

Pre-exposure prophylaxis: Utilisation analysis using PBS 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 PBS data.

Data Source / methodology

Data for all medicines used for PrEP listed on the PBS were extracted from the Services Australia PBS supplied prescriptions database for the 3 years from April 2018 to March 2021.

Key Findings

- Between 1 April 2018 and 31 March 2021, a total of 352,427 prescriptions for PrEP were dispensed for 44,303 patients.
- There was an 80.8% increase in the number of prescriptions for PrEP dispensed between the first and second years since PBS listing, from 77,512 to 140,142 prescriptions.
- There were 134,773 prescriptions for PrEP dispensed in the third year since listing (1 April 2020 to 31 March 2021), representing a 3.8% reduction compared to the second year, likely explained by the impacts of the COVID-19 restrictions.
- In the third year since listing, the cost to government for PrEP was \$11.4 million, a decrease of \$8.9 million when compared to expenditure on PrEP in the first year since listing, due to price disclosure reductions.
- In the third year since listing, approximately 77.9% of dispensed prescriptions for PrEP were prescribed by GPs. Specialists accounted for another 11.3% of prescriptions and nurse prescribers 1.2% of prescriptions each year, with a further 9.6% of prescriptions with unassigned or missing prescriber details.
- In the first year since PBS listing, 22,403 patients were dispensed a PrEP prescription at least once, increasing by 39.1% in the second year to 31,159 people and 31,124 people in the third year since listing.
- The number of patients newly dispensed a PrEP prescription decreased year on year from 22,403 patients in the first year since listing to 8640 patients in the third year.

- The annual number of patients dispensed PBS-subsidised PrEP under the Closing the Gap program increased from 218 patients in the first year since listing to 443 patients in the third year (noting these findings will underestimate the true rate of dispensing to Aboriginal and Torres Strait Islander people).
- Sociodemographic characteristics were similar for patients prescribed PrEP during the first 18 months since PBS listing and the following 18 months. These results were mirrored in the companion MedicineInsight analysis.
 - Across both time periods, most patients dispensed PBS-subsidised PrEP were male (98.7%) and the mean age was 37.1 years.
 - Supply of PrEP was highest among patients aged 30–39 years followed by those aged 20–29 years.
 - Four fifths of patients dispensed PrEP resided in a major city and approximately 11% resided in inner regional areas, with most patients residing in NSW or Victoria
 - A slightly higher proportion of patients accessed PrEP via the Closing the Gap subsidy program in the latter 18-month period (1.7% compared with 1.3%).
- Patients had a mean average of 8.0 prescriptions for PrEP over the 3-year study period or 4.4 prescriptions per person-year, which equates to a medication possession ratio (MPR) of 36.7%. This finding was much lower when compared to the MPR of 80.8% in the MedicineInsight report on prescribing and might be explained by an increase in on-demand use since the guideline change in 2020, non-adherence, changes in behaviour since COVID-19 restrictions or access to PrEP via self-importation (the cost of which is now less than the PBS-subsidised general patient co-payment).
- The mean duration of PrEP use was 1.8 years, similar to the MedicineInsight report at 1.5 years.
- Among 29,569 patients identified as having a gap in PrEP use >21 days, the mean time to first discontinuation was 110 days.
- Among 44,303 patients dispensed PrEP during the 3-year period, a fifth (19.6%) were only dispensed PrEP once, 13.7% had continuous supply and two thirds (66.7%) had non-continuous supply (i.e. one or more gaps of >21 days during the 3 years)
- According to the PBS data non-continuous PrEP use appears to be more common than continuous use, whereas a similar proportion of patients in the MedicineInsight report appeared to have continuous or non-continuous PrEP use.
- The analysis of PrEP user status at 31 March 2021 found that 54.0% had a current prescription and 46.0% had discontinued PrEP.
- The proportion of new HIV diagnoses in patients, at least 31 days following PrEP initiation, was 0.2 per 100 person-years (95% CI 0.2–0.3); higher than the incidence seen in the EPIC-NSW study (0.048 per 100 person-years; 95% CI 0.012–0.195) and similar to the accompanying MedicineInsight report (0.3 per 100 person-years; 95% CI 0.2–0.5)

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 PBS analysis.

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 PrEP¹ 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 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

¹ 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).

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.

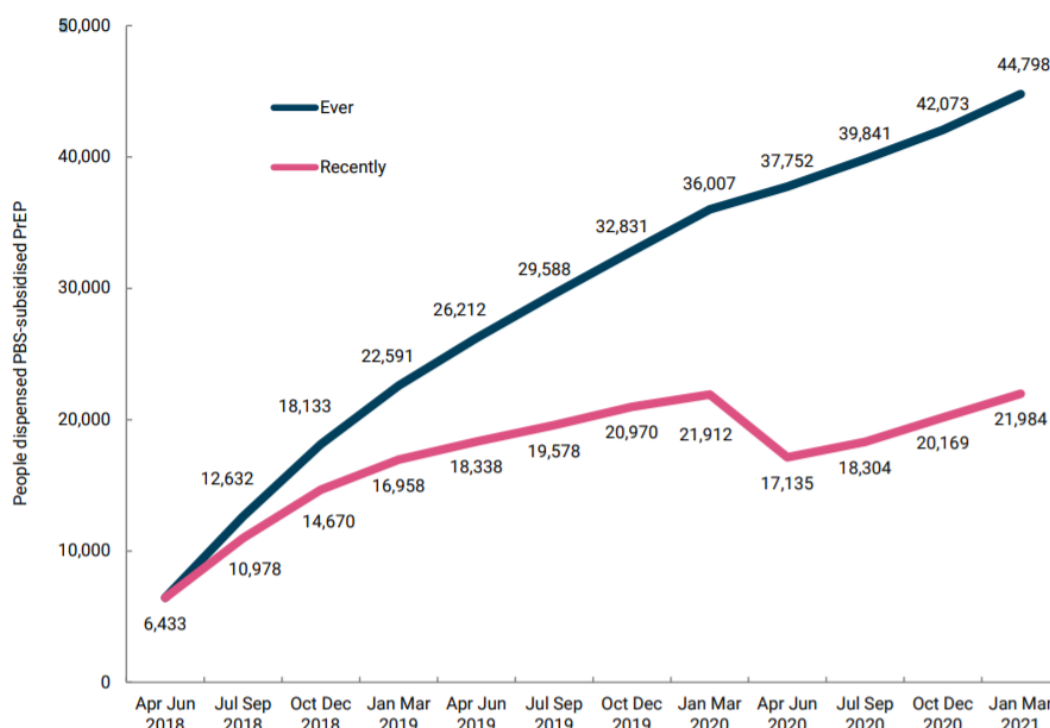


Figure 1. Cumulative (total) number of people with one or more dispensed PBS-subsidised PrEP prescription from 1 April 2018 (ever) compared to the estimated number who have used PBS-subsidised PrEP in each quarter (recently)⁴

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). There are separate PBS items codes for use of tenofovir disoproxil + emtricitabine tablets for the indication of HIV treatment and the indication of PrEP (Table 1).

