
<td>$a^*$</td>
<td>21,34,52</td>
</tr>
<tr>
<td>Multiplying factor for the reduction in number of sexual partners for men in AIDS stage disease</td>
<td>0.1–0.4</td>
<td>21</td>
</tr>
<tr>
<td>Percentage of sexual partnerships in which penile–anal intercourse occurs</td>
<td>10–40%</td>
<td>20–28</td>
</tr>
<tr>
<td>Multiplying factor for the change in number of sexual partners post diagnoses of HIV infection (this reflects a possible range from 50% decrease to 10% increase)</td>
<td>0.4–1.1</td>
<td></td>
</tr>
<tr>
<td>Proportion of partnerships in which serostatus is disclosed (in negotiating condom usage)</td>
<td>Regular 0.8–0.9, Casual h*</td>
<td>29,30,53,54</td>
</tr>
<tr>
<td>Proportion of acts in which condoms are used</td>
<td>e*</td>
<td>29,30</td>
</tr>
<tr>
<td>Efficacy of condom protection per act</td>
<td>0.85–0.9</td>
<td>55–59</td>
</tr>
<tr>
<td>Baseline viral load during chronic infection</td>
<td>$10^4$–$10^5$ copies/mL</td>
<td>10–60–63</td>
</tr>
<tr>
<td>Average viral load at primary infection stage</td>
<td>$10^5.5$–$10^6$ copies/mL</td>
<td>10.60,61,63,64</td>
</tr>
<tr>
<td>Average viral load at AIDS</td>
<td>$10^5$–$10^6$ copies/mL</td>
<td>61,65,66</td>
</tr>
<tr>
<td>Average viral load in effectively treated individual</td>
<td>10–100 copies/mL</td>
<td>67–69</td>
</tr>
<tr>
<td>Proportion of individuals on antiretroviral therapy in which viral load is suppressed</td>
<td>d*</td>
<td>20,34,70,71</td>
</tr>
<tr>
<td>Probability of HIV transmission per act from an individual in chronic stage of infection</td>
<td>0.0015–0.0025</td>
<td>72–77</td>
</tr>
<tr>
<td>Probability of HIV transmission per act from an individual in primary or AIDS stage of infection</td>
<td>e</td>
<td>8</td>
</tr>
<tr>
<td>Probability of HIV transmission per act from a treated individual</td>
<td>0.05–0.15</td>
<td>79,80</td>
</tr>
<tr>
<td>The multiplicative increase in transmission probability due to the presence of other STIs</td>
<td>2–5</td>
<td>81–87</td>
</tr>
<tr>
<td>Average number of anal intercourse acts per regular partner per week</td>
<td>1.6–2.4</td>
<td>88</td>
</tr>
<tr>
<td>Average number of anal intercourse acts per casual partner (over duration of casual relationship)</td>
<td>1–2</td>
<td>54,88</td>
</tr>
<tr>
<td>Proportion of MSM that test for HIV infection each year</td>
<td>h*</td>
<td>30</td>
</tr>
<tr>
<td>Average time from the beginning of AIDS before individual is likely to be diagnosed with infection</td>
<td>2–4 months</td>
<td>9–11</td>
</tr>
<tr>
<td>Average time for untreated individuals to progress from primary infection to chronic infection</td>
<td>3–9 months</td>
<td>60,65,89–92</td>
</tr>
<tr>
<td>Average time for individuals to progress from chronic infection to AIDS</td>
<td>8–12 years</td>
<td></td>
</tr>
<tr>
<td>Proportion of people diagnosed in primary infection that will commence treatment</td>
<td>i</td>
<td></td>
</tr>
<tr>
<td>Average time to cease treatment for individuals with primary infection</td>
<td>6–12 months</td>
<td></td>
</tr>
<tr>
<td>Proportion of people who started ART in primary infection and continue ART after finishing dosing schedule</td>
<td>65–75%</td>
<td></td>
</tr>
<tr>
<td>Proportion of people in chronic infection that will commence treatment</td>
<td>65–75%</td>
<td>16,29,30,34</td>
</tr>
<tr>
<td>Proportion of people with AIDS that commence treatment that experience treatment failure</td>
<td>0–0.1</td>
<td></td>
</tr>
<tr>
<td>Average time before individuals with AIDS commence therapy</td>
<td>1–3 months</td>
<td></td>
</tr>
<tr>
<td>Average time before diagnosed individuals in chronic infection commence therapy</td>
<td>2–10 years</td>
<td>34</td>
</tr>
<tr>
<td>Average time to cease treatment for individuals with chronic infection</td>
<td>6–12 years</td>
<td>34</td>
</tr>
<tr>
<td>Average time to cease treatment for individuals with AIDS</td>
<td>8–14 years</td>
<td></td>
</tr>
<tr>
<td>Average time for individuals to ‘retire’ out of sexually active population (no longer obtaining new partners)</td>
<td>30–35 years</td>
<td>$j^{01}$</td>
</tr>
<tr>
<td>Proportion of untreated MSM in chronic infection who die each year</td>
<td>1–2%</td>
<td>93–97</td>
</tr>
<tr>
<td>Proportion of treated MSM in chronic infection who die each year</td>
<td>1–2%</td>
<td>93–97</td>
</tr>
<tr>
<td>Average time until death from the onset of AIDS for untreated individuals</td>
<td>0.5–1.5 years</td>
<td>97–100</td>
</tr>
<tr>
<td>Average time until AIDS-related death for individuals in AIDS stage but on ART (with treatment failure)</td>
<td>0.5–5 years</td>
<td>91,97,99,101–107</td>
</tr>
<tr>
<td>Average time of disease progression for treated individual with chronic infection to progress to AIDS</td>
<td>$1/\omega_i &lt;1/t_i &lt;20$</td>
<td></td>
</tr>
<tr>
<td>Number of new susceptible individuals entering the MSM population per year (this is approximately 3.0–3.5% of men)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nationally</td>
<td>2000–2500</td>
<td>$k$</td>
</tr>
<tr>
<td>NSW/ACT</td>
<td>35–40%</td>
<td></td>
</tr>
<tr>
<td>Vic.</td>
<td>22–27%</td>
<td></td>
</tr>
<tr>
<td>Qld</td>
<td>17–22%</td>
<td></td>
</tr>
</tbody>
</table>

