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Alberta Real-World Evidence Consortium

Retrospective Database Analysis to Estimate Adherence Rates in PLHIV in Canada

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Executive Summary

Background

The development of highly efficacious antiretroviral therapy (ART) has drastically reduced the mortality and morbidity of Human Immunodeficiency Virus (HIV) patients in Canada and other high-income countries [1-3]. ART works by inducing viral suppression and slowing down disease progression. However, ART is associated with side effects and a complex pill burden which might in turn influence adherence [4]. All treatment regimens require daily, multi drug and lifelong therapy administration [5] to achieve viral suppression.

Multiple studies have shown that optimal adherence levels required to achieve viral suppression and prevent disease transmission are as high as 90-95% [7-9]. Newer ARTs might be able to achieve similar results with lower levels of adherence [10]. However, many patients living with HIV remain at suboptimal adherence levels [4, 7, 11, 12]. Suboptimal adherence has both clinical and economic consequences, including onwards transmission of the disease, decreased health related quality of life and higher healthcare costs.

New therapies that aim to improve adherence through simplified regimens (i.e. single tablets) or less frequent administration (i.e. long-acting treatments) have the potential to address significant gaps in the care pathway. However, there is a lack of evidence on the 'real-world' adherence patterns and number of patients who fail to achieve optimal adherence in Canada.

The aims of this study pertain to the patients living with HIV in the province of Alberta and are as follows: a) to describe adherence rates to ART, b) to describe baseline characteristics (demographic and co-medications), c) to compare ART adherence rates for different baseline characteristics and estimate predictors of adherence, and d) to describe how ART adherence rate changes overtime.

Methods

A research team at the University of Calgary examined data sourced for Saskatchewan, Manitoba, New Brunswick, Newfoundland, and Ontario from the National Prescription Drug Utilization Information System [17] via the Canadian Institute for Health Information data holdings. Alberta prescription claims data was sourced from the Pharmaceutical Information Network database [18]. Each dispensation was used as a proxy for drug use of a patient. This is a retrospective, observational cohort study of HIV patient's medication history. Patients were enrolled in the study if they had ART claims in the data sets from April 1st, 2010 to December 31st, 2019, with follow-up starting from the date of first dispensation of a core agent ART or single-tablet regiment on or after April 1st, 2010. Methods for defining covariates like comorbid conditions, pill burden, chronic disease score, treatment-naive vs treatment-experienced, are all explained in this report. The outcome variable is adherence, calculated based on proportion of days covered by filled prescriptions. Using Anatomical Therapeutic Chemical codes,

rigorous methods were undertaken to prepare the data for accurate counts of single and multi-tablet regimens, and to identify comorbid conditions mapped to prescribed medications when that data was available. Descriptive statistics, univariate, and multivariate binomial regression were used to describe the sample characteristics and factors associated with adherence. Sensitivity analyses were performed to compare the effect of different simulated levels of interruption and of different definitions for multi-tablet regimens on adherence. The impact of missing claims in some provinces (i.e. private claims) was also investigated for Manitoba and Saskatchewan where all claims (public and private) were available.

Results

Of the 16,391 patients studied in Canada, the overall adherence rate was high (mean 93.71%). Using Ontario as reference, overall adherence rate remained statistically consistent across the provinces except for Saskatchewan, where it was lower. For Canada, 72.02% were male with the majority being ≥35 and <65 years of age. For Western Canada where concomitant drugs were available, pill burden score was just below 1 and patients most frequently reported between 1 and 2 comorbid conditions. Most frequently appearing HIV specific comorbid conditions were depression, insomnia, hypertension, hyperlipidemia, psychotic illness, and opioid dependence.

When examining factors affecting adherence, there was no difference between single or multi-drug regimes. Men were 1.37 times more likely to be adherent than women. There were also greater odds of adherence in the older subgroups ≥35 to <65 and ≥65.

Predictors of adherence were conducted for patients with 6 months of baseline characteristics. Men were statistically more adherent, although mean/median differences may not be clinically significant. By age, the older the subgroup, the greater level of adherence. Unlike the analysis above, single treatment regimens were associated with higher overall adherence than multi-tablet regimens. These results were robust to sensitivity analysis for different simulated levels of interruption. Several HIV-specific comorbid conditions were significantly associated with higher adherence levels, namely, hyperlipidemia, hypertension, and diabetes. Paradoxically, higher pill burden was associated with a higher adherence.

Using different definitions for multi-tablet regimens had a stronger impact on the results than changing the level of interruption.

Supplementary analysis of medications, funded by public vs private insurance, seemed to indicate that missing private claims would yield to overestimate adherence when a simple definition for multi-tablet regimens was considered, and to underestimate adherence when a more refined definition for multi-tablet regimens was considered.

Abbreviations

ATC	Anatomical Therapeutic Chemical
ART	Antiretroviral Therapy
CA	Core Agent
CDS	Chronic Disease Score
DHHS	Department of Health and Human Services
HIV	Human Immunodeficiency Virus
ID	Identification
IQR	Interquartile Range (Median)
INSTI	Integrase Strand Transfer Inhibitor
MTR	Multi-Tablet Regimen
NPDUIS	National Prescription Drug Utilization Information System
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
NRTI	Nucleoside/Nucleotide Reverse Transcriptase Inhibitor
OR	Odds Ratio
PDC	Proportion of Days Covered
PI	Protease Inhibitor
PIN	Pharmaceutical Information Network
PLHIV	Patients Living with Human Immunodeficiency Virus
SD	Standard Deviation (Mean)
STR	Single-Tablet Regimen

Introduction

Background

The development of highly efficacious antiretroviral therapy (ART) has drastically reduced the mortality and morbidity of Human Immunodeficiency Virus (HIV) patients in Canada and other high-income countries [1-3]. ART works by inducing viral suppression and slowing down disease progression. However, ART is associated with side effects and a complex pill burden which might in turn influence adherence [4]. All treatment regimens require daily, multi drug and lifelong therapy administration [5] to achieve viral suppression.

The July 2019 the Department of Health and Human Services (DHHS) guidelines state that an ART regimen should consist of two nucleoside reverse transcriptase inhibitors (NRTIs) administered in combination with a core agent (CA) from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) [5]. In Canada, physicians generally follow the DHHS guidelines except for British Columbia and Quebec which have developed independent provincial guidelines, however, in each case, the DHHS guidelines remain an important reference [6]. Importantly all treatment regimens require daily, multi drug and lifelong therapy administration [5].

Multiple studies have shown that optimal adherence levels required to achieve viral suppression and prevent disease transmission are as high as 90-95% [7-9]. Newer ARTs might be able to achieve similar results with lower levels of adherence [10]. However, many patients living with HIV (PLHIV) remain at suboptimal adherence levels [4, 7, 11, 12]. Poor adherence is associated with various social factors such as age, socio-economic status and drug or alcohol use [14]. Consequently, suboptimal adherence has both clinical and economic effects, including transmission of the disease, decreased health related quality of life, and higher healthcare costs. In addition, there is a strong association between complex treatment regiments (i.e. daily administration and multiple pills) and poor adherence [4, 8, 12-16]. In Canada, a study of HIV positive, illicit drug users showed just 27% were optimally adherent (≥95%) [12]. Adherence in the US ranges from 65% in Medicaid-insured populations to 79% in commercially insured populations [11].

Rationale

Adherence to ART for patients living with human immunodeficiency virus (PLHIV) has been shown to be suboptimal across different geographies. Adherence is critical to the effectiveness of treatment of HIV in maintaining viral suppression and reducing transmission as well as reducing the risk of developing resistance to ART. In recent years, a variety of highly efficacious treatment regimens have been developed that have turned HIV infection into a chronic yet manageable condition. Despite this, many patients remain sub-optimally adherent.

New therapies that are associated with improved adherence through simplified regimens (i.e. single tablets) or less frequent administration (e.g. long-acting treatments) have the potential to address significant gaps in the care pathway however, there is a lack of evidence quantifying suboptimal adherence in Canada. Robust data on 'real-world' adherence patterns are thus required to fill the evidence gap.

Objectives

The aim of this study was to increase understanding of adherence patterns and the number of patients that have challenges with daily adherence to their ART across Canada, Western Canada, and Alberta.

The primary objectives of this study of HIV patients are:

1. To describe adherence rates to ART in PLHIV

The secondary objectives of this study of HIV patients are:

2. To describe baseline PLHIV characteristics (demographic and co-medications)
3. To describe and compare ART adherence rates for different baseline characteristics of PLHIV and estimate predictors of adherence
4. To describe how ART adherence rates change over time in PLHIV

Methods

Ethics

Ethics approval for this study was obtained from the University of Calgary Conjoint Health Research Ethics Board (CHREB).

Data Sources

Prescription claims data were sourced for Saskatchewan (SK), Manitoba (MB), New Brunswick (NB), Newfoundland (NF) and Ontario (ON) from the National Prescription Drug Utilization Information System (NDPUIS) [17] via the Canadian Institute for Health Information (CIHI) data holdings. Alberta prescription claims data was sourced directly from the Pharmaceutical Information Network (PIN) database [18]. Each record in each database represents a drug dispensation which was used as a proxy for drug use of a patient. Raw variables included the Anatomical Therapeutic Chemical (ATC) code, brand name, dispensation date, and supply days. Demographic information for the patient (age and gender) were also included. For SK and MB, all the claims were available, and it was known whether these claims were public or private. For AB, all the claims were also available, but the information on public vs private was not labelled in the database. For all the other provinces (i.e., NL, NB, and ON)

only public claims were available. Finally, for AB, SK, and MB, concomitant drugs were made available. This is summarized in Table 1.

Province	Database	Start of the	End of the	Public/Private claim	Concomitant drugs
AB	PIN	2009/10/01	2019/12/31	No	Yes
MB	NDPUIS	2015/04/01	2019/03/31	Yes	Yes
NL	NDPUIS	2010/04/01	2019/03/31	No	No
NB	NDPUIS	2010/04/01	2019/03/31	No	No
ON	NDPUIS	2010/04/01	2019/03/31	No	No
SK	NDPUIS	2010/04/01	2019/03/31	Yes	Yes

Table 1: Database characteristics.

Study Design

This is a retrospective, observational cohort study focussed on HIV patients in Canada, with a particular focus on western provinces and Alberta. To address the study objectives, Canadian secondary data sources containing prescription drug claim information were utilized to extract and analyse individual-level data.