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 Items (PReP)	PBS Items (HIV)
tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet	Truvada	J05AR03	11276L	10347N
			11296M	10946D
tenofovir disoproxil fumarate 300 mg + emtricitabine 200 mg tablet	Tenofovir/Emtricitabine APOTEX		11306C	10966E
			12542D	11146P
tenofovir disoproxil maleate 300 mg + emtricitabine 200 mg tablet	Tenofovir Disoproxil Emtricitabine Mylan			11149T
tenofovir disoproxil phosphate 291 mg + emtricitabine 200 mg tablet	Tenofovir EMT GH			12506F

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

The analyses used 3 years of data from the PBS supplied prescriptions database, managed by Services Australia, for dates of supply from 1 April 2018 up to and including 31 March 2021; extracted August 2021. The PBS supplied prescriptions database includes data submitted to Services Australia for payment of a PBS or Repatriation PBS (RPBS) subsidy by the Government by all approved pharmacies in Australia. These prescription data were used to determine the number of prescriptions supplied, patient category (general/RPBS, concessional or under co-payment) and for the PBS expenditure analysis.

Study ethics and approval

This project was given approval in July 2021 by the Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee (NREEC 21-086).

The release of PBS data for this study was approved by the Department of Health's Data Access and Release Policy committee and the public interest certificate (PIC) for use of PBS data for this study was approved by the Chief Data Steward.

Patient count analysis

To be eligible for inclusion in the study, patients must have had at least one PBS or RPBS prescription for tenofovir disoproxil + emtricitabine, identified using the PBS item numbers listed in Table 1, dispensed between 1 April 2018 and 31 March 2021, and no HIV antiretroviral medicine prior to or up to 7 days after the first prescription for tenofovir disoproxil + emtricitabine. Only patients aged 18 or older in each time period were included in analyses.

Patients who were dispensed tenofovir disoproxil + emtricitabine under the PBS item number for HIV treatment were included in the PrEP cohort, if they had previously been prescribed this medicine under a PBS item for PrEP and were not dispensed any other antiretroviral medicine for HIV throughout the study period. Patients who were dispensed tenofovir disoproxil + emtricitabine under the PBS item number for HIV treatment but had not previously been prescribed this medicine under a PBS item for PrEP were excluded from the PrEP cohort (n=596).

Prevalent patients were counted per year for the following periods:

- April 2018 to March 2019 (2018–19)
- April 2019 to March 2020 (2019–20)
- April 2020 to March 2021 (2020–21)

Prescription count analysis

Prescriptions (PBS and RPBS) for PrEP dispensed to patients included in the study (as per the patient count analysis described above) between 1 April 2018 to 31 March 2021 were identified.

Prescriber type (specialist, GP, nurse) was attributed to the de-identified approval number of the prescriber by Services Australia and was based on the major field of specialty, derived from the combination of the current registered specialty and the most PBS services provided per quarter. Prescribers can work in several different specialties but are allocated by Services Australia to one major field of specialty per quarter.

Analysis of expenditure

Expenditure was analysed for prescriptions dispensed to patients included in the study (as per the patient count analysis described above) between 1 April 2018 to 31 March 2021. This analysis used information from the PBS supplied prescriptions database on the 'benefit paid by government, less patient co-payment' based on the published listed price. The analysis did not include any changes in the cost of other drugs.

As this analysis uses date of supply prescription data, there may be small differences compared with publicly available Services Australia Medicare date of processing data. The publicly available Medicare data only includes subsidised R/PBS prescriptions with prescriptions under the patient co-payment not included. The data used in this report includes under co-payment prescriptions from 1 April 2012.

Closing the gap (CTG) indicator

This analysis used information from the Closing the Gap (CTG) PBS Co-payment Program. This program is available to Aboriginal and Torres Strait Islander people of any age who are:

- registered with Medicare;
- in the opinion of a prescriber or Aboriginal Health Practitioner would experience setbacks in the prevention or ongoing management of a condition if the person did not take the prescribed medicine and
- unlikely to adhere to their medicines regimen without assistance.

PBS prescriptions dispensed under the CTG program were used as a proxy for indigenous status, noting that not all Aboriginal and Torres Strait Islander people will participate in the program and this will underestimate the true rate of dispensing to Aboriginal and Torres Strait Islander people.

Patterns of PrEP use

Continuous or non-continuous patterns of PrEP use were defined based on gaps between dispensed PrEP prescriptions. A patient's pattern of PrEP use was classified as 'continuous' if they never had more than a 21-day gap between the expected end of one dispensed PrEP prescription (i.e. 30 days after the date of supply) and the date of the next dispensed PrEP

prescription. Patients had a 'non-continuous' pattern if they had one or more gaps of > 21 days. 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

If the last date of supply was 120 days or less than the end of the study period (31 March 2021), the patient was classified as actively using PrEP. If their last dispensed PrEP was more than 120 days before the end of the study period the patient was classified as having discontinued. The 120 day period was chosen to account for 30 days of supply plus an additional 90 days to account for missed doses, non-adherence, and intermittent or on demand use.

Calculating duration of PrEP use (in days)

The duration of PrEP use was calculated from the date of supply of their first dispensed PrEP during the study period (the index date) until the date of supply of their last dispensed PrEP plus 120 days.

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

Patient time (follow-up) in the study commenced on the date of supply of the patient's first dispensed PrEP (the index date) and ended at the earliest of:

- the end of the study (31 March 2021)
- the first date of supply of a medicine indicated for the treatment of HIV, other than tenofovir disoproxil + emtricitabine (a proxy for HIV diagnosis).

Date of death was not available for this report. Person time may have been overestimated for patients who died or left Australia during the study period.

HIV diagnoses among patients prescribed PrEP

Patients who were dispensed a prescription for an HIV antiretroviral medicine before, or up to 7 days after, their first dispensed PrEP were excluded.

Patients were considered to have been diagnosed with HIV if they were dispensed an HIV antiretroviral medicine (other than tenofovir disoproxil + emtricitabine) at least 8 days following their first dispensed PrEP.

A sensitivity analysis excluding patients who had a prescription dispensed for an HIV medicine, before, or up to 30 days after, their first dispensed PrEP was conducted. In the sensitivity analysis patients were considered to have been diagnosed with HIV if they were dispensed an HIV antiretroviral medicine (other than tenofovir disoproxil + emtricitabine) at least 31 days following their first dispensed PrEP.

Statistical analysis

Analyses of the data were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Statistics included frequencies, proportions and measures of central tendency of numeric data as appropriate.

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.

Results

Study Selection Flow Chart

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

There were 44,931 patients with a prescription for tenofovir disoproxil + emtricitabine dispensed at least once between 1 April 2018 and 31 March 2021. After excluding patients aged <18 years and patients who appeared to be taking tenofovir disoproxil + emtricitabine for the treatment of HIV, there were 44,303 adult patients dispensed PrEP during the study period (Figure 1). This is similar the most recent numbers reported in the 2021 Australian HIV surveillance report published by the Kirby Institute⁴ which reported 44,798 people had received PBS-subsidised PrEP at least once in the period up until 31 March 2021.