Compared untreated MSM who are undiagnosed with those who are diagnosed but untreated; we found that although there are almost three times as many diagnosed but untreated MSM as undiagnosed MSM, the undiagnosed HIV-infected MSM contributed greater numbers of new infections (Table 2).

A type of reproductive ratio $R_i$ per compartment can be obtained by scaling the number of infections caused by people in each compartment by the number of people in each compartment. We calculated two reproductive ratios: the average number of new HIV infections caused per MSM per year while (i) in primary infection, and (ii) undiagnosed. These ratios were calculated to be 0.54 (median, interquartile range (IQR) (0.44–0.64)) and 0.31 (median, IQR (0.28–0.35)), respectively; note that we standardised these ratios to the rate per year for comparative purposes. Since PHI lasts for ~3–6 months, we estimate that the average number of
infections caused per HIV-infected MSM through the duration of PHI is ~0.14–0.28. This is consistent with independent estimates. Sensitivity analyses of these ratios to the model input parameters revealed that the viral load in PHI, the duration of PHI, and the frequency of sexual acts were the most important parameters in determining the number of HIV transmissions from MSM in PHI and undiagnosed MSM. The average number of infections caused per MSM while undiagnosed v: the duration of PHI is shown in Fig. 2. The strong positive association suggests that targeting undiagnosed HIV-infected MSM for testing and treatment, particularly during PHI, could be an effective public health prevention strategy.

We used our model to estimate the potential impact of changes in the proportion of diagnosed PHI cases who initiate cART, assuming the annual proportion of men who are tested for HIV remains at current levels (~50–60%).