Prescription drug claims data is often used in longitudinal studies for measuring drug adherence [4, 11]. The databases include a unique patient identifier (ID), which can enable a longitudinal look at patients to analyze drug adherence via dispensed prescription patterns for ART medications. These sources are used for high quality observational studies and external communication with the scientific community.

Patients from AB, SK, NB, NL, and ON with ART claims were enrolled into the study from April 1st, 2010 onwards with MB patients enrolled from April 1st, 2015 onwards (due to data availability). The follow-up period is from the index date (defined as the date of first dispensation of an ART on or after the corresponding enrollment date stated) and lasts at least 12 months until the end of the study period (defined as December 31st, 2019, date of last ART dispensation, or the end of database register, whichever comes first).
The baseline period is defined as 6 months prior to the index date. For AB, the baseline period is equal to 6 months for all the patients as data 6 months prior to April 1st, 2010 was made available. For all the other provinces, the baseline period could be less than 6 months.

Study Population

For a patient to be eligible for this study, they fell within the following inclusion and exclusion criteria. To be included, the patient must have at least one claim for dispensation of ART recorded between the corresponding enrollment dates stated above and the last available date at the time of extraction. Patients were excluded if they

were less than 18 years old at the index date, did not have at least one claim for dispensation of an ART (as defined in Table 16, see Appendix A), did not have a follow-up recorded in the dataset more than 12 months following the index date, or had a treatment interruption within 12 months following the index date. Treatment interruption is further defined in *Data Processing* below.

Variables

Co-variables:

The co-variables are defined as:

- Age: defined at index date and was treated as a continuous variable
- Sex: male or female at index date as a categorical variable
- Type of treatment regimen at index date (categorical):
    - Single tablet regimen period (STR)
    - Multi tablet regimen period (MTR)
- Treatment-naïve / Treatment-experienced: patients are considered naïve to treatment if they have no CA or STR (defined in Table 16, see Appendix A) dispensations in the baseline period. Otherwise, patients are considered treatment experienced. Also, if, for a patient, the baseline period is less than 6 months, the patient is treatment experienced.

Comorbidities and Co-medications:

In this study, common HIV comorbid conditions were analysed using concomitant medications as a proxy for the condition or illness following previous study methods (Table 18, see Appendix A) [19]. The baseline period was used for comorbidity identification. The presence of hepatitis B, hepatitis C, hyperlipidemia, hypertension, depression, psychotic illness, diabetes, liver failure, insomnia, osteoporosis, and opioid dependence were evaluated separately for their existence in the baseline period. The condition was considered present if at least one dispensation of a medication for the specific disease was identified in the baseline period.

Chronic Disease Score (CDS) was calculated based on the presence of ATC codes for select chronic conditions and was used to evaluate baseline comorbidities of HIV patients [20]. The CDS is widely used in epidemiological studies to report on comorbidities based on the presence and complexity of prescription medications for select chronic conditions (categorized by ATC codes). The CDS contains 24 distinct comorbidities as shown in Table 17 (see Appendix A). The CDS was reported as both numerical and categorical. The numeric score was calculated by recording dispensations for any drug that falls into any category, as per Table 17 (see Appendix A). However, each category was only counted once (i.e., prescriptions in the category of anxiety and tension contributed only 1 point

to the CDS, regardless of the number of prescriptions recorded). Each comorbidity category was summed into a single CDS for each patient ranging from 0-24.

$$\text{Chronic Disease Score} = \sum \text{comorbidity categories}$$

Next, the CDS distribution was divided into high (CDS >= 4), medium (CDS = 1, 2, or 3), and low (CDS = 0) [20].

Pill burden, defined as the average number of pills (non-HIV specific) consumed, was approximated as follows using the baseline period:

$$\text{Pill burden} = \frac{\sum Number\ of\ days\ supply\ by\ medication\ i}{Length\ of baseline\ period}$$

Pill burden is a continuous variable. The pill burden distribution was then divided into tertiles with high, medium, and low pill burden.

Province	Age	*Sex*	Treatment*	Regimen	CDS*	Pill Burden*
AB	Yes	*Yes*	*Yes*	*Yes*	Yes	Yes
MB	Yes	*Yes*	*No*	*Yes*	Yes	Yes
NL	Yes	*Yes*	*No*	*Yes*	No	No
NB	Yes	*Yes*	*No*	*Yes*	No	No
ON	Yes	*Yes*	*No*	*Yes*	No	No
SK	Yes	*Yes*	*No*	*Yes*	Yes	Yes

Table 2: Availability of the co-variables.

(*) Note that CDS and Pill burden are only calculated whenever the baseline period is 6 months. Also, as already mentioned, patients with a baseline period less than 6 months are considered as experienced.

Outcome Variables:

Outcome variables were represented as adherence estimates during the follow-up period for eligible patients measured by the proportion of days covered (PDC). PDC is a common tool for assessing adherence when using dispensation data. PDC was used to calculate the ratio of "number of days the patient is covered by medication during a specific period" to "the total number of days in that period". The PDC ratio was referred to as the adherence rate and denoted as a range between 0-100%.

$$PDC_{overall}\ (period) = \frac{100.0 * \sum Days\ covered\ by\ complete\ ARV\ regimen\ during\ the\ period}{Length\ of\ period}$$

Moreover, a patient may experience several switches during follow-up from MTR to STR or vice versa. PDC was therefore also specifically calculated for STR and MTR.

$$PDC_{STR}\ (period) = \frac{100.0 * \sum Days\ of\ adherence\ during\ period\ when\ TYPE=STR}{\sum Length\ of\ period\ when\ TYPE=STR}$$

$$PDC_{MTR}\ (period) = \frac{100.0 * \sum Days\ of\ adherence\ during\ period\ when\ TYPE=MTR}{\sum Length\ of\ period\ when\ TYPE=MTR}$$

Data Quality

Of the patients selected from the NDPUIS dataset, there was no missing data (i.e., start date of dispensation, days supply, ATC code, sex, age) except for ON, where patient sex was unknown for a subset of patients.

Similarly, of the patients selected from the PIN dataset, there was no missing data (i.e., start date of dispensation, days supply, ATC code, sex, age). For the PIN dataset, the pill supply was also provided as a data element. It was therefore possible to examine the validity of supply days. Of the 411,592 ART dispensations identified for the study period, 400,224 had pills as a unit of measure. Of these 400,224, only 87 had a ratio of days supply/pills supply greater than 7 (a pill will be consumed more than once a week), or less than 0.1 (more than 10 pills will be taken every day), indicating a very high level of validity for supply days.

Data Processing

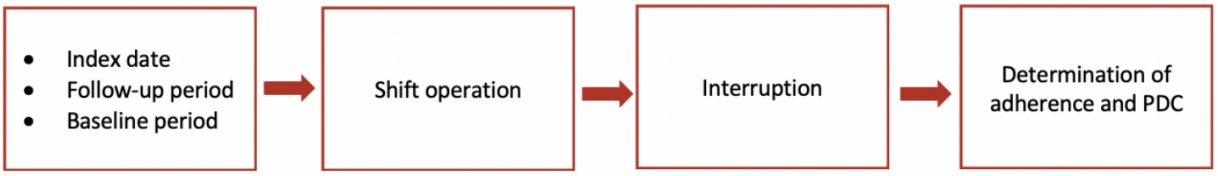

Figure 1: Data processing pipeline.

Step 1

The data processing pipeline started by calculating the index date, the follow-up period, and the baseline period for each patient. Then, the following variables were determined: age, sex, treatment-naïve / treatment-experienced status, CDS, and pill burden.

Step 2

For cases when the patient dispensed a new medication before the supply period of the previous dispensation was finished, the overlapping days were carried over to the end of the later dispensation supply period. Consequently, the refill date was 'shifted' forward to the day after the end of supply of the previous fill. This 'shift' of overlapping

days was only done for overlapping dispensations with the same ATC code [21]. If the 'shifted' days' extended beyond the end of the follow-up of the patient, they were excluded from the PDC calculation.

Step 3

Treatment interruption was assumed when the period between the end of the supply of the current dispensation and the next dispensation was greater than n*1.5, where n= the number of days of the current ART dispensation. To account for cases with low prescribed quantity, a minimum of 45 days between the end of supply of one dispensation to the next dispensation was considered. This would correspond to a treatment interruption definition for a dispensation covering 30 days. Patients were followed only up to their first interruption and were excluded if this first interruption happened within 12 months of the index date.

Step 4

Adherence was calculated based on the qualifications described in Table 3 (see also Table 16 in Appendix A). On any given day during the follow-up period, adherence could be None, MTR, or STR.

	Dispensation		
Adherence	**Other**	**CA**	**STR**
None	None + Other -> None	None + CA -> MTR	None + STR -> STR
MTR	MTR + Other -> MTR	MTR + CA -> MTR	MTR + STR -> STR
STR	STR + Other -> STR	STR + CA -> STR	STR + STR -> STR

Table 3: Adherence regimen qualifications.

Once adherence was obtained for all days in the follow-up period, the days not covered by any ART or covered by a non-adherent regimen were considered to belong to the treatment type prior to switching. For example, if a patient switched from MTR to STR with a gap (drug holiday), the gap period was counted into the MTR period. Next, $PDC_{overall}$, PDC_{STR}, and PDC_{MTR} were calculated. Finally, treatment regimen at index date, CDS and pill burden (categorical) were determined.

Sensitivity Analyses

Sensitivity analyses were conducted to test how robust the results were to changes in MTR adherence definition and varying degrees of treatment interruption.

1. The default definition for MTR adherence is given above in Table 3. Definitions for the treatment interruption that were considered:

1. n = 1.5 by default as discussed in Step 3 above
2. n = 1.25, referred to as Interruption_125
3. n = 1.75, referred to as Interruption_125
4. 90 days: a fixed number of 90 days was used to determine treatment interruption, referred to as Interruption_90
5. no treatment interruption, referred to as No_Interruption

2. The revised definition for MTR adherence is given in Table 4, and corresponds to CA plus Other drug or CA plus another CA. In this case, Other HIV medication dispensations were used in the definition of the follow-up period. MTR adherence was calculated in two steps. First, using Table 2 in "Step 4" above (replacing Table 3). Second, setting days with Other and CA as non-adherent (=None). Definitions for the treatment interruption that were considered:

    1. n = 1.5 by default
    2. 90 days
    3. no treatment interruption

	Dispensation		
Adherence	**Other**	**CA**	**STR**
None	None + Other -> Other	None + CA -> CA	None + STR -> STR
Other	Other + Other -> Other	Other + CA -> MTR	Other + STR -> STR
CA	CA + Other -> MTR	CA + CA -> MTR	CA + STR -> STR
MTR	MTR + Other -> MTR	MTR + CA -> MTR	MTR + STR -> STR
STR	STR + Other -> STR	STR + CA -> STR	STR + STR -> STR

Table 4: Adherence regimen qualifications for the new definition of MTR adherence.

