Implementing HIV pre-exposure prophylaxis (PrEP): let’s not get caught with our pants down

Peter J Saxton, Massimo Giola, Edward P Coughlan, Joseph G Rich, Sunita Azariah, Adrian H Ludlam, Christy O'Toole, Mike Pohl, Jason M Myers

ABSTRACT

HIV pre-exposure prophylaxis (PrEP) is a daily pill that prevents HIV acquisition. In March 2018, New Zealand became one of the first countries in the world to publicly fund PrEP for individuals at high risk. PrEP promises significantly improved HIV control but is unfamiliar to most health practitioners here, compromising its potential. In this article we review the rationale for PrEP and identify barriers to rapid implementation. The latter include: consumer and health practitioner awareness; acceptability; scale-up targets; prescribing and pharmacy bottlenecks; service capacity to manage follow-up; primary care training; monitoring systems for uptake and quality; equity; eligibility; risk compensation and policy. Many of these areas are ripe for research and innovation. By addressing these obstacles we can realise the potential of PrEP and move closer to ending HIV in Aotearoa/New Zealand.
Effectiveness data at the population level is emerging, with NSW recording a 29% reduction. London reported a 32% decline in recent HIV cases after implementing large scale PrEP services although this coincided with increased HIV testing and prompt treatment of those infected. Mathematical modelling studies continue to be encouraging, a recent systematic review predicting ~95% reduction in HIV transmission if PrEP is effectively targeted and combined with existing interventions. Indeed PrEP has recently been described as a necessary public health intervention if HIV is to be controlled.

PrEP is timely
PrEP comes at a pivotal moment in New Zealand’s HIV epidemic. On the one hand, HIV diagnoses have been rising with the increase mostly affecting GBM. On the other hand we have most people living with HIV diagnosed and on treatment and unable to transmit the virus. We have most GBM who are susceptible to HIV using condoms for casual sex. And we could have the small group of people who struggle with consistent condom use for receptive anal intercourse unable to acquire HIV if they are offered, accept and adhere to PrEP.

This pincer-like prevention approach closes down opportunities for HIV to spread. PrEP, like condoms, removes users from the potential network of transmission and leaves the virus with nowhere to go, akin to herd immunity. PrEP therefore promises both private and public health benefits: protecting the user and their future sexual partners. Taken together, condoms, increased HIV testing, treating HIV, and PrEP can enable New Zealand to regain control and work towards HIV elimination.

PrEP is moral
We can anticipate that some people will have moral objections to the government subsidising PrEP for HIV prevention. People may be concerned that it endorses risky sexual behaviour or will increase transmission of other sexually transmitted infections (STIs). However, publicly funding tools that protect against the health and social consequences of sexual behaviour is not new. PHARMAC funds the Gardasil vaccine for human papillomavirus (HPV), funds contraceptive options, and funds condoms. In July 2017 PHARMAC also removed the CD4 threshold to prescribing funded antiretroviral treatment (ART) for people living with diagnosed HIV, recognising ART’s public health value in preventing HIV transmission. To withhold public funding for PrEP would be inconsistent with these historical decisions and raise valid questions about homophobia or heterosexism, given the need for PrEP and its effectiveness, as the majority of those benefiting from PrEP would be gay and bisexual men. We believe that PrEP is the latest in a procession of innovations arising from the HIV sector and could, in time, transform practices in other public health fields.

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**Figure 1:** Eligibility criteria for initiating funded HIV PrEP (1 March 2018).

<table>
<thead>
<tr>
<th>Both:</th>
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<tr>
<td>1. Patient has tested HIV negative; and</td>
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<td>2. Either:</td>
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<tr>
<td>2.1 All of the following:</td>
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<tr>
<td>2.1.1 Patient is male or transgender; and</td>
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<td>2.1.2 Patient has sex with men; and</td>
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<tr>
<td>2.1.3 Patient is likely to have multiple episodes of condomless anal intercourse in the next 3 months; and</td>
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<tr>
<td>2.1.4 Any of the following:</td>
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<tr>
<td>2.1.4.1 Patient has had at least one episode of condomless receptive anal intercourse with one or more casual male partners in the last 3 months; or</td>
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<tr>
<td>2.1.4.2 A diagnosis of rectal chlamydia, rectal gonorrhoea, or infectious syphilis within the last 3 months; or</td>
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<td>2.1.4.3 Patient has used methamphetamine in the last three months; or</td>
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<tr>
<td>2.2 All of the following:</td>
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<tr>
<td>2.2.1 Patient has a regular partner who has HIV infection; and</td>
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<td>2.2.2 Partner is either not on treatment or has a detectable viral load; and</td>
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<td>2.2.3 Condoms have not been consistently used.</td>
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PrEP increases prevention options for the most vulnerable

