

Pre-exposure prophylaxis: Utilisation analysis using MedicineInsight data

Drug utilisation sub-committee (DUSC)

October 2021

Abstract

Purpose

DUSC requested a review of the utilisation of medicines used for the treatment of Human Immunodeficiency Virus (HIV) and for pre-exposure prophylaxis (PrEP) of HIV at its June 2021 meeting. The analyses in this report are for PrEP and are based on general practice data from MedicineInsight.

Data Source / methodology

This study is a descriptive analysis of MedicineInsight data exploring the prescribing of PrEP for HIV in general practice. It uses de-identified patient data from the clinical information systems (CIS) of 488 participating general practices and 2.2 million adult patients in the general study population. The study covered the period between 1 April 2018 to 31 March 2021.

Key Findings

- Of the 2.2 million eligible patients in the MedicineInsight program, 4,055 (0.2%) patients were prescribed PrEP at least once between 1 April 2018 and 31 March 2021.
- 221 patients had a prescription for PrEP recorded in the first month of listing (April 2018), and by 31 March 2021, 4,055 patients had at least one prescription for PrEP recorded. An average of 110 patients per month were prescribed PrEP for the first time.
- Of the 4,055 patients prescribed PrEP at least once during the study period, the majority were male (98.2%), aged 18 to 39 years (63.4%), and resided in Victoria (47.8%) or New South Wales (39.3%), in major cities (88.4%) and in the two most socioeconomically advantaged areas (77.4%).
- Sociodemographic characteristics were similar for patients prescribed PrEP during the first 18 months since PBS listing and during the last 18 months of the study period. There was a slight increase in the proportion of younger patients (18–29), those with a concession/healthcare card and Aboriginal and Torres Strait Islander patients in the second 18 months compared with the first 18 months, however these differences were not statistically significant.
- The majority of high PrEP caseload practices (in the top 5% according to number of patients prescribed PrEP) were in major cities (95.5%) or located in NSW or Victoria

(77.3%), In contrast, approximately half of low PrEP caseload practices were in major cities (57.8%) or in NSW or Victoria (50.5%).

- High PrEP caseload practices had higher numbers of people living with HIV.
- Patients prescribed PrEP at low PrEP caseload practices were younger, more likely to live in regional and more socioeconomically disadvantaged areas and more likely to have a concession/healthcare card than patients prescribed PrEP at high caseload practices.
- A total of 52,935 prescriptions (originals + repeats) for PrEP were recorded for 4055 patients. The mean average number of scripts was 9.7 per person-year. Assuming one prescription covers one month's supply, this equates to a medication possession ratio (MPR) of 80.8%.
- The mean duration of exposure to PrEP therapy was 541 days. Among 1,242 people identified as having a gap in therapy, the mean time to first discontinuation of PrEP was 307 days.
- Among patients who received more than one original prescription for PrEP, just over half had continuous use (52.0%) and just under half had non-continuous use (48.0%).
- Non-continuous PrEP use was associated with PrEP caseload of the patient's practice, anxiety and having a concession/healthcare card. The odds of non-continuous PrEP use was:
 - 40% lower among patients at low PrEP caseload practices (adjusted OR 0.6; 95% CI: 0.5–0.7, $p < 0.0001$) compared to high caseload practices;
 - 30% higher among patients with a recorded diagnosis of anxiety (adjusted OR 1.3; 95% CI: 1.1–1.5, $p = 0.0002$); and
 - 20% lower among patients with a concession/healthcare card (adjusted OR 0.8; 95% CI: 0.6–0.9, $p = 0.0034$) than not.
- At the end of the study (31 March 2021) 48.8% of patients were on active therapy, 19.8% had discontinued therapy and 31.4% were lost to follow-up. Some of this loss to follow-up may reflect patients moving to a new clinic.
- Stopping PrEP was associated with the PrEP caseload of the practice, sex, depression and anxiety. The odds of stopping PrEP was:
 - 2.4 times higher among patients at low PrEP caseload practices (adjusted OR 2.4; 95% CI: 1.7–3.4, $p < 0.0001$) compared to high caseload practices;
 - 3.4 times higher among females (adjusted OR 3.4; 95% CI: 1.5–7.8, $p = 0.012$) than males, although the confidence interval for sex is wide;
 - 50% higher among patients with a recorded diagnosis of depression (adjusted OR 1.5; 95% CI: 1.2–1.8, $p < 0.0001$); and
 - 30% higher among patients with a recorded diagnosis of anxiety (adjusted OR 1.3; 95% CI: 1.0–1.5, $p = 0.0158$).

Purpose of analysis

At its June meeting, PBAC/DUSC requested that the utilisation of medicines for the treatment of HIV, and for PrEP, be reviewed using both PBS dispensing data and MedicineInsight data.

DUSC sought to understand the utilisation of PrEP since its PBS listing. DUSC noted that PrEP guidelines have changed since its initial listing and considered that it was important to understand patterns of use (i.e. continuous versus non-continuous use). DUSC requested that PrEP use be reviewed using both PBS dispensing data and MedicineInsight data.

This paper reports on the MedicineInsight analysis. Unlike PBS data, it captures both PBS and private prescriptions for PrEP. It also describes sociodemographic and clinical characteristics of patients using PrEP.

Background

Clinical situation

PrEP first became available through the PBS on 1 April 2018 for the prevention of HIV infection in adults at medium to high risk of HIV infection as defined by Australasian Society of HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) guidelines.¹

The Therapeutic Goods Administration (TGA) approval is for one tablet per day of tenofovir disoproxil + emtricitabine in HIV-1 uninfected adults. However, on-demand PrEP usage has been investigated. On-demand PrEP^a is highly effective in men who have sex with men (MSM)² and has been recommended by the World Health Organization (WHO)³ and ASHM since 2020 as an option for MSM.¹ The TGA have also approved tenofovir alafenamide + emtricitabine in HIV-1 uninfected adults, however this product is not PBS listed for PrEP.

Questions remain about how people use PrEP in the real world outside the clinical trial setting and whether cost or routine care in general practice would impact utilisation, particularly discontinuation, non-adherence and non-continuous use. This reports aims to address some of these questions.

PrEP uptake since PBS listing

While most patients now access PrEP via the PBS, some patients continue to access PrEP via importation or private prescription. According to a study from the Kirby Institute, of the 37,707 individuals dispensed PBS-subsidised PrEP prescriptions in the first two years and three months after PBS listing, 37,127 (98.5%) were recorded as male. The number of people dispensed PrEP in each calendar quarter (ie. 'recently') increased from 6,433 in Q2 2018, to 21,912 in Q1 2020 and then decreased to 17,135 in Q2, presumably due to the

^a ASHM and the WHO recommend an on-demand dosing schedule of a loading dose of two tablets of tenofovir disoproxil 300 mg + emtricitabine 200 mg 2 to 24 hours before sex, followed by a third pill 24 hours after the first drug intake and a fourth pill 24 hours later (2+1+1).

impacts of COVID-19 restrictions on sexual practice and clinical visits (Figure 1).⁴ In Q1 2021 the number of individuals dispensed PrEP 2020 increased again to 21,984. PBS data is likely to underestimate PrEP coverage, as patterns of legal self-importation of PrEP were established before PBS listing, and the cost of self-importation is now less than the PBS-subsidised general patient co-payment.

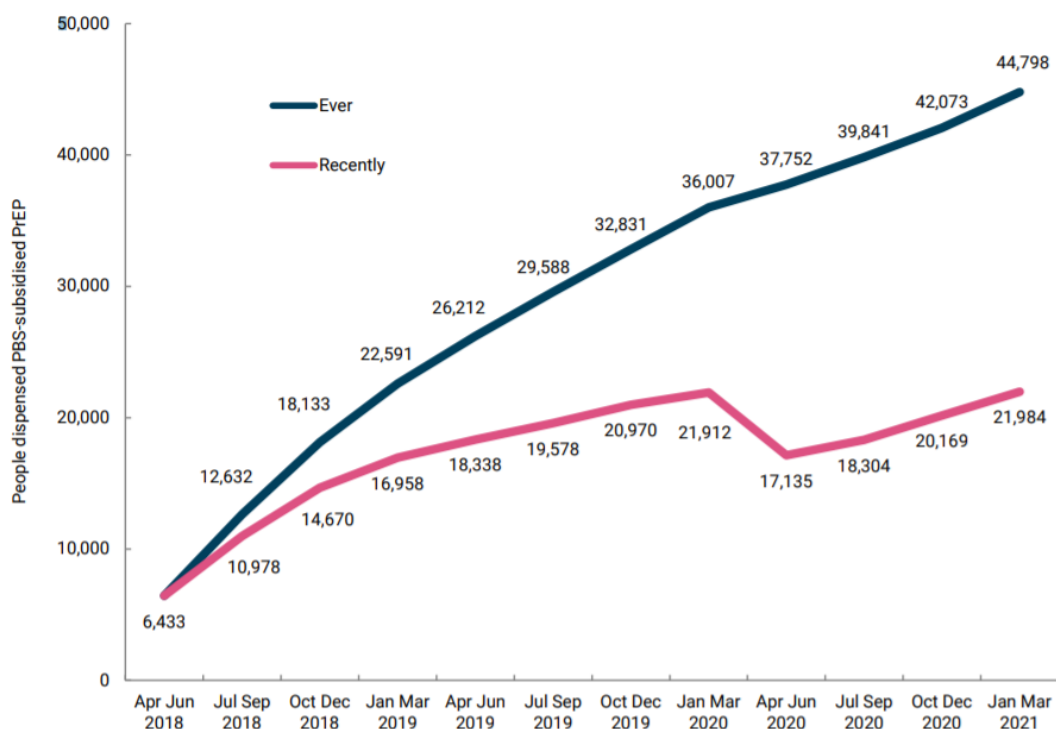


Figure 1. Cumulative (total) number of people with one or more dispensed PBS-subsidised PrEP prescription from 1 April 2018 compared to the estimated number who have used PBS-subsidised PrEP in each quarter (recently)⁴

Pharmacology

Tenofovir disoproxil and emtricitabine belong to the nucleoside and nucleotide reverse transcriptase inhibitors pharmacotherapeutic group (ATC code: J05AF30).