Data Analysis

Analyses were conducted using Python [22-24]. For the first and fourth objectives, Canada and Alberta results were generated. For second and third objectives, i.e., wherever concomitant drugs were part of the analysis, Canada, Western Canada, i.e., AB, MB, and SK (where concomitant drugs were available), and Alberta results were generated. Alberta results are presented in Appendix B.

Endpoints were statistically analysed for the overall population and for subpopulations using the following statistical methods.

Primary objective analysis (Table 6): Adherence rates to ART in PLHIV in Alberta.

The primary objective outcome was analysed with descriptive statistics. PDC was calculated for each patient and then summarized at the population level by descriptive statistics.

Objective 2 analysis (Table 7.1 and 7.2): Description of baseline PLHIV characteristics (demographic and co-medications).

Only patients with a 6 months baseline period were kept. Baseline demographics, ART treatment regimen at index date, pill burden, comorbidity score, and co-medications were summarized with descriptive statistics. Patients were also stratified by age.

Objective 3 analysis (Table 8.1 - 10.2): Description and comparison of adherence rates for different baseline characteristics and estimate predictors of adherence.

Only patients with a 6 months baseline period were kept. As with the primary objective, PDC was calculated for each patient and then summarized at the population level by descriptive statistics.

Each of the strata presented in Tables 8.1 and 8.2 below are grouped into different adherence categories as per cut-off rates used in the primary objective. Mean (SD) and Median (IQR) adherence were computed for each sub-group for the full follow-up period. T-tests for independent samples were used to estimate the statistical significance between subgroups, except for the type of regimen where paired t-test were considered for patients reporting both STR and MTR adherence.

The odds ratio (OR) and 95% confidence interval were calculated for each baseline strata for different adherence rates. An adherence rate higher than (i.e., > 90%) was defined as 1 and adherence rate below 90% was defined as 0. For the type of regimen, McNemar's test (without correction) was employed for patients reporting both STR and MTR adherence. Otherwise, for all other variables (including ART treatment regimen at index date), chi-squared test was employed to test the significance between subgroups. Tables 9.1.1., 9.1.2. show the ORs and p-values which were used to identify the association between adherence and baseline characteristics across provinces, while Tables 9.2.1. and 9.2.2. show the same for Western provinces.

In Tables 10.1 and 10.2, univariate analyses were first conducted to assess the impact of demographic and clinical characteristics, i.e., sex, age, type of regimen, comorbidity score, and pill burden using a binomial regression model (correcting for overdispersion). A multivariate analysis was then performed to estimate each characteristic by controlling for all other confounders. For the analyses in Tables 10.1 and 10.2, the outcome of adherence rate was measured as a continuous variable.

Objective 4 (Tables 11 and 12): Description of the change in rate of adherence over the HIV patient life cycle.

Only naïve patients were kept. Outcomes were analysed with descriptive statistics. This analysis was subsequently refined by keeping only patients with at least four years of follow-up and stratifying by patients solely on STR regimen during their follow-up period or solely on MTR regimen during their follow-up period (Table 11).

Supplementary Analyses (Table 14.1-15.3): Impact of using public claims only for estimating adherence

For ON, NB, and NL, only claims under public program are captured in the database, therefore adherence calculation does not consider claims under private programs. This analysis aims at estimating the impact of not including the private claims for adherence calculation and is restricted to MB and SK where all the claims are recorded and a flag indicating whether the claim was made under a public or a private program is available.

The proposed analysis looks at three exclusive group of patients: patients who recorded public claims only, patients who recorded private claims only, and finally patients who recorded both. The determination of these groups is done on the original dataset. First analysis is to compare adherence for patients recording public claims only and patients who record private claims only. Note that this latter group of patients would not be present at all for ON, NB, and NL. Second analysis is to compare adherence for patients who recorded both public and private claims. We calculate adherence for these patients when all their claims are available and when their private claims have been discarded. Finally, we compare the overall adherence when all the claims are available when with only public claims are available.

Results

All the tables presented in this section are for the default definition of MTR adherence and default definition of interruption.

Population

The population size obtained following the data processing pipeline described in Figure 1 is summarized in Table 5.

Province	Number of patients in database	Patients with index age at least 18 and follow-up more than 12 months	Patients for analysis considering default MTR adherence and default interruption
SK	2697	1832	1182
NB	403	340	318
NL	180	140	118
ON	16287	12543	10053
MB	1616	1259	1057
AB	6156	4648	3663

Table 5: Population in database.

Objective 1: Adherence rates to ART in PLHIV in Canada

Of the 16,391 patients studied in Canada, the overall adherence rate was high (mean 93.71%). Using ON as reference (Table 8.1), overall adherence rate remained statistically consistent across the provinces except for SK, where it was lower ($p < 0.001$). These results were robust to sensitivity analysis except for Interruption_90, where overall adherence rate for AB and NB was statistically larger ($p < 0.001$) (Table 8.1).

Alberta specific adherence rates can be found in Table 19 (see Appendix B).

	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	40%-60%	Mean (SD)	Median (IQR)
Overall (2010-2019)	16391	60.54	17.24	9.52	5.36	7.06	0.26	93.71 (7.72)	96.76 (8.09)
2010-2014	11517	61.54	16.18	9.31	5.60	7.10	0.24	93.83 (7.84)	97.08 (8.24)
2015-2019	13587	66.20	14.73	7.86	4.71	6.01	0.43	94.51 (7.77)	97.78 (7.23)

Table 6: Adherence rate of HIV patients in Canada from 2010-2019. (Total n_{pop} includes patients with adherence < 40% or the lower interval)

Objective 2: Baseline PLHIV characteristics

For Canada, 72.02% were male with the majority being ≥35 and <65 years of age. There were even numbers of patients on both single and multiple drug treatment regimens at index date.

For Western Canada where concomitant drugs were available, pill burden score was just below 1 and patients most frequently reported 1 and 2 comorbid conditions. Most frequently (from higher to lower) appearing HIV specific comorbid conditions were depression, insomnia, hypertension, hyperlipidemia, psychotic illness, and opioid dependence.

Finally, for Alberta where it was possible to capture naïve/experienced status, most patients captured were treatment-naïve (86.02%) (see Table 20, Appendix B).

		Baseline demographics
Province	ON	4787 (49.13%)
	MB	198 (2.03%)
	SK	906 (9.30%)
	NB	131 (1.34%)
	NL	58 (0.60%)
	AB	3663 (37.60%)
Sex	Male	7017 (72.02%)
	Female	2511 (25.77%)
	Unknown	215 (2.21%)
Age	Mean (SD)	43.00 (12.00)
	Median (IQR)	42.30 (17.00)
	≥18 to <35	2692 (27.63%)
	≥35 to <65	6465 (66.36%)
	≥65	586 (6.01%)
	≥18 to <35	2692 (27.63%)
	≥35 to <50	4257 (43.69%)
	≥50	2794 (28.68%)
ART treatment regimen (index date)	STR	4894 (50.23%)
	MTR	4849 (49.77%)

Table 7.1: Baseline demographics of HIV patients in Canada from 2010-2019.

		Baseline demographics
Province	ON	-
	MB	198 (4.15%)
	SK	906 (19.01%)
	NB	-
	NL	-
	AB	3663 (76.84%)
Sex	Male	3297 (69.16%)
	Female	1470 (30.84%)
	Unknown	0 (0.00%)
Age	Mean (SD)	42.88 (11.18)
	Median (IQR)	42.60 (16.20)
	≥18 to <35	1235 (25.91%)
	≥35 to <65	3396 (71.24%)
	≥65	136 (2.85%)

	≥18 to <35	1235 (25.91%)
	≥35 to <50	2247 (47.14%)
	≥50	1285 (26.96%)
ART treatment regimen (index date)	STR	2136 (44.81%)
	MTR	2631 (55.19%)
Treatment experience	ART-naïve	4255 (89.26%)
	ART-experienced	512 (10.74%)
Pill burden	Mean (SD)	0.80 (1.52)
	Median (IQR)	0.05 (0.94)
CDS	Mean (SD)	1.43 (1.87)
	Median (IQR)	1.00 (2.00)
HIV specific comorbidities		
Hepatitis B	Yes	<10 (0.02%)
	No	4766 (99.98%)
Hepatitis C	Yes	10 (0.21%)
	No	4757 (99.79%)
Hyperlipidemia	Yes	372 (7.80%)
	No	4395 (92.20%)
Hypertension	Yes	482 (10.11%)
	No	4285 (89.89%)
Depression	Yes	809 (16.97%)
	No	3958 (83.03%)
Psychotic illness (including bipolar disorders)	Yes	358 (7.51%)
	No	4409 (92.49%)
Diabetes	Yes	212 (4.45%)
	No	4555 (95.55%)
Liver Failure	Yes	86 (1.80%)
	No	4681 (98.20%)
Insomnia	Yes	505 (10.59%)
	No	4262 (89.41%)
Osteoporosis	Yes	22 (0.46%)
	No	4745 (99.54%)
Opioid dependence	Yes	345 (7.24%)
	No	4422 (92.76%)

Table 7.2: Baseline demographics of HIV patients in Western Canada from 2010-2019.

Objective 3: Comparison of adherence rates among baseline characteristics and potential predictors of adherence

Analysis was conducted for patients with 6 months baseline. Patients with unknown gender in ON were discarded.

Patterns of adherence were observed among demographic groups. Men were statistically more adherent, although mean/median differences may not be clinically significant. By age, the older the subgroup, the greater level of adherence. Also, STR overall adherence was higher than MTR adherence. Using ON as reference, overall adherence rate remained statistically consistent across the provinces except for SK, where it was lower ($p < 0.001$). These results were robust to sensitivity analysis.

