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National characteristics and trends in antiretroviral treatment in Australia can be accurately estimated using a large clinical cohort

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Abstract

Objectives: Cohort studies are often used as a national surveillance tool to monitor trends in HIV treatment and morbidity outcomes. However, there are limited studies validating the accuracy of using cohorts as a representation of the overall HIV-positive population. We compared data from a large Australian HIV-positive cohort study (Australian HIV Observational Database [AHOD]) and a 10% longitudinal sample from Australia's subsidized prescription medication scheme (Pharmaceutical Benefits Scheme [PBS]) to assess the use of cohorts for providing representative data for surveillance and monitoring purposes.

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Study Design and Setting: Basic demographics and treatment information from July 1, 2013, to March 31, 2016, were divided into half-yearly periods to compare HIV trends between AHOD ($n = 2,488$) and PBS ($n = 18,409$) patients.

Results: In both data sets, most patients were men, aged above 50 years, and primarily resided in New South Wales. Both data sets revealed a significant shift toward the increased use of integrase strand transfer inhibitors and a gradual decline in the use of protease inhibitors and nonnucleoside reverse-transcriptase inhibitors among the treated population in Australia. Similarly, a substantial increase in the use of once daily, single-tablet, fixed-dose combination regimens was also observed.

Conclusion: Our results show that observational cohort studies can serve as useful surrogate surveillance tools for monitoring patient characteristics and HIV treatment trends.

Keywords

Cohort; HIV infection; Antiretroviral treatment; Observational data; Treatment monitoring; Surveillance

1. Introduction

Antiretroviral therapy (ART) has dramatically improved over the recent decade, with newer antiretroviral regimens becoming more effective, convenient, and well tolerated [1]. During this period, there have been significant changes in treatment initiation recommendations with most recent guidelines recommending immediate initiation of ART for all HIV-infected individuals irrespective of immunological and virological indicators [2]. Together with the introduction of newer antiretroviral regimens, these changes have dramatically improved the quality of life for people living with HIV (PLHIV), resulting in higher life expectancies reaching close to that of the general population, especially for those living in high-income countries such as Australia [3]. In the current context of treatment for all and treatment as prevention, it is important to monitor demographic profiles and patterns of ART use among PLHIV because they are key components of the HIV care continuum. For countries without national HIV surveillance data, observational cohort studies of sufficient size have often been used to provide estimations for treatment and other morbidity outcomes [4–6]. However, the accuracy of using cohorts as a representation of the general population has often remained untested.

There were an estimated 25,313 PLHIV in Australia at the end of 2015, with 75% of the population estimated to be receiving ART [7]. To date, there are no national surveillance data available providing detailed demographic profiles, patterns of ART use, and clinical characteristics of HIV-positive patients in Australia. Since the early ART era, trends in treatment uptake have been reported predominantly via the Australian HIV Observational Database (AHOD), a prospective cohort study of more than 4,000 HIV-positive patients in care throughout most states and territories in Australia [8]. Although many valuable insights have been gained through AHOD [9–12], studies evaluating whether the AHOD cohort is representative of the general HIV-positive population in Australia have never been done.

Recently, data from Australia's Pharmaceutical Benefits Scheme (PBS) have become available to access through the dashboard interface "PharmDash" provided by the company "Prospection" [13]. The data set provides monthly summarized data (updated quarterly) and includes all PBS-listed drugs with HIV indications and tracks patients over time to provide insight to PBS script-purchasing behavior. By analyzing and comparing the PBS data summaries to the AHOD cohort, a more precise representation of the treatment trends in Australia can be uncovered.

In this study, we compare patterns of ART use in Australia using the 10% PBS sample and AHOD data to (1) derive a more comprehensive picture of ART trends in Australia and (2) evaluate the accuracy of using AHOD data at capturing characteristics of Australia's HIV-positive population as part of routine surveillance and monitoring.

2. Methods

The AHOD is an observational cohort study of HIV-infected individuals attending specialized general practitioner sites, sexual health clinics, and tertiary referral centers throughout Australia. It has been ongoing since 1999 with most of the patients recruited before 2004 with a second round of recruitment initiated in 2008. The primary objectives of AHOD are to monitor (1) patterns of ART use, including the efficacy of different treatment regimens related to demographic factors and markers of HIV disease stages; (2) patterns of toxicities/adverse events associated with antiretroviral treatment use; and (3) HIV- and non-HIV-related causes of death [8]. All data collected in AHOD are provided by the clinical or tertiary site that each AHOD participant attends in. No data are self-reported.