Both medicines work by inhibiting viral reverse transcriptase and viral DNA synthesis, preventing HIV replication.

Therapeutic Goods Administration (TGA) approved indications

Tenofovir disoproxil + emtricitabine is indicated in combination with safer sex practices for PrEP to reduce the risk of sexually acquired HIV-1 in adults at high risk. This indication is

based on clinical trials in men who have sex with men (MSM) at high risk for HIV-1 infection and in heterosexual couples where one partner is infected by HIV and the other is not (serodiscordant relationships).

Tenofovir alafenamide + emtricitabine is also indicated for PrEP to reduce the risk of sexually acquired HIV-1 in at-risk adults and adolescents weighing at least 35 kg, excluding individuals at risk from receptive vaginal sex. However, this product is not PBS listed for PrEP and was not included in this study.

Dosage and administration

The TGA approval is one tablet taken orally, once daily, of tenofovir disoproxil + emtricitabine in HIV-1 uninfected adults, preferably with food.

The current Product Informations (PI) and Consumer Medicine Informations (CMI) are available through [the TGA website product information access page](#) and [the TGA website consumer medicines information access page](#).

PBS listing details

Brands of tenofovir disoproxil + emtricitabine that were available on the PBS at any time between 1 April 2018 and 23 June 2021 are listed in Table 1. Irrespective of the salt form, each tablet contains the equivalent of 245mg of tenofovir disoproxil. These forms are bioequivalent for the purposes of substitution.

Note that the Truvada brand was removed from the PBS in April 2020. The other generic brands remain on the PBS.

Tenofovir disoproxil + emtricitabine tablets are also PBS listed for HIV treatment (in conjunction with additional antiretrovirals as part of a three-drug regimen).

Table 1. Tenofovir disoproxil + emtricitabine products available on the PBS at any time between 1 April 2018 and 23 June 2021

Medicine Active ingredients and strengths	Brand name	ATC	PBS Item
tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet	Truvada	J05AR03	11276L
tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet	Tenofovir/Emtricitabine APOTEX		11296M
tenofovir disoproxil maleate 300 mg + emtricitabine 200 mg tablet	Tenofovir Disoproxil Emtricitabine Mylan		11306C
tenofovir disoproxil phosphate 291 mg + emtricitabine 200 mg tablet	Tenofovir EMT GH		12542D

Date of listing on PBS and changes to listing

A summary of the listing dates and relevant changes to the listings of medicines for PrEP from 2018 onwards, can be found in Appendix A.

Current PBS listing details are available from www.pbs.gov.au

Methods

MedicineInsight

MedicineInsight is a large-scale primary care data set of longitudinal de-identified electronic health records (EHR) in Australia. MedicineInsight was initially established by NPS MedicineWise in 2011, with core funding from the Australian Government Department of Health, to collect general practice data to support quality improvement in Australian primary care and post-market surveillance of medicines. The monthly collation of collected data can be analysed for the purposes of improving patient care, quality improvement and evaluation, performing population health analysis, research and developing health policy.

MedicineInsight uses third-party data extraction tools which extract, de-identify, encrypt and securely transmit whole-of-practice data from the CIS of over 700 general practices. Patient level data are de-identified 'at source' meaning patients' personal identifiers such as name, date of birth and address are not extracted by the tool, although year of birth and postcode are extracted, enabling the calculation of age and Socio-Economic Indexes for Areas [SEIFA]. Each patient is assigned a unique number within the dataset which allows all the records (clinical, prescription, referral etc) held in the database to be linked to the associated patient identifying number. Further information is available online: <https://www.nps.org.au/medicine-insight>

This is a descriptive analysis of three years of de-identified patient data (1 April 2018 to 31 March 2021) extracted from 434 general practices sites, including 488 individual general practices which met the standard data quality criteria in the MedicineInsight June 2021 download.

Study ethics and approval

This project was given approval in July 2021 by the RACGP NREEC (NREEC 21-086).

The use of MedicineInsight data for the purposes of this report was approved by the independent Data Governance Committee (2021-012) in July 2021.

Practices and patients that had withdrawn their consent to participate in MedicineInsight were not included in the study.

Eligible practices

Analyses were conducted using de-identified patient data from 488 individual general practices which met the standard data quality criteria.^b

Eligible patients

The study time period included the three-year period starting from the PBS listing of PrEP, from 1 April 2018 to 31 March 2021. Historical records outside of this study period were consulted when exploring patient demographics, diagnoses and prior use of medicines.

Patients were eligible for inclusion in the general study population if they:

- had valid information for age (0–112) and sex (male, female, or indeterminate/intersex)
- were aged 18–74 years on 1 July 2018 (based on year of birth)
- had at least two clinical encounters^c on different days recorded between 1 April 2018 and 31 March 2021
- had a patient status of active, inactive, deceased or visitor (next of kin and emergency contacts were excluded).

The analyses on the changing utilisation of PrEP since PBS listing involved two subpopulations. The **PrEP T1 population** includes patients from the general study population who had a recorded prescription for PrEP during the first time period (T1: 1 April 2018 to 30 September 2019). The **PrEP T2 population** includes patients from the general study population who had a recorded prescription for PrEP during the second time period (T2: 1 October 2019 to 31 March 2021). Patients may be included in both time periods.

PrEP medicines

The PrEP medicines included in this study are listed in Table 2. In the MedicineInsight data PrEP medicines were identified from the 'Script item' table using the 'medicine active ingredient' and 'medicine name' fields. Since these medicines are also used for treating HIV, patients were excluded if they had a diagnosis of HIV recorded before, or 7 days after, the first PrEP prescription or if the term 'post-exposure prophylaxis (PEP)' was recorded during therapy with one of the PrEP medicines. Diagnoses of HIV were identified from the diagnosis, reason for encounter, reason for prescription and authority indication fields.

^b Eligible criteria were that the site had been established for at least 2 years as of May 2021; and had no significant interruptions (of longer than 2 months in the 2 years prior) to their practice data and met the minimum threshold of clinical activity (i.e., at least 50 patients in the last 2 years).

^c A clinical encounter, or any professional exchange between a patient and a healthcare professional (GP or nurse), was defined as all those encounters at the practice site that were: a) not identified as administrator entries nor encounters that have been transferred/imported from another practice and b) were not identified by pre-defined 'administration-type' terms found in the 'reason for encounter' field such as "administrative reasons", "forms", and "recall".

The count of prescriptions included issued prescriptions plus repeats. For example, an issued prescription with 2 repeats was counted as 3 prescriptions and was expected to last 3 months, assuming daily dosing.

Definitions

Socio-demographics in the analysis included age, sex, state or territory, SEIFA, remoteness and Aboriginal and Torres Strait Islander status (as reported in the CIS).

Mental health conditions and drug use disorders were assessed as potential factors that might impact adherence or compliance. Conditions assessed included anxiety, depression, bipolar disorder, schizophrenia, opioid use disorder and alcohol use disorder. Patients were defined as having a condition (Table 2) if they had a relevant coded (Docle, Pyefinch) or free text entry in one of the three diagnosis fields – diagnosis, reason for encounter or reason for prescription - recorded at any time from the patient's earliest record up to the end of the study period.

Table 2: Terms used to identify patients with conditions

Condition	Included terms
alcohol use disorder	(abuse or dependence or addiction) of alcohol, alcohol addiction, alcohol dependence, alcohol related brain injury, alcohol use disorder, alcoholic, alcohol withdrawal, alcoholism, antabuse type reaction, delirium tremens, Korsakoff's dementia
anxiety	anxiety, generalized anxiety disorder, mixed anxiety/depression, obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD)
bipolar disorder	bipolar affective disorder, bipolar 1 disorder, bipolar 2 disorder, bipolar spectrum disorder, manic depressive illness, manic depressive psychosis
depression	depression, post-natal depression, adjustment disorder with depression, mixed anxiety/depression
HIV	HIV, HIV carrier, AIDS, but excludes HIV embryopathy
schizophrenia or schizoaffective disorder	schizophrenia [catatonic, chronic, disorganised, hebephrenic, paranoid, undifferentiated], schizoaffective disorder, schizophreniform disorder, psychosis senile, senile dementia with psychosis, borderline schizophrenia, brief reactive schizophrenia, para schizophrenia.
opioid use disorder	abuse or dependence or addiction) of an opiate, drug addict, IDU, injecting drug user, intravenous drug use, IV drug use, long term opiate use

Patterns of PrEP use

Patterns of PrEP use were defined based on dosage instructions recorded by the prescriber (daily or on-demand regimen) and gaps between prescriptions (continuous or non-continuous use).

