

# BMJ Open NZPrEP Demonstration Project: protocol for an open-label, single-arm trial of HIV pre-exposure prophylaxis (PrEP) to determine feasibility, acceptability, adverse and behavioural effects of PrEP provision to gay and bisexual men in publicly funded sexual health clinics in Auckland, New Zealand

Sunita Azariah,<sup>1</sup> Peter Saxton,<sup>2</sup> Richard Franklin,<sup>3</sup> Rose Forster,<sup>1</sup> Suzanne Werder,<sup>1</sup> Renee Jenkins<sup>1</sup>

**To cite:** Azariah S, Saxton P, Franklin R, *et al.* NZPrEP Demonstration Project: protocol for an open-label, single-arm trial of HIV pre-exposure prophylaxis (PrEP) to determine feasibility, acceptability, adverse and behavioural effects of PrEP provision to gay and bisexual men in publicly funded sexual health clinics in Auckland, New Zealand. *BMJ Open* 2019;**9**:e026363. doi:10.1136/bmjopen-2018-026363

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2018-026363>).

Received 2 September 2018

Revised 2 May 2019

Accepted 2 May 2019



© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Sunita Azariah;  
SunitaA@adhb.govt.nz

## ABSTRACT

**Introduction** New Zealand has experienced a rise in HIV diagnoses in recent years and new interventions are required to address this.

**Methods and analysis** NZPrEP (A demonstration project of HIV preexposure prophylaxis in Aotearoa New Zealand) is an open-label, single-arm treatment evaluation study to investigate feasibility, retention, adherence, and clinical and behavioural outcomes of HIV pre-exposure prophylaxis (PrEP) provision to gay and bisexual men (GBM) in a publicly funded secondary sexual health service in Auckland, New Zealand. The sample size is 150 GBM. Inclusion criteria were specific behavioural risk factors indicating an increased risk of HIV infection. Exclusion criteria were hepatitis B infection, any medical contraindications to prescribing tenofovir/emtricitabine or factors limiting ability to adhere to the study protocol. Eligible participants will be screened for HIV and other sexually transmissible infections (STIs) and for any medical contraindications to PrEP, and enrolled for a maximum follow-up period of 96 weeks. They will be required to attend for 3-monthly testing for HIV and STIs and monitoring for renal and liver toxicity. Participants will also be required to complete an online behavioural survey after each study visit. The outcomes of interest are feasibility of PrEP provision in a sexual health clinic setting, PrEP acceptability, and adverse medical and behavioural effects of PrEP. The study sample is limited to 150 participants due to funding and service constraints. Statistical analysis of all primary and secondary outcomes will be performed using Stata V.14 at the University of Auckland. Results for primary and secondary endpoints will be reported after the conclusion of the study in March 2019.

**Ethics and dissemination** The study was approved by the Health and Disability Ethics Committee on 15 September 2016 (16/NTA/112). Key findings will be

## Strengths and limitations of this study

- The study is using a protocol similar to other pre-exposure prophylaxis (PrEP) demonstration projects, allowing for international comparisons.
- The ethnicity quotas of 50% non-European and 20% indigenous Maori participation will enable us to investigate inequity in sexual health service access and engagement as there is evidence that Maori and non-Europeans with HIV are often diagnosed later.
- PrEP is now funded by the New Zealand government for high-risk gay and bisexual men, meaning our study can inform real-world implementation.
- The small sample size and single-arm design could limit analysis of some objectives, although the study is mainly to determine feasibility and service requirements.
- Factors that could compromise regimen adherence were listed as part of the exclusion criteria, which could potentially result in bias when analysing outcomes for adherence and retention; however, no potential participants were excluded on these grounds.

submitted to peer-reviewed journals. A summary report will be circulated to the study and community stakeholders, and to the Auckland District Health Board, Ministry of Health and Pharmac.