The PBS is a universal program provided by the Australian government that subsidizes prescription medications to all residents of Australia, as well as certain foreign visitors covered by a Reciprocal Health Care Agreement. Data on dispensed prescriptions (a 10% randomized sample) are updated every quarter by the PBS and supplied to a number of approved clients including the company "Prospection" that provides a dashboard interface (PharmDash) for its users to query the data [14]. The 10% PBS sample is randomized at a patient level and is de-identified and rescaled to 100% (multiplied by 10) [15]. The Australian Bureau of Statistics has validated the representativeness of the 10% ensuring equal probability of selection and that the selection method does not appear to be biased and will allow for valid inferences at a broad person level [15]. We also conducted an internal validation in 2015 by comparing the number of people on ART from a 100% cross-sectional PBS sample to the 10% sample. We found the 10% estimate had an error of only 2% nationally. Owing to its accuracy, the 10% PBS sample has been used in the HIV, viral hepatitis, and sexually transmissible infections in Australia: Annual Surveillance Report since 2015 to report estimates for the number of people taking ART each year [7]. Finally, the 10% PBS sample has been used to analyze treatment for hypertension and coronary heart disease [16,17].

The PBS sample provides a comprehensive coverage of certain demographic and treatment information on patients who were dispensed any HIV medication sold in the Australian market (and available on the PBS) at any point in time since mid-2013. The data set contains

170 million script claims and 3 million patients, including all PBS-listed drugs with HIV indications [7,15]. Currently, prophylactic use of antiretrovirals for HIV is not covered by the PBS. As such, all patients who received subsidized HIV medications are HIV positive. Owing to sensitivity and privacy issues, Prospection only provided monthly data summaries to its users. Individualized patient data could not be accessed, thus precluding our ability to perform more in-depth statistical analyses.

For this study, we considered all active AHOD patients and PBS estimates for patients receiving ART between July 1, 2013, and 31 March, 2016. PBS data collected before July 1, 2013, were excluded due to incompleteness of the data. March 2016 was the latest available reporting period for both AHOD and PBS at the time of these analyses. For AHOD, we included any patient reported to be on ART for 2 or more weeks during any of the respective periods to ensure they were on continued therapy. From the PBS sample, we included any patient who had filled at least one antiretroviral medical prescription during the retrospective period. Demographic and HIV treatment data were then summarized for each period. Demographic information included patients' age, sex, and the state/territory they resided in. State/territory was determined by the physical location of the AHOD site that the AHOD patient attended and by the purchase location recorded in the PBS sample.

For each of the respective reporting periods, ART is summarized (presented as N and proportion) in terms of individual drugs and by ART Class, including nucleoside analogue reverse-transcriptase inhibitors (NRTIs), nonnucleoside analogue reverse-transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transfer inhibitors (INSTIs), and entry inhibitors (EIs). For the reporting of ART Class for NRTIs, NNRTIs, PIs, INSTIs, and EIs, to ensure an accurate representation between the two cohorts, the total proportions are calculated after breaking down each combination agent into their respective individual compositions; that is, Truvada into emtricitabine and tenofovir disoproxil fumarate or Triumeq into dolutegravir, abacavir, and lamivudine.

Class Combo (once daily, single-tablet, fixed-dose combinations) was included as an additional category separate to the ART Class categories as means to highlight the growth in popularity of single-tablet fixed-dose combinations. It was also categorized this way in the PharmDash PBS data, where single-tablet combinations consisting of Atripla (emtricitabine/tenofovir disoproxil fumarate/efavirenz), Eviplera (emtricitabine/tenofovir disoproxil fumarate/rilpivirine), Stribild (emtricitabine/tenofovir disoproxil fumarate/elvitegravir/cobicistat), Triumeq (abacavir/lamivudine/dolutegravir), and Genvoya (emtricitabine/tenofovir alafenamide/elvitegravir/cobicistat) were grouped together into a single category called "Class Combo". To allow for comparison, we created a similar category for AHOD with the same set of antiretrovirals that were in the single-tablet fixed-dosed combination form. We further analyzed a subset of AHOD patients who were recruited after 2008 as part of a sensitivity analysis.

3. Results

During the period July 1, 2013, to March 31, 2016, an estimated 18,409 unique PBS patients had treatment dispensed and PBS reimbursement made for HIV medications, and 2,488 unique AHOD patients were reported to be on treatment during this period.

3.1. Demographics

Overall, patient demographics were comparatively similar between PBS data and AHOD (Table 1), with relatively consistent male-to-female proportions across most periods. A shift toward an older population was discovered in both data sets, with almost half of HIV patients on treatment in 2016 aged above 50 years, an approximate 8% and 9% increase (for PBS and AHOD, respectively) since 2013. AHOD patients were observed to be older than PBS patients, with 59% aged above 50 years in 2016 compared with 49% in the PBS. Most patients were living in NSW (40% for AHOD and PBS), followed by VIC and QLD. These three states NSW, VIC, and QLD account for approximately 90% of the HIV population living in Australia.

