HIV treatment-as-prevention and its effect on incidence of HIV among cisgender gay, bisexual, and other men who have sex with men in Australia: a 10-year longitudinal cohort study

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Summary

Background Although HIV treatment-as-prevention reduces individual-level HIV transmission, population-level effects are unclear. We aimed to investigate whether treatment-as-prevention could achieve population-level reductions in HIV incidence among gay, bisexual, and other men who have sex with men (GBM) in Australia's most populous states, New South Wales and Victoria.

Methods TAIPAN was a longitudinal cohort study using routine health record data extracted from 69 health services that provide HIV diagnosis and care to GBM in New South Wales and Victoria, Australia. Data from Jan 1, 2010, to Dec 31, 2019, were linked within and between services and over time. TAIPAN collected data from all cisgender GBM who attended participating services, resided in New South Wales or Victoria, and were 16 years or older. Two cohorts were established: one included HIV-positive patients, and the other included HIV-negative patients. Population prevalence of viral suppression (plasma HIV viral load <200 RNA copies per µL) was calculated by combining direct measures of viral load among the HIV-positive cohort with estimates for undiagnosed GBM. The primary outcome of HIV incidence was measured directly via repeat testing in the HIV-negative cohort. Poisson regression analyses with generalised estimating equations assessed temporal associations between population prevalence of viral suppression and HIV incidence among the subsample of HIV-negative GBM with multiple instances of HIV testing.

Findings At baseline, the final sample (n=101 772) included 90 304 HIV-negative and 11 468 HIV-positive GBM. 59 234 patients in the HIV-negative cohort had two or more instances of HIV testing and were included in the primary analysis. Over the study period, population prevalence of viral suppression increased from 69·27% (95% CI 66·41–71·96) to 88·31% (86·37–90·35), while HIV incidence decreased from 0·64 per 100 person-years (95% CI 0·55–0·76) to 0·22 per 100 person-years (0·17–0·28). Adjusting for sociodemographic characteristics and HIV pre-exposure prophylaxis (PrEP) use, treatment-as-prevention achieved significant population-level reductions in HIV incidence among GBM: a 1% increase in population prevalence of viral suppression corresponded with a 6% decrease in HIV incidence (incidence rate ratio [IRR] 0·94, 95% CI 0·93–0·96; p<0·0001). PrEP was introduced in 2016 with 17·60% uptake among GBM that year, which increased to 36·38% in 2019. The relationship between population prevalence of viral suppression and HIV incidence was observed before the availability of PrEP (IRR 0·98, 95% CI 0·96–0·99; p<0·0001) and was even stronger after the introduction of PrEP (0·80, 0·70–0·93; p=0·0030).

Interpretation Our results suggest that further investment in HIV treatment, especially alongside PrEP, can improve public health by reducing HIV incidence among GBM.

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Introduction

HIV treatment resulting in viral suppression effectively reduces to zero an individual's risk of HIV transmission,[1–3] with universal treatment now a foundation of treatment-as-prevention as a global public health strategy.[4] Despite convincing evidence of the individual-level effectiveness of treatment-as-prevention, evidence of population-level effect is much less clear. Notably, the South African ANRS 12249 randomised controlled trial[5] reported no difference in HIV incidence between community clusters targeted to receive universal treatment and those targeted for standard treatment, a finding attributed to inadequate linkage to care and treatment coverage in the study catchment areas. The SEARCH trial[6] in Kenya and Uganda also found no difference in HIV incidence between groups offered universal versus standard treatment programmes. By contrast, the Ya Tsie Botswanan randomised controlled trial[7] reported

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Research in context

Evidence before this study

On July 1, 2022, we conducted a search of the literature in several databases (ie, Google Scholar, PubMed, and Scopus) using combinations of relevant keywords (ie, HIV, treatment-as-prevention, TasP, treatment, population, gay, MSM, incidence, and biomedical prevention). We sought to identify English-language publications from Jan 1, 2005, to June 30, 2022, which studied the population-level effects of HIV treatment-as-prevention. We identified numerous studies showing the individual-level protection afforded by HIV treatment-as-prevention, which had robust cohort designs or were randomised controlled trials. Two such studies found no sexual transmission among serodiscordant partnerships of gay and bisexual men. We identified four well designed randomised controlled trials, which had mixed results. The ANRS 12249 community cluster (South Africa), SEARCH (Kenya and Uganda), and HPTN 0971 PopArt (South Africa and Zambia) trials found no difference in HIV incidence between early treatment initiation and standard care, whereas the Ya Tsie trial reported 30% lower HIV incidence in communities receiving early treatment initiation and a service linkage intervention compared with those receiving standard care in Botswana. Evidence from the Africa Health Research Institute's large population-based cohort in rural South Africa suggested increasing treatment coverage was associated with decreasing HIV incidence, but the rural context of this research makes it difficult to generalise the findings to other areas, especially those with concentrated HIV epidemics. Furthermore, no study has published data on the population effectiveness of treatment-as-prevention at a jurisdiction level or in any high-income country.