Several HIV-specific comorbid conditions were significantly associated with higher adherence levels, namely, hyperlipidemia, hypertension, diabetes. On the other end, opioid dependence was found to be significantly associated with lower adherence levels. Paradoxically, higher pill burden was associated with a higher adherence level, however, medium pill burden was associated with a lower adherence level. These results were relatively robust to sensitivity analysis, except for Interruption_90: osteoporosis was also found to be significantly associated with higher adherence levels, depression and psychotic illness were also found to be associated with lower adherence levels, and association with hypertension was no longer significant.

For AB, only association with hyperlipidemia and diabetes were consistent across sensitivity analysis (Table 21, see Appendix B).

	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	40%-60%	Mean (SD)	Median (IQR)	P-value (non-paired test)	P-value (paired test)
Province											
ON	4572	61.94	16.01	9.82	5.23	6.76	0.22	93.89 (7.60)	96.95 (7.99)	Refer-ence	-
MB	198	66.67	14.14	8.08	4.04	7.07	0.00	94.51 (6.93)	97.11 (6.88)	0.2	-
SK	906	49.67	20.97	11.04	7.95	9.82	0.44	92.11 (8.51)	94.98 (9.97)	<0.001	-
NB	131	64.89	15.27	7.63	6.87	5.34	0.00	94.19 (7.22)	97.02 (8.27)	0.6	-
NL	58	58.62	20.69	5.17	8.62	5.17	1.72	93.39 (8.40)	95.86 (6.66)	0.6	-
AB	3663	60.11	19.30	9.39	4.64	6.28	0.27	93.93 (7.26)	96.50 (7.57)	0.8	-
Type of regimen (uses PDC_{STR} and PDC_{MTR})											
STR	6467	63.94	16.38	8.50	4.86	5.94	0.31	94.28 (7.67)	97.24 (7.38)	<0.001	<0.001

MTR	5439	59.51	16.20	9.76	5.46	8.07	0.79	93.18 (9.16)	96.76 (9.11)		
Sex (uses $PDC_{overall}$ onwards)											
Men	7017	62.01	17.41	9.06	4.89	6.38	0.23	94.07 (7.36)	96.88 (7.55)	<0.001	-
Women	2511	55.12	18.60	11.39	6.37	8.12	0.36	92.87 (8.06)	95.90 (9.34)		
Age groups											
≥18 to <35	2606	55.76	17.96	11.09	6.56	8.17	0.38	92.91 (8.12)	95.97 (9.37)	Refer-ence	-
≥35 to <65	6338	60.10	18.30	9.69	5.03	6.66	0.22	93.84 (7.43)	96.62 (7.92)	<0.001	-
≥65	584	80.99	10.45	3.25	2.23	2.91	0.17	96.57 (5.51)	98.58 (3.50)	<0.001	-
Age groups											
≥18 to <35	2606	55.76	17.96	11.09	6.56	8.17	0.38	92.91 (8.12)	95.97 (9.37)	Refer-ence	-
≥35 to <50	4159	57.08	18.80	10.75	5.48	7.57	0.31	93.36 (7.74)	96.20 (8.70)	0.02	-
≥50	2763	69.06	15.89	6.73	3.76	4.49	0.07	95.14 (6.52)	97.67 (5.85)	<0.001	-

Table 8.1: ART adherence rates of PLHIV in Canada from 2010-2019, stratified by type of regimen, sex, province, and age at baseline.

	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	40%-60%	Mean (SD)	Median (IQR)	P-value (non-paired test)	P-value (paired test)
Province											
ON	0	-	-	-	-	-	-	- (-)	- (-)	Refer-ence	-
MB	198	66.67	14.14	8.08	4.04	7.07	0.00	94.51 (6.93)	97.11 (6.88)	-	-
SK	906	49.67	20.97	11.04	7.95	9.82	0.44	92.11 (8.51)	94.98 (9.97)	-	-
NB	0	-	-	-	-	-	-	- (-)	- (-)	-	-
NL	0	-	-	-	-	-	-	- (-)	- (-)	-	-
AB	3663	60.11	19.30	9.39	4.64	6.28	0.27	93.93 (7.26)	96.50 (7.57)	-	-
Type of regimen (uses PDC_{STR} and PDC_{MTR})											
STR	2975	63.43	16.84	8.54	4.84	5.88	0.37	94.23 (7.75)	97.09 (7.47)	<0.001	<0.001

MTR		2994	57.15	18.00	10.09	5.58	8.12	0.87	92.96 (9.22)	96.42 (9.27)		
Sex (uses $PDC_{overall}$ onwards)												
Men		3297	60.87	19.11	8.89	4.70	6.19	0.21	94.09 (7.17)	96.67 (7.41)	<0.001	-
Women		1470	52.86	20.07	11.36	6.46	8.78	0.48	92.54 (8.20)	95.42 (9.42)		
Age groups												
≥18 to <35		1235	54.74	17.81	11.50	6.48	8.91	0.49	92.66 (8.29)	95.78 (9.70)	Refer-ence	-
≥35 to <65		3396	59.07	20.17	9.22	4.92	6.39	0.24	93.87 (7.25)	96.43 (7.65)	<0.001	-
≥65		136	75.00	14.71	3.68	2.21	4.41	0.00	95.69 (6.32)	98.34 (4.67)	<0.001	-
Age groups												
≥18 to <35		1235	54.74	17.81	11.50	6.48	8.91	0.49	92.66 (8.29)	95.78 (9.70)	Refer-ence	-
≥35 to <50		2247	55.90	20.61	10.19	5.65	7.30	0.36	93.34 (7.61)	95.99 (8.46)	0.02	-
≥50		1285	66.30	18.83	6.93	3.35	4.59	0.00	94.99 (6.37)	97.34 (6.09)	<0.001	-
CDS groups												
Low		2202	59.26	19.53	9.63	4.72	6.68	0.18	93.79 (7.28)	96.40 (7.80)	Refer-ence	-
Medium		1872	57.91	18.75	9.94	5.45	7.43	0.48	93.38 (7.88)	96.22 (8.48)	0.09	-
High		693	57.00	20.78	8.95	6.35	6.78	0.14	93.65 (7.37)	96.24 (8.28)	0.7	-
HIV specific comorbidities												
Hepatitis B	Yes	<10	100.00	0.00	0.00	0.00	0.00	0.00	99.28 (-)	99.28 (0.00)	-	-
	No	4766	58.39	19.41	9.65	5.25	6.99	0.29	93.61 (7.54)	96.31 (8.07)		
Hepatitis C	Yes	10	80.00	0.00	20.00	0.00	0.00	0.00	96.30 (4.71)	97.97 (1.25)	0.1	-
	No	4757	58.36	19.45	9.63	5.26	7.00	0.29	93.60 (7.54)	96.29 (8.07)		
Hyper-lipidemia	Yes	372	72.31	16.67	5.65	2.15	3.23	0.00	95.88 (5.50)	97.85 (4.80)	<0.001	-
	No	4395	57.22	19.64	9.99	5.51	7.30	0.32	93.42 (7.65)	96.09 (8.40)		
Hyper-tension	Yes	482	62.86	20.54	7.26	3.11	5.81	0.41	94.35 (7.43)	96.97 (6.74)	0.02	-
	No	4285	57.90	19.28	9.92	5.48	7.12	0.28	93.53 (7.55)	96.21 (8.29)		

Depression	Yes	809	54.51	21.14	10.26	5.81	8.16	0.00	93.30 (7.52)	95.75 (8.70)	0.2	-
	No	3958	59.20	19.05	9.53	5.13	6.75	0.35	93.67 (7.54)	96.42 (7.99)		
Psychotic illness	Yes	358	54.47	20.11	11.45	6.70	7.26	0.00	93.24 (7.79)	95.75 (9.36)	0.3	-
	No	4409	58.72	19.35	9.50	5.13	6.96	0.32	93.64 (7.52)	96.36 (7.95)		
Diabetes	Yes	212	64.15	24.53	3.30	1.89	6.13	0.00	94.98 (6.50)	97.24 (6.07)	0.002	-
	No	4555	58.13	19.17	9.95	5.40	7.03	0.31	93.55 (7.58)	96.26 (8.24)		
Liver Failure	Yes	86	60.47	19.77	8.14	5.81	4.65	1.16	93.76 (7.60)	96.02 (7.54)	0.8	-
	No	4681	58.36	19.40	9.68	5.23	7.03	0.28	93.61 (7.54)	96.32 (8.07)		
Insomnia	Yes	505	58.42	19.41	10.10	6.14	5.94	0.00	93.87 (7.17)	96.68 (8.29)	0.4	-
	No	4262	58.40	19.40	9.60	5.14	7.11	0.33	93.58 (7.58)	96.28 (8.04)		
Osteo-porosis	Yes	22	50.00	36.36	9.09	0.00	4.55	0.00	94.73 (4.88)	95.15 (5.44)	0.3	-
	No	4745	58.44	19.33	9.65	5.27	7.00	0.30	93.60 (7.55)	96.32 (8.08)		
Opioid Dependence	Yes	345	46.38	22.90	11.59	6.96	10.72	1.16	91.42 (9.32)	94.41 (10.39)	<0.001	-
	No	4422	59.34	19.13	9.50	5.11	6.69	0.23	93.78 (7.35)	96.43 (7.93)		
Pill burden groups												
Low		2077	59.46	19.35	9.68	4.86	6.50	0.14	93.86 (7.16)	96.42 (7.69)	Refer-ence	-
Medium		2063	55.99	18.86	10.47	5.82	8.29	0.53	93.01 (8.18)	96.02 (9.03)	<0.001	-
High		627	62.84	21.37	6.86	4.63	4.31	0.00	94.77 (6.28)	96.89 (6.38)	0.002	-

Table 8.2: ART adherence rates of PLHIV in Western Canada from 2010-2019, stratified by type of regimen, sex, province, age at baseline, baseline comorbidities, and pill burden.

When examining the OR, the results were consistent with Table 8.1 and 8.2. There was no difference between the STR or MTR (Tables 9.1.1). By this method, men were 1.37 times more likely to be adherent than women (Table 9.1.2). Other similar findings included greater odds of adherence in the older subgroups ≥35 to <65, OR 1.29 [95% CI 1.16, 1.44], and ≥65, OR 3.79 [95% CI 2.80, 5.12]. These results were robust to sensitivity analysis.

