Population-level effectiveness of rapid, targeted, high-coverage roll-out of HIV pre-exposure prophylaxis in men who have sex with men: the EPIC-NSW prospective cohort study

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Summary

Background HIV pre-exposure prophylaxis (PrEP) is highly effective in men who have sex with men (MSM) at the individual level, but data on population-level impact are lacking. We examined whether rapid, targeted, and high-coverage roll-out of PrEP in an MSM epidemic would reduce HIV incidence in the cohort prescribed PrEP and statewide in Australia's most populous state, New South Wales.

Methods The Expanded PrEP Implementation in Communities–New South Wales (EPIC-NSW) study is an implementation cohort study of daily co-formulated tenofovir disoproxil fumarate and emtricitabine as HIV PrEP. We recruited high-risk gay men in a New South Wales-wide network of 21 clinics. We report protocol-specified co-primary outcomes at 12 months after recruitment of the first 3700 participants: within-cohort HIV incidence; and change in population HIV diagnoses in New South Wales between the 12-month periods before and after PrEP roll-out. The study is registered with ClinicalTrials.gov, number NCT02870790.

Findings We recruited 3700 participants in the 8 months between March 1, 2016, and Oct 31, 2016. 3676 (99%) were men, 3534 (96%) identified as gay, and 149 (4%) as bisexual. Median age was 36 years (IQR 30–45 years). Overall, 3069 (83%) participants attended a visit at 12 months or later. Over 4100 person-years, two men became infected with HIV (incidence 0·048 per 100 person-years, 95% CI 0·012–0·195). Both had been non-adherent to PrEP. HIV diagnoses in MSM in New South Wales declined from 295 in the 12 months before PrEP roll-out to 221 in the 12 months after (relative risk reduction [RRR] 25·1%, 95% CI 10·5–37·4). There was a decline both in recent HIV infections (from 149 to 102, RRR 31·5%, 95% CI 11·3 to 47·3) and in other HIV diagnoses (from 146 to 119, RRR 18·5%, 95% CI –4·5 to 36·6).

Interpretation PrEP implementation was associated with a rapid decline in HIV diagnoses in the state of New South Wales, which was greatest for recent infections. As part of a combination prevention approach, rapid, targeted, high-coverage PrEP implementation is effective to reduce new HIV infections at the population level.

Funding New South Wales Ministry of Health, Gilead Sciences.

Introduction

Randomised controlled trials have demonstrated that HIV pre-exposure prophylaxis (PrEP) using co-formulated tenofovir disoproxil fumarate and emtricitabine reduces HIV incidence in men who have sex with men (MSM). Findings from the first published trial, the iPrEx study,[1] showed a 44% reduction in HIV incidence in the intention-to-treat analysis. Medication adherence was relatively poor, and efficacy was closely related to adherence. In an open-label extension,[2] no HIV infections were detected among participants with dried blood spot levels of tenofovir diphosphate consistent with taking at least four pills per week. Two more randomised trials[3,4] in MSM in the UK, France, and Canada reported intention-to-treat effectiveness of 86% with both daily and intermittent PrEP, and HIV infections occurred only in non-adherent individuals. An even higher level of efficacy, of 97%, was found in the open-label extension phase of the French iPERGAY study of intermittent PrEP.[5] These data demonstrate the very high degree of efficacy of PrEP in MSM, and that with the daily-dosing regimen, high levels of efficacy are maintained if at least four pills per week are taken.

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Research in context

Evidence before this study

Randomised controlled trials have demonstrated that HIV pre-exposure prophylaxis (PrEP) using co-formulated tenofovir disoproxil fumarate and emtricitabine reduces HIV incidence in men who have sex with men (MSM), with efficacy approaching 100% in adherent individuals. Mathematical models suggest that the population-level impact of PrEP will be maximised if PrEP is implemented quickly and with high coverage. We searched PubMed for studies published in English from Jan 1, 2010, to July 31, 2018, with the terms "HIV", "pre-exposure prophylaxis", and "impact". Empirical studies have not tested the findings from mathematical modelling, and the size of the effect of PrEP roll-out on population-level HIV incidence remains uncertain.