**Trial registration number** ACTRN12616001387415; Pre-results.

## BACKGROUND

New Zealand has experienced a rise in HIV diagnoses in recent years. In 2016 the highest number of cases (243) was

reported since surveillance began in 1985, with gay and bisexual men (GBM) accounting for more than 80% of locally acquired HIV cases.<sup>1</sup> Previously New Zealand had a relatively successful record controlling HIV, and rates in the late 1990s were low in comparison with most countries including the USA, UK and Australia. During this epidemic nadir fewer than 60 cases in total were reported per year, including just 21 annually among GBM where HIV had been contracted in New Zealand.<sup>2</sup> Then in the early 2000s the number of new HIV diagnoses increased and has fluctuated ever since, with 217 cases reported in 2014 and 225 reported in 2015; over 80% of diagnoses annually were GBM who had contracted HIV locally. The most recent increase in 2016 was at odds with jurisdictions like London, UK and New South Wales, Australia, which have recently experienced a drop in HIV incidence after implementing a number of interventions, including more frequent testing, early antiretroviral treatment and HIV pre-exposure prophylaxis (PrEP).<sup>3,4</sup> Similar approaches are urgently needed in the New Zealand context.<sup>5</sup>

PrEP entails taking a daily dose of tenofovir/emtricitabine in a fixed-dose formulation (Truvada), which was shown in an initial randomised controlled trial (RCT) to be safe and effective at reducing acquisition of HIV in GBM with high-risk sexual behaviour.<sup>6</sup> Subsequently two further RCTs, the PROUD (Pre-exposure option for reducing HIV in the UK: immediate or deferred) study (daily dosing)<sup>7</sup> and IPERGAY (on-demand pre-exposure prophylaxis in men at high risk for HIV-1 infection) study (event-based dosing),<sup>8</sup> both found an 86% relative risk reduction in HIV acquisition in GBM on PrEP compared with those on placebo, although the two studies differed in design. Clinical trials in heterosexuals, including one trial that recruited men and women in heterosexual HIV-discordant relationships<sup>9</sup> and another that recruited heterosexual men and women who were prescribed a fixed-dose combination of tenofovir disoproxil fumarate (TDF) and emtricitabine,<sup>10</sup> also demonstrated a substantial reduction in rates of HIV acquisition. The WHO has recommended demonstration projects in diverse settings to understand potential barriers to PrEP delivery and inform local implementation efforts. In February 2017 Truvada was approved by the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) for use as HIV PrEP, and on 1 March 2018 PrEP became fully funded by the New Zealand government for individuals fulfilling specific behavioural criteria.<sup>11</sup>

Our research team conceived a PrEP demonstration project for GBM in late 2015 ('NZPrEP') in anticipation of future public funding. The five primary aims are to assess (1) the feasibility of PrEP provision in a New Zealand sexual health clinic (SHC) setting; (2) PrEP acceptability to high-risk GBM (study retention); (3) PrEP acceptability to high-risk GBM (medication adherence); (4) clinical outcomes of PrEP use; and (5) behavioural effects of PrEP use.

## METHODS/DESIGN

NZPrEP (a demonstration project of HIV pre-exposure prophylaxis in Aotearoa New Zealand) is an open-label, single-arm treatment evaluation study with a protocol based on the New South Wales demonstration project PRELUDE, (Implementation of HIV pre-exposure prophylaxis with antiretroviral medications among people at high risk of HIV infection : A demonstration project) .<sup>12</sup> The target population is 150 GBM at high risk of HIV acquisition eligible for publicly funded healthcare and residing in the greater Auckland region.

### Study partners and role

The study is being conducted as a collaboration between the Auckland Regional Sexual Health Service (ARSHS), two community non-governmental organisations (NGOs) (New Zealand AIDS Foundation (NZAF) and Body Positive (BP)) and the Gay Men's Sexual Health (GMSH) research group at the University of Auckland School of Population Health. The ARSHS led the study design and conducts the clinical arm, including participant enrolment, testing, clinical management and database linkage. The NZAF and BP are leading the study promotion, communications and website development, and provide database expertise and cultural advice regarding GBM (and more specifically Maori GBM or takataapui), and a peer educator. The GMSH research group will lead the behavioural surveys data collection and analysis. Representatives from each study partner meet regularly to conceive, plan and conduct the study. In addition, although they are not formal study partners, two community pharmacies have agreed to dispense the study medication.

### Sample size

As this was conceived as a demonstration project, overall sample size was determined by sexual health service volume constraints and available funding rather than power calculations. A sample size of 150 participants was considered to be feasible within these parameters.

### Eligibility

Inclusion criteria are GBM aged 18 or over considered to be at high-risk of HIV acquisition by a set of behavioural criteria similar to those defined in the PRELUDE protocol.<sup>10</sup> Participants are required to have a negative HIV antibody test within 2 weeks of commencing PrEP. As the sample size is so limited, the PRELUDE behavioural criteria were amended so that participants have to have a minimum number of sexual contacts in the preceding 6 months, in order to include those who are most likely to benefit (box 1). Participants also have to be able to provide informed written consent for participation, be willing and able to take part in all required study procedures, be willing to provide contact details during the study period, and have reasonable proficiency in written and spoken English.