In Western Canada, there were also greater odds of adherence with the presence of hyperlipidemia, hypertension, and diabetes, and lower odds of adherence with opioid dependence (Table 9.2.1). High pill burden also appeared

associated with greater adherence OR 1.45 [1.14, 1.84], whereas medium pill burden appeared associated with lower adherence OR 0.80 [0.69, 0.93] (Table 9.2.2). These results were relatively robust to sensitivity analysis, except for Interruption_90: depression and psychotic illness showed lower odds of adherence.

For AB, greater odds of adherence with the presence of hyperlipidemia, hypertension, and diabetes were consistently found, and also for naïve patients (Table 22, see Appendix B).

	MTR adherent	MTR non-adherent	Odds ratio	95% confidence interval	P value (chi square test)
Type of regimen (paired test for patients reporting both MTR and STR adherence, i.e., PDC_{STR} and PDC_{MTR})					
STR adherent	1626	308	-	-	-
STR non-adherent	237	207	0.77	[0.65, 0.91]	0.002

Table 9.1.1: Comparing ART adherence using paired test for type of regimen in Canada from 2010-2019.

	Adherent subject	Non-adherent subject	Odds ratio	95% confidence interval	P-value (chi square test)
Province					
ON	3569	1003	-	-	-
MB	160	38	1.18	[0.83, 1.70]	0.4
SK	641	265	0.68	[0.58, 0.80]	<0.001
NB	105	26	1.13	[0.73, 1.75]	0.6
NL	46	12	1.08	[0.57, 2.04]	0.8
AB	2910	753	1.09	[0.98, 1.21]	0.1
ART treatment regimen (index date) (non-paired tests using $PDC_{overall}$ onwards)					
STR (reference)	3811	965	-	-	-
MTR	3620	1132	0.81	[0.73, 0.89]	<0.001
Sex					
Women (reference)	1855	656	-	-	-
Men	5576	1441	1.37	[1.23, 1.52]	<0.001
Age groups					

≥18 to <35 (reference)	1924	682	-	-	-
≥35 to <65	4973	1365	1.29	[1.16, 1.44]	<0.001
≥65	534	50	3.79	[2.80, 5.12]	<0.001
≥18 to <35 (reference)	1924	682	-	-	-
≥35 to <50	3160	999	1.12	[1.00, 1.25]	0.05
≥50	2347	416	2.00	[1.75, 2.29]	<0.001

Table 9.1.2: Comparing ART adherence using non-paired test for a given characteristic in Canada from 2010-2019.

	MTR adherent	MTR non-adherent	Odds ratio	95% confidence interval	P value (chi square test)
Type of regimen (paired test for patients reporting both MTR and STR adherence, i.e., PDC_{STR} and PDC_{MTR})					
STR adherent	*794*	*167*	-	-	-
STR non-adherent	*129*	*112*	0.77	[0.61, 0.97]	0.03

Table 9.2.1: Comparing ART adherence using paired test for type of regimen in Western Canada from 2010-2019.

	Adherent subject	Non-adherent subject	Odds ratio	95% confidence interval	P value (chi square test)
Province					
ON	0	0	-	-	-
MB	160	38	-	-	-
SK	641	265	-	-	-
NB	0	0	-	-	-
NL	0	0	-	-	-
AB	2910	753	-	-	-
ART treatment regimen (index date) (non paired tests using $PDC_{overall}$ onwards)					
STR (reference)	1714	422	-	-	-
MTR	1997	634	0.78	[0.67, 0.89]	<0.001
ART experience					
ART-Naïve (reference)	3329	926	-	-	-
ART-Experienced	382	130	0.82	[0.66, 1.01]	0.06

Sex						
Women (reference)		1073	397	-	-	-
Men		2638	659	1.48	[1.28, 1.71]	<0.001
Age groups						
≥18 to <35 (reference)		897	338	-	-	-
≥35 to <65		2692	704	1.44	[1.24, 1.67]	<0.001
≥65		122	14	3.28	[1.86, 5.79]	<0.001
≥18 to <35 (reference)		897	338	-	-	-
≥35 to <50		1720	527	1.23	[1.05, 1.44]	0.01
≥50		1094	191	2.16	[1.77, 2.63]	<0.001
HIV specific comorbidities (Yes-reference)						
Hepatitis B	Yes	1	0	-	-	-
	No	3710	1056	1.17	[0.05, 28.76]	0.9
Hepatitis C	Yes	8	2	-	-	-
	No	3703	1054	0.88	[0.19, 4.14]	0.9
Hyper-lipidemia	Yes	331	41	-	-	-
	No	3380	1015	0.41	[0.30, 0.57]	<0.001
Hyper-tension	Yes	403	79	-	-	-
	No	3308	977	0.66	[0.52, 0.85]	0.001
Depression	Yes	613	196	-	-	-
	No	3098	860	1.15	[0.96, 1.38]	0.1
Psychotic illness	Yes	268	90	-	-	-
	No	3443	966	1.20	[0.93, 1.54]	0.2
Diabetes	Yes	188	24	-	-	-
	No	3523	1032	0.44	[0.28, 0.67]	<0.001
Liver Failure	Yes	70	16	-	-	-
	No	3641	1040	0.80	[0.46, 1.38]	0.4
Insomnia	Yes	394	111	-	-	-
	No	3317	945	0.99	[0.79, 1.24]	0.9

Osteo-porosis	Yes	19	3	-	-	-
	No	3692	1053	0.55	[0.16, 1.87]	0.3
Opioid Dependence	Yes	241	104	-	-	-
	No	3470	952	1.57	[1.24, 2.00]	<0.001
CDS groups						
Low (reference)		1735	467	-	-	-
Medium		1436	436	0.89	[0.76, 1.03]	0.1
High		540	153	0.95	[0.77, 1.17]	0.6
Pill burden groups						
Low (reference)		1637	440	-	-	-
Medium		1545	518	0.80	[0.69, 0.93]	0.003
High		529	98	1.45	[1.14, 1.84]	0.002

Table 9.2.2 Comparing ART adherence using non-paired test for a given clinical characteristic in Western Canada from 2010-2019.

Using univariate analysis, and after controlling for all other variables, STR at index date was associated with greater adherence across Canada. Other variables also associated with greater adherence were being male and older age (Table 10.1)

In Table 10.2, having a higher pill burden date was associated with greater adherence in Western Canada. Results for comorbidity score were not consistent across sensitivity analysis.

For AB, ART-Naïve patients were associated with greater adherence (Table 23, see Appendix B).

	Coefficient of univariate model (95%CI, P-value)	Coefficient of multivariate model (95%CI, P-value)
ART treatment regimen (index date)	-0.11 ([-0.16, -0.055], <0.001)	-0.12 ([-0.17, -0.073], <0.001)
ART experience	- (-,-)	- (-,-)
Sex	0.20 ([0.14, 0.25], <0.001)	0.13 ([0.077, 0.19], <0.001)
CDS	- (-,-)	- (-,-)
Pill burden	- (-,-)	- (-,-)
Age	0.014 ([0.012, 0.016], <0.001)	0.014 ([0.012, 0.016], <0.001)

Table 10.1: Univariate and multivariate binomial regression models (logit scale) in Canada from 2010-2019.

	Coefficient of univariate model (95%CI, P-value)	Coefficient of multivariate model (95%CI, P-value)
ART treatment regimen (index date)	-0.15 ([-0.22, -0.076], <0.001)	-0.16 ([-0.23, -0.088], <0.001)
ART experience	- (-,-)	- (-,-)
Sex	0.23 ([0.15, 0.30], <0.001)	0.15 ([0.079, 0.22], <0.001)
CDS	0.022 ([0.0028, 0.041], 0.02)	-0.047 ([-0.078, -0.016], 0.003)
Pill burden	0.063 ([0.038, 0.088], <0.001)	0.091 ([0.050, 0.13], <0.001)
Age	0.014 ([0.011, 0.017], <0.001)	0.012 ([0.0086, 0.015], <0.001)

Table 10.2: Univariate and multivariate binomial regression models (logit scale) in Western Canada from 2010-2019.

Objective 4: Change in rate of adherence over the HIV patient life cycle

For treatment-naïve patients, rates of adherence to HIV medication treatment regimens remained high over the patient's life cycle (mean range 93.67 -96.08%) with the lowest being the first year observed (93.97%). This study captured 9,231 treatment-naïve in the first year with only 344 patients remaining to be observed at 9 years (Table 11).

Year after index date	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	<60%	Mean (SD)	Median (IQR)
Year 1	9231	63.17	15.33	8.15	5.89	6.95	0.51	93.97 (8.16)	97.53 (8.49)
Year 2	9231	69.42	10.83	6.26	4.41	7.59	1.48	94.30 (9.68)	98.90 (7.40)
Year 3	6481	70.53	10.69	6.48	4.06	7.25	0.99	94.66 (9.14)	99.18 (6.85)
Year 4	4757	72.10	10.38	5.61	4.25	6.39	1.26	94.92 (9.07)	99.45 (6.10)
Year 5	3370	72.14	10.98	6.20	3.56	5.82	1.31	95.03 (8.90)	99.18 (6.03)
Year 6	2539	74.91	9.18	5.12	3.58	6.34	0.87	95.32 (8.68)	99.45 (5.06)
Year 7	1818	76.07	9.02	5.34	3.63	5.28	0.66	95.75 (8.05)	100.00 (4.90)
Year 8	898	77.06	9.69	3.90	4.01	4.45	0.89	96.07 (7.93)	100.00 (4.11)

Table 11: Adherence rate of HIV naïve patients in Canada from 2010-2019.