Added value of this study

The EPIC-NSW study was a prospective implementation study in New South Wales, Australia, aimed to measure the population-level effect of rapid, targeted, high-coverage PrEP implementation in MSM. State-wide recent HIV infections in MSM declined by almost one-third 1 year after the initial recruitment target was met. By the end of follow-up reported here (Oct 31, 2017), we estimated that 20% of HIV-negative gay men in the study area were receiving PrEP. Declines in recent HIV infections approached 50% among individuals living in the gay suburbs of Sydney, in those born in Australia, and in those aged 45 years and older. Incidence in the treated cohort was less than 1 per 1000 person-years compared with the expected incidence of more than 2 per 100 person-years.

Implications of all the available evidence

In MSM, HIV epidemics with high levels of HIV testing and treatment, rapid PrEP implementation at scale can quickly result in substantial reductions in HIV incidence at the population level. PrEP roll-out should be prioritised as a crucial component of HIV prevention in HIV epidemics predominantly affecting MSM.

Mathematical modelling studies[6] predict that in MSM, a large and early effect on HIV incidence at the population level can be achieved if PrEP is rapidly implemented with high coverage of those at risk. Empirical studies have not tested these findings. Studies of the population-level effects of PrEP would ideally report on population-based HIV incidence as the primary outcome, but these data are not usually available. Time trends in new diagnoses at the population level might not necessarily reflect trends in HIV incidence, because new infections can remain undiagnosed, and some new diagnoses represent infections acquired years previously. In Australia, there is a long-established system to monitor HIV infections likely to have been acquired in the last 12 months (referred to as recent infections).[7] Trends in recent infections are likely to be a more sensitive measure of incidence than trends in all new HIV diagnoses, and thus of the effect of new HIV prevention interventions.

We describe the rapid implementation of PrEP in high-risk MSM in New South Wales, Australia's most populous state. We report HIV incidence within the cohort prescribed PrEP, and state-wide surveillance trends in recent infections and in all other HIV diagnoses.

Methods

Study design and participants

The Expanded PrEP Implementation in Communities New South Wales (EPIC-NSW) study is a single-arm, prospective implementation study of daily, single-dose, oral, co-formulated tenofovir disoproxil fumarate (300 mg) and emtricitabine (200 mg) as HIV PrEP in individuals at high risk of HIV infection. We did the study at 21 clinical sites across New South Wales, Australia. The study was approved by the Ethics Committee of St Vincent's Hospital (Sydney, NSW, Australia). Written informed consent was obtained from all participants. A summary of the study protocol has been published.[8]

We required participants to be 18 years of age or older, and live in New South Wales, or visit often enough to attend follow-up. They were required to have a negative result with a fourth-generation HIV antibody–antigen test within 7 days before commencing PrEP. Participants were assessed as being at high and ongoing risk of HIV infection, as defined by New South Wales HIV PrEP guidelines,[9] or having been a participant in the preceding PrEP demonstration project PrELUDE.[10] The eligibility guidelines require reporting at least one of four behavioural criteria shown in a previous Sydney cohort study to be associated with aN HIV incidence of approximately 2 per 100 person-years or higher.[9,11–13] These criteria were: receptive condomless anal intercourse with casual partners of HIV-positive or unknown status; a diagnosis of rectal chlamydia, rectal gonorrhoea, or infectious syphilis; use of crystal methamphetamine; or condomless anal intercourse with an HIV-positive regular partner who did not have undetectable viral load.[14] Almost the entire study population was anticipated to be gay-identifying men, but other individuals at high risk according to the guidelines were also eligible. Participants were excluded if they tested HIV positive, had symptoms consistent with acute HIV infection, or had an estimated glomerular filtration rate of less than 60 mL/min per 1·73 m².

The study was promoted by New South Wales's largest gay and lesbian health organisation, ACON, in collaboration with other HIV non-governmental organisations, clinicians, researchers, and the New South Wales Ministry of Health. Potential participants received information about EPIC-NSW and were risk assessed using a brief online questionnaire, administered by clinicians or peer educators.[8] To manage demand

on clinical services, substantial pre-consent triaging occurred before screening, meaning we could not document the proportion failing screening.

Procedures

Follow-up was based on New South Wales PrEP guidelines.[9] We required HIV testing at 1 month, 3 months, and every 3 months thereafter, in addition to testing every 3 months for sexually transmissible infections and monitoring every 6 months of renal function.[8] To assess follow-up, we calculated the proportion of participants who had an HIV test or a record of being dispensed PrEP within contiguous time-windows around scheduled visits, based on the date of the baseline visit. Sites kept logs of each dispensing episode.