A patient's pattern of PrEP use was classified as 'continuous' if they never had more than a 21-day (or more than 63 days for an issued prescription with 2 repeats) gap between the

expected end of one prescription and the date of the next prescription for PrEP. Patients had a 'non-continuous' pattern if they had on-demand regimen recorded by the prescriber or had one or more gaps of > 21 days (or > 63 days for an issued prescription with 2 repeats) between the expected end of one prescription and the date of the next prescription for PrEP. The expected end of one prescription (no repeats) is 30 days after the date of the prescription. The 21-day gap was chosen as a conservative estimate of the number of days a patient could maintain a protective dose of four pills per week with a 30-day prescription.^{2,5}

PrEP status at the end of the study

PrEP status at the end of the study was assessed as active, discontinued, or lost to follow-up as defined below:

- active: Patient had a 'current prescription for PrEP' at 31 March 2021
- discontinued: Patient did not have a prescription for PrEP at 31 March 2021 and their last visit at the practice was after the expected end of the last prescription for PrEP
- lost to follow-up: Patient did not have a prescription for PrEP at 31 March 2021 and no visit recorded after the last prescription for PrEP.

A patient was considered to have 'a current prescription for PrEP' from the date of their first prescription for a PrEP medicine until the earlier of 'the date of cessation' or 'the end of the study time period'. The date of cessation of PrEP was defined as either the 'cease date' if this was recorded by the prescriber, or a derived cease date defined as the last prescription date plus the number of days of therapy prescribed (assumed to be 30 days for each issued prescription, multiplied by the number of repeats, where applicable) plus an additional 90 days to account for missed doses, intermittent use and lag between filling a prescription at the pharmacy.

Practice PrEP caseload

High PrEP caseload practices were defined as those with at least 16 patients prescribed PrEP during the study and were the top 5% of all general practice sites with at least one patient prescribed PrEP during the study. Low PrEP caseload practices included those with no PrEP patients up to 15 patients prescribed PrEP. While a number of high PrEP caseload practices had fewer than 100 patients prescribed PrEP, this somewhat crude categorisation of caseload was necessary to protect the confidentiality of practices in MedicineInsight.

Calculating patient time (follow-up) in person-years

The index date was defined for each patient as the date of their first prescription for PrEP during the study period. Patient time (follow-up) in the study commenced on the patient's index date and ended at the earliest of:

- the end of the study (31 March 2021)
- 3 months after the patient's last visit to the practice (ie, loss to follow-up)

- date of first HIV diagnosis, or
- date of death (defined as the last visit in their year of death).

HIV diagnoses among patients prescribed PrEP

We described the number of patients in the PrEP population with a recorded diagnosis of HIV at least 7 days following their first prescription for PrEP at a MedicineInsight practice, according to patterns of PrEP use. We excluded patients who had a recorded diagnosis of HIV or a prescription for an ART medicine, before, or 7 days after, their first prescription for PrEP. A patient was considered to have an HIV diagnosis after PrEP based on information recorded in the three diagnosis fields (diagnosis/medical history, reason for encounter, and reason for prescription), the Authority Prescription indication field or if they had a prescription for a medicine used to treat HIV, until 31 March 2021. The definition of HIV was not based on positive HIV test results.

Statistical analysis

Analyses were conducted on the June 2021 download of MedicineInsight data using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA), including the use of the SURVEYFREQ procedure. Measures included descriptive statistics, frequencies, proportions and odds ratios as appropriate. To indicate the reliability of the estimates of prevalence and proportions, 95% confidence intervals (adjusted for clustering by practice site) and p-values are reported as needed.

Multivariable logistic regression was used to assess the association between patterns of use and patient and practice characteristics. The first multivariable models of discontinued (versus active) and non-continuous use (versus continuous) were adjusted for all factors from the univariable analyses, including age, sex, remoteness, socioeconomic status (SEIFA), concession card status, depression, anxiety, bipolar disorder, schizophrenia, opioid or alcohol use disorder, and PrEP caseload of the practice. In the second multivariable models we used backward elimination to remove all variables with P-value >0.05 eliminating one variable with highest p-value at each step.

If a particular result was only reported in 1–4 patients, this result has been reported as < 5 (with the exception of missing variables). Complementary suppression of related cells was undertaken to ensure suppressed results couldn't be deduced from column totals.

Guide to interpreting MedicineInsight data

When interpreting the information presented in this report, readers should note some of the limitations or caveats related to the MedicineInsight data:

- Information in CIS is collected to provide clinical care to a patient, not for research purposes. All analyses are therefore dependent upon the accuracy and completeness of data recorded in, and available for extraction from, the general practice CISs.

- Medicines use information from MedicineInsight relates to records of GP prescribing, and therefore differs in several important ways from national PBS dispensing data as not all prescriptions and repeats will be dispensed. Specialist and hospital prescriptions are not included. There may be a delay of up to 12 months between prescribing and dispensing.
- Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out.
- Due to confidentiality issues we do not have access to progress notes or access to correspondence, which may contain further information on reasons for prescriptions, reasons for encounters and diagnoses.
- Patients are free to visit multiple other practices. We do not have data on patients from non-MedicineInsight clinics. Currently we cannot identify patients who have attended multiple MedicineInsight practices.

Results

Study Selection Flow Chart

The selection process and number of patients at each step is described in Figure 2 below.

There were 2,207,710 patients eligible for inclusion in the general study population from whom subsequent PrEP populations were derived (Figure 2), representing approximately 11.2% of the Australian adult population (≥ 18 years). The average age for the general study population was 43.9 years, and the majority were female (56.4%) and resided in major cities (65.5%) (Table B1). The average age for the male general study population was 44.7 years and the majority of males resided in major cities (64.3%) (Table 3).

Of the 2.2 million general study patients, 4,055 (0.2%) patients were prescribed PrEP at least once between 1 April 2018 and 31 March 2021 (Figure 2: The PrEP population).

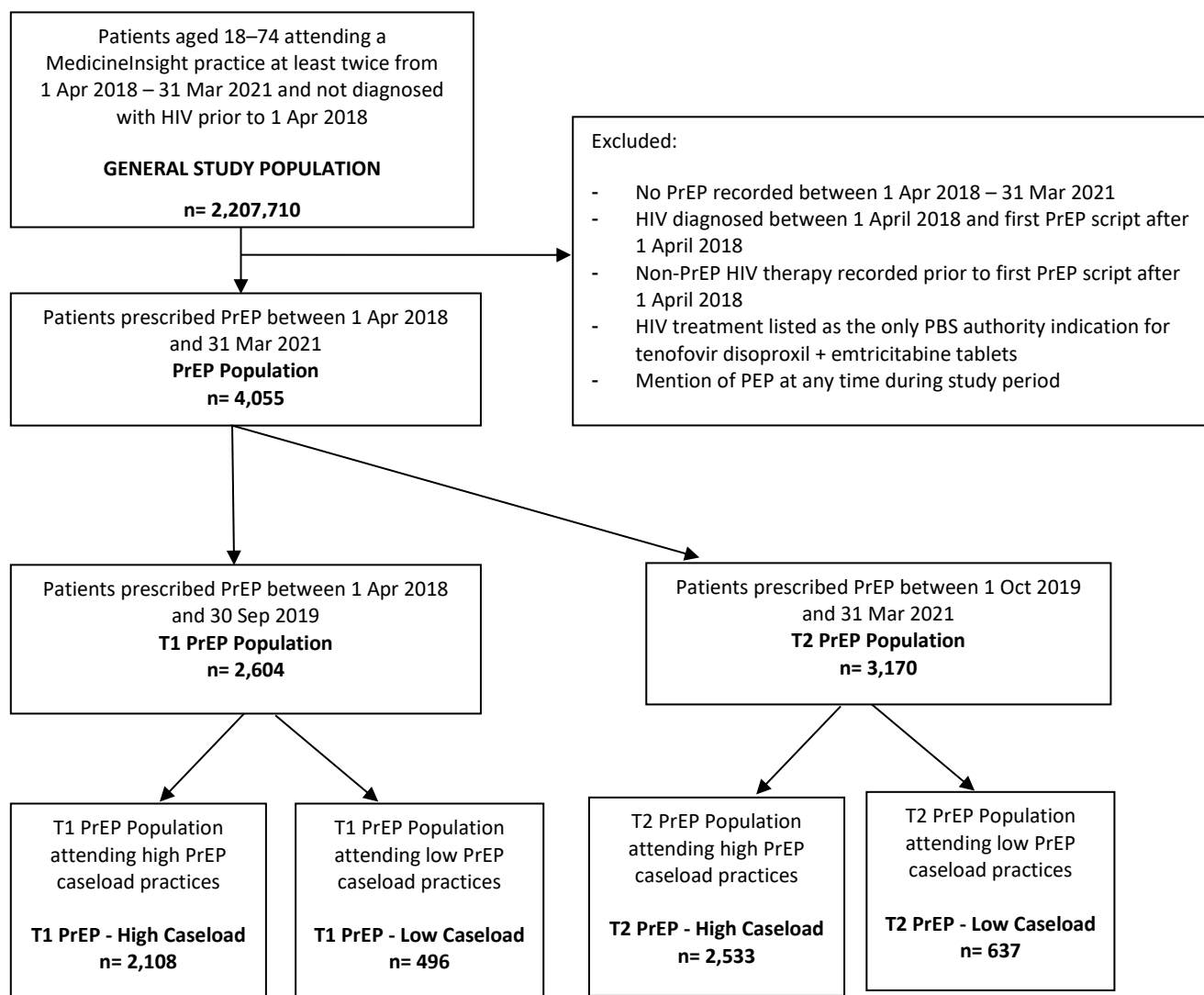


Figure 2: Flow diagram for cohort selection of the PrEP populations from the general study population

The monthly cumulative number of patients prescribed PrEP from 1 April 2018 to 31 March 2021.

