Patient Preference and Adherence

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ORIGINAL RESEARCH

# Impact of the COVID-19 Pandemic on Adherence to Most Costly Chronic Disease Medications in British Columbia, Canada: A Population-Based Interrupted Time Series Analysis

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**Purpose:** To address limited population-level data on prescription medication taking during COVID-19, we assessed the impact of the pandemic on adherence to the costliest drug classes prescribed for chronic diseases in British Columbia (BC).

**Patients and Methods:** Of the 100 top drug classes contributing to total drug spending in 2020, we categorized those prescribed for chronic diseases into 26 drug groups; specifically, drugs for psychiatric and neurologic, cardiac and respiratory, hormone-related, and immune and musculoskeletal conditions. Using administrative health data on all dispensed medications, we quantified adherence by monthly proportion of days covered (PDC) and performed interrupted time-series analysis (ITS) to estimate changes in PDC trends 1-year before and after the implementation of pandemic mitigation measures.

**Results:** We included 3,906,377 adults with ≥1 prescription to ≥1 included drug groups. The most common prescriptions among our study population were for antidepressants (45.0%), drugs for obstructive airway diseases (41.6%), renin-angiotensin system agents (30.5%), diuretics (28.2%), and lipid modifying agents (24.8%). ITS models for 22 of 26 drug groups showed statistically significant changes in monthly PDC trends, with the greatest change occurring among parenteral immunosuppressants, injectable insulins and analogues, and renin-angiotensin system agents.

**Conclusion:** Findings suggest that the pandemic did not substantially impact adherence to commonly used medications; however, adherence was found to be suboptimal across all drug groups regardless of the impact of COVID-19. Medication adherence remains a critical therapeutic challenge requiring our attention irrespective of major healthcare system stressors such as COVID-19.

**Keywords:** medication adherence, chronic conditions, interrupted-times series analysis, COVID-19, administrative health data

## Introduction

For patients living with chronic conditions, medications are necessary healthcare interventions for disease management and prevention of morbidity and mortality. However, taking medications as prescribed ("medication adherence") is a challenge that undermines the effectiveness of treatment leading to adverse patient outcomes and wasted healthcare resources.[1] In December 2019, SARS-CoV-2 was identified as the cause of COVID-19, a respiratory illness declared a pandemic by the World Health Organization (WHO) on March 11, 2020.[2–4] COVID-19 and the public health measures implemented to mitigate its spread have significantly impacted population health, including delays or missed access to healthcare services, such as routine physician visits.[3–5] Consequently, there has been considerable interest in evaluating the impact of COVID-19 on medication adherence.

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In the Five Dimensions of Adherence framework, the WHO describes how medication adherence is influenced by patient, social/economic status, and the healthcare system factors,[1] all of which have been impacted by COVID-19. A 2022 systematic review[6] identified barriers to medication-taking among patients with chronic conditions during the pandemic but did not address the actual burden on medication adherence. Moreover, studies of medication adherence during COVID-19, like broader research in the area, have been disease- or drug-specific[7] and do not align with how pharmaceutical care is administered in Canada (ie, according to drug class through formularies). To provide an understanding of how significant stressors affect healthcare systems, such as a once in a lifetime pandemic, our objective was to conduct a disease-agnostic population-based evaluation of the impact of COVID-19 on adherence, specifically implementation of prescribed dosing regimens,[8] to drugs for chronic diseases that have the greatest bearing on public drug spending in Canada.

# Materials and Methods

## Data Sources

We conducted a population-based cohort study using linked administrative health data holdings from Population Data BC[9] and PharmaNet.[10] Population Data BC captures individual-level, de-identified, longitudinal data on health services for all residents of BC (~5.2 million in 2020[11]), including outpatient healthcare services in the Medical Services Plan (MSP) database,[12,13] hospitalizations in the Discharge Abstract Database,[14] and vital statistics since 1985, with this comprehensive data capture facilitated by the Canada's universal health care system. Under the Pharmaceutical Services Act, PharmaNet[10] captures complete information on all prescriptions dispensed from community pharmacies in BC, including dispensation date and days' supply, regardless of payer since 1996.[9,15] Prescriptions dispensed in hospitals are not captured in PharmaNet.

## Study Population

Individuals 18 years or older were included if they resided in BC (ie, had >12 months of continuous enrollment with the provincial MSP) before the first date of observation and had filled ≥ 1 prescription for ≥ 1 of the drug groups of interest in the 1-year period before and after the index date, set as March 11$^{th}$, 2020.

## Drug Groups

Using 2020 data from the Canadian Institute of Health Information (CIHI),[16,17] we identified the 100 costliest drug classes in BC, categorized by their 4$^{th}$ level Anatomical Therapeutic Chemical (ATC) classification codes (see Supplemental File Table S1). After excluding drug classes typically prescribed as needed (eg, drugs used for erectile dysfunction) and for acute use (eg, antibiotics), the remaining ATC classes were grouped into 26 drug groups by similar therapeutic/pharmacological properties (ie, based on 1$^{st}$ level ATC codes) and further consolidated into 4 broader categories by indication: 1) psychiatric and neurologic conditions; 2) cardiac and respiratory conditions; 3) hormone-related conditions; and 4) immune and skeletal system conditions (see Supplemental File Table S2). Drug group assignment was conducted by the first author (NR), a pharmacist, with expertise in pharmacotherapeutics and pharmacology.

## Medication Adherence

To capture the dynamic nature of medication taking for varying regimens, we applied a flexible, data-driven framework for measuring medication adherence (see Figure 1). As our focus was on the implementation of prescribed dosing regimens, we used information on days' supply from sequential prescription fills to define drug course windows for each drug class (ie, 4$^{th}$ level ATC code) in each drug group. To account for real world medication use, we calculated an allowable gap between fills (eg, 30 days) plus a grace period equivalent to the last days' supply (eg, +30 days) and days of stockpiled medication (ie, difference between the days since the index prescription and sum of all days' supply dispensed).[18] For each drug course window, we then calculated the proportion days covered (PDC) as the ratio of the number of days covered by the medication to the number of days in the drug course window.