Year after index date	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	<60%	Mean (SD)	Median (IQR)
All naïve patients with at least 4 years of follow-up starting at index date									
Year 1	3773	62.60	13.86	7.45	6.44	7.90	1.75	93.05 (10.94)	97.53 (9.32)
Year 2	3773	69.26	11.21	6.20	4.53	6.81	1.99	93.89 (11.64)	98.63 (7.12)
Year 3	3773	68.59	11.45	6.12	4.37	7.32	2.15	93.60 (12.29)	98.63 (7.67)
Year 4	3773	66.18	11.87	6.20	5.70	7.32	2.73	92.93 (13.31)	98.36 (8.49)
Year 5	2826	67.52	12.00	6.65	4.64	7.11	2.09	93.65 (11.87)	98.63 (7.92)
Year 6	2015	69.03	10.07	5.76	4.67	7.49	2.98	92.93 (14.40)	98.63 (7.80)
Year 7	1003	66.50	11.96	6.88	3.79	6.68	4.19	91.88 (16.88)	98.08 (8.49)
Year 8	375	64.53	13.60	5.60	3.47	10.40	2.40	92.24 (15.58)	98.08 (8.49)
All naïve patients with at least 4 years of STR follow-up starting at index date									
Year 1	1453	70.06	12.46	7.09	4.34	5.71	0.34	95.11 (7.42)	98.36 (6.85)
Year 2	1453	74.95	10.94	5.09	3.37	5.23	0.41	95.79 (7.52)	99.45 (5.19)
Year 3	1453	73.23	10.67	5.99	3.72	5.44	0.96	95.20 (8.78)	99.18 (5.75)
Year 4	1453	71.09	11.36	5.37	5.02	6.19	0.96	94.83 (8.90)	98.90 (6.56)
Year 5	1018	72.20	11.10	6.88	3.24	5.40	1.18	95.08 (8.85)	98.90 (6.03)
Year 6	653	71.06	11.03	5.21	4.90	6.13	1.68	94.32 (11.25)	98.90 (6.30)
Year 7	325	66.15	14.46	5.85	4.00	7.69	1.85	93.53 (12.10)	98.08 (7.95)
Year 8	114	64.91	18.42	6.14	1.75	8.77	0.00	94.63 (7.94)	98.36 (7.95)
All naïve patients with at least 4 years of MTR follow-up starting at index date									
Year 1	1319	57.16	14.33	7.28	8.64	9.70	2.88	91.34 (13.22)	96.71 (11.49)
Year 2	1319	65.81	11.37	6.90	5.23	7.51	3.18	92.55 (14.21)	98.36 (8.77)
Year 3	1319	67.48	10.39	5.91	4.47	8.57	3.18	92.43 (14.90)	98.36 (8.49)
Year 4	1319	63.46	11.07	5.91	6.37	8.49	4.70	91.03 (17.15)	98.09 (10.40)
Year 5	921	65.69	11.62	6.08	5.32	8.03	3.26	92.52 (14.69)	98.36 (8.77)
Year 6	653	68.45	10.57	4.75	4.59	7.50	4.13	92.03 (16.97)	98.90 (7.95)
Year 7	280	65.71	10.36	7.14	2.86	7.50	6.43	89.86 (21.19)	98.90 (9.32)
Year 8	94	69.15	11.70	2.13	2.13	9.57	5.32	90.93 (21.14)	98.90 (7.12)

Table 12: Adherence rate of HIV naïve patients in Canada with at least 4 years of follow up from 2010-2019.

Sensitivity analysis when changing the definition of adherence

Sensitivity analyses were performed to compare the effect of different simulated levels of interruption and of different definitions for multi-tablet regimens on adherence. These analyses are available for each of the objectives and each of the provinces. They can be accessed from the result files using the mapping detailed in Table 13. The sensitivity analyses for the different levels of interruption were already discussed previously. In this

section, we focus on the sensitivity analyses when different definitions for multi-tablet regimens on adherence are considered.

As expected, the overall adherence was lower. STR adherence remained the same but MTR adherence dropped due to considering a stricter definition. Notable difference happened with province where with the new MTR definition overall adherence rate became statistically higher for AB and MB ($p < 0.001$). Diabetes and hyperlipidemia consistently remained significantly associated with higher adherence levels. Univariate and multivariate analyses also remained consistent.

Adherence	Interruption	Tab in Excel file
Default	Default	Default
Default	N=1.25	Interruption_125
Default	N=1.75	Interruption_175
Default	90 days	Interruption_90
Default	No_Interruption	No_Interruption
Revised	Default	Revised_default
Revised	90 days	Revised _Interruption_90
Revised	No_Interruption	Revised _No_Interruption

Table 13: Description of supplementary files

Supplementary Analyses: Impact of using public claims only for estimating adherence

From Table 14.1, we observe the patients with public claims only have a significantly higher adherence than patients with private claims only (for SK 93.77% vs 90.83%). Removing private claims for patients with mixed claims is expected to lower adherence for these patients. However, this effect is balanced by censoring with interruption as shown in Table 14.2. Adherence for patients with mixed claims when private claims are discarded remains similar (for SK, 92.74% vs 92.53%). From these two facts, it is expected that the adherence, if only the public claims would be available, would be higher - as illustrated in Table 14.3 (for SK, 93.24% vs 92.10%). This is not evident when the revised definition for MTR adherence is considered. Like Table 14.1, Table 15.1 shows that patients with public claims only have a significantly higher adherence than patients with private claims only (for SK, 92.80% vs 90.14%). On the other hand, adherence for patients with mixed claims, when private claims are discarded, now becomes significantly lower (for SK, 85.57% vs 91.71%). This is because MTR adherence for the revised definition requires, for example, 2 CA drugs: if one is a private claim and the other is a public claim, then discarding the

private claims will result in no adherence. Finally, it results that the adherence, if only the public claims would be available, is now lower (for SK, 89.02% vs 91.30%).

Province	Patient Type	n_{opt}	Mean (SD)	P-value
MB	Private claims only	176	92.47 (8.54)	-
	Public claims only	488	95.25 (6.52)	<0.001
SK	Private claims only	505	90.83 (8.89)	-
	Public claims only	279	93.77 (7.07)	<0.001

Table 14.1: Comparison of adherence between patients with public claims only and patients with private claims only. Default MTR adherence.

Province	Claim Inclusion	n_{opt}	Mean (SD)	P-value
MB	All	393	93.94 (7.21)	-
	Public only	269	94.88 (6.47)	0.08
SK	All	398	92.53 (8.49)	-
	Public only	297	92.74 (9.54)	0.76

Table 14.2: Comparison of adherence for patients with mixed claims when private claims are discarded. Default MTR adherence.

Province	Claim Inclusion	n_{opt}	Mean (SD)	P-value
MB	All	1057	94.30 (7.21)	-
	Public only	757	95.12 (6.50)	0.01
SK	All	1182	92.10 (8.43)	-0.008
	Public only	576	93.24 (8.44)	-

Table 14.3: Comparison of adherence for all patients when private claims are discarded. Default MTR adherence.

Province	Patient Type	n_{opt}	Mean (SD)	P-value
MB	Private claims only	176	91.81 (8.81)	-
	Public claims only	491	94.82 (6.75)	<0.001
SK	Private claims only	509	90.14 (9.39)	-
	Public claims only	281	92.80 (9.31)	<0.001

Table 15.1: Comparison of adherence for patients with public claims only and patients with private claims only. Revised MTR adherence.

Province	Claim Inclusion	n_{opt}	Mean (SD)	P-value
MB	All	396	93.08 (8.52)	-
	Public only	276	87.04 (21.16)	<0.001
SK	All	400	91.71 (9.32)	-
	Public only	308	85.57 (19.94)	<0.001

Table 15.2: Comparison of adherence for all patients with mixed claims when private claims are discarded. Revised MTR adherence.

Province	Patient Type	n_{opt}	Mean (SD)	P-value
MB	All	1063	93.67 (7.89)	-
	Public only	767	92.02 (14.28)	0.004
SK	All	1190	91.30 (9.40)	-
	Public only	589	89.02 (16.18)	0.002

Table 15.3: Comparison of adherence for all patients when private claims are discarded. Revised MTR adherence.

Disclosure

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Appendix A

Table 16: ATC Code transformation

ATC code	Generic name	Category
J05AR04	zidovudine + lamivudine + abacavir	STR
J05AR05	Zidovudine + lamivudine + nevirapine	STR
J05AR06	efavirenz + emtricitabine + tenofovir disoproxil fumarate	STR
J05AR08	tenofovir disoproxil fumarate + emtricitabine + rilpivirine	STR
J05AR09	elvitegravir + cobicistat + tenofovir disoproxil + emtricitabine	STR
J05AR11	Lamivudine + tenofovir disoproxil + efavirenz	STR
J05AR13	dolutegravir + abacavir + lamivudine	STR
J05AR18	Emtricitabine + tenofovir alafenamide + elvitegravir + cobicistat	STR
J05AR19	Emtricitabine + tenofovir alafenamide + rilpivirine	STR
J05AR20	Emtricitabine + tenofovir alafenamide + bictegravir	STR
J05AR22	Emtricitabine + tenofovir alafenamide + darunavir + cobicistat	STR
J05AR24	Lamivudine + tenofovir disoproxil + doravirine	STR
J05AR21	dolutegravir + rilpivirine	STR
J05AR04	zidovudine + lamivudine + abacavir	Other
J05AF01	zidovudine	Other
J05AF02	didanosine	Other
J05AF03	zalcitabine	Other
J05AF04	stavudine	Other
J05AF06	abacavir	Other
J05AF07	tenofovir disoproxil fumarate	Other
J05AF05	lamivudine	Other
J05AR01	zidovudine + lamivudine	Other

J05AR03	tenofovir disoproxil fumarate + emtricitabine	Other
J05AR02	lamivudine + abacavir	Other
J05AR12	lamivudine + tenofovir disoproxil	Other
J05AR17	emtricitabine + tenofovir alafenamide	Other
V03AX03	cobicistat	Other
J05AE03	ritonavir	Other
J05AR14	darunavir + cobicistat	CA
J05AR15	atazanavir + cobicistat	CA
J05AG01	nevirapine	CA
J05AG02	delavirdine	CA
J05AG03	efavirenz	CA
J05AG06	doravirine	CA
J05AE01	saquinavir	CA
J05AE02	indinavir	CA
J05AE04	nelfinavir	CA
J05AE05	amprenavir	CA
J05AE07	fosamprenavir	CA
J05AE09	tipranavir	CA
J05AX07	enfuvirtide	CA
J05AX09	maraviroc	CA
J05AX08	raltegravir	CA
J05AG04	etravirine	CA
J05AE08	atazanavir	CA
J05AE10	darunavir	CA
J05AX12	dolutegravir	CA

J05AG05	rilpivirine	CA
J05AR10	lopinavir + ritonavir	CA

Note: Single tablet regimen (STR), Other (single nucleoside reverse transcriptase inhibitors, double nucleoside reverse transcriptase inhibitors or boosters), and core agent (CA).