As in the findings from the PBS data⁴ (Figure 1), MedicineInsight data showed that PrEP uptake has increased steadily since its listing on the PBS in April 2018 (Figure 2). In the first month of listing, 221 patients in the MedicineInsight program had a prescription for PrEP recorded and by March 2021 there were 4,055 MedicineInsight patients with at least one prescription for PrEP recorded from 1 April 2018 to 31 March 2021. This equates to an average of 110 patients per month prescribed PrEP for the first time. While this is an 18-fold increase in PrEP uptake, not all the 4,055 patients prescribed PrEP during the study would have had a recent prescription in March 2021.

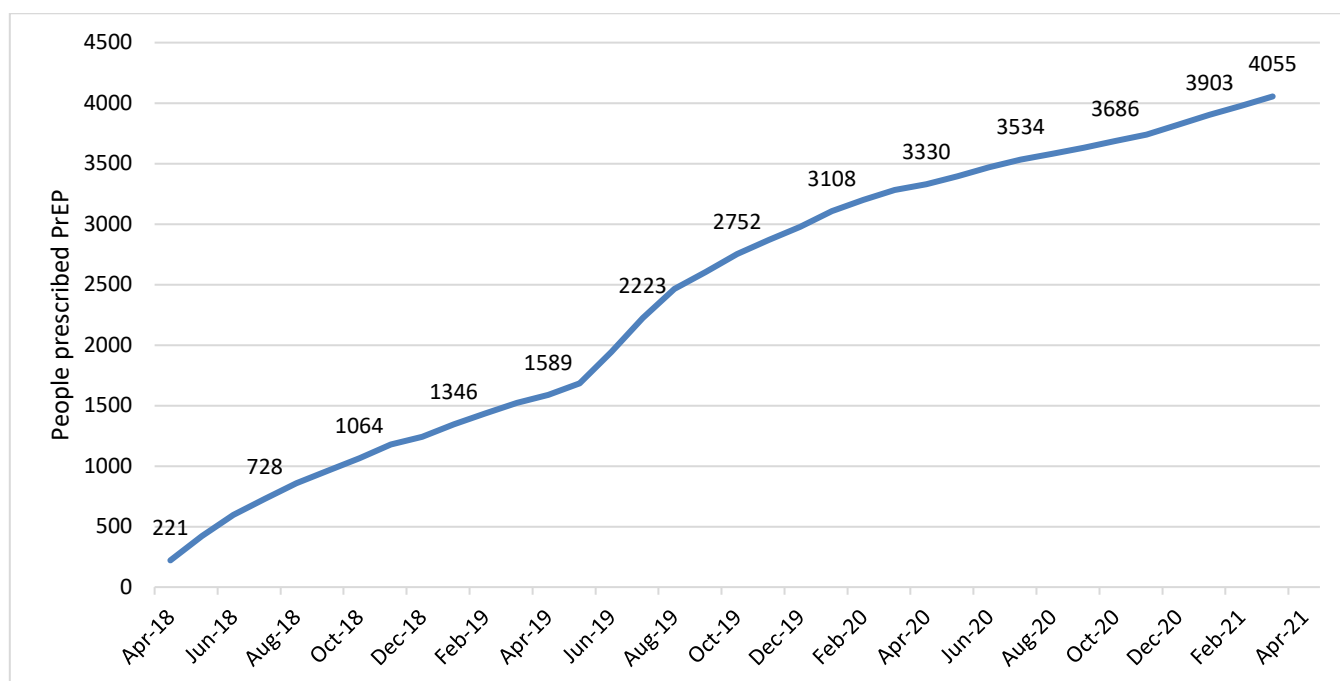


Figure 3: The monthly cumulative (total) number of patients ever prescribed PrEP from 1 April 2018 to 31 March 2021

There were 2,604 patients prescribed PrEP at least once in the first 18 months since PBS listing (T1: 1 Apr 2018 to 30 Sep 2019; Figure 2: the T1 PrEP population) and 3,170 patients prescribed PrEP at least once in the next 18 months (T2: 1 Oct 2019 to 31 Mar 2021; Figure 2: the T2 PrEP population) – a 22% increase. The increase in patients between May and July 2019 evident in Figure 3 appears to be due to the addition of data from one of the high PrEP caseload practices to the MedicineInsight program in June 2019.

Demographics of patients prescribed PrEP

The distribution of sociodemographic characteristics of the male general population, the PrEP population, T1 PrEP population and T2 PrEP population are presented in Table 3. Of the 4,055 patients prescribed PrEP at least once during the study period, the majority were male (98.2%), aged 18 to 39 years (63.4%), and resided in Victoria (47.8%) or New South Wales (39.3%), major cities (88.4%) and the two most socioeconomically advantaged area quintiles (77.4%).

The distribution of sociodemographic characteristics was similar for patients prescribed PrEP during the first 18 months since PBS listing (T1) and during the last 18 months of the study period (T2) (Table 3). There was a slight increase in the proportion of younger patients (18–29), patients with a concession/healthcare card and Aboriginal and Torres Strait Islander patients in the second 18 months (T2) compared with the first (T1), however these differences were not statistically significant.

The distribution of sociodemographic characteristics of the T1 PrEP population and T2 PrEP population at high and low PrEP caseload practices are presented in Table 4. In both time periods, compared to patients prescribed PrEP at high caseload practices, patients prescribed PrEP at low PrEP caseload practices were younger, more likely to live in regional

and more socioeconomically disadvantaged areas and more likely to have a concession/healthcare card (Table 4). In the last 18 months of the study (T2) the proportion of patients prescribed PrEP at low caseload practices who were Aboriginal or Torres Strait Islander was significantly higher (4.4%) than at high caseload practices (0.7%) (Table 4).

Table 3: Sociodemographic characteristics of the male general population and patients prescribed PrEP during time periods T1 (1 April 2018 to 30 September 2019) and T2 (1 October 2019 to 31 March 2021)

Characteristic	1 April 2018 to 31 March 2021				T1: 1 Apr 2018 to 30 Sep 2019		T2: 1 Oct 2019 to 31 Mar 2021	
	Male general population		PrEP population		PrEP T1 population		PrEP T2 population	
	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)
Total	961,408		4055		2,604		3170	
Sex								
Male	961,408	100.0 (100.0–100.0)	3,980	98.2 (97.5–98.8)	2,568	98.6 (98.0–99.2)	3120	98.4 (97.8–99.1)
Female			67	1.7 (1.0–2.3)				
Indeterminate			8	0.2 (0.0–0.3)				
Age mean (SE)	44.7 (0.25)		36.9 (0.88)			38.1 (0.87)		
Age group (years)								
18–19	31,384	3.3 (3.1–3.4)	65	1.6 (0.6–2.6)	25	1.0 (0.3–1.7)	50	1.6 (0.6–2.6)
20–29	175,173	18.2 (17.5–19.0)	1,218	30.0 (24.2–35.9)	692	26.6 (20.7–32.4)	910	28.7 (23.1–34.3)
30–39	192,341	20.0 (19.3–20.8)	1,291	31.8 (28.5–35.1)	828	31.8 (28.3–35.3)	1027	32.4 (29.1–35.7)
40–49	178,651	18.6 (18.2–18.9)	823	20.3 (16.9–23.7)	591	22.7 (19.1–26.3)	657	20.7 (17.9–23.5)
50–74	383,859	39.9 (38.5–41.3)	658	16.2 (12.9–19.6)	468	18.0 (14.3–21.6)	526	16.6 (13.0–20.2)
State / territory								
ACT	23,475	2.4 (0.7–4.2)	46	1.1 (0.0–2.4)	18	0.7 (0.0–1.6)	33	1.0 (0.0–2.3)
NSW	342,248	35.6 (29.9–41.3)	1,595	39.3 (3.3–75.4)	1,084	41.6 (1.3–82.0)	1176	37.1 (0.5–73.7)
NT	14,133	1.5 (0.3–2.6)	<5		<5		<5	
QLD	196,112	20.4 (16.1–24.7)	259	6.4 (1.3–11.4)	135	5.2 (0.8–9.5)	187	5.9 (0.9–10.9)
SA	18,092	1.9 (0.6–3.1)	<15		<5		<10	
TAS	69,268	7.2 (3.9–10.5)	60	1.5 (0.2–2.8)	36	1.4 (0.1–2.6)	36	1.1 (0.0–2.3)
VIC	180,093	18.7 (14.0–23.4)	1,937	47.8 (11.3–84.2)	1,259	48.3 (8.5–88.1)	1621	51.1 (13.2–89.1)
WA	117,987	12.3 (8.3–16.2)	145	3.6 (0.5–6.6)	66	2.5 (0.3–4.8)	106	3.3 (0.3–6.3)