Table 2. Estimated percentage of HIV-infected men who have sex with men (MSM) in each model compartment in 1999 (stage of disease and diagnosis/treatment status) and the estimated percentage of new HIV infections attributable to HIV-infected MSM in each model compartment

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>Undiagnosed</th>
<th>Diagnosed and untreated</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary infection</strong></td>
<td>1.9% (1.2–2.7%)</td>
<td>0.46% (0.23–0.84%)</td>
<td>0.53% (0.28–0.81%)</td>
</tr>
<tr>
<td><strong>Chronic infection</strong></td>
<td>6.8% (4.2–9.3%)</td>
<td>29.0% (24.9–34.8%)</td>
<td>58.1% (52.6–63.1%)</td>
</tr>
<tr>
<td><strong>AIDS</strong></td>
<td>0.12% (0.07–0.17%)</td>
<td>0.44% (0.35–0.57%)</td>
<td>3.6% (2.6–5.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease stage</th>
<th>Undiagnosed</th>
<th>Diagnosed and untreated</th>
<th>Treated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary infection</strong></td>
<td>16.2% (9.9–22.7%)</td>
<td>1.48% (0.67–2.81%)</td>
<td>0.46% (0.22–0.79%)</td>
</tr>
<tr>
<td><strong>Chronic infection</strong></td>
<td>13.5% (8.5–18.2%)</td>
<td>16.0% (12.8–20.0%)</td>
<td>48.5% (39.8–57.5%)</td>
</tr>
<tr>
<td><strong>AIDS</strong></td>
<td>0.14% (0.09–0.23%)</td>
<td>0.18% (0.13–0.26%)</td>
<td>0.8% (0.5–1.2%)</td>
</tr>
</tbody>
</table>
found that the epidemiological impact of increasing treatment in diagnosed PHI would be low (Fig. 3a). Indeed, if no diagnosed PHI cases received cART, ~611 HIV infections are estimated in Australian MSM per year (after 10 years) compared with ~580 infections if all diagnosed cases of PHI initiated cART (Fig. 3a); that is, ~5% reduction in incidence. The number of notifications observed (as opposed to total incident infections) would also not change substantially with increases in the proportion of PHI cases that receive treatment (Fig. 3a). The minimal epidemiological impact resulting from treatment of MSM diagnosed in PHI is due to insufficient timely detection of newly-infected individuals following seroconversion. Based on our model results we predict that even with relatively high proportions of men tested for HIV each year, as observed in the Australian MSM community, treating a large proportion of PHI cases will not have a substantial public health benefit.

In contrast, we found that increases in the proportion of men who are tested for HIV each year could have substantial epidemiological consequences. We investigated the impact of changes in testing coverage on the number of HIV infections and notifications. HIV-infected MSM who become aware of their serostatus generally reduce the acquisition of new sexual partners. They might also have the opportunity to receive cART. We found that the behavioural consequences of HIV diagnosis (and clinical consequences to a smaller degree) greatly influence HIV epidemiology. If the coverage of HIV testing was to decrease (from the current level whereby 50–60% of Australian MSM test each year) then large increases in HIV incidence could be expected. If there was no testing for HIV then the number of HIV infections per year could approximately treble (to ~1600 per year, after 10 years) (Fig. 3b). Of course, if testing was low then the number of notifications would also be low (Fig. 3b). There is a testing coverage threshold of ~30%, above which the observed HIV notifications start to decrease in alignment with the decline in HIV incidence (Fig. 3b). For high testing coverage, the gradient of the curves for HIV infections/diagnoses vs. the testing coverage is approximately linear (Fig. 3b). Thus, we estimate that for every 10% incremental increase in the MSM population that is tested annually for HIV, there will be a decrease of ~13 HIV notifications observed each year and a decrease of ~22–27 HIV infections each year. But such reductions will not be observed immediately (results are shown after 10 years). We present surface plots to indicate the number of HIV infections (Fig. 4a) and HIV notifications (Fig. 4b) expected per year v. the testing coverage and number of years post introduction of the intervention. The infections v. testing coverage profile changes over time and the cumulative benefit of an intervention based on increased testing will increase with time. Clearly, also increasing the frequency of testing (to multiple times per year, especially for MSM at higher risk of HIV acquisition) will further increase the epidemiological benefits of campaigns for HIV testing. Testing more frequently than yearly could also be very important for detecting people in PHI, given the relatively short duration of acute infection. However, our simulations revealed that 100% coverage, at a frequency of once per year, would result in close to the maximum reduction in incidence that is possible due to testing; that is, higher
frequencies would not result in a significant further decrease in the total expected number of new HIV infections.