3.2. ART use

In 2013, the ART Class proportions reported from the PBS was NRTIs (57%), PIs (19%), NNRTIs (17%), InSTIs (6.6%), and EIs (0.5%). In AHOD, similar figures were also reported with NRTIs (54%), PIs (21%), NNRTIs (16%), InSTIs (6.6%), and EIs (0.7%). By 2016, there was a considerable drop in PI and NNRTI rates reported in both the PBS and AHOD, while at the same time, InSTI rates experienced a significant increase (Table 2). For PBS, the rates of PI use decreased from 19% in 2013 to 12% in 2016, and the rates of NNRTIs decreased from 17% to 13%, whereas the rate of InSTIs increased from 7% to 18%. Similarly, for AHOD, both PI and NNRTI rates decreased to 15% and 13%, respectively, and InSTI rates increased to 17%. The rate of NRTI and EI use remained stable throughout the 3-year period at approximately 55% and 0.5%, respectively, for both data sets. In terms of Class Combo use, the PBS data and the AHOD cohort experienced similar rates of increase (PBS: 70%, AHOD: 64%), where during the 3-year period, Class Combo use increased from 9% to 16% for PBS and 6% to 10% for AHOD. Figure 1 illustrates the rate of change in ART classes between the two data sets across the 2013 to 2016 period.

Table 3 presents the proportions of individual antiretroviral drugs used across the 3-year reporting period. In 2013, Truvada, ritonavir, and raltegravir were the top three most frequently used or purchased drugs for both PBS and AHOD. This remained unchanged for AHOD throughout the 3-year reporting period, whereas for PBS, Trimeq had replaced ritonavir as the second most frequently purchased drug by the start of 2016.

In the sensitivity analysis (restricting the ART summaries in AHOD to patients recruited after 2008), the proportions of patients on PIs (12.3%), NRTIs (52.1%), NNRTIs (12.9%), InSTIs (22.4%), EIs (0.4%), and Class Combo (16.3%) during the 2016 period strongly resembled the PBS data. With the exception of NRTIs and InSTIs, every other ART Class category revealed a < 1% difference compared to their PBS counterpart (Tables 1 and 2).

4. Discussion

In our comparison of the PBS data to the AHOD cohort, we observed similar demographic profiles where most HIV patients on treatment were men, with more than half aged above 50 years, and primarily resided in NSW, followed by VIC and QLD, accounting for more than 90% of the total HIV population in Australia. Very similar ART use was observed in both data sets across the 3-year reporting period, with a progressive decline found in NNRTI and PI use, while at the same time, a significant increase toward InSTI use was observed. The rate of NRTI and EI use remained stable during this period at approximately 55% and 0.4%, respectively, whereas in terms of Class Combo use, a considerable increase was observed similar to that of InSTI use.

Overall differences between the two data sets include the AHOD cohort containing a slightly higher proportion of older patients and that a greater proportion were from QLD. The AHOD is essentially a closed cohort study with most patients recruited during 1999–2000. As such, it would contain a higher proportion of older, more treatment-experienced HIV population. To refresh, the cohort efforts were made to replace lost to follow-up and deaths, along with a new recruitment round in 2008. The higher proportion of QLD patients may be an artifact of the early recruitment process, along with poorer rates of replacing patients. We do not expect any significant biases to be caused from this because the treatment guidelines remain the same across every state and territory. In terms of ART use, slight differences in the total proportions of PI, NNRTI, and Class Combo use were observed. However, the rate of change in each of the ART classes remained the same across the 3-year period in both data sets, indicating that the AHOD cohort was able to fully capture the trends displayed from the PBS data.

In terms of Class Combo use (fixed-dose single-tablet combinations), owing to the way the proportions of ART classes were calculated after breaking down each combination drug into individual components, the full effect of the increase in Class Combo use over the 3-year period was distributed across classes. As all Class Combo drugs are composed of three-to-four individual antiretrovirals (2 NRTIs + NNRTIs/InSTIs), if it was to be regarded as an entirely new ART class category, a significant decrease in the use of NRTIs would have been observed, while similarly, the increase in InSTI use would not be as obvious. Overall, the shift toward an increased Class Combo use among PLHIV in Australia was not an unexpected finding, as single-tablet regimens have been shown to improve adherence, lower health care costs, and provide greater patient satisfaction while maintaining similar levels of tolerance, safety, and reductions in mortality rates [18,19]. As recent guidelines have started to recommend for more combinations that can be purchased in a single-tablet form as part of the first-line regimen for treatment-naïve patients [20], a greater proportion of newly diagnosed patients are expected to be on Class Combo ART.