Table 17: ATC Category code transformation for chronic disease score

ATC code	Comorbidity	Drug Identifier
N05B	Anxiety & Tension	AT
C01, C03C, C03EB01	Cardiac Disease	CD
A07EC, excluding A07EC01	Crohn's & Ulcerative Colitis	CU
B01A, C04AD03	Coronary & Peripheral Vascular Disease	CP
A09AA02	Cystic Fibrosis	CF
N06AA, N06AB, N06AE, N06AF, N06AG, N06AX	Depression	DE
A10A, A10B	Diabetes	DI
N03A, excluding N03AE01	Epilepsy	EP
S01E	Glaucoma	GL
M04A	Gout	GO
C10A	Hyperlipidemia	HY
C02, C03A, C03EA01, C07, C08, C09A, C09B	Hypertension	HT
A04AA, L01, excluding L01BA01, L03AA	Malignancies	MG
N02A	Pain	PA
M01A	Pain & Inflammation	PI
N04B	Parkinson's Disease	PD
A02A, A02B	Peptic Acid Disease	PA

N05A	Psychotic Illness	PI
B03XA01, V03AE01	Renal Disease (including End Stage)	RD
R03	Respiratory Illness	RI
A07EC01, H02, L01BA01, M01CB, M01CC01, P01BA02	Rheumatologic Conditions	RC
H03A, H03B	Thyroid Disorders	TD
L04AA01, L04AA05, L04AA06, L04AX01	Transplants	TP
J04A	Tuberculosis	TB

Table 18: ATC category code transformation for HIV specific comorbidities

ATC code	Comorbidity Category/Drug Identifier	Drug Identifier
Hepatitis		
J05AF08, J05AF10, J05AF11	Hepatitis B	HB
J05AB54, L03AB10, L03AB11, L03AB60, L03AB61, J05AE14, J05AE11–J05AE12, J05AX14, J05AX15, J05AX65, J05AB04	Hepatitis C	HC
Cardiovascular diseases		
C10A	Hyperlipidemia	HL
C02, C03A, C03EA01, C07, C08, C09A, C09B	Hypertension	HT
Mental health disorders		
J05AF08, J05AF10, J05AF11	Hepatitis B	HB
J05AB54, L03AB10, L03AB11, L03AB60, L03AB61, J05AE14, J05AE11–J05AE12, J05AX14, J05AX15, J05AX65, J05AB04	Hepatitis C	HC
C10A	Hyperlipidemia	HL
C02, C03A, C03EA01, C07, C08, C09A, C09B	Hypertension	HT
N06AA, N06AB, N06AE, N06AF, N06AG, N06AX	Depression	DE

N05A	Psychotic illness (including bipolar disorders)	PI
A10A, A10B	Diabetes	DI
A06AD11, A07AA11	Liver failure	LF
N05C	Insomnia	IN
M05BA	Osteoporosis	OS
N07BC	Opioid dependence	OD

Appendix B: Alberta Results

	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	40%-60%	Mean (SD)	Median (IQR)
Overall (2010-2019)	3663	60.11	19.30	9.39	4.64	6.28	0.27	93.93 (7.26)	96.50 (7.57)
2010-2014	2514	58.07	19.69	10.26	5.41	6.32	0.24	93.81 (7.45)	96.58 (8.58)
2015-2019	3321	65.91	15.66	8.13	4.40	5.51	0.36	94.67 (7.58)	97.76 (7.25)

Table 19: Adherence rate of HIV patients in Alberta from 2010-2019. (Total n_{pop} includes patients with adherence < 40% or the lower interval

		Baseline demographics
Province	ON	-
	MB	-
	SK	-
	NB	-
	NL	-
	AB	3663 (100.00%)
Sex	Male	2605 (71.12%)
	Female	1058 (28.88%)
	Unknown	<10 (0.00%)
Age	Mean (SD)	43.73 (11.10)
	Median (IQR)	43.60 (16.00)
	≥18 to <35	865 (23.61%)
	≥35 to <65	2683 (73.25%)
	≥65	115 (3.14%)
	≥18 to <35	865 (23.61%)
	≥35 to <50	1742 (47.56%)
	≥50	1056 (28.83%)
ART treatment regimen (index date)	STR	1652 (45.10%)
	MTR	2011 (54.90%)
Treatment experience	ART-naive	3151 (86.02%)
	ART-experienced	512 (13.98%)
Pill burden	Mean (SD)	0.75 (1.53)
	Median (IQR)	0.01 (0.75)
CDS	Mean (SD)	1.23 (1.75)
	Median (IQR)	0.00 (2.00)
HIV specific comorbidities		

Hepatitis B	Yes	<10 (0.03%)
	No	3662 (99.97%)
Hepatitis C	Yes	10 (0.27%)
	No	3653 (99.73%)
Hyperlipidemia	Yes	318 (8.68%)
	No	3345 (91.32%)
Hypertension	Yes	340 (9.28%)
	No	3323 (90.72%)
Depression	Yes	526 (14.36%)
	No	3137 (85.64%)
Psychotic illness (including bipolar disorders)	Yes	236 (6.44%)
	No	3427 (93.56%)
Diabetes	Yes	147 (4.01%)
	No	3516 (95.99%)
Liver Failure	Yes	64 (1.75%)
	No	3599 (98.25%)
Insomnia	Yes	408 (11.14%)
	No	3255 (88.86%)
Osteoporosis	Yes	18 (0.49%)
	No	3645 (99.51%)
Opioid dependence	Yes	42 (1.15%)
	No	3621 (98.85%)

Table 20: Baseline demographics of HIV patients in Alberta from 2010-2019.

	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	40%-60%	Mean (SD)	Median (IQR)	P-value (non-paired test)	P-value (paired test)
Province											
ON	0	-	-	-	-	-	-	- (-)	- (-)	Reference	-
MB	0	-	-	-	-	-	-	- (-)	- (-)	-	-
SK	0	-	-	-	-	-	-	- (-)	- (-)	-	-
NB	0	-	-	-	-	-	-	- (-)	- (-)	-	-
NL	0	-	-	-	-	-	-	- (-)	- (-)	-	-
AB	3663	60.11	19.30	9.39	4.64	6.28	0.27	93.93 (7.26)	96.50 (7.57)	-	-
Type of regimen (uses PDC_{STR} and PDC_{MTR})											

STR		2280	63.95	17.32	8.33	4.47	5.48	0.39	94.42 (7.48)	97.12 (7.06)	<0.001	0.009
MTR		2269	59.19	17.50	10.18	5.07	7.23	0.57	93.38 (8.92)	96.67 (8.87)		
Sex (uses $PDC_{overall}$ onwards)												
Men		2605	62.23	19.04	8.52	4.22	5.80	0.19	94.31 (6.95)	96.77 (6.94)	<0.001	-
Women		1058	54.91	19.94	11.53	5.67	7.47	0.47	93.01 (7.90)	95.86 (8.91)		
Age groups												
≥18 to <35		865	56.99	18.03	11.56	5.55	7.51	0.35	93.28 (7.66)	96.07 (8.94)	reference	-
≥35 to <65		2683	60.49	19.87	8.91	4.47	6.00	0.26	94.06 (7.17)	96.62 (7.36)	0.009	-
≥65		115	74.78	15.65	4.35	1.74	3.48	0.00	95.98 (5.58)	98.43 (4.77)	<0.001	-
Age groups												
≥18 to <35		865	56.99	18.03	11.56	5.55	7.51	0.35	93.28 (7.66)	96.07 (8.94)	reference	-
≥35 to <50		1742	57.06	20.44	10.05	5.28	6.77	0.40	93.51 (7.56)	96.12 (8.21)	0.5	-
≥50		1056	67.71	18.47	6.53	2.84	4.45	0.00	95.16 (6.21)	97.47 (5.87)	<0.001	-
CDS groups												
Low		1881	59.60	19.46	9.62	4.68	6.49	0.16	93.88 (7.20)	96.44 (7.61)	reference	-
Medium		1352	59.62	19.45	9.54	4.51	6.36	0.52	93.81 (7.49)	96.45 (7.94)	0.8	-
High		430	63.95	18.14	7.91	4.88	5.12	0.00	94.56 (6.76)	97.10 (6.98)	0.06	-
HIV specific comorbidities												
Hepatitis B	Yes	<10	100.00	0.00	0.00	0.00	0.00	0.00	99.28 (-)	99.28 (0.00)	-	-
	No	3662	60.10	19.31	9.39	4.64	6.28	0.27	93.93 (7.26)	96.50 (7.57)		
Hepatitis C	Yes	10	80.00	0.00	20.00	0.00	0.00	0.00	96.30 (4.71)	97.97 (1.25)	0.1	-
	No	3653	60.06	19.35	9.36	4.65	6.30	0.27	93.93 (7.27)	96.48 (7.58)		
Hyper-lipidemia	Yes	318	73.27	15.41	5.66	2.20	3.46	0.00	95.92 (5.58)	97.98 (4.67)	<0.001	-
	No	3345	58.86	19.67	9.75	4.87	6.55	0.30	93.74 (7.37)	96.29 (7.94)		
Hyper-tension	Yes	340	65.29	19.41	6.76	3.53	4.71	0.29	94.78 (6.96)	97.43 (6.80)	0.02	-

	No	3323	59.58	19.29	9.66	4.75	6.44	0.27	93.85 (7.29)	96.44 (7.74)		
Depression	Yes	526	59.32	19.77	9.32	4.94	6.65	0.00	94.04 (6.90)	96.26 (7.40)	0.7	-
	No	3137	60.25	19.22	9.40	4.59	6.22	0.32	93.91 (7.32)	96.55 (7.60)		
Psychotic illness	Yes	236	57.63	21.19	9.75	5.93	5.51	0.00	93.91 (7.28)	96.15 (8.61)	1	-
	No	3427	60.29	19.17	9.37	4.55	6.33	0.29	93.93 (7.26)	96.51 (7.50)		
Diabetes	Yes	147	67.35	21.77	3.40	2.04	5.44	0.00	95.32 (6.39)	97.89 (6.26)	0.008	-
	No	3516	59.81	19.20	9.64	4.75	6.31	0.28	93.87 (7.29)	96.46 (7.69)		
Liver Failure	Yes	64	70.31	14.06	6.25	3.12	4.69	1.56	94.51 (7.81)	96.74 (6.04)	0.5	-
	No	3599	59.93	19.39	9.45	4.67	6.31	0.25	93.92 (7.25)	96.49 (7.60)		
Insomnia	Yes	408	59.31	18.87	10.78	5.88	5.15	0.00	94.06 (7.07)	96.83 (8.45)	0.7	-
	No	3255	60.22	19.35	9.22	4.49	6.42	0.31	93.92 (7.29)	96.47 (7.47)		
Osteo-porosis	Yes	18	55.56	33.33	5.56	0.00	5.56	0.00	94.86 (5.15)	96.11 (5.62)	0.5	-
	No	3645	60.14	19.23	9.41	4.66	6.28	0.27	93.93 (7.27)	96.50 (7.59)		
Opioid Dependence	Yes	42	47.62	21.43	7.14	7.14	16.67	0.00	91.89 (8.19)	94.67 (10.56)	0.1	-
	No	3621	60.26	19.28	9.42	4.61	6.16	0.28	93.96 (7.25)	96.51 (7.55)		
Pill burden groups												
Low		1820	59.23	19.62	9.67	4.78	6.54	0.16	93.84 (7.21)	96.40 (7.65)	reference	-
Medium		1383	59.51	18.58	9.76	4.84	6.80	0.51	93.66 (7.69)	96.51 (8.20)	0.5	-
High		460	65.43	20.22	7.17	3.48	3.70	0.00	95.13 (5.95)	97.28 (6.42)	<0.001	-

Table 21: ART adherence rates of PLHIV in Alberta from 2010-2019, stratified by type of regimen, sex, province, age at baseline, baseline comorbidities, and pill burden.