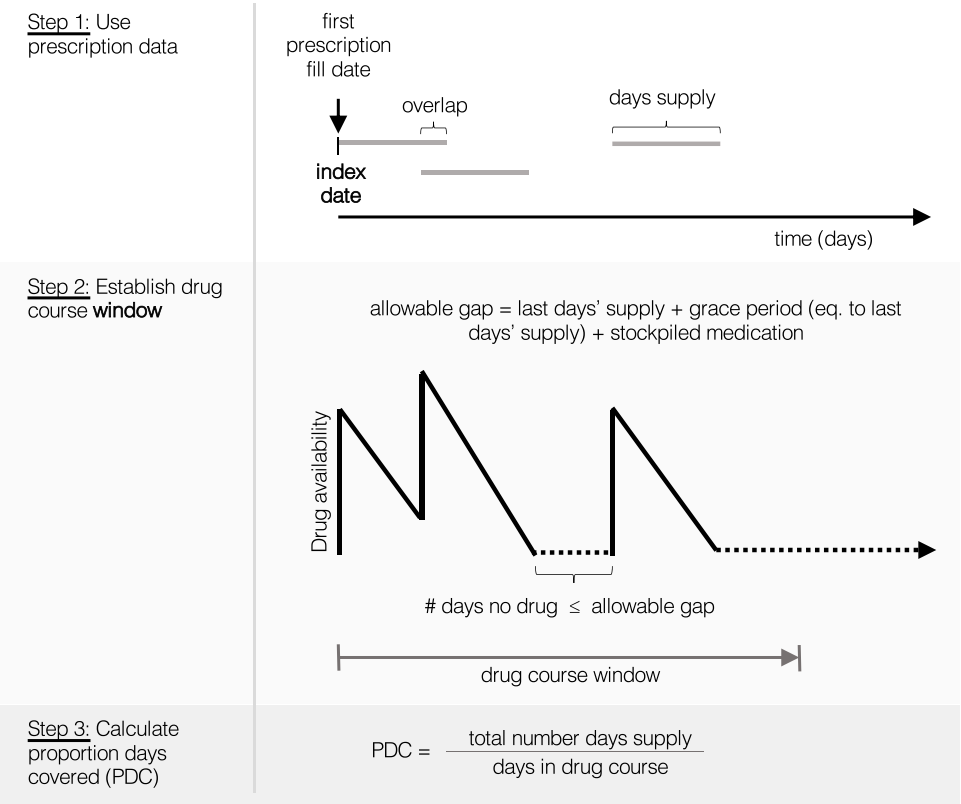


**Figure 1** Framework for measuring implementation of prescribed dosing regimen.

## Statistical Analysis

Mean 1-year PDC was calculated for the 1-year periods before and after the index date, and differences were tested using t-tests, with a p-value of <0.05 considered statistically significant.

We then conducted an interrupted time series (ITS) analysis[19,20] of monthly trends in mean proportion of days covered (PDC) for each drug using generalized least squares (GLS) regression. Autoregressive and moving average terms were selected based on visual inspection of autocorrelation and partial autocorrelation plots. All models were fitted using the most commonly observed lag structure (ie, no lag) to ensure comparability across drugs. Specifically, monthly mean PDC was plotted over a 2-year observation period, and separate ITS models were constructed for the pre-COVID and post-COVID one-year periods. To explore differences in parametrization, we specified models using two reference periods: one with pre-COVID as the baseline and another with post-COVID as the baseline. Each model estimated the slope within each period and the change in slope at the onset of COVID (via an interaction term). Based on visual inspection of trend lines, models were constrained to join at the time of the COVID onset (the "join point"). Model fit was assessed using normal quantile-quantile plots of residuals, and $R^2$ was computed for each model. We conducted analyses for the whole population and stratified by sex. Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

## Ethics

This study was approved by the University of British Columbia (UBC) Behavioural Research Ethics Board (H20-03241). Informed consent was not required as this research involved secondary use of de-identified administrative health data. Access to data provided by the Data Stewards is subject to approval but can be requested for research projects through them or their designated service providers. The following data sets were used in this study: Medical Services Plan, Discharge Abstract Database, Vital Statistics, and PharmaNet. All inferences, opinions, and conclusions drawn in this publication are those of the author(s), and do not reflect the opinions or policies of the Data Steward(s). Further

information regarding these data sets can be found on the PopData projects webpage (https://www.popdata.bc.ca/ria/projects) or project webpage (https://my.popdata.bc.ca/project_listings/21-001/collection_approval_dates).

## Results

The study population included 3,906,377 individuals who were predominantly female (56.0%) with a mean age of 59.5±21.8 years (Table 1). The most common prescriptions among our study population were for antidepressants (45.0%), drugs for