The majority of most-at-risk individuals do use condoms for casual sex, but we need new options to prevent HIV acquisition and transmission in GBM who have difficulty sustaining condom use. Many struggle with condom use because they are vulnerable, as a result of substance addiction, poor mental health, or difficulties negotiating condom use with a sexual partner due to power asymmetry (interpersonal differences in language, age, sexual experience, openness about sexuality). Others struggle with condoms due to perceived reductions in intimacy or sensation, or because of erectile dysfunction or latex allergies. Publicly-funding PrEP can disproportionately benefit the neediest in our communities.

PrEP addresses health inequalities

Improving HIV prevention options for GBM via PrEP can help narrow health inequalities, as GBM in New Zealand are around 40 times more likely than heterosexual individuals to have HIV. Within GBM communities, publicly-funded PrEP can also help reduce inequalities for Māori, Pacific and Asian men, for younger men and for transgender individuals. These sociodemographic groups may face greater barriers to consistent condom use, and are likely to face disproportionate financial barriers if their only option is to pay the full price for PrEP or to import PrEP from overseas pharmacies.

PrEP can be cost-effective

PHARMAC already faces sizeable costs for New Zealand’s failure to eliminate HIV transmission, as treating HIV is lifelong and expensive. PHARMAC’s published spend on HIV antiretrovirals doubled in five years from $16 million in 2011 to $32 million in 2016 due to ongoing infections and low mortality. A well-targeted PrEP programme with high uptake will prevent HIV transmissions and limit PHARMAC’s burden. Savings can be redirected into funding other medicines and vaccines. The cost of PrEP should also decline over time as medicines come off patent and cheaper generics are negotiated. From 1 July 2018 the list price for PrEP medication Truvada™ dropped by 77% and further reductions are likely. The cost-effectiveness of a targeted programme like New Zealand’s is sensitive to the medication price, meaning PrEP could soon become cost-saving.

PrEP can improve HIV testing and outcomes for people living with HIV

PrEP is likely to increase HIV testing among individuals most at risk. Commencing PrEP requires a confirmed HIV negative result, and only half of all GBM test for HIV annually. Consequently PrEP can help reduce the pool of undiagnosed HIV, estimated at 21% of GBM infected. Furthermore a third to a half of individuals with newly diagnosed HIV are diagnosed late (CD4 count <350). Individuals whose HIV is not diagnosed and treated are infectious and they play a disproportionate role in sustaining ongoing transmission in the community. Offering PrEP can engage such individuals in sexual health services resulting in earlier diagnosis and treatment. PrEP can also protect the HIV negative regular partners of diagnosed positive individuals whose virus is not fully suppressed, sharing responsibility for avoiding transmission.

PrEP can improve STI testing and treatment

Similarly, PrEP will increase the frequency and comprehensiveness of STI check-ups in a population experiencing a high burden of STIs. Although PrEP itself offers no protection against non-HIV STIs, each three-monthly PrEP prescription requires an STI screen. This should diagnose and treat bacterial STIs early; and help break chains of STI transmission in the community.

Expert recommendations and international experience

Finally, targeted access to PrEP in New Zealand is consistent with international recommendations from WHO, CDC and agencies in Europe, Britain and Australasia. Policy change also reflects the HIV Consensus Statement in Aotearoa/New Zealand and the New Zealand AIDS Foundation’s (NZAF) Strategic Plan 2016–19. A small number of countries now appear to have funded PrEP programmes (Table 1). Several Australian States also have large-scale PrEP demonstration projects, including NSW, Victoria and Queensland.
Table 1: National and sub-national funded PrEP programmes. Note: GBM = gay and bisexual men.