Characteristic	1 April 2018 to 31 March 2021				T1: 1 Apr 2018 to 30 Sep 2019		T2: 1 Oct 2019 to 31 Mar 2021	
	Male general population		PrEP population		PrEP T1 population		PrEP T2 population	
	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)
Rurality								
Major city	617,802	64.3 (59.1–69.4)	3,583	88.4 (79.9–96.9)	2,311	88.7 (79.5–98.0)	2831	89.3 (81.3–97.4)
Inner regional	219,382	22.8 (18.5–27.1)	364	9.0 (1.9–16.1)	224	8.6 (1.0–16.2)	265	8.4 (1.6–15.1)
Outer regional	107,820	11.2 (8.5–13.9)	96	2.4 (0.7–4.0)	61	2.3 (0.5–4.2)	65	2.1 (0.6–3.5)
Remote/very remote	16,404	1.7 (0.9–2.5)	12	0.3 (0.0–0.6)	8	0.3 (0.0–0.7)	9	0.3 (0.0–0.6)
Socioeconomic status (SEIFA quintile)								
1 (most disadvantaged)	147,606	15.4 (12.7–18.0)	220	5.4 (2.6–8.2)	130	5.0 (2.0–7.9)	169	5.3 (2.5–8.2)
2	175,863	18.3 (15.4–21.2)	273	6.7 (2.6–10.8)	170	6.5 (2.0–11.0)	208	6.6 (2.6–10.5)
3	211,175	22.0 (18.9–25.0)	421	10.4 (5.4–15.3)	266	10.2 (4.6–15.8)	313	9.9 (5.3–14.5)
4	209,918	21.8 (18.8–24.9)	779	19.2 (12.7–25.7)	477	18.3 (11.9–24.7)	594	18.7 (12.0–25.4)
5 (most advantaged)	2168,46	22.6 (19.0–26.1)	2,362	58.2 (42.8–73.7)	1,561	59.9 (43.4–76.5)	1886	59.5 (44.4–74.6)
Concession status								
No concession	739,050	76.9 (75.5–78.3)	3,487	86.0 (82.1–89.9)	2,301	88.4 (84.7–92.0)	2734	86.2 (82.4–90.1)
Concession/Healthcare card	222,358	23.1 (21.7–24.5)	568	14.0 (10.1–17.9)	303	11.6 (8.0–15.3)	436	13.8 (9.9–17.6)
Aboriginal and Torres Strait Islander Status								
Aboriginal and Torres Strait Islander	22,915	2.4 (1.9–2.8)	60	1.5 (0.7–2.3)	25	1.0 (0.4–1.5)	45	1.4 (0.5–2.3)
Not Aboriginal and Torres Strait Islander	744,417	77.4 (74.8–80.1)	3,063	75.5 (62.5–88.6)	1,982	76.1 (60.6–91.7)	2425	76.5 (63.1–89.9)
Not reported	194,076	20.2 (17.5–22.9)	932	23.0 (10.1–35.9)	597	22.9 (7.5–38.3)	700	22.1 (8.9–35.3)

Table 4. Sociodemographic characteristics of the patients prescribed PrEP at high vs low PrEP caseload practices for time periods T1 (1 April 2018 to 30 September 2019) and T2 (1 October 2019 and 31 March 2021)

Characteristic	T1: 1 April 2018 to 30 September 2019				T2: 1 October 2019 to 31 March 2021			
	PrEP T1 High caseload		PrEP T1 Low caseload		PrEP T2 High caseload		PrEP T2 Low caseload	
	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)
Total	2,108		496		2,533		637	
Sex								
Male	2,084	98.9 (98.4–99.3)	484	97.6 (96.2–98.9)	2,504	98.9 (98.5–99.3)	616	96.7 (95.1–98.3)
Female	24	1.1 (0.7–1.6)			24	0.9 (0.5–1.3)		
Indeterminate	0	0.0 (0.0–0.0)			5	0.2 (0.0–0.4)		
Age mean (SE)	38.3 (1.01)		37.2 (0.65)		37.5 (0.98)		35.7 (0.61)	
Age group (years)								
18–19	13	0.6 (0.1–1.1)	12	2.4 (1.1–3.7)	26	1.0 (0.3–1.8)	24	3.8 (2.3–5.2)
20–29	520	24.7 (18.8–30.6)	172	34.7 (30.2–39.2)	678	26.8 (21.0–32.5)	232	36.4 (32.0–40.8)
30–39	707	33.5 (29.9–37.2)	121	24.4 (20.2–28.6)	865	34.1 (31.0–37.3)	162	25.4 (22.0–28.9)
40–49	502	23.8 (20.2–27.5)	89	17.9 (14.7–21.2)	545	21.5 (18.4–24.6)	112	17.6 (14.4–20.7)
50–74	366	17.4 (12.8–21.9)	102	20.6 (16.8–24.4)	419	16.5 (12.1–21.0)	107	16.8 (13.6–20.0)
State/Territory								
ACT	8	0.4 (0.0–1.2)	10	2.0 (0.5–3.5)	14	0.6 (0.0–1.7)	19	3.0 (0.4–5.6)
NSW	913	43.3 (0.0–92.8)	171	34.5 (26.6–42.4)	954	37.7 (0.0–83.4)	222	34.9 (26.7–43.0)
NT	0	0.0 (0.0–0.0)	<5		<5		<5	
QLD	30	1.4 (0.0–3.3)	105	21.2 (14.6–27.7)	42	1.7 (0.0–4.1)	145	22.8 (15.5–30.0)
SA	<5		<5		<5		<10	
TAS	<5		34	6.9 (3.1–10.6)	<5		34	5.3 (1.5–9.1)
VIC	1,142	54.2 (4.5–100.0)	117	23.6 (16.2–31.0)	1,496	59.1 (12.8–100.0)	125	19.6 (12.8–26.5)
WA	9	0.4 (0.0–1.2)	57	11.5 (6.3–16.7)	21	0.8 (0.0–2.2)	85	13.3 (6.7–20.0)

Characteristic	T1: 1 April 2018 to 30 September 2019				T2: 1 October 2019 to 31 March 2021			
	PrEP T1 High caseload		PrEP T1 Low caseload		PrEP T2 High caseload		PrEP T2 Low caseload	
	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)	Number	% (95% CI)
Rurality								
Major city	1,979	93.9 (85.6–100.0)	332	66.9 (59.7–74.2)	2,390	94.4 (87.3–100.0)	441	69.2 (62.0–76.4)
Inner regional	116	5.5 (0.0–13.1)	108	21.8 (15.4–28.1)	126	5.0 (0.0–11.4)	139	21.8 (15.4–28.2)
Outer regional	<20		50	10.1 (6.0–14.2)	<20		49	7.7 (4.5–10.9)
Remote/very remote	<5		6	1.2 (0.0–2.9)	<5		8	1.3 (0.1–2.4)
Socioeconomic status								
1 (most disadvantaged)	67	3.2 (0.8–5.6)	63	12.7 (8.6–16.8)	90	3.6 (1.1–6.0)	79	12.4 (8.5–16.3)
2	100	4.7 (0.3–9.2)	70	14.1 (9.8–18.5)	109	4.3 (0.8–7.8)	99	15.5 (11.1–20.0)
3	158	7.5 (2.2–12.7)	108	21.8 (17.2–26.3)	190	7.5 (3.0–12.0)	123	19.3 (14.9–23.7)
4	381	18.1 (10.3–25.8)	96	19.4 (14.8–23.9)	470	18.6 (10.3–26.8)	124	19.5 (15.1–23.8)
5 (most advantaged)	1,402	66.5 (50.0–83.1)	159	32.1 (24.9–39.2)	1,674	66.1 (50.6–81.5)	212	33.3 (25.9–40.7)
Concession status								
No concession	1,923	91.2 (88.3–94.1)	378	76.2 (72.0–80.4)	2,249	88.8 (85.4–92.2)	485	76.1 (72.6–79.7)
DVA/Concession	185	8.8 (5.9–11.7)	118	23.8 (19.6–28.0)	284	11.2 (7.8–14.6)	152	23.9 (20.3–27.4)
Aboriginal and Torres Strait Islander Status								
Aboriginal and Torres Strait Islander	13	0.6 (0.2–1.1)	12	2.4 (1.1–3.8)	17	0.7 (0.2–1.1)	28	4.4 (2.6–6.2)
Not Aboriginal and Torres Strait Islander	1,558	73.9 (55.3–92.6)	424	85.5 (81.7–89.2)	1,930	76.2 (59.5–92.9)	495	77.7 (73.4–82.0)
Not reported	537	25.5 (7.1–43.8)	60	12.1 (8.5–15.7)	586	23.1 (6.6–39.6)	114	17.9 (13.8–22.0)

Characteristics of high and low PrEP caseload practices

A higher proportion of high PrEP caseload practices (95.5%) were located in major cities than low PrEP caseload practices (57.8%), and in NSW and Victoria (77.3% of high caseload practices and 50.5% of low caseload practices) (Table 5). High PrEP caseload practices also had higher numbers of people living with HIV, with 5 (22.5%) high caseload practices having 100 or more HIV-positive patients each.

The characteristics of the practices with at least 1 patient prescribed PrEP during the time periods T1 and T2 are presented in Appendix B (Table B2).

Table 5. Characteristics of the high and low PrEP caseload practices (1 April 2018 to 31 March 2021)

Characteristic		High PrEP caseload practices		Low PrEP caseload practices	
		Number	% (95% CI)	Number	% (95% CI)
Total		22		412	
State/Territory					
	ACT	<4	4.5 (0.0–13.3)	8	1.9 (0.6–3.3)
	NSW	9	40.9 (20.3–61.5)	142	34.5 (29.9–39.1)
	NT	0	0.0 (0.0–0.0)	7	1.7 (0.4–3.0)
	QLD	<4	13.6 (0.0–28.0)	95	23.1 (19.0–27.1)
	SA	0	0.0 (0.0–0.0)	10	2.4 (0.9–3.9)
	TAS	0	0.0 (0.0–0.0)	33	8.0 (5.4–10.6)
	VIC	8	36.4 (16.2–56.5)	66	16.0 (12.5–19.6)
	WA	<4	4.5 (0.0–13.3)	51	12.4 (9.2–15.6)
Rurality					
	Major city	21	95.5 (86.7–100.0)	238	57.8 (53.0–62.6)
	Inner regional	1	4.5 (0.0–13.3)	100	24.3 (20.1–28.4)
	Outer regional	0	0.0 (0.0–0.0)	60	14.6 (11.1–18.0)
	Remote/very remote	0	0.0 (0.0–0.0)	14	3.4 (1.6–5.2)
Number of people living with HIV					
	≥ 100	5	22.7 (5.1–40.3)	0	
	< 100	17	77.3 (59.7–94.9)	412	100.0 (100.0–100.0)

Patterns of PrEP utilisation

A total of 52,935 prescriptions (originals + repeats) for PrEP were recorded for 4055 patients. The mean average number of scripts per patient was 13.1 (95% CI: 11.4–14.7) over the 3-year study period, however not all patients were present and attending the practice during the entire study period (Table 7). To account for differences in available follow-up for patients, the average number of scripts was also calculated per person-year at 9.7 scripts for PrEP per person-year. Assuming one prescription equates to one month's supply, this equates to a medication possession ratio (MPR) of 80.8%.