Outcomes

The protocol specified two co-primary endpoints: HIV incidence in the cohort dispensed PrEP in the 12 months after recruitment of 3700 participants; and the change in HIV diagnoses in MSM in New South Wales surveillance data between the 12 months before commencement of recruitment (March 1, 2015, to Feb 28, 2016; ie, before PrEP roll-out) and the 12 months after recruitment of 3700 participants (Nov 1, 2016, to Oct 31, 2017; ie, after PrEP roll-out).

A new HIV diagnosis required a repeatedly reactive laboratory-based antibody–antigen result, plus a positive western blot or positive HIV nucleic acid amplification test. New HIV infections in the cohort were detected using overlapping methods. First, an HIV diagnosis was a protocol-specified serious adverse event. Second, data for all HIV test results in participants were extracted from electronic patient medical records, except in four clinics, where data were entered onto a study database. The other 17 clinics were part of an existing sentinel surveillance network, which electronically extracts and collates HIV test results. Third, in consenting participants (2954 [80%] individuals), data were linked to state-wide HIV surveillance data by the New South Wales Health Centre for Health Record Linkage. Linkage used five deterministic passes matching date of birth, postcode of residence, country of birth, sex, and first two letters of given name and surname.

Statistical analysis

The cohort size of 3700 to be recruited over 12 months was based on a balance between the aim of quickly providing high-level PrEP coverage to all eligible MSM, and pragmatic considerations of how quickly the clinic network could recruit. Our method for estimation of the cohort size has been published.[8] Briefly, it was based on the number of gay-identifying men in New South Wales (2·3% of men), the proportion of these who are sexually active (81·9%), minus those HIV positive. The result was then multiplied by the proportion of HIV-negative MSM in New South Wales who reported the eligibility behaviours listed above in behavioural surveillance studies, plus additional requirements of frequent risk behaviour to indicate likely ongoing exposure.[8] Overall, we estimated that 8·6% of 38872 sexually active gay men in New South Wales who were HIV negative or status unknown would be eligible (3343), and set a higher target of 3700 to allow for loss to follow-up.[8] After recruitment of 3700 individuals in 8 months, with clear ongoing demand for PrEP from high-risk MSM, we formally amended the protocol to specify that recruitment of high-risk people could continue beyond 3700 without a cap.

This analysis is based on 12 months of follow-up after the recruitment of 3700 high-risk participants who were dispensed PrEP at least once. We grouped countries of birth into continental regions, except for those born in Canada, Ireland, New Zealand, the UK, and the USA, which were grouped as high-income English-speaking countries. For area of residence, we present data on participants living in one of the seven contiguous postcodes in inner Sydney where more than 10% of adult men identify as gay (referred to as gay Sydney suburbs),[15] elsewhere in Sydney, and outside of Sydney.

We calculated medication possession ratio for the first 12 months as the number of PrEP pills dispensed during the first year divided by 365 days for all individuals dispensed PrEP at baseline. We truncated pills dispensed at 365 doses, and we included only dispensed pills that could have been taken by the end of 12 months of follow-up, assuming daily dosing. Based on a previous study, we defined possible poor adherence as a medication possession ratio of less than 80%.[16]

For HIV incidence, we calculated person-years at risk from the date of first PrEP dispensing until the first of the date of a confirmed HIV positive test, the last HIV negative test, or Oct 31, 2017 (for those with a later HIV negative test result available). We did a modified intention-to-treat analysis, which included all participants who were dispensed at least one dose of study drug. No imputations were made for ongoing use of PrEP or other missing data. Participants who formally withdrew from the study (49 [1%] individuals) were censored at their date of withdrawal. Incidence and CIs were calculated using Poisson regression.

For the HIV surveillance analysis, we present the difference in numbers of HIV diagnoses in MSM in New South Wales before and after PrEP roll-out. We hypothesised that the reduction in recent HIV infections among MSM would be greater than the reduction in other HIV diagnoses. For analysis, we assumed the denominator was the number of gay-identifying men in New South Wales at risk of HIV infection (n=38872). Because this denominator is large and unlikely to change substantially over 2 years, the relative risk reduction (RRR) calculated from surveillance data is likely to be a robust comparative estimation. The RRR [(1−relative risk [RR])×100)] and the 95% CIS were calculated using the Poisson distribution. We used the surveillance definition of recent infection to