### Box 1 NZPrEP : A demonstration project of HIV preexposure prophylaxis in Aotearoa New Zealand behavioural inclusion criteria

- ▶ Person is a gay or bisexual man who has sex with other men.
  - ▶ AND is likely to have multiple events of condomless anal intercourse (CAS) in the next 3 months (sustained risk) AND has had sex with at least five casual male partners in the preceding 3 months or at least 10 casual male partners in the preceding 6 months.
- AND any of the following:
- ▶ A regular sexual partner of an HIV-infected man who is not on antiretroviral therapy or has detectable viral load with whom condomless anal sex has occurred in the previous 3 months.
  - ▶ OR at least one episode of receptive CAS with any casual male partner with HIV infection who is not on antiretroviral therapy or with a male partner of unknown HIV test status in the previous 3 months.
  - ▶ OR a diagnosis of syphilis, rectal gonorrhoea or rectal chlamydia during the previous 3 months.
  - ▶ OR a history of methamphetamine use in the previous 3 months.

Exclusion criteria are being HIV-1-infected, having an estimated glomerular filtration rate of <60 mL/min, any contraindication to taking TDF and/or emtricitabine, infection with hepatitis B virus, any mental health issues, memory loss, cognitive impairment or other intellectual disability that could compromise participant safety or regimen adherence, any conditions which could compromise a participant's retention in the study, or being unwilling to adhere to any of the required procedures. Participants with hepatitis B infection will be excluded as liver transaminases are being monitored as part of the assessment for clinical safety outcomes.

#### Equity quotas

As several PrEP demonstration projects internationally have shown poorer study retention and adherence outcomes for GBM of non-white ethnicity,<sup>4 13</sup> the protocol has been designed to recruit 50% participants of non-European ethnicity, including 20% participants of indigenous Maori ethnicity. This will allow us to try and identify if there are suboptimal outcomes for ethnic minorities (see Power calculations and data analysis section). Ethnicity will be self-determined by participants when they enrol in the study. Participants will self-report their ethnicity in their initial online baseline behavioural survey, which allows multiple responses (see Behavioural surveys section).

#### Enrolment and recruitment

Enrolment will take place at all four publicly funded ARSHS clinics and will be conducted by clinical staff. Participants will be recruited from patients attending SHCs, an online study waiting list coordinated by the NZAF, a dedicated study website, targeted promotion on social media and dating apps, community partner organisation (NZAF and BP) networks and media releases, and/or self-referral.

#### Study visits

These are summarised in [table 1](#). Prior to enrolment (visit 0), patients who wish to participate and who fit the inclusion criteria will undergo testing for HIV, chlamydia, gonorrhoea, syphilis, hepatitis A, B and C, and baseline renal and liver function tests. Each potential participant will be given a participant information sheet (PIS) explaining the study and a follow-up appointment arranged (visit 1) with the research nurse. Visit 1 is to discuss and review results from the initial visit, treat any diagnosed sexually transmissible infection (STI) and obtain informed written consent to participate in the study. Free hepatitis A and B vaccination will be offered if not immune and human papilloma virus (HPV) vaccination offered if eligible (those aged 26 and under). Participants will also have a risk reduction counselling session with a peer educator from BP. Participants will then be given a prescription for Truvada, which is to be dispensed at one of two participating community pharmacies. Study medication will be supplied by Gilead Sciences (Foster City, USA). Follow-up study visit participants will be scheduled 12-weekly ([table 1](#)) for testing, repeat prescriptions, assessment of risk as well as adverse events, laboratory testing, and self-report of medication adherence.

#### Clinical safety and medication adherence

We will assess clinical safety by monitoring adverse events during the study period. Serious adverse events are those considered life-threatening, including anaphylaxis or severe renal injury. Data regarding frequency of less serious adverse events will be collected, including abnormal liver transaminases, reduction in creatinine clearance, gastrointestinal intolerance and potential drug–drug interactions.

Adherence will be assessed by participant self-report at follow-up visits, pharmacy dispensing records and responses to behavioural online surveys. Pharmacy dispensing information is automatically entered into each participant's electronic medical record at point of dispensation as per standard pharmacy practice. At each 3-monthly follow-up visit, participants will be asked to estimate the number of pills taken in the preceding 4 weeks, categorised as 7 pills per week, 4–6 pills per week, 1–3 pills per week or none. The 3-monthly behavioural survey asks specific questions on adherence. Data on average study retention time and clinician adherence to protocols will be extracted from the research database.