Discussion

Our study confirms the disproportionate nature of HIV transmission between different stages of disease and by diagnosis status for the MSM population in Australia. We have estimated that ~3% and ~9% of HIV-infected MSM in Australia are in PHI or are undiagnosed, respectively, but they are responsible for ~19% and 31% of the new HIV infections, respectively. These ratios will differ between locations depending on behaviour and clinical practice specific to each setting. However, the qualitative conclusions of our analyses are generally applicable to other locations. We have shown that the coverage of testing for HIV can have substantial epidemiological impacts. In locations where HIV testing rates are low, even small changes in the coverage and frequency of testing, if accompanied with changes in behaviour similar to those which we have assumed, might have very significant reductions in incidence. The relative benefit of increased testing decreases with higher testing coverage. However, even if testing rates are relatively high, further increases in the coverage and frequency of testing for HIV might still result in noticeable reductions in HIV incidence. An implication of this is that if the rate of testing for HIV is relaxed then there is the danger of large consequent increases in HIV incidence. Promoting increases in the coverage and frequency of testing for HIV has benefits at numerous levels: for the HIV-infected patient, for the partners of HIV-infected individuals, and at the population-level. Testing for HIV informs individuals of their actual serostatus and is likely to lead to a decrease in risky behaviour and subsequent reduction in the risk of onward HIV transmission to partners of HIV-infected individuals. Our model.

Fig. 4. Surface plots fitted through model-generated data indicating the expected number of (a) HIV infections over time v. the proportion of men who have sex with men (MSM) who test for HIV each year and the primary HIV infection (PHI) treatment coverage, (b) HIV notifications over time v. the proportion of MSM who test for HIV each year and the PHI treatment coverage. Here, all model parameters are set to their median values except for the proportion of MSM who are tested for HIV each year.
suggests that promoting testing can be a highly-effective public health intervention.

In contrast to the large potential impact of increases in testing, our model suggests that the population-level impact of interventions based on promoting early treatment of patients diagnosed in PHI is likely to be modest at best. If testing rates were much higher, such that the majority of newly-infected individuals were diagnosed and received treatment, then the population-level benefit of early treatment would be greater. As we have shown, this cannot be achieved on a large scale just by increasing the coverage of HIV testing. To identify large numbers of PHI cases, much more frequent testing than yearly would be required. For individuals who are diagnosed in PHI and are in serodiscordant partnerships, treatment during PHI could reduce the chance of onward transmissions and thus have preventative benefits for sexual partners. However, the primary purpose of cART must be to benefit the patient infected with HIV. The evidence supporting benefits for HIV-infected patients who receive early cART is currently not substantial. Thus, caution must be exercised when considering promoting treatment of PHI for the purposes of public health interventions to reduce population-level incidence. Treating PHI could be considered for reducing the risk of HIV transmission in serodiscordant partnerships, but further evaluation of its long-term effects on HIV-infected individuals is required.

The objective of early treatment is to preserve immune function and enhance viral control in order to attenuate long-term clinical outcomes. The first randomised controlled trial (RCT) of treatment in PHI demonstrated beneficial clinical outcomes for patients receiving monotherapy with zidovudine for 6 months. Subsequently, there have been various observational studies investigating different therapies in PHI. However, currently there are no data addressing the impact of cART in PHI on long-term clinical outcomes. Results from observational studies highlight the need for RCTs to be conducted. But most treatment guidelines do not recommend cART for treating PHI due to the lack of RCT evidence, along with drug toxicity, the risk of selecting for drug-resistant strains of HIV, and financial implications.