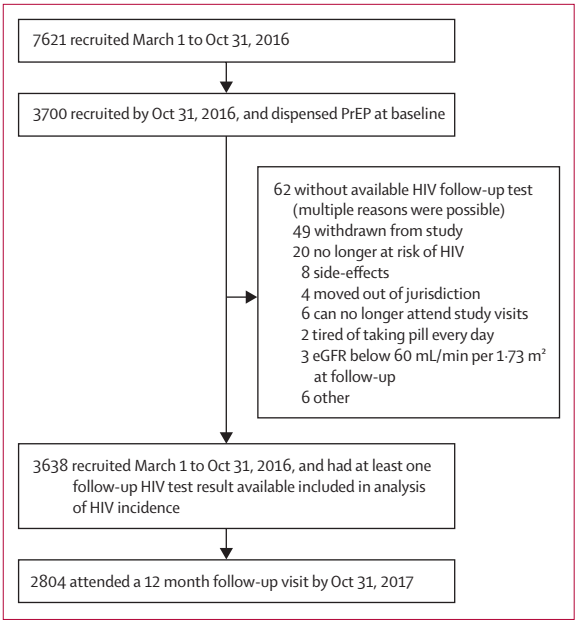

Figure 1: **Flow-diagram for the EPIC-NSW cohort**
Follow-up defined as having had a post-baseline HIV test. eGFR= estimated glomerular filtration rate.

define recent HIV infections as those with at least one of the following three characteristics in the 12 months before diagnosis: a negative or indeterminate HIV test; an indeterminate or negative western blot; or a medical diagnosis of HIV seroconversion illness.[7] We compared trends in recent infections to trends in all other HIV diagnoses, which mostly represent infections that have been established for more than 12 months.

All calculations were performed using Stata version 14.2 (StataCorp, College Station, TX, USA).

The study is registered with ClinicalTrials.gov, number NCT02870790.

Role of the funding source

The study was funded by the New South Wales Ministry of Health, and Gilead provided 2000 person-years of Truvada (the remainder of study drug was purchased from Mylan). As an implementation study, the Ministry had an active role in the design, conduct and analysis of the study, and a number of Ministry staff were included as manuscript coauthors (CS, JH, H-MAS, KC, BT). Gilead played no role in the collection, analysis, and interpretation of data or the writing of the report or the decision to submit the paper for publication.

Results

Recruitment commenced on March 1, 2016, and target recruitment of the initial 3700 individuals was completed on Oct 31, 2016. Recruitment continued after Oct 31, 2016, and by the end of the 12-month follow-up (Oct 31, 2017), 7621 participants were enrolled, an estimated 19·6% of 38872 sexually active gay men in New South Wales who were HIV negative or status unknown (figure 1). Subsidised availability of HIV PrEP through Australia's Pharmaceutical Benefits System commenced on April 1, 2018, and enrolment ceased on April 30, 2018, with 9714 participants enrolled.

	Number (%)
Age (years)	
18–24	297 (8%)
25–34	1356 (37%)
35–44	1086 (29%)
≥45	961 (26%)
Gender	
Male	3676 (99%)
Female	1 (<1%)
Transgender, male to female	15 (<1%)
Transgender, female to male	7 (<1%)
Other	1 (<1%)
Sexual identity	
Gay or homosexual	3534 (96%)
Bisexual	149 (4%)
Heterosexual	9 (<1%)
Other	8 (<1%)
Country of birth	
Australia	2057 (56%)
Canada, Ireland, New Zealand, USA, or UK	422 (11%)
Asia	328 (9%)
Europe (excluding UK and Ireland)	155 (4%)
Africa	78 (2%)
South America, Central America, or Caribbean	119 (3%)
Other countries	60 (2%)
Missing	481 (13%)
Area of residence	
Sydney, gay postcodes*	1413 (38%)
Other Sydney	1847 (50%)
Other	423 (11%)
Missing	17 (<1%)
Type of recruiting site	
Public sexual health clinic	1741 (47%)
Private general practice	1797 (49%)
Hospital	162 (4%)

Total number of participants was 3700. EPIC-NSW=Expanded PrEP Implementation in Communities–New South Wales. *Postcodes 2008, 2010, 2011, 2016, 2021, 2042, and 2204.[15]