<table>
<thead>
<tr>
<th>Location</th>
<th>Date</th>
<th>Funding type</th>
<th>Eligibility</th>
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<tbody>
<tr>
<td>United States</td>
<td>2014</td>
<td>Not public per se but criteria inform health</td>
<td>1) GBM, 2) heterosexual men and women, 3) people who inject drugs&lt;sup&gt;g&lt;/sup&gt;</td>
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<td></td>
<td></td>
<td>insurance coverage</td>
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<tr>
<td>South Africa</td>
<td>2016</td>
<td>Funded PrEP offered to high risk patients</td>
<td>1) GBM, 2) sex workers (includes males, females, and transgendered individuals), 3) serodiscordant couples, 4) adolescent girls and young women, as per WHO guidelines&lt;sup&gt;e&lt;/sup&gt;</td>
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<tr>
<td>France</td>
<td>2016</td>
<td>Funded by social security and state medical aid.</td>
<td>1) GBM, 2) transgendered individuals, 3) people who inject drugs, 4) sex workers engaging in unprotected sex, 5) any vulnerable person who has engaged in unprotected sex&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Oslo, Norway</td>
<td>Nov 2016</td>
<td>Funded for patients attending the Olafia Sexual Health Clinic</td>
<td>Individuals at significant risk of HIV&lt;sup&gt;e&lt;/sup&gt;</td>
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<tr>
<td>Belgium</td>
<td>June 2017</td>
<td>Heavily subsidised on reimbursement from an individual’s health insurance provider</td>
<td>1) GBM, 2) people who inject drugs, 3) sex workers, 4) partners of people with HIV&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Scotland</td>
<td>July 2017</td>
<td>Funded via Scottish NHS</td>
<td>1) GBM, 2) transgender individuals, 3) partners of people with HIV, 4) case-by-case on opinion of specialist&lt;sup&gt;f&lt;/sup&gt;</td>
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<tr>
<td>Ontario, Canada</td>
<td>Sep 2017</td>
<td>Funded for individuals: aged under 25; Ontario Drug Benefit; Non-insured Drug Benefits Program for First Nations and Inuit. Discounted for: Private health insurance; Trillium Drug Program</td>
<td>1) GBM, 2) transgender individuals, 3) heterosexual men and women, 4) people who inject drugs&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Brazil</td>
<td>Dec 2017</td>
<td>Funded via 35 clinical sites</td>
<td>1) GBM, 2) sex workers, 3) people who inject drugs&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>British Columbia, Canada</td>
<td>Jan 2018</td>
<td>Funded via BC Centre for Excellence Drug Treatment Program</td>
<td>1) GBM, 2) transgender individuals, 3) heterosexual men and women, 4) people who inject drugs&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>New Zealand</td>
<td>Mar 2018</td>
<td>Funded via PHARMAC</td>
<td>1) GBM, 2) transgender individuals, 3) partners of people with HIV&lt;sup&gt;i&lt;/sup&gt;</td>
</tr>
<tr>
<td>Australia</td>
<td>Apr 2018</td>
<td>Funded via Pharmaceutical Benefits Scheme</td>
<td>1) GBM, 2) transgender, 3) heterosexual men and women, 4) people who inject drugs, 5) case-by-case basis&lt;sup&gt;i&lt;/sup&gt;</td>
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<sup>g</sup> http://www.get-prep.com/prep-costs


Implementation uncertainties

Acceptability
High risk GBM are interested in PrEP with 150 successfully enrolled in the NZPrEP demonstration project in Auckland. However the extent of PrEP awareness and acceptability in the broader GBM community in New Zealand is unknown and needs to be assessed and monitored. Demand for PrEP in this early phase has largely been driven by non-government agencies (NGOs) such as NZAF, through social marketing, community forums and media, in partnership with community activists and clinician-champions. This energy may not be sustainable without extra resources as it competes with condom promotion. A risk is that unbalanced marketing and advocacy will under-promote condoms, leading to behavioural risk compensation and cannibalising the prevention gains possible with PrEP.

Targets
PHARMAC estimated that 4,000 individuals would be eligible under the targeted publicly funded programme. Researchers have since revised this to 5,816 individuals using updated data, estimating that 17.9% of sexually active HIV negative GBM would meet the criteria. If 50% of GBM live in Auckland, 2,900 need access in that city alone. Such numbers are well beyond current sexual health service capacity, meaning PrEP delivery in primary care is crucial to meeting these scale-up targets.