Although the AHOD cohort revealed a similar rate of increase in Class Combo use during the 3-year period, the total proportions were lower than the PBS data. One reason could be due to the reporting of fixed-dose combinations varied by sites in AHOD, with certain sites reporting only in individual components rather than as a fixed-dose combination. Another reason might be attributed to the AHOD cohort having a higher proportion of treatment-

experienced patients. As a closed cohort where most of the patients began treatment before 2004, it would be less likely for those who have been on longer durations of stable ART to switch to a newer regimen. This was evident in the sensitivity analysis, where among the group of AHOD patients recruited after 2008, comparatively higher proportions (16.3%) were found to be receiving Class Combo ART, a <1% difference to the PBS data. Similarly for the PBS data, despite the significant increase in Class Combo use observed during the 3-year period, in terms of individual drug usage, Truvada (emtricitabine/tenofovir disoproxil fumarate) and ritonavir have remained as two of the top three most dominant antiretroviral drugs for both PBS and AHOD patients, suggesting that a significant proportion of HIV patients have remained on their existing regimen. Truvada, a fixed-dose combination comprising two NRTI medications, is often taken together with an additional PI or InSTI such as ritonavir-boosted darunavir or raltegravir. This type of multiple-tablet regimen was the most common approach and is still widely prescribed today. Nevertheless, we anticipate that the usage of Class Combo ART will continue to rise as more single-tablet regimens are introduced to the HIV therapy market.

Although the PBS data offered many advantages and was able to provide a broader perspective on the overall treatment trends occurring in Australia, a number of limitations still exist such as the inability to perform statistical comparisons with AHOD due to the restrictions placed on accessing the data set (only data summaries can be obtained within PharmDash), and therefore, we were unable to track individual patients and obtain their treatment history, including ART switching. More importantly, it is limited to only tracking and monitoring data related to national prescription purchase. Many key markers such as CD4 count and viral load measurement could not be obtained from just national prescription purchase data alone, and as part of the care continuum and the need to meet the UNAIDS 90-90-90 targets, it is important to keep track of these information pieces that are best managed and obtained via observational cohorts.

In the absence of clinical data being available in the national prescription data set, cohorts should potentially be regarded as important secondary or complimentary data sources in particular for understanding treatment use and the impact on short-term (CD4 count and viral load) and long-term outcomes (such as death). Through the comparison with the AHOD data, we were able to demonstrate similarities between the two cohorts especially in terms of ART use. As such, it may be reasonable to hypothesize that the CD4 and viral load measurements as observed in AHOD patients might more broadly reflect the HIV-treated population; however, further research is required to validate this. By using data obtained from AHOD as a surrogate, our study estimates that over 70% of the PBS population (a surrogate of the Australian treated population) would have a CD4 count of 500 or above, with as little as 7.5% (95% CI: 5.8%–9.2%) having a viral load measurement of >50 copies/mL or 4.5% (95% CI: 3.1%–5.1%) with >200 copies/mL. When compared to an estimated figure of 10% population having detectable viral load (> 200 copies/mL) among patients on treatment in the United States [21], the rate of virological suppression in Australia is comparably higher among high-income countries.

Overall, we have shown that treatment data reported in the AHOD is similar to the ART treatment trends among similar patient demographics reported by the national prescription

database PBS. Observational cohort studies such as AHOD may therefore serve as useful surveillance tools for the monitoring of treatment use, especially in countries without national treatment data, and can further enhance surveillance by providing additional insight to treatment response and outcomes, which are often not available in national treatment data set such as the PBS.

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What is new?**Key Findings**

- Similar demographic profiles were observed between a large Australian HIV-positive cohort study (Australian HIV Observational Database [AHOD]) to a 10% longitudinal sample from Australia's subsidized prescription medication scheme (Pharmaceutical Benefits Scheme [PBS]) data. In both data sets, most patients were men, aged above 50 years, and primarily resided in New South Wales.
- Very similar treatment trends were observed between the two data sets. A significant shift toward the increased use of integrase strand transfer inhibitors and a gradual decline in the use of protease inhibitors and nonnucleoside reverse-transcriptase inhibitors were observed over the 3-year reporting period (2013-2016).

What this adds to what was known?

- Cohort studies are often used as a national surveillance tool to monitor trends in HIV treatment and morbidity outcomes. However, there are limited data validating the accuracy of using cohorts as a representation of the overall HIV-positive population. In our comparison of the AHOD cohort to the PBS data, our results show that minimal differences were observed between the two data sets.

What is the implication and what should change now?