**Table 1** Characteristics of Study Population Overall and Stratified by Sex

| Characteristic | All | Male | Female |
|---|---|---|---|
| **N** | 3,906,377 | 1,720,467 | 2,185,910 |
| **Age**, mean (SD) | 59.5 (21.8) | 60.7 (21.2) | 58.5 (22.1) |
| **Sex**, n (%) | | | |
| Female | 2,185,910 (56.0) | – | 2,185,910 (100.0) |
| Male | 1,720,467 (44.0) | 1,720,467 (100.0) | – |
| **Neighborhood income quintile**[a], n (%) | | | |
| 1 - Lowest | 845,286 (21.6) | 379,034 (22.0) | 466,252 (21.3) |
| 2 | 787,305 (20.2) | 346,962 (20.2) | 440,343 (20.1) |
| 3 | 780,690 (20.0) | 341,964 (19.9) | 438,726 (20.1) |
| 4 | 772,468 (19.8) | 337,672 (19.6) | 434,796 (19.9) |
| 5 - Highest | 720,628 (18.5) | 314,835 (18.3) | 405,793 (18.6) |
| **Type of Residence**[b], n (%) | | | |
| Urban | 3,441,778 (88.1) | 1,506,053 (87.5) | 1,935,725 (88.6) |
| Rural | 464,599 (11.9) | 214,414 (12.5) | 250,185 (11.4) |
| **Charlson Comorbidity Score**[c], mean (SD) | 0.4 (1.1) | 0.4 (1.2) | 0.3 (1.0) |
| **No. of hospitalizations**, mean (SD) | 0.2 (0.7) | 0.2 (0.7) | 0.2 (0.6) |
| **No. of outpatient visits**, mean (SD) | 7.2 (11.6) | 7.1 (12.3) | 7.4 (11.0) |
| **Drug group**[d], n (%) | | | |
| Antidepressants | 1,758,922 (45.0) | 707,121 (41.1) | 1,051,801 (48.1) |
| Drugs for obstructive airway diseases | 1,624,270 (41.6) | 732,849 (42.6) | 891,421 (40.8) |
| Renin-angiotensin system agents | 1,190,441 (30.5) | 619,930 (36.0) | 570,511 (26.1) |
| Diuretics | 1,103,121 (28.2) | 478,736 (27.8) | 624,385 (28.6) |
| Lipid modifying agents | 968,450 (24.8) | 548,145 (31.9) | 420,305 (19.2) |
| Antiepileptics | 944,184 (24.2) | 405,457 (23.6) | 538,727 (24.6) |
| Beta blocking agents | 888,744 (22.8) | 437,081 (25.4) | 451,663 (20.7) |
| Oral hormonal contraceptives | 716,526 (18.3) | 927 (0.1) | 715,599 (32.7) |
| Estrogens | 540,935 (13.8) | 3,264 (0.2) | 537,671 (24.6) |
| Calcium channel blockers | 699,447 (17.9) | 342,254 (19.9) | 357,193 (16.3) |
| Thyroid hormones | 513,995 (13.2) | 125,707 (7.3) | 388,288 (17.8) |
| Antipsychotics | 506,921 (13.0) | 242,785 (14.1) | 264,136 (12.1) |
| Antithrombotic agents | 465,293 (11.9) | 269,715 (15.7) | 195,578 (8.9) |
| Vasodilators | 462,808 (11.8) | 250,555 (14.6) | 212,253 (9.7) |
| Blood glucose lowering drugs (excluding insulin) | 458,358 (11.7) | 244,993 (14.2) | 213,365 (9.8) |
| Alpha-adrenoreceptor antagonists | 329,550 (8.4) | 300,316 (17.5) | 29,234 (1.3) |
| Stimulants and centrally acting antiadrenergic agents | 240,867 (6.2) | 119,928 (7.0) | 120,939 (5.5) |
| Bisphosphonates | 228,712 (5.9) | 37,190 (2.2) | 191,522 (8.8) |
| Uric acid inhibitors | 173,013 (4.4) | 124,427 (7.2) | 48,586 (2.2) |
| Injectable insulins and analogues | 147,976 (3.8) | 74,442 (4.3) | 73,534 (3.4) |
| Dopaminergic and anticholinergic agents | 103,713 (2.7) | 54,368 (3.2) | 49,345 (2.3) |
| Intestinal anti-inflammatory agents | 97,286 (2.5) | 42,577 (2.5) | 54,709 (2.5) |
| Antidementia drugs | 76,670 (2.0) | 32,244 (1.9) | 44,426 (2.0) |

(*Continued*)

**Table 1** (Continued).

| Characteristic | All | Male | Female |
|---|---|---|---|
| Oral immunosuppressants | 49,854 (1.3) | 20,806 (1.2) | 29,048 (1.3) |
| Parenteral immunosuppressants | 22,835 (0.6) | 10,209 (0.6) | 12,626 (0.6) |
| Immunostimulants | 16,553 (0.4) | 9,829 (0.6) | 6,724 (0.3) |

**Notes**: [a]Determined using neighbourhood income per person equivalent adjusted for household size. [b]Determined using Census Metropolitan Area/Census Agglomeration from geographical census data.[c] Predicts the ten-year mortality for a patient who may have a range of comorbid conditions.[d]Cumulative percentage may be greater than 100, as individuals may be prescribed multiple drug classes.

obstructive airway diseases (41.6%), renin-angiotensin system agents (30.5%), diuretics (28.2%), and lipid modifying agents (24.8%). The mean PDC 1-year before and after the index date for the population and stratified by sex are presented in Table 2. Mean PDC 1-year among the 26 drug groups showed significant differences among all but 3 groups; specifically, antidepressants, drugs for obstructive airway diseases, and lipid modifying agents. Mean PDC among all drug groups was <80% in both the before and after periods.

Results of ITS analysis for the study population is presented in Table 3 and visualized in Figure 2 while sex stratified analyses are presented in Supplementary File Tables S3 and S4 and Figures S1 and S2.

## Psychiatric & Neurologic Conditions

ITS models for the 6 drug groups used for psychiatric and neurologic conditions are presented in Figure 2a. The estimated annual change in PDC showed statistically significant increases in slope among 5 drug groups, with the greatest impact occurring among antidementia drugs (0.21%; 95% CI: 0.15%, 0.27%), followed by antidepressants (0.11%; 95% CI: 0.06%, 0.17%), stimulants and centrally acting antiadrenergic agents (0.16%; 95% CI: 0.11%, 0.22%), antiepileptics (0.07%; 95% CI: 0.04%, 0.10%), and antipsychotics (0.05%; 95% CI: 0.002%, 0.09%).