Added value of this study

Across an Australian network of clinical services representing high jurisdictional coverage of HIV testing and treatment, a population-level estimate of viral suppression among gay, bisexual, and other men who have sex with men (GBM) was calculated alongside directly measured HIV incidence to assess the impact of treatment-as-prevention. We found that as the population prevalence of viral suppression increased, HIV incidence decreased. This relationship was observed even when accounting for individual-level risk factors, sociodemographic variations, and use of HIV pre-exposure prophylaxis (PrEP). Although the relationship between treatment-as-prevention and HIV incidence was evident before the widespread availability of PrEP, treatment-as-prevention and PrEP were most impactful in combination. This study provides important evidence on the population-level effects of treatment-as-prevention in a concentrated epidemic and a well funded public health system.

Implications of all the available evidence

The results of population-level studies of treatment-as-prevention suggest that, as a biomedical prevention strategy, treatment-as-prevention can achieve reductions in HIV incidence among GBM, but doing so requires very high rates of HIV diagnosis and treatment uptake, including among subpopulations. Treatment-as-prevention is a potentially powerful public health strategy, but further efforts are needed to maximise treatment coverage and reduce undiagnosed infections, especially in settings with generalised HIV epidemics. To meet global HIV prevention targets, both PrEP and treatment-as-prevention are needed.

30% lower HIV incidence in communities receiving early treatment initiation and a service linkage intervention compared with those receiving standard care. Finally, the HPTN 071 PopART randomised controlled trial[8] in Zambia and South Africa found no difference in HIV incidence between groups receiving standard care versus universal treatment with a combination prevention intervention, although incidence was 30% lower in a third cluster with standard care and a prevention intervention.

Surveillance data from many parts of the world have shown increases in HIV treatment uptake over the past two decades but stable or increasing HIV notifications.[9,10] These data, alongside the inconclusive population-level randomised controlled trial results, led Baral and colleagues to conclude that there was a "disconnect between individual-level and population-level HIV prevention benefits of antiretroviral treatment".[10] Despite this claim, there is some cohort-derived evidence from South Africa that increases in primary prevention and antiretroviral therapy (ART) coverage were associated with a decline in HIV incidence in a rural area where HIV was hyperendemic.[11] Although suggestive, that study and the previously described African randomised controlled trials (with the exception of SEARCH[6]) did not account for undiagnosed infections, despite their important role in HIV transmission.[12,13]

It is also necessary to consider the heterogeneity of HIV epidemics between countries, areas, and populations.[10,13] This point is especially important given that studies assessing the effect of treatment-as-prevention have largely occurred in the context of generalised epidemics in sub-Saharan Africa, although many countries have epidemics concentrated among key populations, including gay, bisexual, and other men who have sex with men (GBM). In one of the only population-level studies among GBM, from 1996 to 2013 researchers in Denmark found an association between increasing HIV treatment and decreasing incidence.[14] However, that study indirectly measured HIV incidence via CD4-stage back-calculations, which is an imprecise method for categorising more recent infections.[15] Furthermore, the study ended as treatment-as-prevention was being adopted globally and before many countries introduced HIV pre-exposure prophylaxis (PrEP).

Following decades of increasing HIV diagnoses concentrated among GBM,[16] in 2014, Australia introduced treatment-as-prevention to its national HIV strategy.[17] We aimed to assess the population-level effects of treatment-as-prevention on directly measured HIV incidence among GBM in Australia's two most populous states, accounting for undiagnosed HIV and within-population heterogeneity of sociodemographic characteristics, sexual and drug use behaviours, and PrEP use.

Methods

Study design and participants

TAIPAN (Treatment with Antiretroviral and their Impact on Positive and Negative Men) was a longitudinal cohort study of routine clinical data extracted and linked across a network of health services that provide HIV diagnosis and care to GBM in New South Wales and Victoria, Australia. The study was started in August, 2015, and deidentified data were extracted retrospectively (ie, before August, 2015) and prospectively (ie, from August, 2015) for the 10-year period from Jan 1, 2010, to Dec 31, 2019. The TAIPAN protocol has been published previously.[18]

TAIPAN increased coverage of an existing national sentinel surveillance system for bloodborne viruses and sexually transmitted infections.[19] Specifically, the number of participating services was increased through targeted recruitment of health services identified in state health systems as maintaining 20 or more patients with HIV, 50 or more patients who were GBM, or diagnosing five or more patients with HIV annually. The final sample comprised 69 health services, including 35 publicly funded sexual health clinics, 25 general practices, five community-based HIV testing services, three hospitals, and one drug and alcohol service. The majority of services (n=57) provided care to both HIV-negative and HIV-positive GBM. Regarding coverage, across both states our sample included nearly all (95%) sexual health clinics, all community-based HIV testing services, three of the largest hospital-based HIV clinics, and 73% of all HIV treatment prescribers.[20]

TAIPAN collected data from all GBM who attended participating services, resided in New South Wales or Victoria, and were 16 years or older. Participation was limited to cisgender men, a necessity because most services recorded transgender as a single category without disaggregation between men and women. Two cohorts were established: (1) HIV-negative patients, comprising GBM whose first test during the study period was negative, and (2) HIV-positive patients, comprising GBM with a positive diagnostic test, recorded diagnosis, or HIV management tests (eg, viral load). The cohorts were dynamic, with ongoing enrolment of new patients who attended at any point during the study period and GBM who were newly diagnosed moved prospectively to the HIV-positive cohort.