- Observational cohorts, especially those of sufficient sample size, can serve as useful surrogate surveillance tools for monitoring patient characteristics and HIV treatment trends.

Fig. 1.
ART Class trend from July 2013 to March 2016. Proportions are calculated using data from Table 2.

Table 1.

Demographic data for PBS and AHOD from July 2013 to March 2016

Variables	Jul-Dec 2013		Jan-Jun 2014		Jul-Dec 2014		Jan-Jun 2015		Jul-Dec 2015		Jan-Mar 2016	
	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Total	15,630	2,313	16,350	2,268	16,890	2,205	17,290	2,157	18,150	2,070	15,130	1,451
Age, years												
<21	100 (0.64)	1 (0.04)	130 (0.8)	1 (0.04)	120 (0.71)	0 (0)	140 (0.81)	2 (0.09)	180 (0.99)	2 (0.1)	130 (0.86)	1 (0.07)
21–30	790 (5.05)	98 (4.24)	740 (4.53)	89 (3.92)	900 (5.33)	66 (2.99)	930 (5.38)	71 (3.29)	1,070 (5.9)	77 (3.72)	790 (5.22)	58 (4)
31–40	2850 (18.23)	329 (14.22)	2840 (17.37)	308 (13.58)	3,100 (18.35)	257 (11.66)	3,040 (17.58)	265 (12.29)	3,320 (18.29)	239 (11.55)	2640 (17.45)	175 (12.06)
41–50	5,510 (35.25)	732 (31.65)	5,410 (33.09)	694 (30.6)	5,490 (32.5)	620 (28.12)	5,270 (30.48)	618 (28.65)	5,530 (30.47)	558 (26.96)	4,200 (27.76)	367 (25.29)
51–60	4,120 (26.36)	689 (29.79)	4,700 (28.75)	703 (31)	4,790 (28.36)	739 (33.51)	5,180 (29.96)	709 (32.87)	5,310 (29.26)	690 (33.33)	4,710 (31.13)	479 (33.01)
61–70	1,700 (10.88)	334 (14.44)	1,880 (11.5)	340 (14.99)	1,880 (11.13)	364 (16.51)	1,980 (11.45)	342 (15.86)	2000 (11.02)	349 (16.86)	1,890 (12.49)	238 (16.4)
>70	560 (3.58)	130 (5.62)	650 (3.98)	133 (5.86)	610 (3.61)	159 (7.21)	750 (4.34)	150 (6.95)	740 (4.08)	155 (7.49)	770 (5.09)	133 (9.17)
Sex												
Female	1,580 (10.11)	184 (7.96)	1,720 (10.52)	177 (7.8)	1,790 (10.6)	177 (8.03)	1,920 (11.1)	175 (8.11)	2020 (11.13)	165 (7.97)	1,640 (10.8)	129 (8.89)
Male	14,050 (89.89)	2,129 (92.04)	14,630 (89.48)	2,091 (92.2)	15,100 (89.4)	2,028 (91.97)	15,370 (88.9)	1,982 (91.89)	16,130 (88.87)	1,905 (92.03)	13,490 (89.2)	1,322 (91.11)
State												
ACT	220 (1.39)	-	240 (1.45)	-	250 (1.47)	-	270 (1.55)	-	270 (1.47)	-	210 (1.39)	-
NSW	6,650 (42.14)	926 (40.03)	6,890 (41.71)	903 (39.81)	6,950 (40.76)	874 (39.64)	7,070 (40.56)	851 (39.45)	7,290 (39.58)	809 (39.08)	6,210 (41.04)	576 (39.7)
NT	130 (0.82)	23 (0.99)	120 (0.73)	22 (0.97)	140 (0.82)	23 (1.04)	120 (0.69)	23 (1.07)	100 (0.54)	24 (1.16)	70 (0.46)	21 (1.45)
QLD	2610 (16.54)	551 (23.82)	2680 (16.22)	539 (23.77)	2870 (16.83)	527 (23.9)	2930 (16.81)	512 (23.74)	3,270 (17.75)	489 (23.62)	2750 (18.18)	321 (22.12)
SA	670 (4.25)	24 (1.04)	710 (4.3)	24 (1.06)	750 (4.4)	24 (1.09)	720 (4.13)	24 (1.11)	810 (4.4)	24 (1.16)	670 (4.43)	20 (1.38)
TAS	150 (0.95)	-	150 (0.91)	-	170 (1)	-	200 (1.15)	-	200 (1.09)	-	180 (1.19)	-
VIC	4,260 (27)	693 (29.96)	4,540 (27.48)	687 (30.29)	4,640 (27.21)	664 (30.11)	4,800 (27.54)	656 (30.41)	5,100 (27.69)	636 (30.72)	4,000 (26.44)	458 (31.56)
WA	1,090 (6.91)	96 (4.15)	1,190 (7.2)	93 (4.1)	1,280 (7.51)	93 (4.22)	1,320 (7.57)	91 (4.22)	1,380 (7.49)	88 (4.25)	1,120 (7.4)	55 (3.79)

Abbreviations: PBS, Pharmaceutical Benefits Scheme; AHOD, Australian HIV Observational Database.