## Cardiac & Respiratory Conditions

ITS models for the 8 drug groups used for cardiac and respiratory conditions are presented in Figure 2b. The estimated annual change in PDC showed statistically significant increases in slope among 4 drug groups, with the greatest impact occurring among calcium channel blockers (0.30%; 95% CI: 0.19%, 0.42%), followed by antithrombotic agents (0.17%; 95% CI: 0.12%, 0.21%), alpha-adrenoreceptor antagonists (0.11%; 95% CI: 0.06%, 0.16%), and vasodilators (0.04%; 95% CI: 0.02%, 0.07%). Three drug groups had statistically significant decreases in slope, with the greatest impact occurring among renin-angiotensin system agents (−0.31%; 95% CI: −0.41%, −0.22%), followed by beta blocking agents (0.27%; 95% CI: −0.33%, −0.20%) and drugs for obstructive airway diseases (−0.18%; 95% CI: −0.34%, −0.02%).

## Hormone-Related Conditions

ITS models for the 6 drugs used for hormone-related conditions are presented in Figure 2c. The estimated annual change in PDC showed statistically significant increases in slope among 4 drug groups, with the greatest impact occurring among injectable insulins and analogues (0.85%; 95% CI: 0.60%, 1.09%), followed by estrogens (0.10%; 95% CI: 0.06%, 0.14%), other blood glucose lowering drugs (0.08%; 95% CI: 0.02%, 0.14%), and oral hormonal contraceptives (0.04%; 95% CI: 0.02%, 0.06%).

## Immune & Skeletal System Conditions

ITS models for the 6 drugs used for immune and skeletal system conditions are presented in Figure 2d. The estimated annual change in PDC showed statistically significant increases in slope among all 6 drug groups, with the greatest estimated change occurring among parenteral immunosuppressants (1.91%; 95% CI: 1.45%, 2.36%), followed by oral immunosuppressants (0.17%; 95% CI: 0.11%, 0.23%), bisphosphonates (0.10%; 95% CI: 0.07%, 0.13%), uric acid inhibitors (0.09%; 95% CI: 0.03%, 0.15%), intestinal anti-inflammatory agents (0.06%; 95% CI: 0.02%, 0.10%), and immunostimulants (0.01%; 95% CI: 0.007%, 0.02%).

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**Table 2** Mean PDC (%) 1-year Before and After the Implementation of Mitigation Measures Against the COVID-19 Pandemic Among Study Population Overall and Stratified by Sex

| Drug Group | All | | | Male | | | Female | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1-Year Before March 11, 2020 | 1-Year After March 11, 2020 | P-value | 1-Year Before March 11, 2020 | 1-Year After March 11, 2020 | P-value | 1-Year Before March 11, 2020 | 1-Year After March 11, 2020 | P-value |
| **Drugs for psychiatric and neurologic conditions** | | | | | | | | | |
| Antidementia drugs | 27.0 | 24.1 | <0.05 | 30.0 | 27.3 | <0.05 | 25.0 | 22.1 | <0.05 |
| Dopaminergic and anticholinergic agents | 25.4 | 23.9 | <0.05 | 28.5 | 26.9 | <0.05 | 22.3 | 20.8 | <0.05 |
| Antipsychotics | 23.3 | 22.6 | <0.05 | 23.6 | 23.0 | <0.05 | 22.9 | 22.3 | <0.05 |
| Antidepressants | 21.7 | 21.6 | 0.66 | 18.7 | 18.3 | <0.05 | 23.6 | 23.7 | 0.50 |
| Antiepileptics | 16.9 | 16.5 | <0.05 | 16.5 | 16.0 | <0.05 | 17.1 | 16.9 | <0.05 |
| Stimulants and centrally acting antiadrenergic agents | 10.3 | 9.1 | <0.05 | 10.3 | 9.1 | <0.05 | 10.3 | 9.1 | <0.05 |
| **Drugs for cardiac and respiratory conditions** | | | | | | | | | |
| Renin-angiotensin system agents | 50.5 | 51.5 | <0.05 | 51.4 | 52.1 | <0.05 | 49.5 | 50.9 | <0.05 |
| Calcium channel blockers | 47.5 | 45.4 | <0.05 | 49.5 | 47.4 | <0.05 | 45.6 | 43.5 | <0.05 |
| Beta blocking agents | 37.1 | 33.1 | <0.05 | 42.4 | 37.9 | <0.05 | 32.2 | 28.7 | <0.05 |
| Antithrombotic agents | 34.1 | 32.4 | <0.05 | 33.4 | 31.5 | <0.05 | 35.2 | 33.7 | <0.05 |
| Diuretics | 29.0 | 26.8 | <0.05 | 30.9 | 28.6 | <0.05 | 27.6 | 25.5 | <0.05 |
| Alpha-adrenoreceptor antagonists | 19.8 | 19.0 | <0.05 | 21.6 | 20.8 | <0.05 | 3.9 | 3.3 | <0.05 |
| Drugs for obstructive airway diseases | 8.8 | 8.7 | 0.94 | 9.0 | 8.9 | 0.44 | 8.5 | 8.6 | 0.77 |
| Vasodilators | 5.4 | 4.9 | <0.05 | 5.0 | 4.5 | <0.05 | 6.0 | 5.4 | <0.05 |
| **Drugs for hormone-related conditions** | | | | | | | | | |
| Thyroid hormones | 71.8 | 71.3 | <0.05 | 71.7 | 71.1 | <0.05 | 71.8 | 71.3 | <0.05 |
| Lipid modifying agents | 61.5 | 61.7 | 0.08 | 64.3 | 64.5 | 0.08 | 57.9 | 58.1 | 0.09 |
| Blood glucose lowering drugs (excluding insulin) | 52.9 | 51.5 | <0.05 | 57.6 | 56.2 | <0.05 | 47.9 | 46.5 | <0.05 |
| Injectable insulins and analogues | 44.4 | 36.4 | <0.05 | 54.4 | 45.1 | <0.05 | 35.6 | 28.8 | <0.05 |
| Oral hormonal contraceptives | 9.7 | 8.3 | <0.05 | 1.1 | 1.0 | <0.05 | 9.7 | 8.3 | <0.05 |
| Estrogens | 7.8 | 6.9 | <0.05 | 7.1 | 4.6 | <0.05 | 7.8 | 6.9 | <0.05 |
| **Drugs for immune and skeletal system conditions** | | | | | | | | | |
| Parenteral immunosuppressants | 48.3 | 34.3 | <0.05 | 53.4 | 38.1 | <0.05 | 44.3 | 31.2 | <0.05 |
| Uric acid inhibitors | 47.5 | 46.4 | <0.05 | 50.1 | 49.1 | <0.05 | 39.8 | 38.0 | <0.05 |
| Oral immunosuppressants | 33.0 | 30.7 | <0.05 | 36.0 | 33.4 | <0.05 | 31.0 | 28.8 | <0.05 |
| Bisphosphonates | 17.9 | 17.1 | <0.05 | 18.9 | 17.9 | <0.05 | 17.1 | 16.4 | <0.05 |
| Intestinal anti-inflammatory agents | 20.4 | 18.8 | <0.05 | 21.3 | 19.1 | <0.05 | 20.2 | 18.7 | <0.05 |
| Immunostimulants | 1.9 | 1.7 | <0.05 | 0.9 | 0.9 | <0.05 | 3.1 | 2.8 | <0.05 |