Study procedures were approved by the University of New South Wales's human research ethics committee (HC16560).[18] Informed consent was provided by participating services, with individual patient consent waived given TAIPAN's low risk. Participating services were asked to notify patients of the study and their opt-out options via clinic intake procedures and publicly displayed notices in waiting and consultation rooms. Since inception, the larger surveillance network recorded three opt-outs of data among millions of patients.

Procedures

Specialised software installed on participating sites' patient management systems facilitated monthly data extractions.[21] For each clinical visit, extracted line-listed data included sociodemographic characteristics, date of visit, test requests and results for the diagnosis and management of HIV and other sexually transmitted infections, and ART prescriptions coded as post-exposure prophylaxis, PrEP, or HIV treatment. Sexual health clinics and community-based testing services also collected data on sexual and drug use behaviours, which were extracted as available; patients with these variables were included in an enhanced primary analysis. The extraction software facilitated deidentified record linkage between participating services by assigning non-reversible encrypted codes generated from identifying information (eg, date of birth), a process with 95% sensitivity and 99% specificity.[21] This linkage was important given the potential for individuals to access multiple health services.

Outcomes

Extracted health record data were used to calculate our primary and secondary outcome variables, as well as several covariates.[18] Study variables were calculated overall and by calendar year, with baseline defined as each patient's first visit to a TAIPAN site during the study period. Study variables were also stratified by age.

The primary outcome was HIV incidence, calculated directly among the HIV-negative cohort with a previously validated measure that used the Poisson binomial method to estimate an infection date between instances of repeat testing.[22] An incident case was defined as a positive test following a previous negative result. HIV incidence was calculated among GBM with two or more HIV tests during the study period, with HIV testing data extracted 1 year before and after the study period (ie, 2009 and 2020) to improve inter-test interval accuracy.

Population prevalence of viral suppression was the primary predictor variable, defined for each calendar year as the proportion of GBM with HIV (diagnosed and undiagnosed) who were virally suppressed. Viral suppression among GBM with diagnosed HIV was calculated as the proportion of the HIV-positive cohort with fewer than 200 RNA copies per µL at their last viral load test in a calendar year. Viral suppression among GBM with undiagnosed HIV was estimated as the proportion of GBM with fewer than 200 RNA

copies per µL at the point of diagnosis, per data from Australia's National Notifiable Diseases Surveillance System. Back-projection modelling using the HIV Modelling Tool (European Centre for Disease Prevention and Control) estimated annual proportions of undiagnosed HIV among HIV-positive GBM in New South Wales and Victoria.[12] The modelling tool used CD4 lymphocyte count at diagnosis, AIDS diagnoses, deaths, and emigration rates to estimate undiagnosed HIV; previous comparisons with prevalence survey data in Australia suggest this estimate is reliable.[12] Resulting estimates of undiagnosed HIV weighted each group's relative contribution to population prevalence of viral suppression (appendix pp 4–6).

See Online for appendix

Three secondary descriptive outcomes were examined given their relevance to treatment-as-prevention as an overarching public health strategy. First, incidence of HIV treatment initiation among GBM who were newly diagnosed during the study period was calculated as the first record of an ART prescription following diagnosis. Second, sustained viral suppression incidence among the HIV-positive cohort was defined as consecutive viral load test results of fewer than 200 RNA copies per µL over at least 3 months. Third, repeat HIV testing incidence was calculated as a subsequent test within 1·5–12·0 months of an index test among the HIV-negative cohort. For these measures, the period of follow-up was censored after 24 months without a clinical visit but resumed when future visits were recorded.

	All participants (n=101 772)	HIV-negative cohort† (n=90 304)	HIV-positive cohort (n=11 468)
Median age, years	33 (27–43)	32 (26–41)	43 (35–51)
Indigenous status			
Aboriginal or Torres Strait Islander	1833 (1·80%)	1599 (1·77%)	234 (2·04%)
Non-Indigenous	99 939 (98·20%)	88 705 (98·23%)	11 234 (97·96%)
Area of residence‡			
Regional or rural area	7779 (7·77%)	6254 (7·05%)	1525 (13·42%)
Major city	92 340 (92·23%)	82 500 (92·95%)	9840 (86·58%)
GBM prevalence in home postcode‡			
<5% total adult male population	52 826 (52·76%)	46 665 (52·52%)	6161 (54·21%)
≥5% total adult male population	47 290 (47·23%)	42 086 (47·42%)	5204 (45·79%)
Recent rectal sexually transmitted infection diagnosis§¶	8238 (8·09%)	7314 (8·10%)	924 (8·06%)
Recent sex and drug use practices¶‖			
Median number of sexual partners	4 (0–10)	4 (0–10)	0 (0–4)
Sex work	1186 (2·09%)	1109 (2·12%)	77 (1·78%)
Injecting drug use	1219 (2·15%)	986 (1·88%)	233 (5·38%)

Data are median (IQR) or n (%). GBM=gay, bisexual, and other men who have sex with men. *Baseline defined as each participant's first visit to a TAIPAN site during the study period. †GBM newly diagnosed during the study period (n=1183) were HIV-negative at baseline and are, therefore, reported in this table as part of the HIV-negative cohort. ‡Excluding GBM without a recorded postcode (n=1653; HIV-negative n=1550 missing, HIV-positive n=103 missing). §Diagnosis with rectal infection of chlamydia, gonorrhoea, or both used as a marker of condomless anal sex. ¶Self-reported for the 12 months before each participant's first (ie, baseline) visit. ‖Behavioural data available only for GBM attending sexual health clinic or community testing site at baseline (n=56 677; HIV-negative n=52 345, HIV-positive n=4332).