We have shown that treating PHI cannot be highly effective in reducing incidence when rates of testing for HIV are low-to-moderate. We have also shown that increasing average coverage levels of HIV testing can have large public health benefits. Benefits of undiagnosed HIV-infected individuals becoming aware of their serostatus include the tendency for sexual behaviour to decrease and treatment also becomes an option. Both of these lower the risk of HIV transmission. Our results are highly dependent on behaviour change post-diagnosis. Many behavioural studies provide evidence that risky sexual behaviour decreases after HIV diagnosis. However, some individuals diagnosed with HIV might increase transmission risk events, because they are no longer susceptible. Therefore, we investigated a range for the average change in behaviour, from a 10% increase to a 50% decrease; this is in agreement with behavioural studies that have investigated this issue. If these trends for reducing risk are reversed or are different in other settings, such that diagnosed HIV-infected individuals increase behaviour that leads to the transmission of HIV, then our conclusions on the benefits of testing would then not hold. A limitation of our model is that we only considered the annual coverage of HIV testing and not the frequency of testing and its correlation with risk behaviour. To investigate this would require a more detailed model than the one developed for this analysis and would be of interest for future research.

The feasibility of increasing HIV testing rates differs between settings. In Australia, unlike some other regions, the health care system and infrastructure is well equipped to conduct screening for HIV. But greater efforts might be required to reach individuals who are not regularly tested for HIV, and this might include extending hours of operation of sexual health clinics or providing alternative testing facilities. The proportion of Australian MSM who are tested for HIV at least once per year is already relatively high. This proportion has been slowly increasing and its increase should be promoted further. Furthermore, persons who have higher HIV risk exposure tend to test more frequently but there might be a saturation level to the frequency of testing that is attainable.

Increasing HIV diagnoses requires educating susceptible populations to seek HIV testing on the basis of indicators such as a known exposure to HIV or early recognition of symptoms. This could be complemented by population-level interventions to reduce factors that potentiate the transmission of HIV, including promoting condom use, strategic positioning, and testing and treatment of other sexually transmissible infections. This is especially important as most forms of HIV counselling have little effect on the behaviour of HIV-negative people. But as we have demonstrated, the potential impact of promoting HIV testing could be substantial in reducing secondary transmissions from HIV-positive individuals.

Conflicts of interest
None declared.

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Appendix 1

a: We use behavioural data on the proportion of men that have 0, 1, 2–10, 11–50, >50 partners to calculate a weighted average at each available time point, to obtain the following trends:

b: Serosorting and disclosure of serostatus are discussed in the Appendix methods section. Our model requires estimates of the proportion of partnerships in which serostatus is disclosed in order to negotiate condom usage. We use data on the percentage of men who reported unprotected anal intercourse and always disclosed serostatus:

c: Condom usage will vary between types of relationships and the disclosure of HIV serostatus. For relationships in which serostatus is not ascertained we use the data from the State gay periodic surveys to obtain the following trends over time:

In regular relationships that are serodiscordant we assume that average condom usage is high. Based on the Futures study we assume condoms are used in 75–85% of anal intercourse acts between discordant men who have sex with men (MSM). However, in regular relationships that are seroconcordant we assume that average condom usage is relatively low; we assume condoms are used in 5–10% of acts. In casual relationships, serological disclosure is not as common as in regular relationships, but if the MSM in a casual relationship determine the relationship is serodiscordant then we assume condoms are used in 95–100% of acts. We assume that condoms are used more frequently in casual partnerships than in regular partnerships.
There is evidence to suggest that the percentage of treated patients with undetectable virus has increased over time. This could be due to numerous factors such as greater adherence or different drug regimes. We use data from the Australian HIV Observational Database (AHOD) database:

\[ \beta_C \times 2.45^{\log_{10}(V/V_C)} \text{ if } V > V_C \]

\[ \beta_C / 2.45^{\log_{10}(V_C/V)} \text{ if } V < V_C \]

Although this relationship was originally determined for heterosexual penile–vaginal intercourse, we use a greater baseline transmission probability for homosexual penile–anal intercourse, \( \beta_C \), and assume that the same multiplicative increase in transmission holds with changes in viral load. This relationship was established based on empirical data in a cohort of African heterosexual couples. In the absence of information to the contrary, we assume that this relationship holds for penile–anal transmission and that it applies across the range of viral loads, including those that are below detectable levels, regardless of whether or not a person is under treatment with antiretroviral therapy. However, the baseline transmission probability differs between the different modes of transmission.