		Adherent subject	Non-adherent subject	Odds ratio	95% confidence interval	P value (chi square test)
Province						
ON		0	0	-	-	-
MB		0	0	-	-	-
SK		0	0	-	-	-
NB		0	0	-	-	-
NL		0	0	-	-	-
AB		2910	753	-	-	-
Type of regimen (paired test for patients reporting both MTR and STR adherence, i.e., PDC_{STR} and PDC_{MTR})						
STR adherent		593	125	-	-	-
STR not adherent		87	81	0.70	[0.53, 0.92]	0.009
ART treatment regimen (index date) (non paired tests using $PDC_{overall}$ onwards)						
STR (reference)		1348	304	-	-	-
MTR		1562	449	0.78	[0.67, 0.92]	0.003
ART experience						
ART-Naïve (reference)		2528	623	-	-	-
ART-Experienced		382	130	0.72	[0.58, 0.90]	0.004
Sex						
Women (reference)		792	266	-	-	-
Men		2118	487	1.46	[1.23, 1.73]	<0.001
Age groups						
≥18 to <35 (reference)		649	216	-	-	-
≥35 to <65		2157	526	1.36	[1.14, 1.64]	<0.001
≥65		104	11	3.15	[1.66, 5.97]	<0.001
≥18 to <35 (reference)		649	216	-	-	-
≥35 to <50		1351	391	1.15	[0.95, 1.39]	0.2
≥50		910	146	2.07	[1.64, 2.62]	<0.001
HIV specific comorbidities (Yes-reference)						
Hepatitis B	Yes	<10	<10	-	-	-

	No	2909	753	1.29	[0.05, 31.63]	0.9
Hepatitis C	Yes	<10	<10	-	-	-
	No	2902	751	0.97	[0.20, 4.56]	1
Hyperlipidemia	Yes	282	36	-	-	-
	No	2628	717	0.47	[0.33, 0.67]	<0.001
Hypertension	Yes	289	51	-	-	-
	No	2621	702	0.66	[0.48, 0.90]	0.008
Depression	Yes	417	109	-	-	-
	No	2493	644	1.01	[0.81, 1.27]	0.9
Psychotic illness	Yes	187	49	-	-	-
	No	2723	704	1.01	[0.73, 1.40]	0.9
Diabetes	Yes	131	16	-	-	-
	No	2779	737	0.46	[0.27, 0.78]	0.003
Liver Failure	Yes	55	<10	-	-	-
	No	2855	744	0.63	[0.31, 1.28]	0.2
Insomnia	Yes	320	88	-	-	-
	No	2590	665	1.07	[0.83, 1.38]	0.6
Osteoporosis	Yes	16	<10	-	-	-
	No	2894	751	0.48	[0.11, 2.10]	0.3
Opioid Dependence	Yes	30	12	-	-	-
	No	2880	741	1.55	[0.79, 3.05]	0.2
CDS groups						
Low (reference)		1487	394	-	-	-
Medium		1069	283	1.00	[0.84, 1.19]	1
High		354	76	1.23	[0.94, 1.62]	0.1
Pill burden groups						
Low (reference)		1435	385	-	-	-
Medium		1080	303	0.96	[0.81, 1.13]	0.6
High		395	65	1.63	[1.23, 2.17]	<0.001

Table 22: Comparing ART adherence using non-paired test for a given clinical characteristic in Alberta from 2010-2019.

	Coefficient of univariate model (95%CI, P-value)	Coefficient of multivariate model (95%CI, P-value)
ART treatment regimen (index date)	-0.14 ([-0.22, -0.063], <0.001)	-0.17 ([-0.24, -0.087], <0.001)
ART experience	-0.19 ([-0.28, -0.099], <0.001)	-0.24 ([-0.33, -0.15], <0.001)
Sex	0.19 ([0.11, 0.28], <0.001)	0.13 ([0.050, 0.22], 0.002)
CDS	0.044 ([0.020, 0.067], <0.001)	-0.022 ([-0.063, 0.018], 0.3)
Pill burden	0.072 ([0.043, 0.10], <0.001)	0.079 ([0.030, 0.13], 0.002)
Age	0.013 ([0.0091, 0.016], <0.001)	0.011 ([0.0074, 0.015], <0.001)

Table 23: Univariate and multivariate binomial regression models (logit scale) in Alberta from 2010-2019.

Years after index date	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	<60%	Mean (SD)	Median (IQR)
Year 1	4255	61.01	15.04	8.72	6.79	7.85	0.59	93.59 (8.46)	97.26 (9.59)
Year 2	4255	69.24	11.05	6.53	4.30	7.36	1.53	94.38 (9.57)	98.98 (7.40)
Year 3	3076	69.51	11.22	6.53	4.19	7.57	0.98	94.55 (9.33)	99.32 (7.12)
Year 4	2227	72.03	10.64	5.03	4.22	7.05	1.03	94.91 (9.18)	99.73 (6.28)
Year 5	1614	72.06	11.21	6.20	3.59	5.58	1.36	95.13 (8.62)	99.45 (6.30)
Year 6	1241	74.86	8.86	5.00	3.87	6.61	0.81	95.29 (8.71)	99.60 (5.21)
Year 7	930	76.34	8.71	5.38	4.09	4.95	0.54	95.92 (7.81)	100.00 (4.66)
Year 8	403	74.44	11.17	3.97	4.22	5.21	0.99	95.73 (8.22)	100.00 (5.21)

Table 24: Adherence rate of HIV naïve patients in Alberta from 2010-2019.

Years after index date	n_{pop}	>=95%	90%-95%	85%-90%	80%-85%	60%-80%	<60%	Mean (SD)	Median (IQR)
All naïve patients with at least 4 years of follow-up starting at index date									
Year 1	1320	65.53	12.27	8.26	6.29	7.27	0.38	94.16 (8.13)	98.08 (9.02)
Year 2	1320	74.92	10.76	5.30	3.41	5.00	0.61	95.79 (7.47)	99.45 (5.20)
Year 3	1320	72.20	11.67	5.30	3.94	6.36	0.53	95.33 (8.09)	99.45 (6.29)
Year 4	1320	71.29	11.44	5.23	4.47	6.74	0.83	94.95 (8.49)	99.18 (6.56)
Year 5	1031	72.36	12.61	5.72	3.20	5.43	0.68	95.45 (7.76)	99.18 (6.16)
Year 6	797	73.78	8.66	5.27	4.27	7.40	0.63	95.02 (8.77)	99.45 (5.48)
Year 7	338	71.30	10.95	5.62	4.44	7.40	0.30	94.89 (8.28)	98.90 (5.48)
Year 8	159	64.15	18.24	6.29	3.14	8.18	0.00	94.59 (7.91)	98.08 (7.26)
All naïve patients with at least 4 years of STR follow-up starting at index date									
Year 1	576	67.88	12.33	7.81	5.03	6.42	0.52	94.72 (7.83)	98.36 (7.67)
Year 2	576	78.65	8.68	5.73	2.26	4.17	0.52	96.41 (6.89)	99.73 (3.84)

Year 3	576	75.17	11.46	5.73	3.47	4.17	0.00	96.12 (6.72)	99.73 (4.93)
Year 4	576	74.48	9.90	4.34	5.56	5.21	0.52	95.56 (7.69)	99.45 (5.48)
Year 5	418	72.97	12.92	5.74	3.35	3.83	1.20	95.51 (8.04)	98.90 (5.48)
Year 6	292	74.32	8.90	3.77	4.79	7.53	0.68	95.07 (8.69)	99.18 (5.21)
Year 7	139	66.91	12.95	4.32	5.76	9.35	0.72	93.83 (9.53)	98.36 (6.58)
Year 8	71	63.38	18.31	8.45	2.82	7.04	0.00	94.47 (8.04)	97.81 (7.95)
All naïve patients with at least 4 years of MTR follow-up starting at index date									
Year 1	470	63.19	11.28	8.30	8.09	8.72	0.43	93.37 (8.72)	97.26 (9.86)
Year 2	470	72.55	13.19	4.68	4.26	4.89	0.43	95.61 (7.51)	99.18 (5.62)
Year 3	470	73.40	10.21	4.47	3.19	7.66	1.06	95.15 (8.95)	100.00 (5.48)
Year 4	470	70.43	11.49	5.53	4.47	6.81	1.28	94.76 (8.96)	99.73 (6.57)
Year 5	337	75.96	10.39	5.34	2.37	5.64	0.30	96.06 (7.10)	99.73 (4.93)
Year 6	268	79.10	7.46	4.85	2.99	5.22	0.37	95.98 (8.32)	100.00 (3.15)
Year 7	75	76.00	10.67	8.00	2.67	2.67	0.00	96.55 (6.42)	100.00 (4.93)
Year 8	28	64.29	25.00	3.57	0.00	7.14	0.00	95.77 (5.96)	98.36 (7.12)

Table 25: Adherence rate of HIV naïve patients in Alberta with at least 4 years of follow up from 2010-2019.