The mean duration of exposure to PrEP therapy was 541 days. Among 1,242 patients identified as having a gap in therapy, the mean time to first discontinuation of PrEP was 307 days.

Table 7: Average number of scripts for the PrEP initiator population (initiations between 1 April 2018 and 31 March 2021)

Characteristic	2018-2020 PrEP population	
	Number	95% CI
Number of individuals	4055	
Person-years		
<i>Total</i>	5432	
<i>Mean per patient</i>	1.3	1.1–1.5
<i>Range (min-max)</i>	0.0 – 3.0	
Total prescriptions	52,935	
<i>Mean</i>	13.1	11.4–14.7
<i>Median (IQR)</i>	8.7 (2.9-17.9)	
<i>Number of scripts per person-year</i>	9.7 scripts per person-year	
Duration (person-days) of PrEP exposure	1,826,988	
<i>Mean</i>	451	383–518
<i>Median (IQR)</i>	392 (179 – 642)	
Mean time to first discontinuation		
<i>Person-days to discontinuation (mean)*</i>	307	282–332

* The analysis of mean time to first discontinuation of PrEP was restricted to those 1,242 patients where a true treatment gap could be demonstrated.

According to the dosage instructions recorded by GPs on prescriptions, 186 patients (4.6%) were prescribed on-demand use. According to the dosage instructions recorded by GPs on prescriptions, and an analysis of gaps between prescriptions, 36.3% were on continuous therapy, 33.4% appeared to have non-continuous PrEP use and 30.3% of patients had only one original script for PrEP recorded (not assessable). Excluding people who were not assessable,

just over half had continuous use (52.0%) and just under half had non-continuous use (48.0%). (Table 8)

The analysis of PrEP user status at the end of the study period (31 March 2021) found that 48.8% were on active therapy, 19.8% had discontinued therapy and 31.4% could not be assessed as they were lost to follow-up (Table 8). Some of this loss to follow-up may reflect patients moving to a new clinic.

Table 8: Patterns of use for the PrEP population (between 1 April 2018 and 31 December 2021)

Characteristic	PrEP population	
	Number	% (95% CI)
Number of individuals	4055	
Patterns of PrEP use (n=4,055)		
<i>Continuous (no significant gaps between scripts)</i>	1470	36.3 (34.5–37.9)
<i>Non-continuous (gaps between scripts or on-demand dosing)</i>	1356	33.4 (28.2–38.7)
<i>Not assessable (only one script)</i>	1229	30.3 (24.0–36.6)
PrEP status at end of follow-up (n=4,055)		
<i>Active PrEP at end of study</i>	1980	48.8 (44.5–53.2)
<i>Discontinued PrEP at end of study</i>	802	19.8 (15.1–24.4)
<i>Lost to follow-up</i>	1273	31.4 (30.2–32.6)
Patterns of use in patients with active PrEP use at end of study (n=1,980)		
<i>Continuous (no significant gaps between scripts)</i>	754	38.1 (36.6–39.6)
<i>Non-continuous (gaps between scripts or on-demand dosing)</i>	906	45.8 (40.9–50.7)
<i>Not assessable (only prescribed 1 original prescription)</i>	320	16.2 (10.7–21.6)

Predictors of stopping PrEP

The baseline demographic and clinical characteristics of patients in the PrEP population are presented in Table 3 and Appendix B (Table B3).

The crude (unadjusted) univariable analyses to test the association between stopping PrEP and potential predictors among the entire PrEP population found that, compared to patients on active PrEP at the end of the study period, patients who discontinued were more likely to:

- be female,
- be younger than 30,
- have a recorded diagnosis of depression, anxiety or bipolar disorder,
- live in outer regional areas or more disadvantaged socioeconomic areas,
- have a concession/healthcare card, and
- attend a low PrEP caseload practice (Table 9).

There was weak evidence ($p=0.053$) that having an opioid or alcohol use disorder was associated with discontinuation of PrEP by the end of the study.

After adjusting for confounding, the strongest predictors of discontinuation were being female and attending a low caseload practice. Having a recorded diagnosis depression or anxiety were also predictors of discontinuation but there was no longer good evidence for an association between discontinuing PrEP and age, having a recorded diagnosis of bipolar disorder, living in outer regional or more disadvantaged socioeconomic areas, or having a concession/healthcare card. (Table 9)

In the final multivariable model, after adjusting for sex, depression, anxiety and PrEP caseload of the patient's practice, we found the odds of stopping PrEP was 1.4 times higher among patients at low PrEP caseload practices (adjusted OR 2.4; 95% CI: 1.7–3.4, $p < 0.0001$) compared to high caseload practices and 2.4 times higher among females (adjusted OR 3.4; 95% CI: 1.5–7.8, $p=0.012$) than males, although the confidence interval for sex is wide. The odds of stopping PrEP was 50% higher among patients with a recorded diagnosis of depression (adjusted OR 1.5; 95% CI: 1.2–1.8, $p < 0.0001$) and 30% higher among patients with a recorded diagnosis of anxiety (adjusted OR 1.3; 95% CI: 1.0–1.5, $p=0.0158$). (Table 9)

Table 9. Patient and practice characteristics associated with stopping PrEP among PrEP users at the end of the study (1 April 2018 to 31 March 2021)

	Discontinued (n=799) vs active (n=1,973) PrEP status					
	Univariable analyses		Multivariable analysis 1*		Multivariable analysis 2†	
	OR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Sex						
Male (reference group)	1.0					
Female	4.2 (1.8–9.6)	0.0009	3.4 (1.4–7.9)	0.0053	3.4 (1.5–7.8)	0.0041
Age group						

	Discontinued (n=799) vs active (n=1,973) PrEP status					
	Univariable analyses		Multivariable analysis 1*		Multivariable analysis 2†	
	OR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
18–19	1.9 (1.1–3.3)	0.0275	1.4 (0.8–2.5)	0.2341		
20–29	1.3 (1.1–1.7)	0.0134	1.2 (0.9–1.5)	0.2236		
30–39 (reference group)	1.0					
40–49	1.2 (0.9–1.4)	0.1877	1.1 (0.8–1.4)	0.6012		
50–74	1.3 (1.0–1.7)	0.0364	1.2 (1.0–1.5)	0.1135		
Remoteness						
Major city (reference group)	1.0					
Inner regional	1.3 (1.0–1.8)	0.0947	0.9 (0.6–1.3)	0.5710		
Outer regional	2.8 (1.4–5.5)	0.0039	1.6 (0.8–3.1)	0.2054		
SES						
Disadvantaged SES (SEIFA 1-3)	1.5 (1.2–1.8)	0.0001	1.0 (0.8–1.4)	0.8020		
Advantaged SES (SEIFA 4-5)	1.0					
Concession status						
No concession	1.0					
DVA/Concession	1.4 (1.2–1.8)	0.0011	1.0 (0.8–1.2)	0.8201		
Clinical condition						
Depression	1.8 (1.3–2.3)	0.0001	1.4 (1.2–1.8)	0.0003	1.5 (1.2–1.8)	0.0001
Anxiety	1.5 (1.2–2.0)	0.0022	1.3 (1.0–1.5)	0.0210	1.3 (1.0–1.5)	0.0158
Bipolar disorder	2.0 (1.3–3.2)	0.003	1.4 (0.7–2.5)	0.3234		
Schizophrenia	1.4 (0.7–3.1)	0.3552	0.7 (0.3–1.7)	0.4592		
Drug or alcohol use disorder	1.4 (1.0–2.1)	0.0535	1.2 (0.8–1.7)	0.4213		
Practice type						
Low PrEP caseload	2.6 (1.8–3.7)	<.0001	2.3 (1.6–3.3)	<.0001	2.4 (1.7–3.4)	<.0001
High PrEP caseload	1.0					

OR: Odds Ratio, aOR: Adjusted Odds Ratio, CI: Confidence Interval, SES: Socioeconomic status, SEIFA: Socio-Economic Indexes for Areas

* The first multivariable models of discontinued (versus active) and non-continuous use (versus continuous) were adjusted for all factors from the univariable analyses, including age, sex, remoteness, socioeconomic status (SEIFA), concession card status, depression, anxiety, bipolar disorder, schizophrenia, opioid or alcohol use disorder, and PrEP caseload of the practice.

†The final multivariable analyses of discontinued versus active status at the end of the study were adjusted for sex, depression, anxiety, and PrEP practice caseload.

Predictors of non-continuous PrEP use

The unadjusted univariable analyses to test the associations between non-continuous PrEP use and potential predictors among the entire PrEP population found that, compared to patients with continuous PrEP use throughout the study, patients with non-continuous use were less likely to: be younger (20-29 years), live in inner regional areas or more disadvantaged areas, have a concession/healthcare card or attend a low PrEP caseload practice (Table 10). Compared to patients with continuous PrEP use, patients with non-continuous use were more likely to have a recorded diagnosis of anxiety.