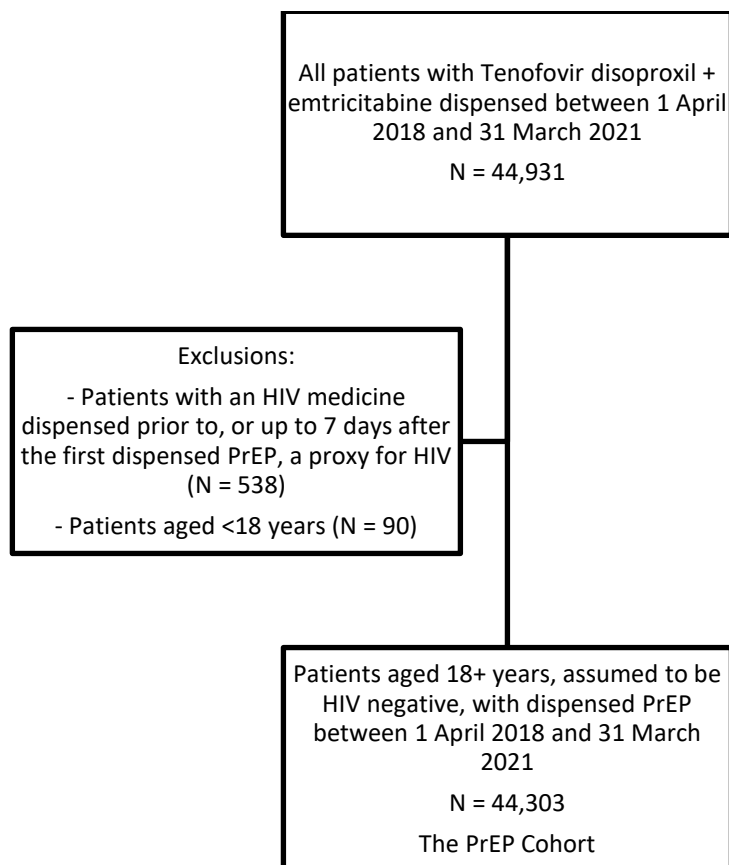


Figure 2: Study flow chart of patients

Number of prescriptions for PrEP dispensed

In the first year since PBS listing (1 April 2018 to 31 March 2019), 77,512 PrEP prescriptions were dispensed, and in the second year since listing (1 April 2019 to 31 March 2020) this figure increased by 80.8% to 140,142 prescriptions. There were 134,773 prescriptions for PrEP dispensed in the third year since listing (1 April 2020 to 31 March 2021), representing a 3.8% reduction compared to the second year (Table 2, Figure 3); this reduction is likely explained by the impacts of the COVID-19 restrictions on sexual practice and visits to healthcare providers.

Expenditure

Government expenditure on PrEP in the first year since PBS listing (2018–19) was \$20.3 million (Table 2; Figure 3). Expenditure on PrEP rose only slightly in the second year (2019–20), to \$21.3 million, despite an 88.8% increase in the total number of prescriptions dispensed and then almost halved in the third year (2020–21) to \$11.4 million despite prescription numbers only falling by 3.8%. (Table 2; Figure 3). This is due to a 58% reduction in price from an approved ex-manufacturer price (AEMP) of \$220.34 per pack of 30 at the time of listing to \$92.49 as of 1 August 2020.⁶ These reductions have largely been driven by price disclosure. Price disclosure reductions were applied to PrEP in April 2019 and April 2020,⁷ reflected in the average cost per prescription steadily decreasing from \$262 per

prescription the first year since PBS listing (2018–19) to \$85 per prescription by the third year (2020–21) (Table 2; Figure 4).

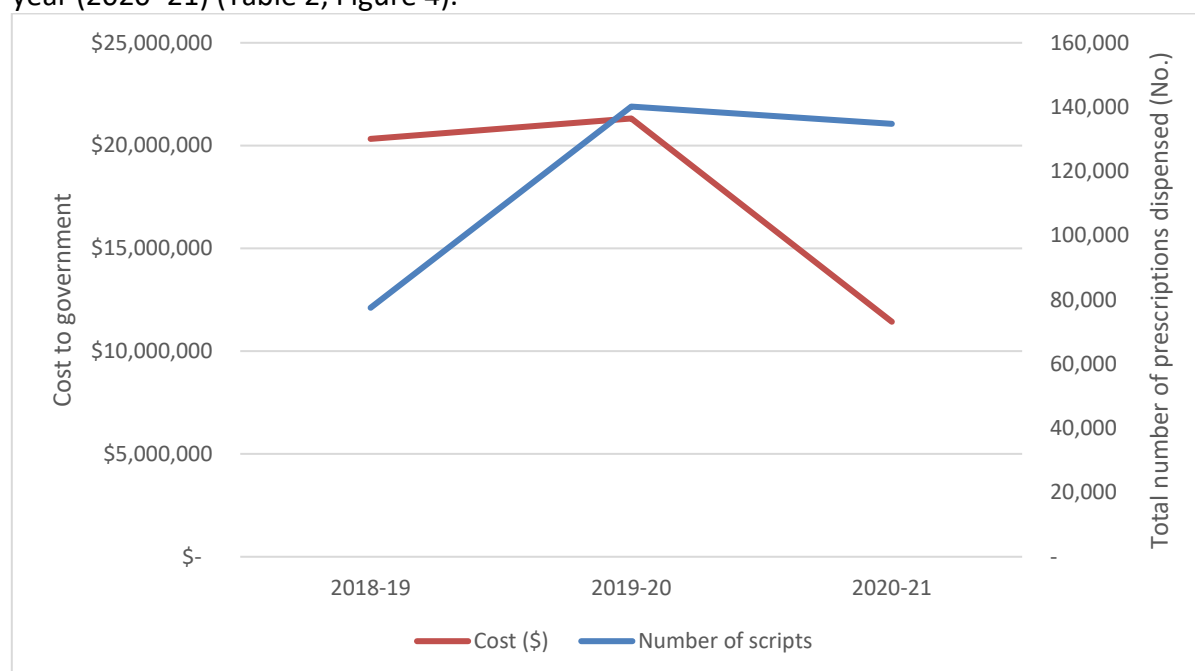


Figure 3: Number of prescriptions for PrEP dispensed and cost to government for prescriptions supplied for PrEP(\$), since listing on 1 April 2018 to 30 March 2021.

2018-19 - 1 April 2018 to 31 March 2019; 2019-20 - 1 April 2019 to 31 March 2020; 2020-21 - 1 April 2020 to 31 March 2021.