Prescribing bottlenecks
Identifying efficiencies in the PrEP prescribing and care process would be a valuable area of innovation. Subsidised PrEP can only be prescribed on special authority from an approved HIV prescriber, currently found on a list of specialists managed by the Ministry of Health. This numbers around 45 prescribers, most of whom presently focus on treatment of adults living with HIV, not those at HIV risk. New Zealand only has 8.0 FTE sexual health physicians, with uneven regional distribution and many DHBs not employing sexual health specialists at all or sub-contracting from other DHBs. Ten of the 20 DHBs have no-one listed as an HIV prescriber, making access to HIV care and prevention inequitable.

PHARMAC has addressed this by stating it is sufficient for a medical practitioner to have a documented recommendation from a named specialist, but it immediately raises questions about prescriber access, workload, service capacity and the consultation quality. In several centres, sexual health and infectious diseases physicians are facilitating virtual and remote consultations via e-referrals, and have developed a form for GPs to complete and return so an HIV prescriber can recommend approval if appropriate. However widening the range of PrEP prescribers at initial application, for example to include all sexual health physicians and registered medical doctors who have completed an accredited PrEP prescribing course, would better help reduce prescribing bottlenecks and improve access.

Pharmacy delays
Many pharmacies may be reluctant to carry stock due to Truvada’s currently high list price. Anecdotally, this is resulting in further delays, on top of some patients having to wait up to a week for a special authority to be processed before they can get a prescription (pers comm “PrePing NZ” closed Facebook group). This could be mitigated by GPs with high PrEP patient caseloads developing relationships with a local pharmacy to hold stock or couriering prescriptions overnight for remote patients.

Clinic capacity
Three-monthly repeats can be prescribed by GPs and nurse practitioners who have undertaken an accredited PrEP training course, but the patient has to be seen in person for the necessary STI screening, safety monitoring and risk reduction counselling. To meet the 5,816 scale-up target, health services must seek to minimise prescribing delays and manage the increased volume of initial and three-monthly repeat in-person patient appointments. For example, a 12-month PrEP programme for 5,816 patients would require 29,080 PrEP clinical encounters nationwide (initial plus four three-monthly reviews), or around 14,540 extra encounters in Auckland. Screening, scheduling and treating STIs are not factored into this time and should not be underestimated. Sexual
health service laboratory budgets may blow out due to increased NAAT testing, and high STI incidence among PrEP patients can erode clinicians’ time. Solutions include increased funding for sexual health staff and laboratory testing, and pooling laboratory specimens.

**Primary care training**

PrEP is also a sexual health care programme, not just a prescription. Improving primary care competencies in sexual health history taking, STI diagnosis and risk reduction counselling is fundamental as this is not currently well covered in medical or nursing training curricula. Worryingly, only half of GBM are “out” to their GP,

Improving primary care competencies in sexual health history taking, STI diagnosis and risk reduction counselling is fundamental as this is not currently well covered in medical or nursing training curricula. Worryingly, only half of GBM are “out” to their GP,

Addressing this will require a cultural transformation in the way primary care meets the needs of non-heterosexual and transgender patients. PrEP patients themselves have higher rates of prevalent and incident non-HIV STIs,

ASHM has published local PrEP clinical guidelines,

Equity

PrEP should benefit those most at risk, not those most able to navigate healthcare systems. Non-European minority GBM are less likely to access and adhere to PrEP in overseas studies.

In New Zealand, Māori, Pacific and Asian GBM are not more likely to acquire HIV, but evidence does suggest later diagnosis, implying barriers to clinical services. PrEP
implementation here must ensure multiple entry points and appropriate follow-up, potentially including community-led and pharmacy-led delivery models, to avoid generating inequalities. Although PrEP is fully funded for those most at risk, visiting a GP every three months is not free and this will disproportionately deter some GBM.

**Widening eligibility**

PHARMAC’s initial funding criteria are deliberately narrowly targeted. Their origins are the ASHM “high risk” clinical guidelines which themselves are derived from an Australian cohort study. Eligibility for public funding should be based on need, but could in future be broadened to increase access and maximise public health benefit, presumably after the price of PrEP falls and when the issues raised by this article have been addressed. For example, the ASHM guidelines also propose “medium risk” and “case by case” categories for GBM (which would include GBM engaging in repeated insertive condomless anal intercourse with serononconcordant partner/s), and specific guidelines for people who inject drugs, transgender and heterosexual individuals. These are obvious candidates to consider in the New Zealand context. However, each country has a unique HIV epidemiology, and decisions about widening eligibility should be based on evidence to avoid wasting public funds.