#### Behavioural surveys

Participants will be required to self-complete an anonymous behavioural survey online using SurveyMonkey at baseline enrolment and within 3 days of each 3-monthly follow-up study visit. The survey was adapted from the Australian VicPrEP study (The Victorian preexposure prophylaxis demonstration project-VicPrEP HIV prevention trial for people at risk of HIV)<sup>14</sup> by the University of Auckland GMSH research team that has experience conducting HIV behavioural research. Reminders to

**Table 1** NZPrEP: A demonstration study of HIV pre-exposure prophylaxis in Aotearoa New Zealand study procedures

Procedures		Visit 0	Visit 1 Week 1	Visit 2 Week 4	Visit 3 Week 12	Visit 4 Week 24	Visit 5 Week 36	Visits 6–10 until study completion Week 96	Exit
Consent form		X*	X†						
Assessment of eligibility criteria		X	X						
Review of medical history‡		X	X						
Sexual history§		X	X	X	X	X	X	X	X
Review of concomitant medications		X	X	X	X	X	X	X	X
Review of adherence				X	X	X	X	X	X
Behavioural survey		X			X	X	X	X	X
Truvada prescription			X¶	X**	X††	X††	X††	X††	
Physical examination	Symptom-directed	X		X	X	X	X	X	X
	Observations (BP, BMI)		X						
Assessment of adverse events				X	X	X	X	X	X
Clinical laboratory	HIV test	X‡‡		X§§	X§§	X§§	X§§	X§§	X§§
	Creatinine, eGFR	X			X	X	X	X	X
	Liver Function Tests	X			X	X	X	X	X
	Urine P/Cr ratio	X					X		X
	Urinalysis¶¶	X		X	X	X	X	X	X
Concomitant STIs	Syphilis serology	X		X	X	X	X	X	X
	Multisite g***	X		X	X	X	X	X	X
Hepatitis screening	HAV and HBV serologies†††	X							
	Hepatitis C Virus Antibody	X					X		X

Criteria for premature discontinuation: (1) positive HIV test result (see below), (2) renal toxicity, (3) non-adherence to medication or appointments, (4) using the medication for other purposes than intended (eg, giving it to others, using it on demand and so on), (5) reduction of risk behaviours to such extent that PrEP is no longer indicated, and (6) patient's request.

\*Give and discuss consent form and other patient information material.

†Discuss and sign consent form.

‡Take full family and personal medical history and vaccinations (HAV, HBV, HPV).

§Partners (number, gender, casual/regular, HIV status), practices (oral/anal intercourse, sex toys, 'chem sex' and so on), condom use and history of STIs (what, when, treatments and so on).

¶Prescribe 30 tablets.

\*\*Prescribe 60 tablets.

††Prescribe 90 tablets.

‡‡HIV enzyme immunoassay (EIA) fourth-generation (Antigen/Antibody combination) must be negative at baseline visit (day 0), and the prescriber must document that history and clinical examination do not raise the suspicion of recently acquired HIV infection still in the window period. DO NOT PRESCRIBE Truvada if criteria are not met; patients will be eligible for PrEP if a repeat HIV test 4 weeks later (with no additional risk in the mean time) is still negative.

§§A positive HIV test at any visit after baseline (day 0) is a criteria for premature discontinuation. If signs/symptoms of acute retroviral infection at any visit after baseline, send for HIV RNA together with HIV EIA combo Ag/Ab. Terminate the study, obtain confirmatory test (western blot, HIV RNA including genotype for drug resistance) and discuss options with the patient regarding ongoing care.

¶¶For proteinuria.

\*\*\*Urinary, pharyngeal and rectal chlamydia and gonorrhoea testing by strand displacement amplification (BD Viper™).

†††Hepatitis A virus and hepatitis B virus; Vaccinate if not immune as per standard protocol.

BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; PrEP, pre-exposure prophylaxis; STI, sexually transmissible infection.