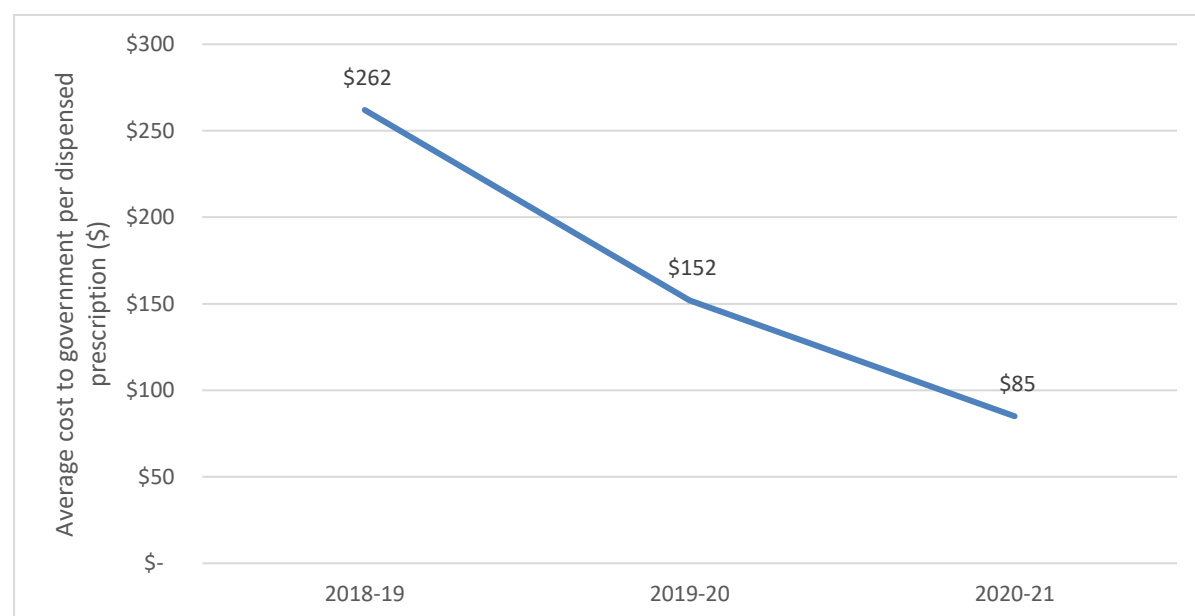


Figure 4: Average cost to government per script (\$) by since listing on 1 April 2018 to 30 March 2021

2018-19 - 1 April 2018 to 31 March 2019; 2019-20 - 1 April 2019 to 31 March 2020; 2020-21 - 1 April 2020 to 31 March 2021.

Table 2: Number of prescriptions supplied for PrEP (No.) and cost to government (\$) of all supplied prescriptions for PrEP by calendar year

	April 2018 to March 2019 (2018-19)	April 2019 to March 2020 (2019-20)	April 2020 to March 2021 (2020-21)
PrEP (No.)	77,512	140,142	134,773
Cost (\$)	20,330,934	21,318,400	11,432,061
Average cost per script (\$)	262	152	85

Prescriptions by prescriber type

The majority of dispensed PrEP prescriptions were from GPs (Table 3; Figure 5). Excluding prescriptions where the prescriber type was missing or unassigned, GP prescribing accounted for 84% to 86% of all prescriptions since the PBS listing, specialist prescribing from 15% to 13% and nurse prescribing 1%.

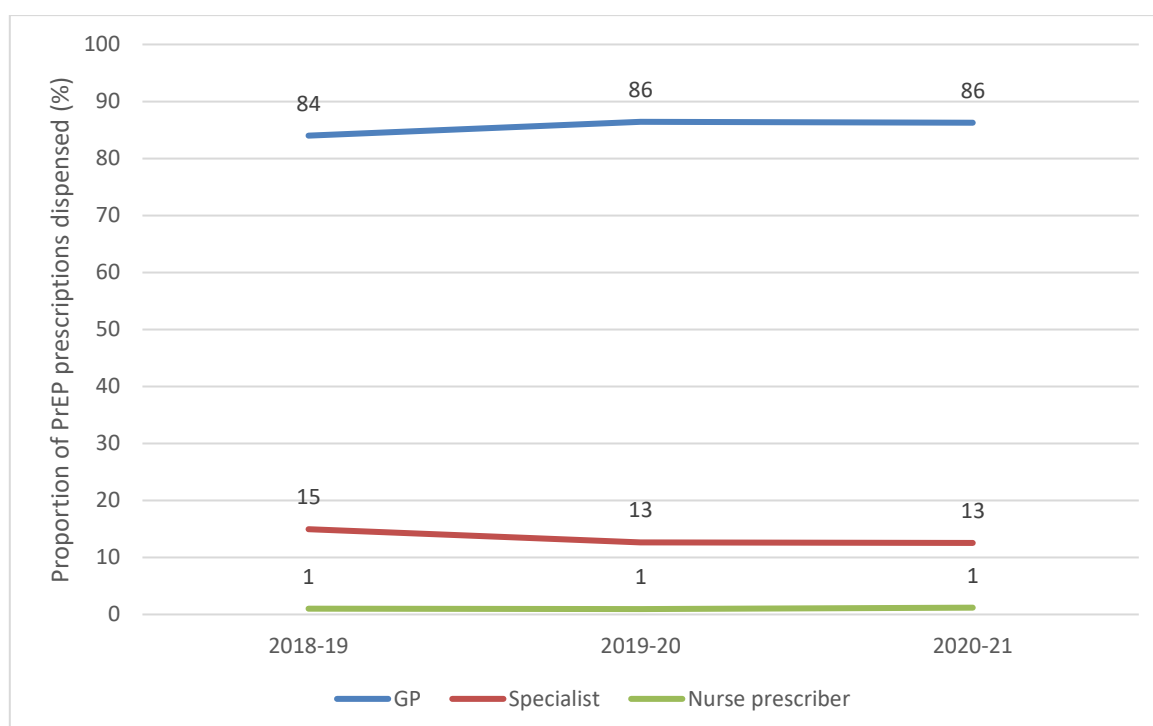


Figure 5: Proportion (%) of dispensed prescriptions for PrEP by prescriber type (excluding prescriptions with missing prescriber type), since listing on 1 April 2018 to 30 March 2021

2018–19 - 1 April 2018 to 31 March 2019; 2019–20 - 1 April 2019 to 31 March 2020; 2020–21 - 1 April 2020 to 31 March 2021.

Table 3: Number and proportion of dispensed prescriptions for PrEP by prescriber type

Prescriber type	April 2018 to March 2019 (2018-19) No. (%)	April 2019 to March 2020 (2019-20) No. (%)	April 2020 to March 2021 (2020-21) No. (%)
Total	77,512 (100%)	140,142 (100%)	134,773 (100%)
Prescriber			
GP	62,935 (81.2)	111,275 (79.4)	104,945 (77.9)
Specialist	11,209 (14.5)	16,259 (11.6)	15,246 (11.3)
Nurse prescriber	778 (1.0)	1219 (0.9)	1651 (1.2)
Missing	2590 (3.3)	11,389 (8.1)	12,931 (9.6)

Number of patients dispensed PrEP

Prevalent

In the first year since PBS listing, 22,403 patients were dispensed a PrEP prescription and in the second year after listing this figure increased by 39.1% to 31,159 people (Table 4; Figure 6). In the third year after listing the number of patients dispensed PrEP remained similar, at 31,124 people (Table 4; Figure 6).