**Ineligible patients**

Temporary migrants who meet the PrEP behavioural risk criteria are not however eligible for funded healthcare. Notably this includes international students, a sexually active population many of whom may have chosen to study in New Zealand because of our progressive laws and social acceptance of homosexuality. Other patients, ineligible for public funding because they fail to meet the behavioural criteria can still be prescribed the medication and then purchase PrEP unsubsidised at $250-$350 per month. Importing generic versions of PrEP from trusted overseas pharmacies is a popular alternative option and costs as little as $70 per three-month supply. These provide an alternative avenue for individuals who still feel at risk of HIV and could benefit from PrEP.

**Promoting confidence in condoms**

Why do otherwise low-risk patients feel so vulnerable to HIV? Is it overestimation of personal risk? Or lack of confidence in condoms? Promoting the value of pharmaceuticals such as PrEP should not result in scaring people or exaggerating HIV risks, making GBM feel powerless or that they lack agency without the medication, or that effective interventions such as condoms are now inadequate, passé or unsophisticated.

In New Zealand, local HIV transmission is concentrated among GBM who account for 89% of diagnoses. Condoms prevent transmission 100% of the time if used consistently and correctly and they remain intact. Condoms also possess many qualities not shared by PrEP, such as reducing transmission of undiagnosed STIs which are endemic among sexually-active GBM, and being visually verifiable, meaning sexual partners don’t have to rely on full and accurate disclosure of sexual history, STI and medication status prior to casual sex. These messages should be reinforced in consultations with patients, safe sex social marketing and in policy formulation.

**Policy**

At the time of writing the Government had no HIV or sexual health action plan to guide planning, workforce training, delivery or research into PrEP. Jurisdictions such as NSW cite government leadership as central to their rapid successes in deploying PrEP, including aspirational targets with short time frames (eg, Ending HIV by 2020). Here, DHBs and PHOs will also play an important role by ensuring that sexual health services have adequate capacity and expertise and by training primary health care to be PrEP-ready.

**Conclusion**

Now that biomedical PrEP for HIV prevention is funded, we should aim to implement it with a “hit early and hit hard” mentality. Non-biomedical community-based and behaviour-change approaches like condom use should continue and PrEP should be matrixed within these. That promises the best impact but requires a short-term, deliberate, focused and energetic response across the health sector, not merely HIV and...
sexual health agencies alone. After sustained annual increases, new HIV diagnoses in 2017 declined by 21% — a glimpse of what's possible. International observers will be watching to see if New Zealand displays the same verve behind implementing PrEP as we did to fast-track funding. Let's not get caught with our pants down.

Competing interests:
Gilead Sciences has funded study medication, extra laboratory costs and a research nurse on the separate NZPrEP demonstration project at Auckland Sexual Health Service (lead PI Dr Azariah). PHARMAC has provided salary support for behavioural analysis on NZPrEP (Dr Saxton).

Acknowledgements:
The New Zealand AIDS Foundation Fellowship funded Dr Saxton's time on this work. The authors acknowledge the efforts and perspectives of many HIV and sexual health clinicians, GPs, NGO staff and gay community members surrounding PrEP in New Zealand that have informed this viewpoint.

Author information:
Peter Saxton, Director, Gay Men's Sexual Health Research Group, Department of Social and Community Health, University of Auckland, Auckland; Massimo Giola, Infectious Diseases Specialist and Sexual Health Physician, Tauranga Hospital, Tauranga; Edward Coughlan, Director, Christchurch Sexual Health Service and President, New Zealand Sexual Health Society, Christchurch; Joe Rich, Operations Director, New Zealand AIDS Foundation, Auckland; Sunita Azariah, Sexual Health Physician, Auckland Sexual Health Service, Auckland; Adrian Ludlam, Policy and Science Manager, New Zealand AIDS Foundation, Auckland; Christy O'Toole, Year 5 Medical Student, University of Auckland, Auckland; Mike Pohl, General Practitioner, Auckland; Jason Myers, Executive Director, New Zealand AIDS Foundation, Auckland.

Corresponding author:
Dr Peter Saxton, Department of Social and Community Health, University of Auckland, Private Bag 92109, Auckland.
p.saxton@auckland.ac.nz

URL:

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