#### References

- Guidance for the Use of Pre-Exposure Prophylaxis (PrEP) to Prevent HIV Infection, New York State Department of Health AIDS Institute (NYSDOH AI), [www.hivguidelines.org](http://www.hivguidelines.org) (accessed 21/08/2015).
- Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline, CDC/DHHS/US Public Health Service, [www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf](http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf) (accessed 21/08/2015).
- Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Providers' Supplement, CDC/DHHS/US Public Health Service.

complete the surveys will be issued by email and text message by the SHC research nurse. The survey data will be held securely at the University of Auckland, separate from clinic records. Data linkage is via a unique study number. The baseline behavioural survey collects data on participant sociodemographics (6 items), PrEP awareness (6 items), reasons for accepting PrEP (5 items), HIV and STI screening history (8 items), sexual behaviour (11 items), substance use (4 items), previous PrEP and post-exposure prophylaxis (4 items), beliefs and attitudes about STIs (5 items), HIV (3 items), anti-retroviral therapy (ART) (8 items), PrEP (28 items), condoms (8 items) and experiences of the clinic visit (9 items). Enrolled participants will not be offered financial incentives to complete the survey. Follow-up surveys are shorter and will focus on PrEP adherence (17 items), communication (5 items), sexual behaviour (15 items), STIs (3 items), alcohol and drug use (4 items), future intentions (4 items) and study experiences (12 items). Participants who choose to exit the study early will be asked to complete a brief early exit survey that assesses reasons for exiting (6 items), alternative PrEP sources (1 item), future intentions (3 items) and study experiences (3 items).

### Primary endpoints

There are five primary endpoints related to the primary aims. Feasibility of PrEP implementation among high-risk GBM at a sexual health service in Auckland, New Zealand will be assessed by time to full enrolment of 150 eligible GBM. PrEP acceptability to high-risk GBM (study retention) will be assessed by the proportion completing all study visits at 12 months. The rationale for this endpoint is that a participant's willingness to physically attend regular clinic appointments provides an indication of PrEP's acceptability to this population as a prevention method. Medication adherence will be assessed by the number and proportion of PrEP pills taken and missed. The rationale for this endpoint is that a participant's willingness to take a daily pill also provides a measure of this HIV prevention method's acceptability. Clinical outcomes related to PrEP use will be measured by an aggregate measure of HIV seroconversion and adverse events. Behavioural effects of PrEP will be measured by the change in the proportion of participants reporting 10 or more condomless receptive anal intercourse partners in the previous 3 months from baseline to 12-month follow-up.

### Secondary endpoints

In addition, we propose the following secondary endpoints. These are grouped under the relevant five primary endpoints (box 2): (1) feasibility: clinician and participant adherence to study protocol; (2) acceptability (study retention): study retention at 6 and 12 months; proportion of participants reporting that PrEP is acceptable; attitudes towards PrEP; (3) acceptability (medication adherence): number and proportion of PrEP pills taken and missed (clinician-recorded); time to PrEP discontinuation; (4) clinical outcomes related

## Box 2 Primary (italics) and secondary endpoints of NZPrEP: A demonstration project of HIV preexposure prophylaxis in Aotearoa New Zealand related to study aims

### Feasibility of delivering PrEP to 150 high-risk GBM in publicly funded SHC in Auckland:

- ▶ *Time to full enrolment.*
  - Clinician adherence to study protocol.
  - Participant adherence to study protocol.

### Acceptability of PrEP to high-risk GBM (study retention).

- ▶ *Proportion completing all study visits at 12 months.*
  - Study retention at 6 months and 12 months.
  - Proportion reporting that PrEP is acceptable to them.
  - Attitudes towards PrEP.

### Acceptability of PrEP to high-risk GBM (medication adherence).

- ▶ *Number and proportion of PrEP pills taken.*
  - Behavioural survey responses.
  - Clinician-recorded responses.
  - Time to PrEP discontinuation.

### Clinical outcomes related to PrEP use.

- ▶ *Aggregate measure of HIV seroconversion and adverse events.*
  - HIV seroconversion.
  - Serious adverse events.
  - Other adverse events.

### Behavioural effects of PrEP use.

- ▶ *Proportion reporting 10+ condomless receptive anal intercourse partners in the last 3 months.*
  - Number of male sexual partners in the last 3 months.
  - Incident rectal gonorrhoea or chlamydia.
  - Incident STIs (aggregate).
  - Illicit drug use in the last 3 months.

GBM, gay and bisexual men; PrEP, pre-exposure prophylaxis; SHC, sexual health clinic; STI, sexually transmissible infection.

to PrEP use: HIV seroconversion; adverse events; and (5) behavioural effects of PrEP use: number of male sexual partners in the previous 3 months; incident rectal gonorrhoea or chlamydia; any incident STI; and illicit drug use in the previous 3 months, including methamphetamine use and injecting drugs.