Table 1: **Baseline* characteristics, overall and by HIV status**

Covariates recorded at each patient's first visit (ie, baseline) and updated as new data became available included age, Indigenous status, and home postcode. Postcode was used to categorise regionality defined by the Australian Bureau of Statistics and population prevalence of adult gay men.[23] Other time-varying covariates included sexual partner numbers, injecting drug use, and sex work based on patient self-report at each visit to a sexual health clinic or community testing site and applied to the 12 previous months. Data on condom use were not routinely collected, thus diagnosis with a rectal sexually transmitted infection at any TAIPAN service was used as a surrogate marker of condomless sex[24,25] (noting repeated behavioural surveys found 65–79% of GBM each year reported rectal screening).[26,27] PrEP use was defined from prescription data starting in 2016 when PrEP became widely available. Given the generally low and stable uptake of post-exposure prophylaxis among GBM during the study period,[26,27] we did not account for it in these analyses.

Statistical analysis

Population averaged participant-level repeated measures models using generalised estimating equations were fitted to investigate temporal associations between population prevalence of viral suppression and HIV incidence. The unit of analysis was calendar year of observation, with the outcome participant-level HIV incidence as assigned proportionally to time periods where cases were diagnosed at first test in a calendar year.[22] For example, a patient with a last negative HIV test in June and a first positive HIV test in March the following year would be allocated 0·67 HIV incidents in the first year and 0·33 HIV incidents in the second year. Duration-based weighting adjusted for incomplete annual exposures associated with delayed study entry and early study exit. Poisson pseudo-maximum likelihood estimation accommodated this non-integer repeated measure.[28] An exchangeable covariance structure with robust standard errors accounted for intra-patient correlation while being robust to misspecified variance structure. This approach assumed annual HIV infection risk associated with population prevalence of viral suppression was independent of other years. These methods were deemed robust for the study's open and dynamic cohort design, especially given the imprecise assessment of event-time via repeat testing.

Sociodemographic characteristics, PrEP use, and rectal sexually transmitted infection diagnoses were included as control variables. The analysis was repeated for the period before (ie, 2010–16) and after (ie, 2016–19) PrEP was available and among the subsample for whom enhanced behavioural data were available. Incidence rate ratios (IRRs) and 95% CIs were calculated, with exposure as person-years and IRR as incidence rate (given population prevalence of viral suppression percentage + 1%) / incidence rate (given population prevalence of viral suppression percentage).

We did three sensitivity analyses. First, we repeated the primary analysis with viral suppression defined as fewer than 1000 RNA copies per µL, which some view as a more pragmatic threshold for assessing public health impact.[29] Second, per previous Australian estimates, we assumed up to 8·6% of GBM with diagnosed HIV were not linked to care and therefore not captured in the TAIPAN cohort.[30] For these men and for GBM in the HIV-positive cohort without viral load test results, we repeated the primary analysis assuming 0% and 100% viral suppression. Third, viral suppression was assessed at any test, rather than the last test, in a calendar year.

In addition to the primary and sensitivity analyses, some secondary analyses were conducted. Incidence of HIV treatment initiation, sustained viral suppression, and repeat HIV testing were calculated annually and assessed over time using Poisson regression analyses with year fitted as an independent variable. Given the function of HIV testing in supporting treatment-as-prevention, a further Poisson regression analysis investigated any temporal relationship between the incidence of repeat testing and prevalence of undiagnosed HIV.

All analyses were carried out using Stata version 14.2 using the xtpoisson command.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

101722 GBM attended a participating service during 2010–19. At baseline (ie, their first visit during the study period), 90 304 patients were HIV-negative and