**Table 3** Results of Interrupted Times Series (ITS) Modeling Using Linear Equations to Estimate Change in PDC After the Introduction of Mitigation Measures for the COVID-19 Pandemic for 26 Included Drug Groups Among Study Population

| Drug Group | Model A: 1-year Before March 11, 2020 | | Model B: 1-Year After March 11, 2020 | | Estimated Change[a] | | R-squared |
|---|---|---|---|---|---|---|---|
| | Annual Change in PDC, slope Coefficient (95% CI) | P-value | Annual Change in PDC, slope Coefficient (95% CI) | P-value | Annual Change in PDC, slope Coefficient (95% CI) | P-value | |
| **Drugs for psychiatric and neurologic conditions** | | | | | | | |
| Antidementia drugs | −0.35 (−0.39, −0.32) | <0.05 | −0.14 (−0.17, −0.11) | <0.05 | 0.21 (0.15, 0.27) | <0.05 | 0.95 |
| Dopaminergic and anticholinergic agents | −0.13 (−0.14, −0.11) | <0.05 | −0.13 (−0.14, −0.11) | <0.05 | −0.0006 (−0.03, 0.02) | 0.96 | 0.99 |
| Antipsychotics | −0.09 (−0.11, −0.06) | <0.05 | −0.04 (−0.06, −0.02) | <0.05 | 0.05 (0.002, 0.09) | <0.05 | 0.88 |
| Antidepressants | −0.07 (−0.10, −0.04) | <0.05 | 0.05 (0.02, 0.08) | <0.05 | 0.11 (0.06, 0.17) | <0.05 | 0.21 |
| Antiepileptics | −0.06 (−0.08, −0.05) | <0.05 | 0.003 (−0.01, 0.02) | 0.74 | 0.07 (0.04, 0.10) | <0.05 | 0.69 |
| Stimulants and centrally acting antiadrenergic agents | −0.19 (−0.22, −0.16) | <0.05 | −0.03 (−0.06, 0.002) | 0.06 | 0.16 (0.11, 0.22) | <0.05 | 0.85 |
| **Drugs for cardiac and respiratory conditions** | | | | | | | |
| Renin-angiotensin system agents | 0.27 (0.21, 0.33) | <0.05 | −0.04 (−0.10, 0.007) | 0.09 | −0.31 (−0.41, −0.22) | <0.05 | 0.76 |
| Calcium channel blockers | −0.34 (−0.41, −0.28) | <0.05 | −0.04 (−0.10, 0.02) | 0.17 | 0.30 (0.19, 0.42) | <0.05 | 0.83 |
| Beta blocking agents | −0.19 (−0.23, −0.15) | <0.05 | −0.46 (−0.49, −0.42) | <0.05 | −0.27 (−0.33, −0.20) | <0.05 | 0.96 |
| Antithrombotic agents | −0.23 (−0.26, −0.21) | <0.05 | −0.06 (−0.09, −0.04) | <0.05 | 0.17 (0.12, 0.21) | <0.05 | 0.91 |
| Diuretics | −0.18 (−0.23, −0.14) | <0.05 | −0.21 (−0.25, −0.17) | <0.05 | −0.03 (−0.10, 0.04) | 0.42 | 0.97 |
| Alpha-adrenoreceptor antagonists | −0.13 (−0.16, −0.10) | <0.05 | −0.01 (−0.04, 0.01) | 0.27 | 0.11 (0.06, 0.16) | <0.05 | 0.77 |
| Drugs for obstructive airway diseases | 0.08 (−0.02, 0.17) | 0.10 | −0.10 (−0.19, −0.02) | <0.05 | −0.18 (−0.34, −0.02) | <0.05 | 0.036 |
| Vasodilators | −0.07 (−0.08, −0.05) | <0.05 | −0.02 (−0.04, −0.01) | <0.05 | 0.04 (0.02, 0.07) | <0.05 | 0.88 |
| **Drugs for hormone-related conditions** | | | | | | | |
| Thyroid hormones | −0.07 (−0.10, −0.04) | <0.05 | −0.02 (−0.05, 0.009) | 0.17 | 0.05 (−0.004, 0.11) | 0.07 | 0.67 |
| Lipid modifying agents | 0.03 (−0.01, 0.07) | 0.16 | 0.01 (−0.03, 0.05) | 0.53 | −0.02 (−0.09, 0.05) | 0.61 | 0.23 |
| Blood glucose lowering drugs (excluding insulin) | −0.17 (−0.20, −0.13) | <0.05 | −0.08 (−0.12, −0.05) | <0.05 | 0.08 (0.02, 0.14) | <0.05 | 0.92 |
| Injectable insulins and analogues | −1.09 (−1.24, −0.94) | <0.05 | −0.25 (−0.38, −0.11) | <0.05 | 0.85 (0.60, 1.09) | <0.05 | 0.88 |
| Oral hormonal contraceptives | −0.14 (−0.15, −0.13) | <0.05 | −0.10 (−0.12, −0.09) | <0.05 | 0.04 (0.02, 0.06) | <0.05 | 0.99 |
| Estrogens | −0.12 (−0.14, −0.09) | <0.05 | −0.02 (−0.04, 0.0009) | 0.06 | 0.10 (0.06, 0.14) | <0.05 | 0.80 |
| **Drugs for immune and skeletal system conditions** | | | | | | | |
| Parenteral immunosuppressants | −2.14 (−2.41, −1.87) | <0.05 | −0.23 (−0.48, 0.007) | 0.06 | 1.91 (1.45, 2.36) | <0.05 | 0.84 |
| Uric acid inhibitors | −0.14 (−0.17, −0.11) | <0.05 | −0.05 (−0.08, −0.02) | <0.05 | 0.09 (0.03, 0.15) | <0.05 | 0.95 |
| Oral immunosuppressants | −0.28 (−0.32, −0.24) | <0.05 | −0.11 (−0.14, −0.08) | <0.05 | 0.17 (0.11, 0.23) | <0.05 | 0.85 |
| Bisphosphonates | −0.18 (−0.20, −0.17) | <0.05 | −0.08 (−0.10, −0.07) | <0.05 | 0.10 (0.07, 0.13) | <0.05 | 0.93 |
| Intestinal anti-inflammatory agents | −0.10 (−0.12, −0.07) | <0.05 | −0.04 (−0.06, −0.02) | <0.05 | 0.06 (0.02, 0.10) | <0.05 | 0.88 |
| Immunostimulants | −0.02 (−0.03, −0.02) | <0.05 | −0.009 (−0.01, −0.005) | <0.05 | 0.01 (0.007, 0.02) | <0.05 | 0.95 |