Dashes (–) indicate that data were not available. The state/territory information for each patient is determined by the physical location of the AHOD site that the patient is visiting and the location of where they purchased their scripts for PBS. Owing to patient movements, the proportions do not necessarily add up to 100%.

Table 2.

ART Class distribution for PBS and AHOD from July 2013 to March 2016

Variables	Jul-Dec 2013		Jan-Jun 2014		Jul-Dec 2014		Jan-Jun 2015		Jul-Dec 2015		Jan-Mar 2016	
	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Total drugs	54,160	8,443	57,650	8,531	59,060	8,517	62,610	8,410	64,430	8,002	51,830	5,450
ART Class												
PI	10,320 (19.1)	1,784 (21.1)	10,290 (17.8)	1,742 (20.4)	9,410 (15.9)	1,670 (19.6)	8,750 (14)	1,491 (17.7)	8,070 (12.5)	1,297 (16.2)	6,040 (11.7)	838 (15.4)
NRTI	30,610 (56.5)	4,539 (53.8)	32,370 (56.1)	4,579 (53.7)	33,170 (56.2)	4,576 (53.7)	35,490 (56.7)	4,581 (54.5)	36,590 (56.8)	4,405 (55)	29,470 (56.9)	2,983 (54.7)
NNRTI	9,360 (17.3)	1,377 (16.3)	9,670 (16.8)	1,332 (15.6)	9,350 (15.8)	1,268 (14.9)	9,200 (14.7)	1,194 (14.2)	8,800 (13.7)	1,056 (13.2)	6,550 (12.6)	683 (12.5)
InSTI	3,590 (6.6)	687 (8.1)	5,050 (8.8)	827 (9.7)	6,850 (11.6)	950 (11.2)	8,920 (14.2)	1,094 (13)	10,730 (16.7)	1,198 (15)	9,550 (18.4)	910 (16.7)
EI	280 (0.5)	56 (0.7)	270 (0.5)	51 (0.6)	280 (0.5)	53 (0.6)	250 (0.4)	50 (0.6)	240 (0.4)	46 (0.6)	220 (0.4)	36 (0.7)
Class Combo	5,090 (9.4)	531 (6.3)	5,800 (10.1)	543 (6.4)	6,370 (10.8)	567 (6.7)	7,700 (12.3)	670 (8)	9,680 (15)	769 (9.6)	8,280 (16)	560 (10.3)

Abbreviations: PI, protease inhibitor; NRTI, nucleoside analogue reverse-transcriptase inhibitors; NNRTI, nonnucleoside analogue reverse-transcriptase inhibitors; InSTI, integrase inhibitor; EI, entry inhibitor; Class Combo, single-tablet, fixed-dose combinations; PBS, Pharmaceutical Benefits Scheme; AHOD, Australian HIV Observational Database.

N is the total number of drugs per time period. This number is calculated based on using the data from Table 3, after breaking down every combination drug into its simplest components; for example, Truvada into emtricitabine and tenofovir. Each ART Class and their proportions are also calculated based on individual antiretroviral components.

Table 3.

Frequency and percentage breakdown of individual antiretrovirals for PBS and AHOD from July 2013 to March 2016