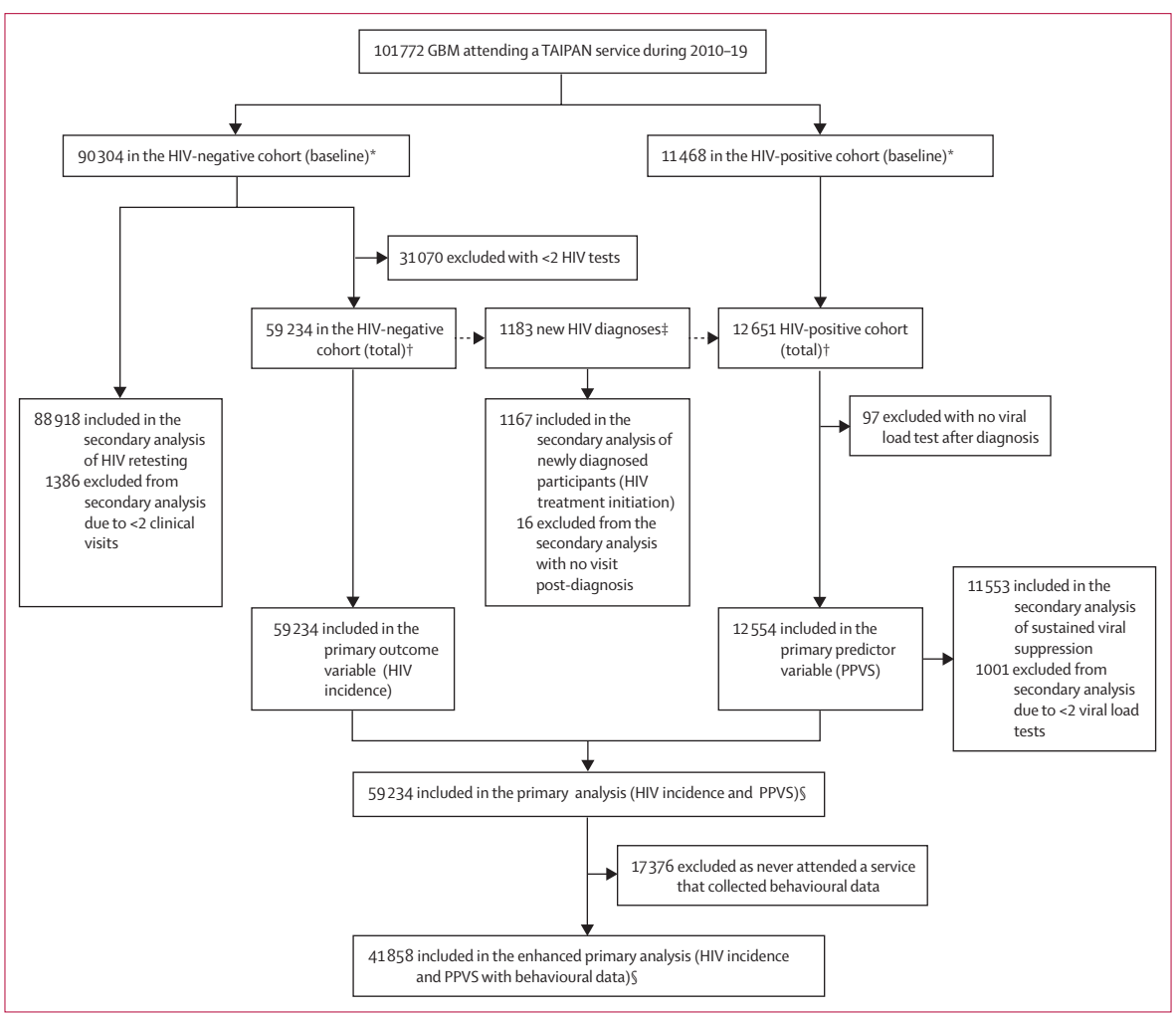

Figure 1: **Flowchart of enrolment and inclusion in each analysis**
GBM=gay, bisexual, and other men who have sex with men. PPVS=population prevalence of viral suppression. *Baseline defined as each participant's first visit to a TAIPAN site during the study period. †Participants newly diagnosed with HIV during the study period were prospectively included in the HIV-positive cohort and are, therefore, counted here as part of the total sample size for each cohort. ‡Includes participants newly diagnosed with HIV during the study period as distinct from those infected (ie, HIV incidence). §As HIV incidence was the outcome, the primary regression analyses sample sizes are limited to the HIV-negative cohort.

11 468 were HIV-positive (table 1; figure 1). Sociodemographic and behavioural characteristics over time are shown in the appendix (p 2). At baseline, 60 318 (59·27%) patients were in New South Wales and 41 454 (40·73%) were in Victoria, which was similar to the overall distribution of GBM between these states.[23] 34 707 (34·1%) patients attended two or more participating services during the study period.

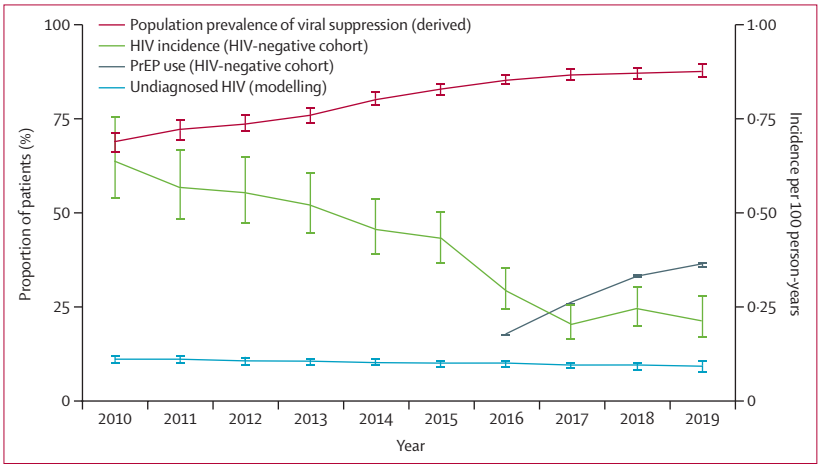

Figure 2: **Population prevalence of viral suppression, HIV incidence, undiagnosed HIV, and PrEP uptake among GBM, by year, 2010–19**

Whiskers are 95% CIs. Population prevalence of viral suppression was derived by combining estimates of undiagnosed infection with viral load results from the HIV-positive TAIPAN cohort. HIV incidence was calculated among the HIV-negative TAIPAN cohort using repeat testing. Undiagnosed HIV was estimated as a proportion of all HIV-positive GBM using back-projection mathematical modelling. PrEP was made widely available to GBM in New South Wales and Victoria from 2016 onward. GBM=gay, bisexual, and other men who have sex with men. PrEP=pre-exposure prophylaxis.