Incident (newly dispensed)

Since PBS listing, the number of patients newly dispensed PBS-subsidised PrEP at least once decreased year on year (Table 5, Figure 6). In the first year since PBS listing, 22,403 patients were dispensed a PrEP prescription for the first time, with this figure decreasing by 40.8% to 13,254 patients dispensed a PrEP prescription for the first time in the second year after listing. Between the second and third years after listing there was a 34.8% reduction in the number of patients incident PrEP, to 8640 patients in the third year (Table 5, Figure 6).

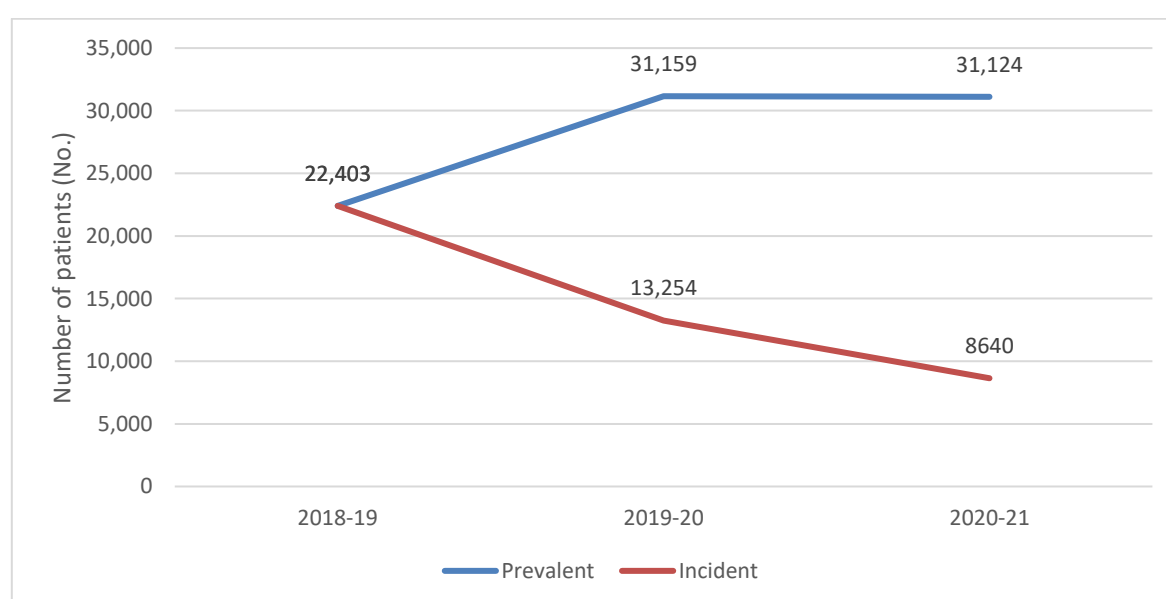


Figure 6: Count of patients prevalent (blue line) and incident (red line) to PrEP per year since listing on 1 April 2018 to 30 March 2021

2018-19 - 1 April 2018 to 31 March 2019; 2019-20 - 1 April 2019 to 31 March 2020; 2020-21 - 1 April 2020 to 31 March 2021.

These findings align with data from the Kirby Institute, showing the number of patients newly dispensed PBS-subsidised PrEP in each calendar quarter decreased over time, with the biggest drop occurring in the first quarter of 2020 (Figure 7), due to the impacts of COVID-19 restrictions on sexual practice and accessing healthcare. However, quarterly data shows that, since the second quarter of 2020, there has been an increase in the number of patients dispensed PrEP for the first time to almost pre-COVID-19 level in the first quarter of 2021.

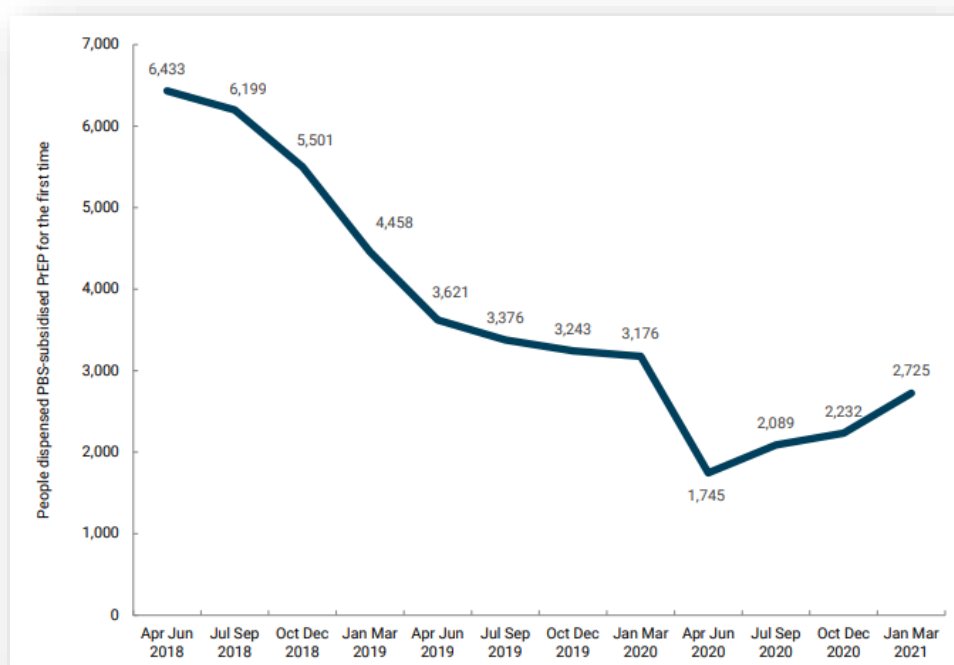


Figure 7: Quarterly count of patients newly dispensed PrEP (incident patients), April 2018 to March 2021 (from the Kirby Institute)⁴

Number of patients dispensed PrEP by demographics, 2018 to 2021

Prevalent

Across all age groups, the number of patients dispensed PrEP at least once increased between the first and the second year after PBS listing (Table 4). However, from the second to the third year after PBS listing there was a small decline in the number of people aged

18–29 and 20–29 years who were dispensed PrEP and a small increase in the number of people aged 30+ years who were dispensed PrEP (Table 4, Figure 8).

The number of males dispensed PrEP at least once increased by approximately 40% from 22,159 male patients in 2018–19 to 30,793 males in 2019–20 and then remained similar in 2020–21 at 30,803 males (Table 4). Similarly, the number of females dispensed PrEP at least once increased by approximately 50%, from 244 female patients in 2018–19 to 366 females in 2019–20 and then decreased slightly in 2020–21 to 321 females (Table 4). The largest decrease in patients dispensed PrEP between 2019–20 and 2020–21 was among females aged 20–29 years (27.5% decrease) (Table 4, Figure 8).

Data from the Kirby Institute shows that across all age groups, the number of individuals who were recently (within the last 3 months) dispensed PrEP in each calendar quarter increased until Q1 2020 before decreasing in Q2 2020. The largest decrease was in people aged under 25 years (27.4% decrease). By the first quarter of 2021, 'recent dispensing' returned to pre COVID-19 levels among all age groups.⁴

The annual number of patients dispensed PBS-subsidised PrEP under the Closing the Gap program increased from 218 patients, or 1.0% of all patients dispensed PrEP, in 2018–19 to 443 patients, or 1.4% of all patients dispensed PrEP, in 2020–21 (Table 4, Figure 9). Not all Aboriginal and Torres Strait Islander people will participate in the CTG PBS program, therefore these findings will underestimate the true rate of dispensing to Aboriginal and Torres Strait Islander people.