Table 1: **Enrolment characteristics of EPIC-NSW study participants**

Baseline demographic data for the initial protocol-specified target of 3700 individuals are presented in table 1. 3676 (99%) participants were male, with 3534 (96%) identifying as gay, and 149 (4%) as bisexual. Median age was 36 years (IQR 30–45). 2057 (56%) participants were born in Australia, followed by 422 (11%) in high-income English-speaking countries, 328 (9%) in Asia, and 412 (11%) in other countries. Data on country of birth were missing for 481 (13%) participants, for

	Number (%)
Receptive condomless anal intercourse with at least one casual male partner of HIV-positive or unknown status	3357 (91%)
Diagnosis of infectious syphilis or anal gonorrhoea or anal chlamydia	632 (17%)
Use of crystal methamphetamine	961 (26%)
Condomless anal intercourse with an HIV-positive regular partner who is not on antiretroviral treatment or has detectable viral load	282 (8%)
Previous PrELUDE study participant	159 (4%)

Table shows data for 3633 of 3700 participants in the EPIC-NSW study; eligibility criteria were missing for 67 participants (2%). Multiple responses were possible. EPIC-NSW=Expanded PrEP Implementation in Communities–New South Wales.

Table 2: **Enrolment behavioural risk eligibility criteria in the 3 months before enrolment**

whom data were not available from the electronic medical records.

High-risk eligibility criteria were available for 3633 (98%) participants (table 2). The most common criterion was receptive condomless anal intercourse with at least one casual partner reported by 3357 (91%) individuals. 2257 (61%) participants reported only one eligibility criterion, 2009 (89%) of whom reported receptive condomless sex with a casual partner, 1103 (30%) reported two, 241 (7%) reported three, and 48 (1%) reported all four risk behaviours. Data were missing for 47 (1%) individuals recruited in the first few weeks because of initial failure of systems to link risk assessment to enrolment details.

The proportion of participants attending a follow-up visit each visit window declined from 88% (n=3259) at 1 month and 90% (n=3333) at 3 months to 76% (n=2804) at 12 months (table 3). In total, 3577 (97%) participants were dispensed study drugs more than once in the year after the first date of dispensing. Median medication possession ratio over the first 12 months was 97·8% (IQR 74·0–100), with a mean of 83·1% (95% CI 82·3–83·9). 1114 (30%) individuals had a low medication possession ratio (<80%). Participants with low medication possession ratio were less likely than others to attend follow-up visits. For example, during the 12-month visit window, 2243 (87%) of 2586 with a high ratio and 421 (38%) of 1114 with a low ratio attended for HIV testing.

Among the 3700 participants, there were two new HIV diagnoses by Oct 31, 2017. Both occurred in men who were clearly non-adherent. One was a participant who was dispensed PrEP but never commenced taking it. The other had an indeterminate western blot assay, indicative of very recent infection, 11 months after being dispensed 3 months of PrEP. There were a total of 4100 person-years of follow-up among 3638 participants with a record of at least one HIV test result after study baseline, among whom HIV incidence was 0·048 (95% CI 0·012–0·195) per 100 person-years. The 4100 person-years of follow-up we documented was 83% of the 4940 person-years expected if everyone had attended as scheduled. There were three additional new HIV diagnoses after the protocol-defined end date, in November and December, 2017. All three individuals were clearly non-adherent to PrEP at the time of infection.

	Number dispensed PrEP or received an HIV test in each visit window (%)	Cumulative number dispensed PrEP or received HIV test in each visit window, or during a later window period (%)
Baseline	3700	3700
1 month	3259 (88%)	3645 (99%)
3 months	3333 (90%)	3569 (96%)
6 months	3131 (85%)	3422 (92%)
9 months	2934 (79%)	3264 (88%)
12 months	2804 (76%)	3069 (83%)

Visit windows were contiguous, with upper and lower boundaries of the window midway between the scheduled visit date and the previous and subsequent scheduled visits, respectively. EPIC-NSW=Expanded PrEP Implementation in Communities–New South Wales. PrEP=pre-exposure prophylaxis.