Among 59 234 GBM with two or more HIV tests during the study period, 1201 incident cases of HIV were identified over 301 313 person-years: an overall rate of 0·40 per 100 person-years. Annually, HIV incidence decreased by 66·37% from 0·64 per 100 person-years (95% CI 0·55–0·76) in 2010 to 0·22 per 100 person-years (0·17–0·28) in 2019 (figure 2). HIV incidence decreased by 88·64% among GBM aged 30–39 years, by 62·67% among those aged 16–29 years, and by 49·45% among those aged 40 years and older (appendix p 8). GBM included in and excluded from these estimates are outlined in the appendix (p 3). Compared with excluded GBM, our sample had a lower proportion of Aboriginal or Torres Strait Islanders, and a higher proportion living in cities, living in neighbourhoods with higher proportions of gay men, and diagnosed with rectal sexually transmitted infections (appendix p 3).

During the study period, population prevalence of viral suppression increased from 69·27% (95% CI 66·41–71·96) in 2010 to 88·31% (86·37–90·35) in 2019, a relative increase of 27·48% (figure 2). This change reflects an increase in the proportion of GBM in the HIV-positive cohort who were virally suppressed (4052 [77·37%] in 2010 to 7917 [96·74%] in 2019) and a decrease in the estimated proportion of all GBM who were HIV-positive and were undiagnosed (10·92% in 2010 to 9·18% in 2019; appendix p 5).

Over time, increasing population prevalence of viral suppression was associated with decreasing HIV incidence (IRR 0·95, 95% CI 0·94–0·96; p<0·0001). This association persisted when adjusting for PrEP use and

	Unadjusted analyses†		Primary analysis‡ (n=59 234)		Enhanced primary analysis§ (n=41 858)	
	IRR (95% CI)	p value	IRR (95% CI)	p value	IRR (95% CI)	p value
Population prevalence of viral suppression at <200 RNA copies per µL	0·95 (0·94–0·96)	<0·0001	0·94 (0·94–0·96)	<0·0001	0·94 (0·93–0·96)	<0·0001
Age	0·98 (0·98–0·99)	<0·0001	0·99 (0·98–0·99)	<0·0001	1·00 (0·99–1·01)	0·54
Urban home neighbourhood (reference rural or regional)	1·04 (0·80–1·35)	0·76	0·93 (0·71–1·21)	0·57	0·80 (0·58–1·12)	0·20
≥5% GBM prevalence in home neighbourhood (reference <5%)	1·05 (0·93–1·18)	0·46	1·04 (0·92–1·19)	0·48	1·03 (0·88–1·20)	0·75
Aboriginal or Torres Strait Islander (reference non-Indigenous)	1·41 (0·93–2·13)	0·10	1·32 (0·87–2·00)	0·20	1·13 (0·67–1·93)	0·64
On PrEP (reference not on PrEP)	0·31 (0·24–0·41)	<0·0001	0·26 (0·19–0·35)	<0·0001	0·30 (0·21–0·43)	<0·0001
Recent rectal sexually transmitted infection diagnosis (reference no diagnosis)¶‖	4·50 (3·96–5·11)	<0·0001	6·45 (5·61–7·42)	<0·0001	4·10 (3·48–4·84)	<0·0001
Recent number of sexual partner numbers‖	1·00 (1·00–1·01)	<0·0001	..	..	1·00 (0·99–1·00)	0·14
Recent sex work‖ (reference no recent sex work)	1·12 (0·69–1·85)	0·63	..	..	0·87 (0·53–1·44)	0·59
Recent injecting drug use‖ (reference no recent injecting drug use)	3·97 (3·05–5·15)	<0·0001	..	..	3·39 (2·57–4·47)	<0·0001

IRR=incidence rate ratio. GBM=gay, bisexual, and other men who have sex with men. PrEP=pre-exposure prophylaxis. *Analyses conducted with generalised estimating equations and robust error estimates. †Results are reported for bivariable associations between each variable and HIV incidence (primary outcome). ‡Multivariable model adjusted for sociodemographic characteristics, PrEP use, rectal sexually transmitted infection diagnoses, and year. §Multivariable model adjusted for sociodemographic characteristics, PrEP use, rectal sexually transmitted infection diagnoses, year, and enhanced behavioural data. ¶Used as a proximal marker for condomless anal sex. ‖Recent defined as the 12 months before a clinical visit.

Table 2: **Results of Poisson regression analyses* investigating the relationship between population prevalence of viral suppression and HIV incidence**

sociodemographic characteristics (0·94, 0·93–0·96; p<0·0001) and when adjusting for sex and drug use behaviours (0·93, 0·93–0·96; p<0·0001; table 2). PrEP uptake among the HIV-negative cohort increased from 5951 (17·60%) in 2016 (the year it was widely introduced) to 12 189 (36·38%) in 2019 (figure 2; appendix p 8). Increasing population prevalence of viral suppression was associated with decreasing HIV incidence in the years before the availability of PrEP in Australia (0·98, 0·96–0·99; p<0·0001), an association strengthened after its introduction in 2016 (0·80, 0·70–0·93; p=0·0030).