Incident (newly dispensed)

Across most age groups, the annual number of patients newly dispensed PBS-subsidised PrEP at least once decreased year on year. The exception was among patients aged 18–19 years where the number of patients newly prescribed PrEP increased from the first to the second year after PBS listing before decreasing thereafter (Table 5).

The number of females who were newly dispensed PrEP, although small compared to males, increased between 2018 and 2019 and decreased thereafter (Table 5, Figure 6).

The annual number of patients newly dispensed PBS-subsidised PrEP under the Closing the Gap program decreased from 218 patients, or 1.0% of all patients dispensed PrEP, in 2018–19 to 116 patients, or 1.3% of all patients newly dispensed PrEP, in 2020–2021 (Table 5, Figure 9).

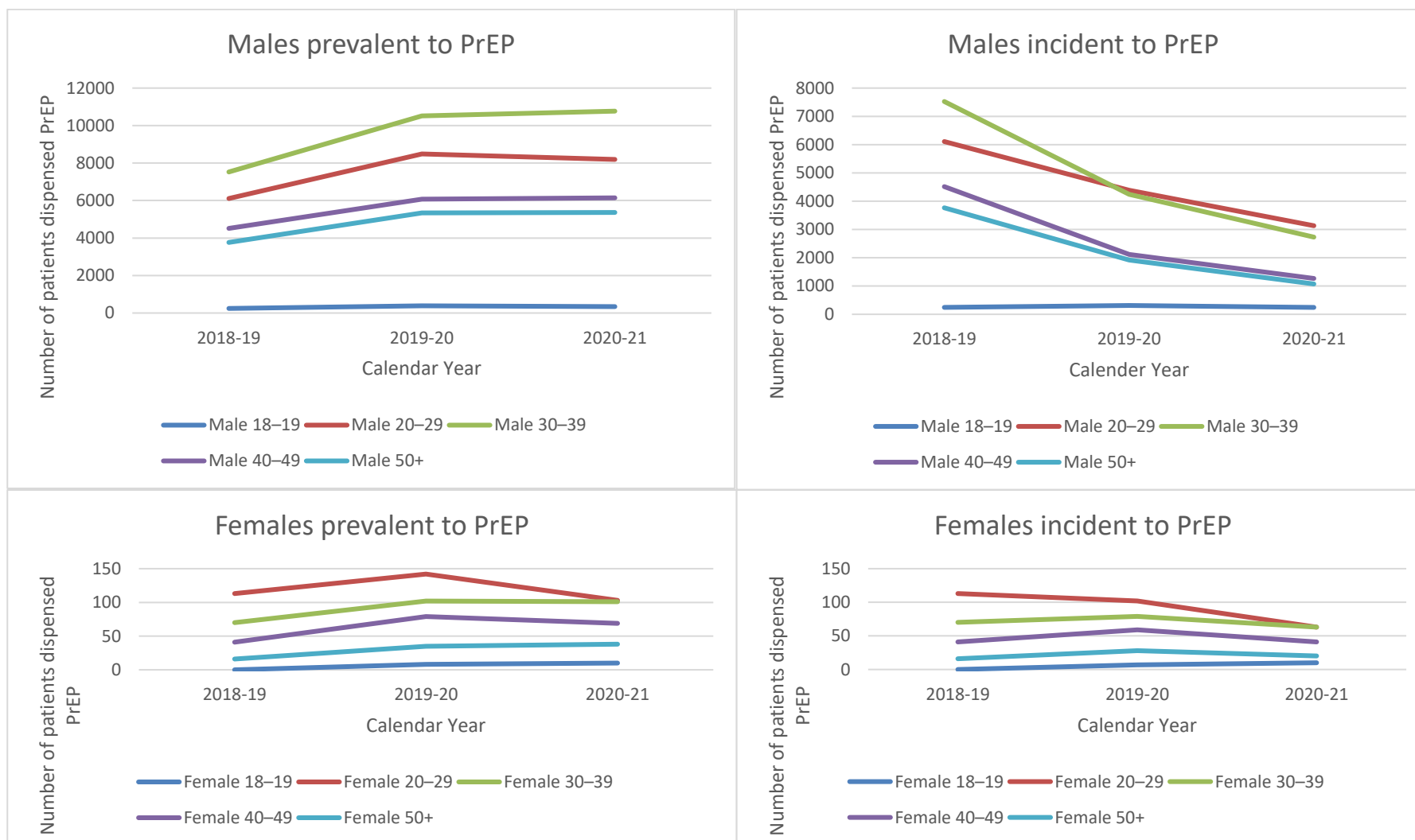


Figure 8: Annual count of patients prevalent to PrEP (males top left, females bottom left) and incident to PrEP (males top right, females bottom right) by age group, 1 April 2018 to 30 March 2021

2018-19 - 1 April 2018 to 31 March 2019; 2019-20 - 1 April 2019 to 31 March 2020; 2020-21 - 1 April 2020 to 31 March 2021.

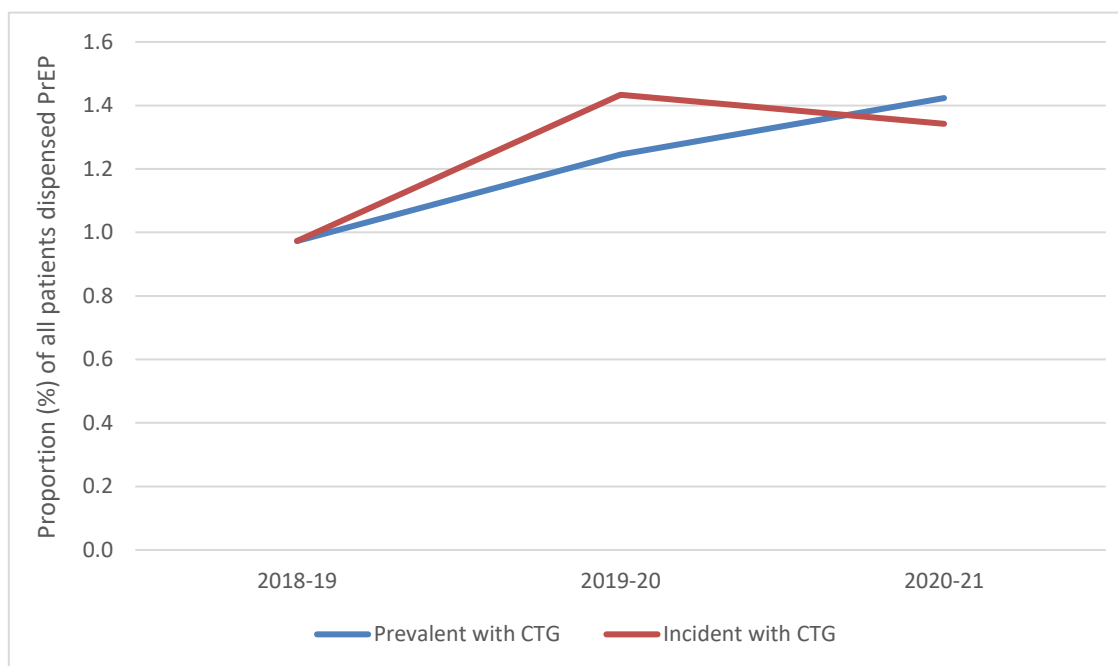


Figure 9: Annual proportion (%) of patients dispensed PrEP at least once (prevalent) with the Closing The Gap (CTG) indicator and annual proportion (%) of patients newly dispensed PrEP (incident) with the CTG indicator, 1 April 2018 to 30 March 2021

2018-19 - 1 April 2018 to 31 March 2019; 2019-20 - 1 April 2019 to 31 March 2020; 2020-21 - 1 April 2020 to 31 March 2021.