**Notes**: [a]Estimated change defined as difference between the predicted PDC and the modeled PDC (**Model B**) for 1-year period after the index date computed using fitted linear models for 1-year before and after March 11, 2020.

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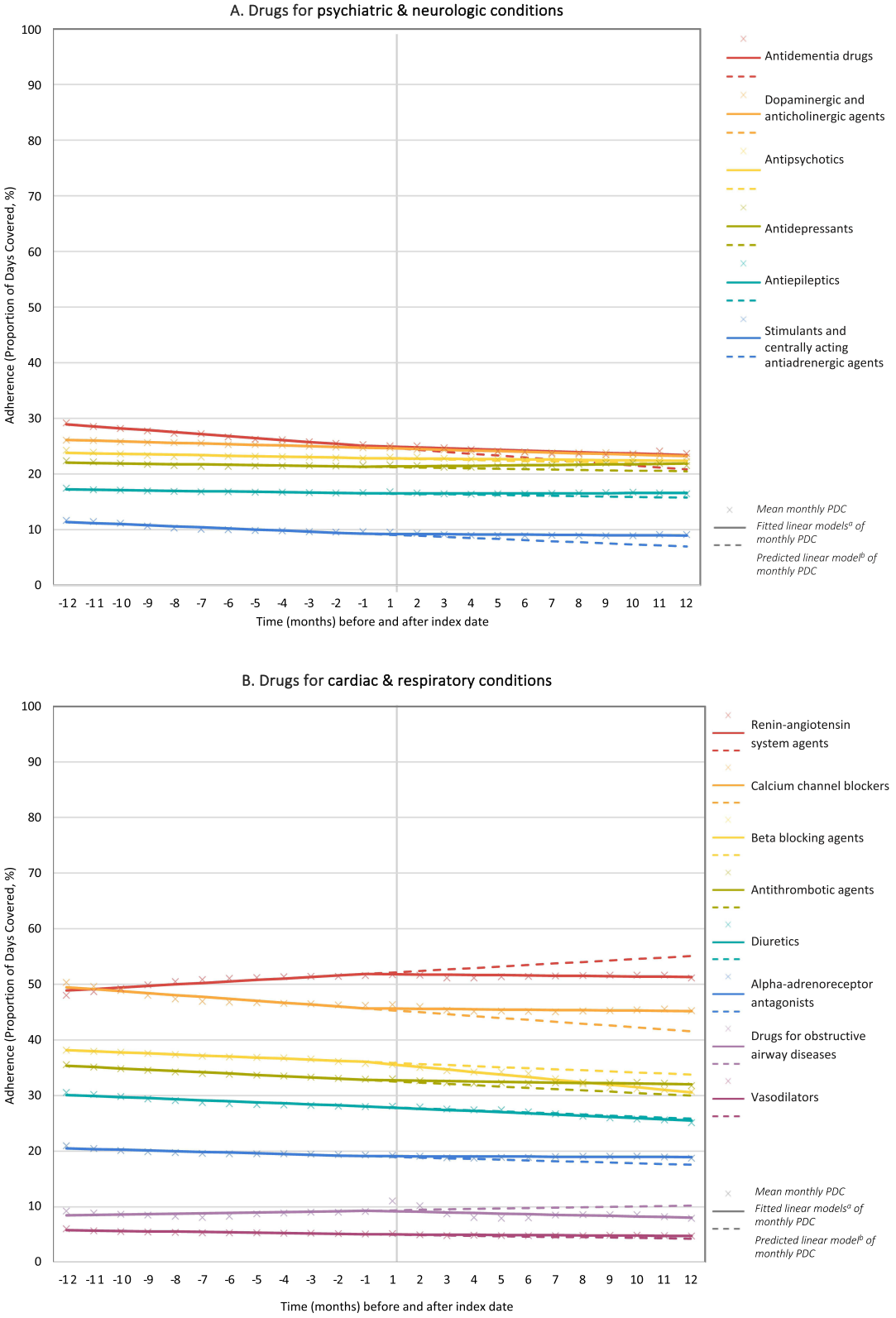