In order to model the impact of sexually transmissible infections (STIs) on HIV transmission it is necessary to estimate the proportion of MSM with other STIs as well as trends over time and by state. This is problematic for several reasons. First, while there are indications that the prevalence of some STIs, notably syphilis, is increasing in MSM in Australia, most data are reported only as
notifications, not as the proportion of tests that are positive. Furthermore, the National Centre for HIV Social Research reports significant increases in testing (10–20%) in the past few years. Second, much of the published data on STIs in MSM in Australia is from the HIM (Health in Men) study and the incidence of STIs has decreased in this Sydney-based HIV-negative cohort over the past few years. Third, there are little data on trends in STI incidence and prevalence in MSM for the other states. Fourth, the most prevalent STI associated with HIV transmission is herpes simplex virus-2 (HSV-2) with prevalence in the HIM cohort estimated at ~23% masking any trends that might be occurring with other STIs. Of course, HSV-2 is latent for significant proportions of time in infected people and virus is shed periodically; thus, the effective prevalence of HSV-2 for which it increases HIV transmissibility is reduced. Given the uncertainty, we assume that the average proportion of MSM with STIs (ulcerative or non-ulcerative, that contribute to increasing HIV transmissibility) is in the range 5–15% initially (that is, at 1999). To investigate national HIV trends we do not distinguish STI levels between states. Although there are currently no published data, the prevailing perception among epidemiologists and sexual health clinicians is that there has been a rise in the number of STIs in recent years. However, because the magnitude of increase is different between different STIs we do not use STI data. Our initial analyses are based on an initial uncertainty range of 5–15% but constant over time. We then investigate numerous rates of increase in the prevalence of other STIs to determine the influence of increasing STIs on the HIV epidemic.

g: There is strong evidence that both ulcerative and non-ulcerative STIs can increase the probability of HIV transmission by augmenting HIV infectiousness and susceptibility. Reciprocally, HIV infection can enhance the transmission of other STIs. This is a complex synergy and the results of several prospective studies estimate the relative risks of HIV infection due to infection with other STIs in the range 2 to 24, but largely clustering between 2 and 5. We therefore assume that the multiplicative increase in transmission probability due to concurrent infection with another STI is in the range 2–5.

h: Data from the Gay periodic surveys over time for the percentage of MSM who tested for HIV in the past 12 months are used as shown in the graph below:

![Graph showing percentage of MSM tested for HIV over time in different states (NSW, VIC, QLD)]

i: We evaluated available data from primary infection cohorts of the percentage of HIV-infected MSM who commenced antiretroviral therapy (ART) within 1 year of HIV diagnosis, including patients recruited to the Acute Infection and Early Disease Research Program (CORE 01) protocol established by the National Institute of Health, and the Primary HIV and Early Disease Research: Australian Cohort (PHAEDRA) established by the National Centre in HIV Epidemiology and Clinical Research. These data have large uncertainty (summarised in Glenday et al.16), is limited in time and only includes NSW and Vic. Sample sizes are also not sufficient (as low as four in some years for Vic. and six for NSW). Consequently, this has been used as a rough guide but we make assumptions in the trends in early treatment based on personal communications with clinicians (e.g. Professor Tony Kelleher). We estimate the basic anecdotal trends observed over the past few years by the figure below. But since there are no firm data for the trends, we include greater uncertainty bounds on this time-dependent parameter than on the others (we use a multiplicative uncertainty range on these trends of 0.6–1.2.

We then assume that the initial dosing schedule for these patients who commence treatment in primary infection is 6–12 months, after which time 60–70% of these patients will continue ART and the remaining patients will discontinue therapy until a later time.

j: We assume that individuals who have not been diagnosed with HIV infection, but are infected, will have the same lifetime duration (30–35 years) of sexual activity (in terms of choosing new partners) as those that are uninfected or at different disease stages. However, the number of partners chosen will differ between some disease stages.
This leads to ~150,000–175,000 MSM nationally. The proportion of new MSM in NSW/ACT, Vic., Qld each year as a subset of the total national number are indicated.