Table 4: Annual count of patients prevalent to PrEP overall, by age, sex and age-sex groups since listing on 1 April 2018 to 30 March 2021

Characteristic	2018 – 19 No.	2019 – 20 No.	2020 – 21 No.
Total	22,403	31,159	31,124
Age*			
18–19	248	392	345
20–29	6222	8628	8294
30–39	7595	10,613	10,870
40–49	4556	6151	6213
50+	3782	5375	5402
Sex			
Female	244	366	321
Male	22,159	30,793	30,803
Sex-Age group			
Female 18–19	<5	8	10
Female 20–29	113	142	103
Female 30–39	70	102	101

Characteristic	2018 – 19 No.	2019 – 20 No.	2020 –21 No.
Female 40–49	41	79	69
Female 50+	16	35	38
Male 18–19	244	384	335
Male 20–29	6109	8486	8191
Male 30–39	7525	10,511	10,769
Male 40–49	4515	6072	6144
Male 50+	3766	5340	5364
Closing The Gap (CTG) indicator			
CTG	218	388	443
No CTG	22,185	30,771	30,681

* Age calculated at the first prescription in each time period.

Table 5: Annual count of patients incident to PrEP overall, by age, sex and age-sex groups since listing on 1 April 2018 to 30 March 2021

Characteristic	2018 – 19 No.	2019 – 20 No.	2020 –21 No.
Total	22,403	13,254	8640
Age			
18–19	248	318	253
20–29	6222	4488	3195
30–39	7595	4319	2792
40–49	4556	2178	1308
50+	3782	1951	1092
Sex			
Female	244	275	197
Male	22,159	12,979	8443
Sex-Age group			
Female 18–19	<5	7	10
Female 20–29	113	102	63
Female 30–39	70	79	63
Female 40–49	41	59	41
Female 50+	16	28	20
Male 18–19	244	311	243
Male 20–29	6109	4386	3132

Characteristic	2018 – 19 No.	2019 – 20 No.	2020 – 21 No.
Male 30–39	7525	4240	2729
Male 40–49	4515	2119	1267
Male 50+	3766	1923	1072
Closing The Gap (CTG) indicator			
CTG	218	190	116
No CTG	22,185	13,064	8524

* Age calculated at the first prescription in each time period.

Demographics of patients dispensed PrEP

We compared the demographic characteristics of the 29,978 patients dispensed PrEP at least once during the first 18 months since PBS listing (T1: 1 April 2018 to 31 September 2019) to that of 37,665 patients dispensed PrEP in the following 18-month period (T2: 1 October 2019 to 31 March 2021) which included the COVID-19 period (Table 5). No significant differences were evident between patients dispensed PrEP in the two time periods (T1 and T2), in terms of age, gender, state, remoteness and participation in the CTG PBS subsidy program.

Across both time periods, most patients dispensed PBS-subsidised PrEP were male (98.7%) and the mean age was 37.1 years (Table 6). Supply of PrEP was highest among patients aged 30–39 years (33.3% and 34.1% in T1 and T2, respectively), followed by those aged 20–29 years (29.5% and 29.1% in T1 and T2, respectively). Four fifths of patients dispensed PrEP resided in a major city and around 11% resided in inner regional areas. Most patients resided in NSW (T1: 39.4%) or Victoria (T1: 32.5%). A slightly higher proportion of patients accessed PrEP via the CTG subsidy program in the latter 18 month period (1.7% in T2 compared with 1.3% in T1). Table 5.

Table 6. Sociodemographic characteristics of patients prescribed PrEP at least once during two time periods (1 April 2018 to 30 September 2019 and 1 October 2019 to 31 March 2021)

Characteristic	1 April 2018 to 30 September 2019 PrEP population N= 29,978		1 October 2019 to 31 March 2021 PrEP population N=37,665	
	Number	%	Number	%
	Sex			
Male	29,600	98.7	37,188	98.7
Female	378	1.3	477	1.3

Characteristic	1 April 2018 to 30 September 2019 PrEP population N= 29,978		1 October 2019 to 31 March 2021 PrEP population N=37,665	
	Number	%	Number	%
Age				
<i>Age mean (SE)</i>	37.1 (11.8)		37.1 (11.8)	
<i>Age group (years)</i>				
18–19	398	1.3	563	1.5
20–29	8842	29.5	10,972	29.1
30–39	9993	33.3	12,883	34.2
40–49	5830	19.4	7113	18.9
50+	4915	16.4	6134	16.3
Sex-Age group (years)				
Female 18–19	6	0.0	17	0.0
Female 20–29	168	0.6	165	0.4
Female 30–39	111	0.4	133	0.4
Female 40–49	68	0.2	107	0.3
Female 50+	25	0.1	55	0.1
Male 18–19	392	1.3	546	1.4
Male 20–29	8674	28.9	10,807	28.7
Male 30–39	9882	33.0	12,750	33.9
Male 40–49	5762	19.2	7006	18.6
Male 50+	4890	16.3	6079	16.1
State/Territory				
ACT	695	2.3	933	2.5
NSW	11,805	39.4	14,773	39.2
NT	155	0.5	187	0.5
QLD	4562	15.2	5895	15.7
SA	1091	3.6	1385	3.7
TAS	311	1.0	387	1.0

Characteristic	1 April 2018 to 30 September 2019 PrEP population N= 29,978		1 October 2019 to 31 March 2021 PrEP population N=37,665	
	Number	%	Number	%
VIC	9754	32.5	11,811	31.4
WA	1605	5.4	2294	6.1
Remoteness				
Major city	24,101	80.4	30,323	80.5
Inner regional	3412	11.4	4234	11.2
Outer regional	1633	5.4	2102	5.6
Remote/very remote	313	1.0	404	1.1
Missing	519	1.7	602	1.6
Closing The Gap (CTG) identifier				
No CTG	29,592	98.7	37,042	98.3
CTG	386	1.3	623	1.7

Patterns of PrEP utilisation

Between 1 April 2018 and 31 March 2021, a total of 352,427 prescriptions for PrEP were dispensed for 44,303 patients. The mean average number of scripts per patient was 8.0 (95% CI: 7.9–8.0) over the 3-year study period (Table 7). To account for differences in available follow-up for patients from their first prescription for PrEP until the end of the study period, or first prescription for another antiretroviral for HIV (indicating an HIV diagnosis), the average number of scripts was also calculated per person-year at 4.4 scripts for PrEP per person-year (Table 7). Assuming one prescription equates to one month's supply, this represents a medication possession ratio (MPR) of 36.7%.