Table 3: **Distribution of participants attending each follow-up visit for PrEP dispensing or an HIV test in each visit window in the EPIC-NSW study**

The number of HIV diagnoses in MSM in New South Wales declined from 295 in the 12 months before PrEP roll-out to 221 in the 12 months after PrEP roll-out (RRR 25·1%, 95% CI 10·5–37·4), the lowest annual HIV diagnosis count in MSM recorded in New South Wales since the beginning of HIV surveillance in 1985. There was a decline in recent HIV infections (from 149 to 102, RRR 31·5%, 95% CI 11·3–47·3) and a non-significant decline in other HIV diagnoses (from 146 to 119, RRR of 18·5%, 95% CI –4·5 to 36·6). The declines in recent HIV infection were greatest in Australia-born individuals (48·7%), and were lower in those born in high-income English-speaking countries (33·3%), Asia (21·4%), and other countries (increase of 23·5%). Declines were greatest in the gay suburbs of Sydney (51·8%) and in New South Wales outside of Sydney (54·2%) than in other Sydney suburbs (7·3%). Declines were seen at all ages but were greatest in men aged 45 and older (48·4%; figure 2). CIs for these declines could not be calculated because of a lack of reliable information on the size of the denominator for these subgroups. The declines we documented after PrEP roll-out contrasted with the stable number of recent HIV infections in the 2 years before roll-out of 143 and 146, respectively (RR 1·02, 95% CI 0·81–1·29; figure 3).

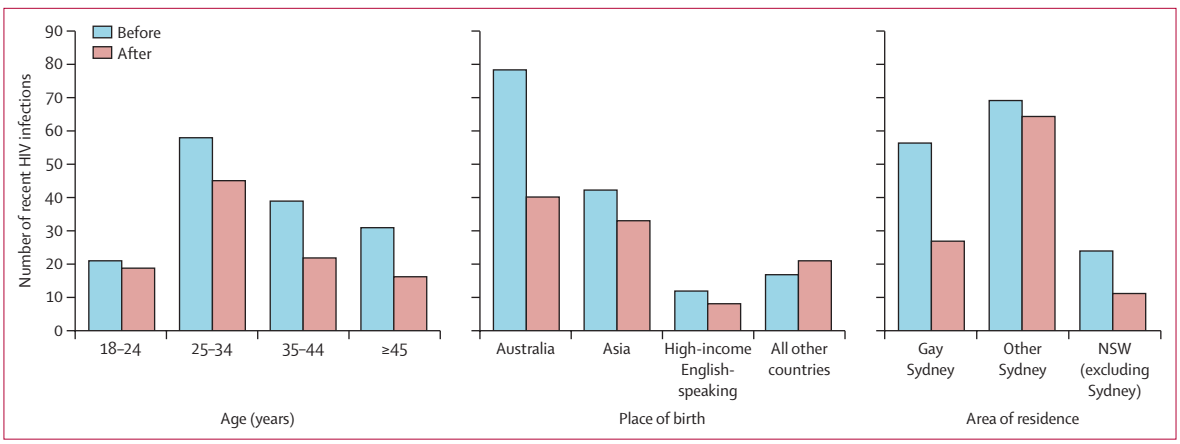

Figure 2: **Number of recent HIV infections in New South Wales**
Figure shows data for the 12 months before commencement of recruitment to EPIC-NSW (n=149, "before") and the 12 months after the 3700th EPIC-NSW participant was recruited (n=102, "after") by age, country or region of birth, and area of residence. NSW=New South Wales.

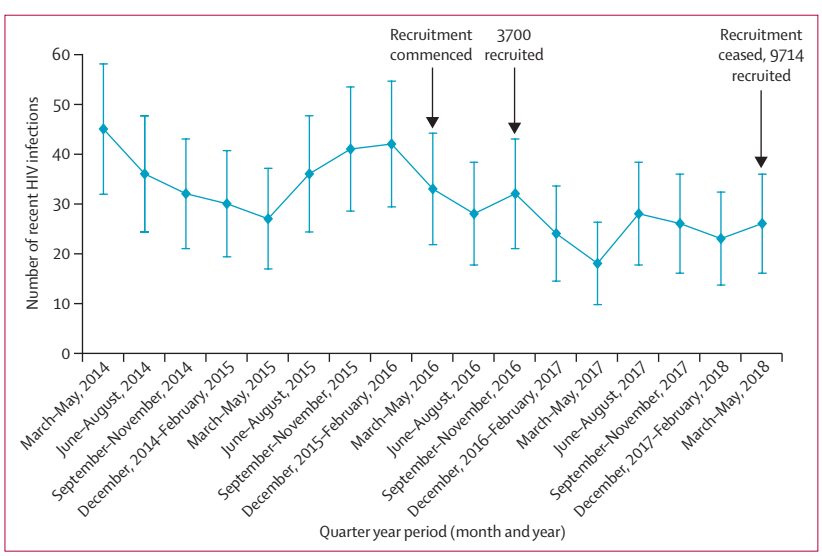

Figure 3: **Trend of recent HIV infections in men who have sex with men in New South Wales by quarter, March 1, 2014, to May 31, 2018**
95% CIs were calculated as the normal approximation from the Poisson distribution of number of recent HIV infections. These should be interpreted as an indicator of random variation, and should not be used to infer statistical significance of the difference between points.