Variables	Jul-Dec 2013		Jan-Jun 2014		Jul-Dec 2014		Jan-Jun 2015		Jul-Dec 2015		Jan-Mar 2016	
	PBS N (%)	AHOD N (%)	PBS N (%)	AHOD N (%)	PBS N (%)	AHOD N (%)	PBS N (%)	AHOD N (%)	PBS N (%)	AHOD N (%)	PBS N (%)	AHOD N (%)
Total	33,600	5,949	35,240	5,981	35,220	5,938	36,200	5,733	35,140	5,290	27,360	3,532
PI												
Amprenavir	-	15 (0.3)	-	16 (0.3)	-	9 (0.2)	-	8 (0.1)	-	6 (0.1)	-	4 (0.1)
Atazanavir	2800 (8.3)	434 (7.3)	2750 (7.8)	417 (7)	2330 (6.6)	394 (6.6)	2040 (5.6)	342 (6)	1,850 (5.3)	285 (5.4)	1,270 (4.6)	178 (5)
Kaletra	1,050 (3.1)	128 (2.2)	980 (2.8)	117 (2)	850 (2.4)	99 (1.7)	670 (1.9)	80 (1.4)	460 (1.3)	64 (1.2)	300 (1.1)	41 (1.2)
Indinavir	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	-
Nelfinavir	-	3 (0.1)	-	4 (0.1)	-	3 (0.1)	-	3 (0.1)	-	4 (0.1)	-	2 (0.1)
Ritonavir	3,720 (11)	717 (12.1)	3,770 (10.7)	708 (11.8)	3,520 (10)	698 (11.8)	3,430 (9.5)	626 (10.9)	3,310 (9.4)	554 (10.5)	2510 (9.1)	368 (10.4)
Saquinavir	-	14 (0.2)	-	11 (0.2)	-	10 (0.2)	-	9 (0.2)	-	9 (0.2)	-	5 (0.1)
Intravir	40 (0.1)	8 (0.1)	30 (0.1)	6 (0.1)	30 (0.1)	5 (0.1)	30 (0.1)	3 (0.1)	30 (0.1)	3 (0.1)	30 (0.1)	2 (0.1)
Fortovase	-	2 (0.0)	-	1 (0.0)	-	1 (0.0)	-	1 (0.0)	-	1 (0.0)	-	1 (0.0)
Tipranavir	30 (0.1)	2 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)	30 (0.1)	1 (0.0)
Fosamprenavir	140 (0.4)	12 (0.2)	120 (0.3)	11 (0.2)	100 (0.3)	8 (0.1)	100 (0.3)	7 (0.1)	70 (0.2)	7 (0.1)	50 (0.2)	3 (0.1)
Lopinavir	-	47 (0.8)	-	44 (0.7)	-	35 (0.6)	-	30 (0.5)	-	17 (0.3)	-	9 (0.3)
Darunavir	1,460 (4.3)	273 (4.6)	1,600 (4.5)	288 (4.8)	1,670 (4.7)	307 (5.2)	1,750 (4.8)	300 (5.2)	1,830 (5.2)	281 (5.3)	1,520 (5.5)	183 (5.2)
Evotaz	-	-	-	-	-	-	-	-	-	-	-	-
NRTI												
Abacavir	390 (1.2)	186 (3.1)	410 (1.2)	184 (3.1)	400 (1.1)	189 (3.2)	410 (1.1)	196 (3.4)	340 (1)	182 (3.4)	210 (0.8)	126 (3.6)
Combivir	370 (1.1)	82 (1.4)	400 (1.1)	76 (1.3)	360 (1)	71 (1.2)	340 (0.9)	67 (1.2)	310 (0.9)	59 (1.1)	200 (0.7)	35 (1)
Didanosine	130 (0.4)	18 (0.3)	130 (0.4)	18 (0.3)	100 (0.3)	16 (0.3)	80 (0.2)	15 (0.3)	50 (0.1)	11 (0.2)	30 (0.1)	6 (0.2)
Lamivudine	630 (1.9)	278 (4.7)	610 (1.7)	288 (4.8)	590 (1.7)	293 (4.9)	660 (1.8)	312 (5.4)	600 (1.7)	301 (5.7)	490 (1.8)	202 (5.7)
Stavudine	60 (0.2)	12 (0.2)	50 (0.1)	12 (0.2)	50 (0.1)	6 (0.1)	40 (0.1)	5 (0.1)	40 (0.1)	5 (0.1)	30 (0.1)	5 (0.1)
Trizivir	100 (0.3)	20 (0.3)	100 (0.3)	19 (0.3)	90 (0.3)	17 (0.3)	60 (0.2)	15 (0.3)	50 (0.1)	15 (0.3)	30 (0.1)	8 (0.2)
Zidovudine	80 (0.2)	25 (0.4)	60 (0.2)	22 (0.4)	70 (0.2)	20 (0.3)	50 (0.1)	20 (0.4)	50 (0.1)	19 (0.4)	30 (0.1)	13 (0.4)
Emtricitabine	60 (0.2)	112 (1.9)	80 (0.2)	113 (1.9)	90 (0.3)	132 (2.2)	120 (0.3)	135 (2.4)	110 (0.3)	128 (2.4)	110 (0.4)	79 (2.2)
Truvada	5,500 (16.3)	779 (13.1)	5,630 (15.9)	780 (13)	5,510 (15.6)	732 (12.3)	5,360 (14.8)	662 (11.6)	5,250 (14.9)	579 (11)	4,160 (15)	415 (11.8)