The annual incidence of HIV treatment initiation among GBM who were newly diagnosed during the study period increased from 14·52 per 100 person-years in 2010 to 82·90 per 100 person-years in 2019 (IRR 1·19, 95% CI 1·16–1·22; p<0·0001; figure 3). Among HIV-positive GBM with two or more viral load tests, incidence of sustained viral suppression increased from 46·46 per 100 person-years in 2010 to 336·73 per 100 person-years in 2019 (1·33, 1·31–1·36; p<0·0001; figure 3). Among the HIV-negative cohort, repeat testing incidence increased from 94·75 per 100 person-years in 2010 to 247·60 per 100 person-years in 2019 (1·14, 1·13–1·14; p<0·0001; figure 3). Over time, increasing repeat testing was associated with decreasing estimated prevalence of undiagnosed HIV (0·87, 0·87–0·88; p<0·0001). The incidences of treatment initiation and viral suppression were consistent between GBM of different age groups; repeat diagnostic testing was consistently lower among GBM aged 40 years and older but over time increased by a similar rate across age groups (see appendix p 9).

Full results of the sensitivity analyses are provided in the appendix (p 7). First, adjusting the definition of population prevalence of viral suppression to fewer than 1000 RNA copies per µL showed a similar association with HIV incidence (IRR 0·94, 95% CI 0·92–0·95; p<0·0001) as in the primary analysis. Second, population prevalence of viral suppression remained associated with HIV incidence when, among HIV-positive GBM not accessing care, we assumed no viral suppression (0·94, 0·93–0·95; p<0·0001) or total viral suppression (0·92, 0·91–0·93; p<0·0001). Third, when viral suppression was assessed at any rather than just the last test of a year period (0·95, 0·94–0·96; p<0·0001) results were similar to the primary analysis.

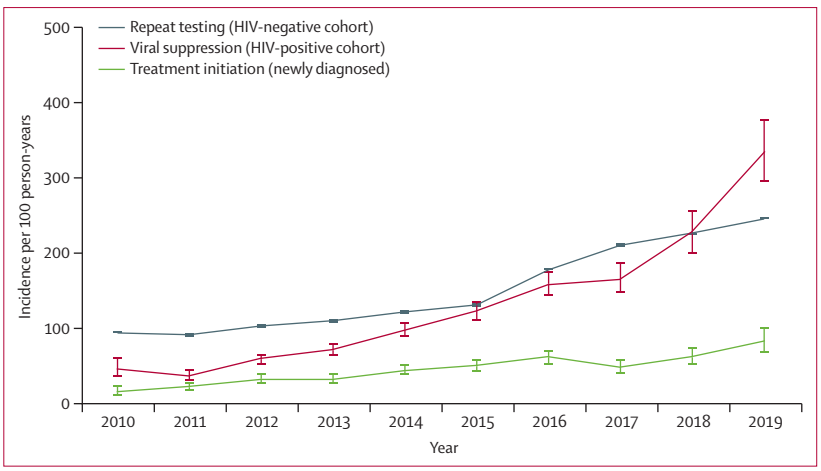

Figure 3: **Incidence of HIV treatment initiation, sustained viral suppression, and repeat diagnostic testing among GBM, by year, 2010–19**

Whiskers are 95% CIs. HIV treatment initiation was assessed among GBM who were newly diagnosed with HIV during the study period (n=1183). Sustained viral suppression was assessed among GBM in the HIV-positive cohort who had two or more viral load tests during the study period (n=11 535); viral suppression was defined as two consecutive test results of fewer than 200 RNA copies per µL. Repeat diagnostic testing was assessed among GBM in the HIV-negative cohort (n=88 918). GBM=gay, bisexual, and other men who have sex with men.

Discussion

From 2010 to 2019, the population-level prevalence of viral suppression increased by 27·48%, while HIV incidence decreased by 66·37% among GBM in Australia's two most populous states. We found that increasing population prevalence of viral suppression was associated with decreasing HIV incidence: a 1% increase in the proportion of HIV-positive GBM with viral loads of fewer than 200 RNA copies per µL corresponded with a 5% decrease in new infections. Methodologically, this study comes at a time when other countries are implementing real-world investigations of population-targeted HIV prevention interventions, including with direct measures of HIV incidence.[31]

Although our findings show a relationship between population prevalence of viral suppression and HIV incidence that was evident well before PrEP was introduced in Australia, the association was even stronger after PrEP's introduction in 2016. Despite decreasing most dramatically from 2015 to 2017 when PrEP became available, HIV incidence among GBM levelled off from 2017 to 2019. This stabilisation could indicate the saturation of treatment-as-prevention and PrEP among some GBM subpopulations, but not others. For example, earlier research reported GBM who were migrants to Australia had lower rates of HIV diagnosis, treatment, and viral suppression.[32] In this context, our findings suggest that although treatment-as-prevention and PrEP are both important public health strategies, their true potential is unlocked in combination and when delivered equitably among subpopulations.

We observed substantial increases in HIV treatment initiation, sustained viral suppression, and HIV testing among GBM. Governments, clinics, and community-based organisations in New South Wales and Victoria have worked to remove ART prescribing restrictions, enabled community pharmacy dispensing, reduced patient treatment costs, and educated those at risk of HIV about the individual and prevention benefits of early and sustained treatment. Furthermore, there have been a range of HIV testing initiatives targeting GBM, including quick and simplified express options, peer-led and community-based testing sites, rapid diagnostic tests, and (since 2016) quarterly testing to access PrEP. These initiatives probably explain the observed increases in

testing and treatment as important components of treatment-as-prevention.