### Adverse events

All serious adverse events will be reported to the NZPrEP steering group, and any deemed to be related to the study drug by the lead investigator will be reported to Gilead Sciences and to the Auckland District Health Board safety management system (Datix). Participants will be advised to report any adverse effects or untoward medical occurrences at each quarterly visit, or if they present to the clinic between study visits. All participants who have an adverse event will be followed clinically until it is resolved or stabilised. Participants who acquire HIV during the study will be managed according to the Australasian Society for HIV Medicine guidelines.<sup>15</sup>

### Power calculations and data analysis

The unique study identification number allocated to each participant will link clinical and behavioural outcomes across separate databases and will enable each participant to be followed longitudinally through the study. We made the following power calculations based on the study recruitment quotas and selected study aims and endpoints:

- ▶ Power calculation 1: We have 85% power to detect if retention of non-Europeans at 48 weeks is 60% or lower vs 80% in Europeans if non-Europeans comprise half (n=75) the entry sample.
- ▶ Power calculation 2: We have 72% power to detect if retention of indigenous Maori at 48 weeks is 60% or lower vs 80% in non-Maori if Maori comprise 20% of the entry sample (n=30).
- ▶ Power calculation 3: We have 81% power to detect a change in high-risk behaviour (10 or more receptive condomless anal intercourse partners in the prior 3 months) from 10% at baseline to 21% at 48 weeks if 120 participants (80%) are retained.

We will conduct statistical analysis of key study endpoints over 12 months' follow-up, including PrEP acceptability and clinical and behavioural outcomes. We propose to undertake this using logistic regression and using binomial or normal distributions to model outcomes in dichotomous or count or ordinal data, respectively. We will use ethnicity, age and time as covariates where appropriate. Findings for key endpoints will be presented as ORs or as ORs adjusted for potential confounders. STI incidence will be presented per 100 person years, and incidence rate ratios will be used to compare outcomes over time. An alpha of  $p=0.05$  will be set for all analyses. Where appropriate and where the sample size permits, we will examine whether primary and secondary endpoints are associated with key variables including sociodemographic (eg, age, ethnicity), behavioural (eg, sexual behaviour, drug use), attitudinal (eg, attitudes towards PrEP, condoms, HIV, STIs) and study experience (eg, PrEP initiation status, study participation feedback) items.

Statistical analysis of all primary and secondary outcomes will be performed using Stata V.14 at the University of Auckland. The NZPrEP study will commence enrolment in February 2017 and will be completed in February 2019.

### Dissemination and knowledge translation

Key findings describing the sample at baseline and the primary and secondary endpoints will be prepared for submission to peer-reviewed journals. The research team will prepare a summary report and circulate this to the study stakeholders, and to the Auckland District Health Board, Ministry of Health and Pharmac. The research team will also prepare recommendations based on the study findings to inform future PrEP implementation. Key findings and recommendations will be disseminated to study participants and will be proffered to HIV and community stakeholder meetings in New Zealand and internationally. Beyond these planned research outputs,

study data will be available for further analysis on application to and with the approval of the principal investigator.

The study has been registered with the Australian New Zealand Clinical Trials Registry.

### Patient and public involvement

Patients were not involved in the design and conduct of the study. Two community NGOs were involved in the set-up and design of the study (NZAF and BP), and they led the community engagement and communications with the Auckland GBM community and specifically with indigenous Maori GBM or takataapui. This consultation informed the dissemination of information, the PIS and the questions included in the behavioural survey. A peer educator from BP will carry out the risk reduction counselling for study participants at enrolment. The Health and Disability Ethics Committee, which reviewed the study, included consumer and community representatives.

### DISCUSSION

Although studies have shown that PrEP is efficacious, several countries have PrEP demonstration projects under way to better understand implementation barriers in local settings as per WHO recommendations. NZPrEP will inform the feasibility, acceptability and optimal adherence to PrEP in the Auckland, New Zealand context, which has a concentrated low-level HIV epidemic, with a small but highly ethnically diverse population and where HIV incidence appears to be rising. This distinguishes our study from some other larger demonstration projects of GBM communities with higher HIV prevalence, and therefore it may offer more relevant insights for settings that are similar. Furthermore, we believe our study is unique in having equity quotas for ethnic minorities, including for indigenous Maori GBM, which will enable us to try and identify any suboptimal outcomes for such GBM should they be experienced. Finally, New Zealand has recently become one of the first countries to publicly fund PrEP, and the findings from our study on PrEP feasibility, acceptability, adherence and behavioural impacts among GBM accessing the medication through SHCs can inform the development of PrEP prescribing guidelines in this country.<sup>16</sup>