Variables	Jul-Dec 2013		Jan-Jun 2014		Jul-Dec 2014		Jan-Jun 2015		Jul-Dec 2015		Jan-Mar 2016	
	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD	PBS	AHOD
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
NNRTI												
Kivexa	3,170 (9.4)	395 (6.6)	3,180 (9)	412 (6.9)	3,230 (9.2)	437 (7.4)	3,270 (9)	407 (7.1)	2110 (6)	337 (6.4)	1,390 (5)	182 (5.2)
Tenofovir	700 (2.1)	274 (4.6)	710 (2)	263 (4.4)	660 (1.9)	255 (4.3)	610 (1.7)	241 (4.2)	550 (1.6)	226 (4.3)	420 (1.5)	144 (4.1)
InSTI												
Efavirenz	910 (2.7)	208 (3.5)	810 (2.3)	183 (3.1)	710 (2)	168 (2.8)	650 (1.8)	148 (2.6)	510 (1.5)	123 (2.3)	340 (1.2)	74 (2.1)
Nevirapine	2740 (8.1)	496 (8.3)	2730 (7.7)	488 (8.2)	2520 (7.1)	469 (7.9)	2430 (6.7)	433 (7.6)	2290 (6.5)	367 (6.9)	1,770 (6.4)	239 (6.8)
Etravirine	540 (1.6)	125 (2.1)	550 (1.6)	129 (2.2)	520 (1.5)	122 (2.1)	520 (1.4)	123 (2.2)	500 (1.4)	116 (2.2)	370 (1.3)	81 (2.3)
Rilpivirine	80 (0.2)	25 (0.4)	110 (0.3)	20 (0.3)	110 (0.3)	21 (0.4)	190 (0.5)	20 (0.4)	200 (0.6)	22 (0.4)	170 (0.6)	18 (0.5)
InSTI												
Raltegravir	3,590 (10.7)	630 (10.6)	3,730 (10.6)	640 (10.7)	3,250 (9.2)	585 (9.9)	3,030 (8.4)	513 (9)	2740 (7.8)	447 (8.5)	2080 (7.5)	299 (8.5)
Dolutegravir	-	11 (0.2)	660 (1.9)	87 (1.5)	1,840 (5.2)	185 (3.1)	2440 (6.7)	253 (4.4)	2000 (5.7)	270 (5.1)	1,610 (5.8)	180 (5.1)
Elvitegravir	-	17 (0.3)	-	16 (0.3)	-	16 (0.3)	-	18 (0.3)	-	17 (0.3)	-	16 (0.5)
Cobicistat	-	13 (0.2)	-	12 (0.2)	-	13 (0.2)	-	19 (0.3)	-	18 (0.3)	-	17 (0.5)
EI												
Maraviroc	250 (0.7)	51 (0.9)	270 (0.8)	46 (0.8)	280 (0.8)	50 (0.8)	250 (0.7)	49 (0.9)	240 (0.7)	45 (0.9)	220 (0.8)	35 (1)
Enfuvirtide	30 (0.1)	5 (0.1)	-	5 (0.1)	-	3 (0.1)	-	1 (0.0)	-	1 (0.0)	-	1 (0.0)
Class Combo												
Atripla	3,560 (10.6)	394 (6.6)	3,510 (9.9)	371 (6.2)	3,360 (9.5)	345 (5.8)	3,030 (8.4)	326 (5.7)	2950 (8.4)	291 (5.5)	2090 (7.6)	183 (5.2)
Eviplera	1,530 (4.5)	129 (2.2)	1,960 (5.6)	141 (2.4)	2130 (6)	143 (2.4)	2380 (6.6)	144 (2.5)	2350 (6.7)	137 (2.6)	1,810 (6.5)	88 (2.5)
Stribild	-	8 (0.1)	330 (0.9)	30 (0.5)	880 (2.5)	72 (1.2)	1,160 (3.2)	91 (1.6)	1,610 (4.6)	102 (1.9)	1,450 (5.2)	87 (2.5)
Triumeq	-	-	-	1 (0.0)	-	7 (0.1)	1,130 (3.1)	109 (1.9)	2770 (7.9)	236 (4.5)	2900 (10.5)	180 (5.1)
Genvoya	-	-	-	-	-	-	-	-	-	3 (0.1)	30 (0.1)	22 (0.6)

Abbreviations: PI, protease inhibitor; NNRTI, nucleoside analogue reverse-transcriptase inhibitor; NNRTI, nonnucleoside analogue reverse-transcriptase inhibitor; InSTI, integrase inhibitor; EI, entry inhibitor; Class Combo, combination ART; PBS, Pharmaceutical Benefits Scheme; AHOD, Australian HIV Observational Database.

Proportion is calculated by the total number of antiretrovirals. Dashes (–) indicate that data were not available. Total cost is calculated as the total value of the PBS benefits paid + patient contributions.