**Figure 2** Continued.

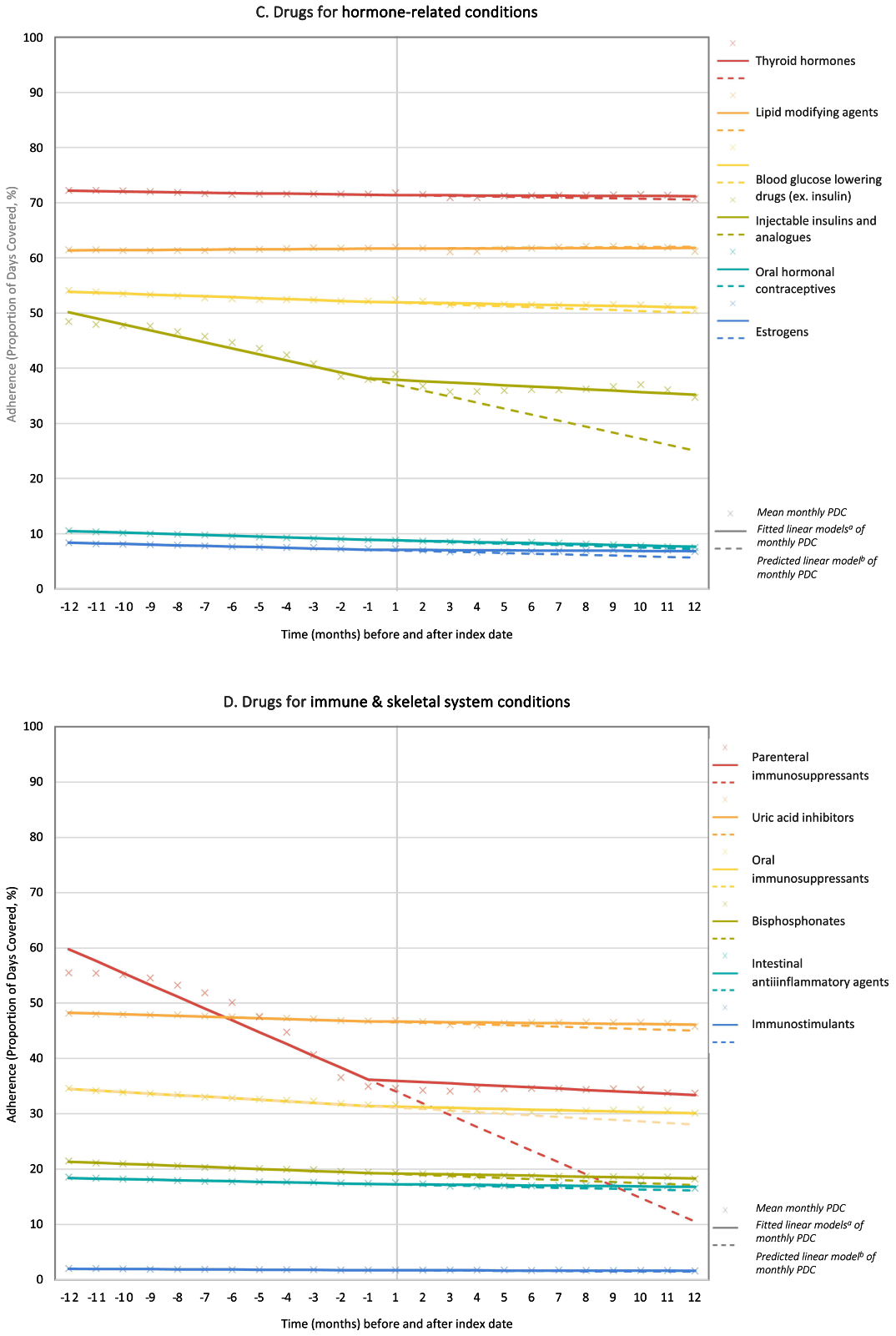


**Figure 2** Interrupted times series models of PDC trajectory 1-year before and after the introduction of mitigation measures for the COVID-19 pandemic of drugs for psychiatric and neurologic conditions (**A**), cardiac and respiratory conditions (**B**), hormone-related conditions (**C**), and immune and skeletal system conditions (**D**) among the study population.

**Notes**: [a]Includes **Model A**, fitted for the mean monthly PDC in the 1-year period before the index date, and **Model B**, fitted for the mean monthly PDC in the 1-year period after the index date (x = 0). [b]Computed using the slope coefficient of the fitted linear model of mean monthly PDC for 1-year period before the index date (**Model B**) to estimate the mean monthly PDC for the 1-year period after the index date.