This project was developed as a collaboration between Auckland District Health Board sexual health clinicians, NGOs and the University of Auckland in the absence of governmental advocacy, policy or funding. It is encouraging that since the study commenced the New Zealand government has funded fully subsidised PrEP access to high-risk individuals (see below). The next requirement is a rapid scale-up of delivery to those most in need in order to maximise the returns on this public health investment, including adequate funding and support of clinical services providing PrEP.

Strengths of the study include its setting in an SHC which is ideally suited to PrEP provision, the similar protocol to the PRELUDE study allowing for international

comparison with other demonstration projects, and the ethnicity quotas that oversample GBM who are non-Europeans and Maori in the New Zealand context. Although such groups are not over-represented in HIV diagnoses,<sup>14</sup> there is evidence that Maori and non-Europeans with HIV are diagnosed later,<sup>17 18</sup> suggesting inequity in sexual health service access and engagement, with obvious implications for PrEP programmes. PrEP demonstration projects in other countries have identified worse outcomes among non-white GBM, and our equity quotas and power calculations were based on these observations.<sup>4 13</sup>

Our study is limited by its small sample size and single-arm design. A potential limitation was the requirement for participants to be able to adhere to all study procedures; however, no potential participants were excluded on the grounds of inability to adhere to the study protocol. Our study was powered to investigate differences in retention for European versus non-European participants, and for Maori versus non-Maori participants; we may lack power to identify other important disparities. As this is a feasibility study, it should provide useful data regarding service requirements (eg, staff resource required, training, clinical protocols, laboratory budgets), the impact of PrEP on sexual behaviour for users, and sociodemographic factors that may impact on PrEP adherence and STI incidence. If successful, it may also itself have an impact on the wider community in Auckland, New Zealand by reducing incident HIV in a high-risk subset of GBM and preventing secondary transmission.

Recent data indicate that STI prevalence and incidence are higher among HIV-negative GBM taking PrEP than those not taking PrEP,<sup>19</sup> so it is important that clinical services are adequately resourced.<sup>20</sup> After this study commenced, the New Zealand drug-buying agency Pharmac approved funding for PrEP in GBM and transgender people at high risk of HIV acquisition,<sup>16</sup> with eligibility criteria very similar to our demonstration project. This is a promising step in the goal to end HIV in New Zealand and will augment other measures including increased testing of those at risk, earlier treatment for those diagnosed and health promotion activities endorsing consistent condom use.<sup>5</sup> Further research should include qualitative work to better understand barriers to PrEP use, quantitative research to investigate the speed and equity of PrEP uptake, and behavioural surveillance to monitor changes in risk and protective practices among all GBM in a context of PrEP availability. Finally, the cost of Truvada in New Zealand has been recently reduced (\$2280 (in New Zealand dollars) per annum per patient), improving the cost-effectiveness of this intervention. Previous studies have found PrEP to be cost-effective if targeted to individuals at high risk of HIV.<sup>21</sup> The availability of cheaper generic drugs in the near future should further reduce the price and potentially enable eligibility criteria to be widened.

#### Author affiliations

<sup>1</sup>Auckland Regional Sexual Health Service, Auckland District Health Board, Auckland, New Zealand

<sup>2</sup>School of Population Health, University of Auckland, Auckland, New Zealand

<sup>3</sup>Self-Employed, Sydney, New South Wales, Australia

**Acknowledgements** The authors would like to thank the men who are participating in the study and the staff at Auckland Sexual Health Service for administering study procedures. The authors would also like to thank Eric Ho and Tony Sie, community pharmacists, for their valuable support. The authors would especially like to thank Dr Dean Murphy, Professor Martin Holt and Associate Professor Iryna Zablotska at the University of NSW, Sydney, Australia for their advice and support.

**Contributors** SA did the ethics application for the study. SA, RfR, RfO, SW and PS designed the protocol for the study. PS designed the behavioural survey and is responsible for data analysis for the survey. RAF secured funding for the study from Gilead Sciences. SW provides liaison with the community pharmacies and Gilead for medication supplies. RJ (research nurse) will enrol participants, manage follow-up and communication with participants, and will manage the clinical database. SA and PS wrote the initial draft for the paper, and all authors critically reviewed and approved the final draft submitted for publication.