Although use of linked data from medical records enabled establishment of two large, population-specific cohorts and provided objective clinical data with which to directly measure HIV incidence, as is common when using routine data for research purposes, our dataset was susceptible to incomplete and missing data. However, sensitivity analyses suggested that incomplete and missing data had minimal effect on our primary findings. Although there were some differences between GBM included and excluded from our analyses (appendix p 3), excluded men were of a lower risk profile and were, therefore, unlikely to have affected the primary results had they been included. Second, our analyses were able to consider only variables within existing electronic health systems, with several relevant factors not assessed (eg, race and ethnicity, and cisgender or transgender status) or assessed indirectly (eg, condomless sex). Third, our sample was limited to GBM attending participating services and could not account for care received at services outside of the network or in other jurisdictions. However, the TAIPAN network had overall high coverage of the underlying population. Including a buffer period for the preceding 6 months (ie, to account for less than annual clinical attendance), in 2019 TAIPAN included 10 118 GBM with diagnosed HIV (estimated as 76·65% of the total population)[16] and 62 130 GBM overall (estimated as 70·61% of the total population).[23] Fourth, our findings show the population-level potential of treatment-as-prevention in a high-income country with a concentrated epidemic and a relatively low level of undiagnosed HIV, which cannot necessarily be generalised to other countries, populations, or health systems.

The design of this research precludes any direct claim of causality; although the results are highly suggestive, they cannot conclusively show that increasing population prevalence of viral suppression was the cause of decreasing HIV incidence. Although steps were taken to control for confounders as alternative explanations, it is possible that changing sexual practices might have influenced HIV incidence in a way not captured here. However, behavioural surveys of GBM in New South Wales and Victoria clearly indicate that condom use declined substantially over the period of this study.[33] The enhanced behavioural data collected via TAIPAN support this contention. Thus, it is very unlikely that changes in sexual practices could explain decreasing HIV incidence. It is also possible that our study's exclusion criteria biased the results, although the effect of this on the primary outcome is likely to be minimal given excluded GBM probably had lower risk for HIV than the included cohort, as evidenced by significantly lower rectal sexually transmitted infection positivity (appendix p 3). However, we acknowledge potential biases introduced by social network dynamics and assortative mixing among excluded subpopulations, for which our analysis cannot account.

Our results suggest that treatment-as-prevention reduced HIV incidence among GBM in Australia, providing evidence to help bridge the disconnect between the individual-level and population-level effects of treatment-as-prevention[10] and challenging assertions of its limited public health potential.[9] Our results suggest that although effective on its own, treatment-as-prevention most effectively reduces HIV incidence when combined with PrEP distribution and low levels of undiagnosed HIV (ie, high rates of testing). Given the individual health benefits of HIV treatment and compelling evidence of its potential to achieve population-level reductions in HIV incidence, increasing treatment access and reducing undiagnosed infections is vital for combatting HIV.

Contributors

RG led this study in partnership with MS and DC; all authors contributed to its design, development, and implementation. Funding for this research was secured by RG, MS, AC, JH, KP, JE, DJT, S-TL, DC, AP, AEG, BD, CKF, MHo, and MHe. DC and JA were responsible for recruitment and data collection from all study sites, with support provided by all other authors. DC and HM collaborated on the analysis plan with support from RG and MS. DC cleaned and organised the study data and conducted quality control checks and conducted all analyses, while HM reviewed all statistical code and outputs to ensure accuracy. RK and JC provided advice on the study's implementation and interpretation relative to people living with HIV, while MHo and AEG provided guidance relative to PrEP and gay, bisexual, and other men who have sex with men. RTG provided guidance on and carried out all mathematical modelling. DC, HM, MS, and RG had access to the full data and code used to generate these analyses. DC and JA accessed and verified the data. All authors were involved in drafting this manuscript, reviewing several iterations, and approving the final version to submit for publication.

Declaration of interests

AC has received research funding from Gilead Sciences, MSD, and ViiV Healthcare; lecture and travel sponsorships from Gilead Sciences and ViiV Healthcare; and has served on advisory boards for Gilead Sciences, MSD, and ViiV Healthcare. JH's institution received reimbursement for her participation in Advisory Boards for Gilead Sciences, Merck Sharp & Dohme, and ViiV Healthcare. JC's affiliated organisation received reimbursement for her participation in advisory boards and for consultancy services from Gilead Sciences and ViiV Healthcare. AEG reports non-financial support from Gilead Sciences and personal fees from ViiV Healthcare for an educational course. RG is a co-investigator on projects that have received non-financial and research support from Gilead Sciences. PK has received payment for consultancy services from Gilead Sciences. AP received funding from Gilead Sciences and AbbVie for research activities unrelated to this work. MHe and MS received funding from Gilead Sciences and AbbVie for investigator-initiated research unrelated to this study. All other authors declare no competing interests.

Data sharing

The protocol for the TAIPAN project has been published previously,[18] as has the protocol for the larger ACCESS project from which this study derives.[19] The ethical conditions under which TAIPAN was approved limit dissemination of study data given their sensitive nature. However, researchers may request access to these and other data collected by the ACCESS project by submitting an analysis plan for review and agreeing to adhere to security, confidentiality, and collaborative conditions. More information can be found by visiting https://accessproject.org.au/data.

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