In the final multivariable model, after adjusting for anxiety, having a concession/healthcare card and PrEP caseload of the patient's practice, we found the odds of non-continuous PrEP use was 40% lower among patients at low PrEP caseload practices (adjusted OR 0.6; 95% CI: 0.5–0.7, $p < 0.0001$) compared to high caseload practices and 20% lower among patients with a concession/healthcare card (adjusted OR 0.8; 95% CI: 0.6–0.9, $p=0.0034$) than not. The odds of non-continuous PrEP use was 30% higher among patients with a recorded diagnosis of anxiety (adjusted OR 1.3; 95% CI: 1.1–1.5, $p=0.0002$). (Table 10)

Table 10. Patient and practice characteristics associated with non-continuous use among PrEP users (1 April 2018 to 31 March 2021)

	Non-continuous use (n=1350) vs continuous use (n=1465)					
	Univariable analyses		Multivariable analysis 1*		Final multivariable analysis†	
	OR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Sex						
Male (reference group)	1.0					
Female	1.1 (0.5–2.4)	0.8366	1.2 (0.6–2.6)	0.6307		
Age group						
18–19	0.6 (0.3–1.2)	0.1287	0.7 (0.4–1.4)	0.3532		
20–29	0.8 (0.6–1.0)	0.0493	0.9 (0.7–1.1)	0.1605		
30–39 (reference group)	1.0					
40–49	1.0 (0.7–1.3)	0.9097	1.0 (0.7–1.4)	0.9355		
50–74	1.0 (0.7–1.5)	0.8296	1.1 (0.8–1.5)	0.5513		
Remoteness						
Major city (reference group)	1.0					
Inner regional	0.7 (0.6–0.9)	0.0013	1.1 (0.8–1.4)	0.7107		
Outer regional	1.1 (0.7–1.9)	0.6045	2.0 (1.2–3.3)	0.0088		
SES						
Disadvantaged SES (SEIFA 1-3)	0.8 (0.6–0.9)	0.0048	0.9 (0.7–1.0)	0.0629		
Advantaged SES (SEIFA 4-5)	1.0					

	Non-continuous use (n=1350) vs continuous use (n=1465)					
	Univariable analyses		Multivariable analysis 1*		Final multivariable analysis†	
	OR (95% CI)	p-value	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Concession status						
No concession	1.0				1.0	
DVA/Concession	0.7 (0.6–0.9)	0.0014	0.9 (0.7–1.0)	0.0629	0.8 (0.6–0.9)	0.0034
Clinical condition						
Depression	1.1 (1.0–1.3)	0.1217	1.1 (0.9–1.3)	0.2457		
Anxiety	1.3 (1.1–1.5)	0.0012	1.3 (1.1–1.5)	0.0121	1.3 (1.1–1.5)	0.0002
Bipolar disorder	1.2 (0.8–1.8)	0.4756	1.3 (0.8–2.3)	0.2877		
Schizophrenia	0.8 (0.4–1.8)	0.6438	1.0 (0.4–2.5)	0.9527		
Drug or alcohol use disorder	0.9 (0.7–1.3)	0.7231	0.8 (0.6–1.2)	0.2407		
Practice type						
Low PrEP caseload	0.6 (0.5–0.7)	<.0001	0.6 (0.5–0.7)	<.0001	0.6 (0.5–0.7)	<.0001
High PrEP caseload	1.0		1.0		1.0	

OR: Odds Ratio, aOR: Adjusted Odds Ratio, CI: Confidence Interval, SES: Socioeconomic status, SEIFA: Socio-Economic Indexes for Areas

* The first multivariable models of non-continuous use (versus continuous) were adjusted for all factors from the univariable analyses, including age, sex, remoteness, socioeconomic status (SEIFA), concession card status, depression, anxiety, bipolar disorder, schizophrenia, opioid or alcohol use disorder, and PrEP caseload of the practice.

†The final multivariable analyses of non-continuous use (versus continuous) were adjusted for concession status, anxiety, and PrEP practice caseload.

Discussion regarding stopping therapy and non-continuous use

Patients who stopped PrEP were more likely to attend a low PrEP caseload practice than a high caseload practice. This finding aligns with a recent study using PBS data that found the discontinuation of PrEP was associated with low PrEP caseload of the patients' prescriber.⁶ High PrEP caseload practices likely include HIV-specialist GPs who are specially trained in prescribing PrEP. This finding could highlight a need for better education for non-HIV specialist GPs and low caseload practices, to help to address this disparity. That patients with depression or anxiety had higher odds of stopping PrEP use is consistent with prior studies that have found an association between mental health disorders and difficulties with continuing with PrEP.⁷

Non-continuous PrEP use may indicate on-demand dosing/ intermittent use or non-adherence to daily dosing, and our data do not enable us to distinguish between these patient groups. Based on the available information on 'directions for use', it appears that 5% of the patients who initiated PrEP were prescribed on-demand dosing, compared to < 0.5% in the previous MedicineInsight PrEP report. Since 2020, the on-demand regimen has been recommended as

an alternative option for MSM, particularly those who have sex less than twice a week and can plan ahead for sex at least 2 hours in advance.¹ The on-demand dosing strategy has the potential to reduce the cost of drugs, pill burden and toxicity and to improve continuation among those who find daily pill-taking challenging.³

Unlike discontinuation of PrEP, non-continuous PrEP use was more common among patients attending a high PrEP caseload practice, where support for using PrEP is arguably highest. This finding could indicate that the non-continuous users in our study are largely made up of experienced on demand/intermittent users rather than non-adherent. Some individuals may be taking PrEP during periods when they are potentially at risk of HIV, a concept called 'prevention-effective adherence' and take fewer pills or cease taking PrEP during periods deemed to be of no or low risk.^{9,10}

We found that patients with a concession card had 20% lower odds of having non-continuous PrEP therapy. As non-continuous PrEP therapy in this study represents a combination of on-demand dosing and non-adherent use, this finding might reflect less knowledge about on-demand dosing among concessional patients and the lower cost of obtaining PrEP for concessional patients (PBS co-payment of \$6.60 for 30 days' supply, assuming daily dosing) compared to the general patients (\$41.00 for 30 days' supply).¹¹ That patients with anxiety had 30% higher odds of non-continuous PrEP use is consistent with prior studies that have found an association between mental health disorders and difficulties with continuing with PrEP.⁷ This highlights potential sub-populations for whom tailored support for continued PrEP use may be beneficial. We did not detect evidence that any of the other patient characteristics were associated with non-continuous therapy. The ability to detect associations in this analysis may have been limited by the heterogeneity of non-continuous users which included both patients with on-demand dosing and non-adherent use.

HIV diagnoses in patients prescribed PrEP

We described the number of patients in the PrEP population with a recorded diagnosis of HIV at least 8 days following their first prescription for PrEP at a MedicineInsight practice, according to patterns of PrEP use (Table 12).

The recorded proportion of new HIV diagnoses in patients, at least 8 days following PrEP initiation, was 0.4% (95% CI 0.2–0.6) and the recorded incidence was 0.3 per 100 person-years (95% CI 0.2–0.5), higher than the incidence seen in the EPIC-NSW study (incidence 0.048 per 100 person-years, 95% CI 0.012–0.195), although the 95% CIs overlap. The proportion and incidence of patients with a new diagnosis of HIV was higher among patients on non-continuous PrEP than continuous PrEP, although this difference was not statistically significant. Encouragingly no HIV diagnoses were identified among patients still on active PrEP at the end of the study who had continuous use. (Table 12)

These findings should be interpreted with caution, noting the possibility that despite our best efforts, a patient with HIV may not have been excluded from the baseline PrEP population if they had diagnoses or prescriptions received from other providers that were not captured by the MedicineInsight program. What may seem like a new diagnosis of HIV after PrEP could have been the GP recording a previous diagnosis at a later date.

Table 12: Proportion of patients with an HIV diagnosis recorded after commencing PrEP, by patterns of use

PrEP status	n	Proportion of PrEP patients with HIV record [% , (95% CI)]	Rate of HIV record while on PrEP [incidence per 100 person years, (95% CI)]
All patients dispensed PrEP	17	0.4 (0.2–0.6)	0.3 (0.2–0.5)
Continuous PrEP	<5	0.2 (0.0–0.5)	0.1 (0.0–0.3)
Non-continuous PrEP	10	0.7 (0.3–1.2)	0.4 (0.1–0.6)
Active	10	0.5 (0.2–0.8)	0.3 (0.1–0.5)
<i>Active with continuous use</i>	0	0.0 (0.0–0.0)	0.0 (0.0–0.0)
<i>Active with non-continuous use</i>	9	1.0 (0.4–1.6)	0.5 (0.2–0.8)
Discontinued PrEP	6	0.7 (0.1–1.4)	0.4 (0.1–0.7)
Lost to follow-up	<5	0.1 (0.0–0.2)	0.1 (0.0–0.3)

Actions undertaken by the DUSC Secretariat

DUSC requested that the report be provided to the PBAC for consideration.