The mean duration of PrEP use was 1.8 years, similar to the MedicineInsight report at 1.5 years. Among 29,567 patients identified as having a gap in therapy >21 days, the mean time to first discontinuation of PrEP was 110 days. This finding contrasts with the MedicineInsight report which found the mean time to first discontinuation to be 307 days. This could be explained by differences between dispensing and prescribing information.

Table 7: Average number of prescriptions for PrEP dispensed between 1 April 2018 and 31 March 2021

Characteristic	2018–2021 PrEP population	
	Number	95% CI
Number of prescriptions for PrEP	352,427	
Number of individuals	44,303	
Person-years		
<i>Total</i>	80,773	
<i>Mean per patient</i>	1.8	1.8–1.8
<i>Range (min-max)</i>	0 – 3.0	
The average number of total prescriptions		
<i>Mean</i>	8.0	7.9–8.0
<i>Median (IQR)</i>	5.1 (1.5–11.1)	
Number of scripts per person-year	4.4 scripts per person-year	
Duration (person-days) of PrEP exposure	29,519,429	
<i>Mean</i>	666	664–669
<i>Median (IQR)</i>	735 (435–935)	
Mean time to first discontinuation		
<i>Person-days to discontinuation (mean)*</i>	110	109–111

* The analysis of mean time to first discontinuation of PrEP was restricted to those 29,567 patients where a treatment gap was identified.

A patient's pattern of PrEP use was classified as 'continuous' if they never had more than a 21-day 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 one or more gaps of > 21 days between the expected end of one prescription and the date of the next prescription for PrEP.

Among 44,303 patients dispensed PrEP during the 3-year period, a fifth (19.6%) were only dispensed PrEP once, 13.7% had continuous supply and two thirds (66.7%) had non-continuous supply (i.e. one or more gaps of >21 days during the 3 years) (Table 8). Non-continuous PrEP use appears to be more common than continuous use according to the PBS data, whereas a similar proportion of patients in the MedicineInsight report appeared to have continuous or non-continuous PrEP use. The MedicineInsight data found that, 30.3% of patients had only one original script for PrEP recorded, 36.3% were on continuous therapy, and 33.4% appeared to have non-continuous PrEP use.

The analysis of PrEP user status at the end of the study period (31 March 2021) found that 54.0% had a current prescription and 46.0% had discontinued PrEP (i.e. their last PrEP purchase was more than 120 days before 31 March 2021).

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

Patterns of PrEP use	PrEP population	
	Number	% (95% CI)
Number of individuals	44,303	
Patterns of PrEP use		
<i>Continuous (no significant gaps between scripts)</i>	6068	13.7 (13.4-14.0)
<i>Non-continuous (gaps between scripts or on-demand dosing)</i>	29,567	66.7 (66.3-67.2)
<i>Not assessable (only one script)</i>	8668	19.6 (19.2-19.9)
PrEP status at end of follow-up		
<i>Active PrEP at end of study</i>	23,921	54.0 (53.5-54.5)
<i>Discontinued PrEP at end of study</i>	20,382	46.0 (45.5-46.5)
PrEP status at end of follow-up counting for patients with HIV		
<i>Active PrEP at end of study</i>	23,918	54.0 (53.5-54.5)
<i>Discontinued PrEP at end of study</i>	20,253	45.7 (45.3-46.2)
<i>Patients lost to follow-up due to HIV</i>	132	0.3 (0.2-0.3)

HIV in patients dispensed PrEP

We described the number of patients in the PrEP population newly dispensed an antiretroviral medicine for HIV at least 8 days following their first prescription for PrEP, according to patterns of PrEP use (Table 9). The proportion of new HIV diagnoses in patients, at least 8 days following PrEP initiation, was 0.3% (95% CI 0.2–0.3) and the incidence was 0.5 per 100 person-years (95% CI 0.3–0.7), higher than the incidence seen in the EPIC-NSW study⁸ (incidence 0.048 per 100 person-years, 95% CI 0.012–0.195).

In the sensitivity analysis we assumed patients who started an antiretroviral medicine for HIV up to 30 days after starting tenofovir disoproxil + emtricitabine, were using tenofovir disoproxil + emtricitabine for HIV all along, rather than PrEP. After excluding these patients from the PrEP cohort the incidence of HIV was 0.2 per 100 person-years (95% CI 0.2–0.3); still higher than the incidence seen in the EPIC-NSW study (0.048 per 100 person-years) but lower than the original analysis (Table 10).

There was no statistically significant difference in the proportion of new HIV diagnoses among patients on continuous versus non-continuous PrEP. The proportion and incidence of patients with a new diagnosis of HIV was higher among patients on continuous PrEP than non-continuous PrEP, although this difference was not statistically significant. (Table 9)

These findings should be interpreted with caution, noting the possibility that despite our best efforts, a patient with HIV may have been misclassified as using tenofovir disoproxil + emtricitabine for PrEP. Also, the reliance on a proxy measure of antiretroviral prescriptions

for HIV diagnosis may have led to misclassification, for example if some people started on tenofovir alafenamide + emtricitabine (Descovy) for PrEP.

Table 9: Proportion of patients on PrEP with an HIV medicine dispensed at least 8 days after commencing PrEP

PrEP status	HIV Medicine dispensed while on PrEP (n=44,303)		
	Number	% (95% CI)	rate per 100 person years, (95% CI)
All patients dispensed PrEP	132	0.3 (0.2-0.3)	0.5 (0.3-0.7)
Continuous PrEP	26	0.4 (0.3-0.6)	0.5 (0.2-0.8)
Non-continuous PrEP	59	0.2 (0.1-0.3)	0.3 (0.2-0.4)
Active	<5	0.0 (0.0-0.0)	0.0 (0.0-0.0)
<i>Active with continuous use</i>	0	-	-
<i>Active with non-continuous use</i>	<5	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Discontinued PrEP	129	0.6 (0.5-0.7)	3.5 (2.2-4.8)

Table 10: Sensitivity analysis - Proportion of patients on PrEP with an HIV medicine dispensed at least 31 days after commencing PrEP

PrEP status	HIV Medicine dispensed while on PrEP (n= 44,269)		
	Number	% (95% CI)	Rate per 100 person years, (95% CI)
All patients dispensed PrEP	121	0.3 (0.2-0.3)	0.2 (0.2-0.3)
Continuous PrEP	25	0.4 (0.3-0.6)	0.5 (0.2-0.8)
Non-continuous PrEP	61	0.2 (0.2-0.3)	0.3 (0.2-0.4)
Active	<5	0.0 (0.0-0.0)	0.0 (0.0-0.0)
<i>Active with continuous use</i>	0	-	-
<i>Active with non-continuous use</i>	<5	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Discontinued PrEP	118	0.6 (0.5-0.7)	1.4 (1.0-1.8)

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	

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