Discussion

PrEP roll-out in New South Wales was associated with a rapid decline in state-wide HIV diagnoses in MSM. Compared to the 12 months immediately before PrEP roll-out, there were 25·1% fewer HIV diagnoses in MSM in New South Wales in the 12 months after PrEP roll-out. There was a 31·5% decline in recent HIV infections, and an 18·5% decline in other HIV diagnoses, reflecting larger reductions in incident HIV infections than in the diagnosis of longer-established infections. The reductions in recent infections were not as large in individuals younger than 35 years, in those born overseas, and in men residing in Sydney outside the gay suburbs, highlighting future challenges in maximising reduction of HIV transmission state-wide. The HIV infection incidence in the cohort of 3700 men dispensed PrEP was less than 1 in 2000 per year, compared with an expected incidence of 2 per 100 per year or higher in the absence of PrEP. Only two new HIV infections were documented in these men, both of whom were clearly not using PrEP at the time of infection. Median medication possession ratio was 96·7%, reflecting high adherence. However, about three in ten men had a medication possession ratio of less than 80%, which could potentially reflect poor adherence, but could also relate to intermittent or periodic use of PrEP, or informed cessation of PrEP related to the end of a period of high-risk behaviour.

In New South Wales, HIV test-and-treat strategies had already been successfully implemented before the implementation of PrEP. By 2016, the UNAIDS 90-90-90 HIV diagnosis and treatment targets were estimated to have been exceeded, and between 2015 and 2017, there were only small increases in already high rates of HIV testing and treatment.[17] Before EPIC-New South Wales, there was little uptake of PrEP in New South Wales. A PrEP demonstration project enrolled 303 high-risk gay men from Nov 13, 2014,[18] but by February 2016, immediately before EPIC-New South Wales recruitment, only 3·9% of non HIV-positive gay men in Sydney reported ever using PrEP.[19] A year later, in February 2017, this figure had increased to 13·9%,[19] relating to our rapid recruitment. Over the period reported in this study, we noted increases in reported condomless anal intercourse in gay men in New South Wales[20] and increased chlamydia and gonorrhoea notifications in men in New South Wales.[21] The decline in HIV we documented, at a time of decreasing condom use and increasing sexually transmitted infections, provides empirical support for the predictions from modelling[6] that rapid high-coverage PrEP roll-out can lead to swift declines in HIV incidence at the population level. Public funding of PrEP from April 1, 2018, now allows PrEP prescription by all

Australian general practitioners, and this should assist in ensuring more equitable reductions in HIV diagnoses. Targeted campaigns promoting PrEP in New South Wales residents who are gay men born in selected non-English-speaking countries have also commenced.

Internationally, there have been few studies of population-level effectiveness of PrEP. Although a number of countries have approved HIV PrEP, uptake has been slower and has been geographically patchy. In the USA, HIV PrEP was approved in 2012, and the Centers for Disease Control and Prevention has estimated that 492 000 MSM, estimated to be 25% of all sexually active MSM, meet the substantial risk indication for PrEP used in the USA.[22] Initial US PrEP uptake was sluggish[23] before accelerating more recently, and by late 2016 it was estimated that 83 672 men in the USA had commenced PrEP.[24] Uptake was highest in the city of San Francisco, where by 2014 an estimated 9·2% of MSM were using PrEP.[25] New HIV diagnoses in MSM in San Francisco declined by 50% over the 5-year period 2012 to 2016 when PrEP was gradually introduced, but trends in recent HIV infection have not been reported.[26,27] In London, reductions in HIV diagnoses were reported in 2017 at some HIV clinics, which has been attributed to a combination of increased testing and treatment, as well as PrEP sourced through trials or privately.[28] Declines in HIV diagnoses in these settings were co-incident with increased implementation of HIV treatment as prevention, so the individual attribution of the effect of PrEP is difficult. In France, 2805 people (97% MSM) were prescribed PrEP in the first 12 months of roll-out in 2016 with only four new HIV infections in this cohort,[29] but population-based trends in HIV have not yet been reported.