Appendices

Appendix A: PBS restriction information for PrEP from 2018 onwards

Table A1: History of PrEP for HIV on the PBS

itm_cd	RESTRICTION_TEXT	RESTRICTION START DATE	RESTRICTION END DATE
11276L	Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection Clinical criteria: * The treatment must be for patients at medium to high risk of HIV infection, as defined by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Guidelines, AND * Patient must have a negative HIV test result prior to treatment with PBS-subsidised therapy with this drug. Population criteria: * Patient must be 18 years or older.	01Apr2018	31Dec2020
11296M	Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection Clinical criteria: * The treatment must be for patients at medium to high risk of HIV infection, as defined by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Guidelines, AND * Patient must have a negative HIV test result prior to treatment with PBS-subsidised therapy with this drug. Population criteria: * Patient must be 18 years or older.	01Apr2018	31Dec2020
11306C	Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection Clinical criteria: * The treatment must be for patients at medium to high risk of HIV infection, as defined by the Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine (ASHM) Guidelines, AND * Patient must have a negative HIV test result prior to treatment with PBS-subsidised therapy with this drug. Population criteria: * Patient must be 18 years or older.	01Apr2018	31Dec2020
12542D	Pre-exposure prophylaxis (PrEP) against human immunodeficiency virus (HIV) infection Clinical criteria: * Patient must have at least one of the following prior to having the latest PBS-subsidised prescription issued: (i) a negative HIV test result no older than 4 weeks, (ii) evidence that an HIV test has been conducted, but the result is still forthcoming.	01Jun2021	

Appendix B: Supplementary tables

Table B1: Baseline characteristics of the general study population (1 April 2018 to 31 March 2021)

	General study population (1 April 2018 to 31 March 2021)	
	Number	% (95% CI)
Sex		
Male	961408	43.5 (43.0–44.1)
Female	1245717	56.4 (55.9–57.0)
Indeterminate	585	0.0 (0.0–0.0)
Average Age (mean (SD))	43.9 (0.25)	
Age group		
18–19	76866	3.5 (3.3–3.6)
20–29	441011	20.0 (19.1–20.8)
30–39	454639	20.6 (19.9–21.3)
40–49	399833	18.1 (17.8–18.5)
50–74	835361	37.8 (36.5–39.1)
State/territory		
ACT	57960	2.6 (0.8–4.5)
NSW	783254	35.5 (29.9–41.1)
NT	31030	1.4 (0.3–2.5)
QLD	459631	20.8 (16.5–25.1)
SA	42884	1.9 (0.7–3.2)
TAS	154137	7.0 (3.8–10.2)
VIC	406330	18.4 (13.8–23.0)
WA	272484	12.3 (8.4–16.3)
Rurality		
Major city	1445135	65.5 (60.4–70.5)
Inner regional	489990	22.2 (18.0–26.4)
Outer regional	238052	10.8 (8.1–13.4)
Remote/ very remote	34533	1.6 (0.8–2.3)
SES (SEIFA)		
1 (most disadvantaged)	327185	14.8 (12.3–17.4)
2	393976	17.8 (15.0–20.7)

	General study population (1 April 2018 to 31 March 2021)	
	Number	% (95% CI)
3	480801	21.8 (18.8–24.8)
4	486740	22.0 (19.1–25.0)
5 (most advantaged)	519008	23.5 (19.8–27.2)
Concession status		
No concession	1645195	74.5 (73.1–76.0)
DVA/Concession	562515	25.5 (24.0–26.9)
Aboriginal and Torres Strait Islander status		
Aboriginal and Torres Strait Islander	54444	2.5 (2.0–2.9)
Not Aboriginal and Torres Strait Islander	1729962	78.4 (75.8–81.0)
Not reported	423304	19.2 (16.5–21.8)
Clinical condition		
Depression (ever)	433176	19.6 (18.9–20.4)
Anxiety (ever)	389587	17.6 (17.0–18.3)
Bipolar disorder	30162	1.4 (1.3–1.5)
Schizophrenia	17416	0.8 (0.7–0.9)
Drug or alcohol use disorder (ever)	33134	1.5 (1.3–1.7)

Table B2. Characteristics of the general practices prescribing PrEP for two time periods (T1:1 April 2018 to 30 September 2021; and T2: 1 October 2019 to 31 March 2021)

Characteristic		T1: 1 April 2018 to 30 September 2019		T2: 1 October 2019 to 31 March 2021	
		Number	% (95% CI)	Number	% (95% CI)
Total		239		254	
State/Territory					
	ACT	8	3.3 (1.1–5.6)	8	3.1 (1.0–5.3)
	NSW	84	35.1 (29.1–41.2)	91	35.8 (29.9–41.7)
	NT	<5	0.8 (0.0–2.0)	<5	
	QLD	49	20.5 (15.4–25.6)	56	22.0 (16.9–27.2)
	SA	<5	0.0 (0.0–0.0)	<5	
	TAS	16	6.7 (3.5–9.9)	15	5.9 (3.0–8.8)

Characteristic		T1: 1 April 2018 to 30 September 2019		T2: 1 October 2019 to 31 March 2021	
		Number	% (95% CI)	Number	% (95% CI)
	VIC	53	22.2 (16.9–27.5)	53	20.9 (15.8–25.9)
	WA	27	11.3 (7.3–15.3)	26	10.2 (6.5–14.0)
Rurality					
	Major city	156	65.3 (59.2–71.3)	171	67.3 (61.5–73.1)
	Inner regional	55	23.0 (17.7–28.4)	58	22.8 (17.7–28.0)
	Outer regional	<30		22	8.7 (5.2–12.1)
	Remote/very remote	<4		3	1.2 (0.0–2.5)
PrEP Caseload					
	High caseload	22	9.2 (5.5–12.9)	22	8.7 (5.2–12.1)
	Low caseload	217	90.8 (87.1–94.5)	232	91.3 (87.9–94.8)

Table B3. Baseline patient and practice characteristics included in the regression analyses among the PrEP population (1 April 2018 to 31 March 2021)

Characteristic	PrEP population (1 April 2018 to 31 March 2021)	
	Number	% (95% CI)
Sex		
Male	3980	98.2 (97.5–98.8)
Female	67	1.7 (1.0–2.3)
Indeterminate	8	0.2 (0.0–0.3)
Age group		
18–19	65	1.6 (0.6–2.6)
20–29	1218	30.0 (24.2–35.9)
30–39	1291	31.8 (28.5–35.1)
40–49	823	20.3 (16.9–23.7)
50–74	658	16.2 (12.9–19.6)
State / territory		
ACT	46	1.1 (0.0–2.4)
NSW	1595	39.3 (3.3–75.4)
NT	3	0.1 (0.0–0.2)
QLD	259	6.4 (1.3–11.4)
SA	10	0.2 (0.0–0.5)
TAS	60	1.5 (0.2–2.8)
VIC	1937	47.8 (11.3–84.2)

Characteristic	PrEP population (1 April 2018 to 31 March 2021)	
	Number	% (95% CI)
WA	145	3.6 (0.5–6.6)
Rurality		
Major city	3583	88.4 (79.9–96.9)
Inner regional	364	9.0 (1.9–16.1)
Outer regional	96	2.4 (0.7–4.0)
Remote/ very remote	12	0.3 (0.0–0.6)
SES		
Disadvantaged SES (SEIFA 1-3)	914	22.5 (11.7–33.4)
Advantaged SES (SEIFA 4-5)	3141	77.5 (66.6–88.3)
Concession status		
No concession	3487	86.0 (82.1–89.9)
DVA/Concession	568	14.0 (10.1–17.9)
Clinical condition		
Depression	974	24.0 (19.9–28.2)
Anxiety	1109	27.3 (22.2–32.5)
Bipolar disorder	90	2.2 (1.4–3.0)
Schizophrenia	37	0.9 (0.5–1.3)
Drug or alcohol use disorder	89	2.2 (1.3–3.1)
Practice type		
Low PrEP caseload	918	22.6 (5.7–39.5)
High PrEP caseload	3137	77.4 (60.5–94.3)

References

1. The Australasian Society of HIV Viral Hepatitis and Sexual Health Medicine (ASHM). *PrEP Guidelines Update. Prevent HIV by Prescribing PrEP*. Sydney: ASHM; 2019 2020.
2. Molina JM, Capitant C, Spire B, et al. On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection. *The New England journal of medicine*. 2015;373(23):2237-2246.
3. (WHO) WHO. *What's the 2+1+1? Event-driven oral pre-exposure prophylaxis to prevent HIV for men who have sex with men: update to WHO's recommendation on oral PrEP*. Geneva: WHO;2019.
4. The Kirby Institute. *Monitoring HIV Pre-exposure Prophylaxis Uptake in Australia (Issue 4)*. Sydney: UNSW Sydney;2021.
5. Anderson PL, Glidden DV, Liu A, et al. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Science translational medicine*. 2012;4(151):151ra125.
6. Medland NG, R. Bavinton B, Keen P. Large differences in discontinuation of PBS-subsidised PrEP in Australia: evaluation using national prescription data: from Abstracts of the Joint Australasian HIV&AIDS and Sexual Health Conferences held 16-20 November 2020 (virtual). *Sex Health*. 2020;17(5):iii-xxix.
7. Krakower D, Maloney KM, Powell VE, et al. Patterns and clinical consequences of discontinuing HIV preexposure prophylaxis during primary care. *J Int AIDS Soc*. 2019;22(2):e25250.
8. Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *The lancet HIV*. 2017;4(9):e402-e410.
9. Bavinton BR, Vaccher S, Jin F, et al. High Levels of Prevention-Effective Adherence to HIV PrEP: An Analysis of Substudy Data From the EPIC-NSW Trial. *J Acquir Immune Defic Syndr*. 2021;87(4):1040-1047.
10. Elsesser SA, Oldenburg CE, Biello KB, et al. Seasons of Risk: Anticipated Behavior on Vacation and Interest in Episodic Antiretroviral Pre-exposure Prophylaxis (PrEP) Among a Large National Sample of U.S. Men Who have Sex with Men (MSM). *AIDS Behav*. 2016;20(7):1400-1407.
11. Australian Medicines Handbook. In:2019: <https://amhonline.amh.net.au/>. Accessed 6 February 2019.