**Funding** This work is supported by Gilead Sciences, which will provide the study medication and funding for a research nurse and some of the study-associated laboratory costs. The Auckland District Health Board is funding the clinician time, clinic visits and the laboratory costs associated with the STI testing and serology for HIV, syphilis and hepatitis. NZAF and BP are providing support through dedicated staff time and resources. Funding for the online behavioural survey is being provided independently by a grant from the New Zealand AIDS Foundation and by Pharmac. None of the funding bodies will be involved in data analysis or dissemination of the study results.

**Competing interests** None declared.

**Patient consent for publication** Not required.

**Ethics approval** The study has received ethics approval from the Health and Disability Ethics Committee (HDEC) 16/NTA/112 on 15 September 2016.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### REFERENCES

1. AIDS Epidemiology Group. AIDS – New Zealand. *Issue* 2017;76.
2. Dickson N, Lee B, Foster T, et al. The first 30 years of HIV in New Zealand: Review of the epidemiology. *N Z Med J* 2015;128:31–47.
3. Brown AE, Mohammed H, Ogaz D, et al. Fall in new HIV diagnoses among men who have sex with men (MSM) at selected London sexual health clinics since early 2015: testing or treatment or pre-exposure prophylaxis (PrEP)? *Euro Surveill* 2017;22:30553.
4. NSW HIV STRATEGY 2016–2020: DATA REPORT. <http://www.health.nsw.gov.au/endinghiv/Publications/q4-2017-and-annual-hiv-data-report.pdf>
5. Consensus statement on comprehensive HIV prevention in Aotearoa/ New Zealand. <https://hivconsensus.org.nz/>
6. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010;363:2587–99.
7. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet* 2016;387:53–60.
8. Molina JM, Capitant C, Spire B, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. *N Engl J Med* 2015;373:2237–46.
9. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med* 2012;367:399–410.
10. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med* 2012;367:423–34.



11. PHARMAC. *Decision to fund HIV pre-exposure prophylaxis (PrEP)*. Wellington, New Zealand: PHARMAC, 2018.
12. Vaccher S, Grulich A, McAllister J, *et al*. Protocol for an open-label, single-arm trial of HIV pre-exposure prophylaxis (PrEP) among people at high risk of HIV infection: the NSW Demonstration Project PRELUDE. *BMJ Open* 2016;6:e012179.
13. Liu AY, Cohen SE, Vittinghoff E, *et al*. Preexposure Prophylaxis for HIV Infection Integrated With Municipal- and Community-Based Sexual Health Services. *JAMA Intern Med* 2016;176:75–84.
14. Lal L, Audsley J, Murphy DA, *et al*. Medication adherence, condom use and sexually transmitted infections in Australian preexposure prophylaxis users. *AIDS* 2017;31:1709–14.
15. ASHM. HIV Management in Australasia. ASHM. 2016. verified 10 Jan 2019 <http://hivmanagement.ashm.org.au/>.
16. Saxton P, Giola M, Coughlan E, *et al*. Implementing HIV pre-exposure prophylaxis (PrEP): let's not get caught with our pants down. *N Z Med J* 2018;131:64–73.
17. Dickson N, McAllister S, Sharples K, *et al*. Late presentation of HIV infection among adults in New Zealand: 2005–2010. *HIV Med* 2012;13:182–9.
18. Saxton PJ, Dickson NP, Griffiths R, *et al*. Actual and undiagnosed HIV prevalence in a community sample of men who have sex with men in Auckland, New Zealand. *BMC Public Health* 2012;12:92.
19. Kojima N, Davey DJ, Klausner JD. Pre-exposure prophylaxis for HIV infection and new sexually transmitted infections among men who have sex with men. *AIDS* 2016;30:2251–2.
20. Traeger MW, Schroeder SE, Wright EJ, *et al*. Effects of Pre-exposure Prophylaxis for the Prevention of Human Immunodeficiency Virus Infection on Sexual Risk Behavior in Men Who Have Sex With Men: A Systematic Review and Meta-analysis. *Clin Infect Dis* 2018;67:676–86.
21. Cambiano V, Miners A, Dunn D, *et al*. Cost-effectiveness of pre-exposure prophylaxis for HIV prevention in men who have sex with men in the UK: a modelling study and health economic evaluation. *Lancet Infect Dis* 2018;18:85–94.