In comparison with these other international settings, PrEP roll-out in New South Wales has been more rapid and at a relatively higher coverage. We met our initial target of 3700 participants on PrEP within 8 months. By the end of 12 months of follow-up of those participants (Oct 31, 2017) we had enrolled 7621 participants, an estimated 19·6% of sexually active gay-identifying men living in New South Wales who were HIV negative or HIV status unknown.[8] The continuing high rate of PrEP initiation in New South Wales reflects a less restrictive definition of high risk than in the initial estimate (which included additional requirements of frequent risk behaviour to indicate likely ongoing exposure), but also reflects increasing rates of condomless anal intercourse. Increasing levels of condomless sex have been reported coincident with PrEP roll-out in both San Francisco[27] and in Victoria and New South Wales in Australia.[19] We will continue to follow up the larger cohort who commenced PrEP to document longer-term trends.

Several characteristics contributed to the success of EPIC-NSW. The previous small-scale PrEP demonstration project PrELUDE documented high levels of adherence and no seroconversions in 2014–16,[10] and provided confidence that international randomised trial data on efficacy could be replicated in Australian gay men. That local experience with PrEP led to the development of PrEP guidelines approved by the state's Ministry of Health.[9] A government strategy which specifically targeted PrEP implementation[30] reflected government leadership. Intensive building of community health literacy was led by ACON. A state-wide network of free-to-consumer and publicly funded sexual health services, and large inner-city private general practices predominantly serving gay men, allowed for a large-scale and truly state-wide response. As a clinical trial, the drug was provided free of charge to consumers. Key to our ability to quickly document the population-level effect of PrEP was the existing surveillance system for recent HIV infection.[7] We ascertained HIV diagnoses through means which would have likely detected HIV diagnosed anywhere in the state. We are only likely to have missed cases of HIV infection in people who had left New South Wales, or in people who stopped testing for HIV.

There are some limitations in the interpretation of these data. First, it is possible that other factors might explain some of the decline in HIV diagnoses. However, the HIV test-and-treat strategy was already rolled out at the commencement of the study, with the 90-90-90 goals met in 2016,[17] and data on behaviours[20] and sexually transmitted infection notifications[21] both suggesting increasing rather than decreasing HIV risk. Second, it is possible that PrEP could have been obtained outside the study by personal importation of generic medication, so that the actual level of coverage might be greater than we have described. In early 2017, 6% of gay men receiving PrEP in New South Wales and Victoria reported they had obtained PrEP in this manner.[20] Third, the fact that 17% of participants did not have an HIV test result available at their 12 month or later visit means it is possible some new HIV infections could have been missed. Fourth, our distinction between recent infections and other diagnoses is unlikely to be 100% accurate. Men with new HIV diagnoses who had not tested in the past 12 months and did not have an indeterminate or negative western blot or seroconversion illness at the time of HIV diagnosis were not included in recent HIV infections, but some probably had been infected recently. This possibility would mean that we underestimated the difference in trends between recent infection and other HIV diagnoses.

Our results support the population-level effectiveness of PrEP less than 2 years after commencement of PrEP roll-out. Rapid, targeted, high-coverage roll-out to scale was accompanied by rapid reductions in HIV incidence at the population level. PrEP is a highly effective element of the combination prevention approach in MSM.

Contributors

AEG, BT, BY, BW, CS, DAC, EEO, FJ, GL, H-MAS, IZ, JA, JH, KP, KLC, LW-S, MAH, NJD, RG, SM, and SV made substantial contributions to the conception or design of the work and the analysis and interpretation

of data for the work. AC, AM, CCO'C, CJC, DAL, DB, DJS, DMA, EYJ, JL, KLC, MB, NR, PR, RFi, RIB, and RFo made substantial contributions to the acquisition and interpretation of data for the work. AEG drafted the work. AC, AM, BT, BY, BW, CCO'C, CS, CJC, DAC, DAL, DB, DJS, DMA, EEO, EYJ, FJ, GL, H-MAS, IZ, JA, JH, JL, KP, KB, KLC, LW-S, MB, MAH, NR, NJD, PR, RG, RFi, RIB, RFo, SM, and SV revised drafts critically for important intellectual content. All authors gave final approval of the version to be published and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Declaration of interests

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