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## Discussion

Using population-based administrative health data and a drug-based analytic framework that aligns with pharmaceutical care delivery, we evaluated adherence to commonly used drugs for chronic conditions before and after the introduction of mitigation measures against the COVID-19 pandemic in BC. Our findings expand on a recent ITS analysis of prescription dispensing rates in BC that showed, after a slight decrease (2.4%) in overall dispensations in March 2020, sustained weekly increases restored dispensations to pre-pandemic trends by January 2021,[21] and a Manitoba study that showed consistent findings.[22] With our current analysis reflecting adherence to the prescribed regimen of medications used to treat chronic conditions, it is important to note that adherence across all 26 drug groups was suboptimal; specifically, mean PDC over both the 1-year before and after periods were well below 80%, the most widely accepted cut-off for satisfactory adherence.[23]

The introduction of mitigation measures showed a heterogeneous impact on medication adherence among individual drug groups. Specifically, we found increasing trends in adherence among 19 drug groups, with the greatest estimated change occurring among parenteral immunosuppressants, injectable insulins and analogues, calcium channel blockers, and antidementia drugs, as well as decreasing trends in adherence among the 3 drug groups (ie, renin-angiotensin system agents, beta blocking agents, and drugs for obstructive airway diseases). Although statistically significant, these trends represent −0.31% to 1.91% changes in PDC, which warrant cautious interpretation of the clinical significance of the impact of the COVID-19 pandemic on medication taking. A population-based study in Manitoba used ITS to examine the impact of the COVID-19 pandemic on psychotropic medication adherence, measured as the proportion of individuals with a medication possession ratio of >80%, and found improved adherence in the 9 months following public health restrictions.[24] In addition to similarly reporting improved adherence among 5 of the 6 drug groups for psychiatric and neurologic conditions, our analysis provided an accurate population-level representation of adherence to prescribed dosing regimens by avoiding the reduction of adherence measures to a dichotomous categorical variable. Furthermore, changes in PDC trends among all included drug groups in our study, whether increasing or decreasing, were in the context of suboptimal PDCs across study periods; therefore, they did not represent a change from what would be considered adherent to non-adherent behaviour (ie, ≥80% to <80%) or vice versa. Unique to our study is sex-stratified analysis which showed similar adherence trends across the 26 drug groups in the year before and after the index date, with mean PDC consistently slightly lower in females across most study periods.

Prior research on medication taking during COVID-19 has relied on subjective, cross-sectional surveys prone to reporting biases and focused mainly on disease-based rather than drug-based adherence. In rheumatology, we conducted a rapid review of 31 peer-reviewed studies and estimated a pooled prevalence of medication non-adherence of 14.8% during the COVID-19 pandemic among patients with rheumatic diseases.[25] Ruksakulpiwat et al conducted a systematic review of medication adherence among patients with chronic diseases and identified barriers to adherence (eg, concern of COVID-19 infection, medication shortage, travel restriction, financial restriction and substance use) and facilitators to adherence (eg, adherence with health guidelines and health information).[6] Our study adds to this literature for several reasons: 1) population-based administrative health data provides generalizable results; 2) use of prescription fills provides an objective measure of adherence; 3) use of ITS is a method that allows for evaluation of the impact of the COVID-19 pandemic on medication adherence; and 4) use of drug-based framework that aligns with pharmaceutical care delivery.

Although ITS analysis helps address several key threats to validity present in observational epidemiologic studies, it is important to discuss limitations of this approach. First, given the global nature of the COVID-19 pandemic, it was not feasible to have a control group. Given data availabilities, our study period was limited to 1-year before and after the start of COVID-19 pandemic (March 11, 2020) and we were not able to evaluate a prolonged pandemic period or related to this, discontinuation of prescriptions given that this necessitates a longer follow-up period. Nonetheless, our study period captures the critical early phase of the pandemic, coinciding with the strictest mitigation measures. Although PDC based on medication refills provides a more objective measure of adherence compared to surveys, it reflects prescription fills rather than actual medication taking. Since information is only available for prescription fills and not for prescriptions written, we were unable to assess primary non-adherence (ie, whether patients initiate their prescribed medications).[8] Moreover, use of administrative health data limits the ability to explore reasons for suboptimal adherence observed,

including cost-related non-adherence. Finally, as we did not have information on prescriptions received in hospital, we were not able to account for potential medications stockpiled during hospitalization. However, as number of hospital stays among our population was low and Parker et al's[18] data-driven approach for handling gaps between prescriptions has shown consistent results regardless of whether stockpiled medication from early fills was accounted for, we do not expect this additional potential stockpile to significantly affect our findings.

Our study provides a valuable overview of the impact of COVID-19 on medication adherence. Although findings suggest that the COVID-19 pandemic did not substantially impact adherence to commonly used medications for chronic diseases in BC, they alarmingly indicate suboptimal adherence across virtually all of drug groups evaluated. Importantly, medication adherence remains a critical therapeutic challenge that requires our attention irrespective of major stressors like the COVID-19 pandemic.

## Conclusion

Findings suggest that the pandemic did not substantially impact adherence to commonly used medications; however, adherence was found to be suboptimal across all drug groups regardless of the impact of COVID-19. Medication adherence remains a critical therapeutic challenge requiring our attention irrespective of major healthcare system stressors such as COVID-19.

## Data Sharing Statement

Access to data provided by the Data Stewards is subject to approval but can be requested for research projects through them or their designated service providers. The following data sets were used in this study: Medical Services Plan, Discharge Abstract Database, Vital Statistics, and PharmaNet. Further information regarding these data sets can be found on the PopData projects webpage (https://www.popdata.bc.ca/ria/projects) or project webpage (https://my.popdata.bc.ca/project_listings/21-001/collection_approval_dates).

## Ethics Approval

This study was approved by the University of British Columbia (UBC) Behavioural Research Ethics Board (H20-03241).

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