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RESEARCH ARTICLE

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The effects of COVID-19 on the dispensing rates of antidepressants and benzodiazepines in Canada

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Abstract

Background: Population studies have shown that rates of depressive and anxious symptoms have increased as a result of COVID-19. We analyzed trends in the dispensing rates of antidepressants and benzodiazepines in Canada to determine whether the pandemic has caused changes in rates of pharmacological treatment for depression and anxiety.

Methods: We conducted a population-based, cross-sectional time-series analysis of antidepressants and benzodiazepines dispensed monthly by Canadian community pharmacies between January 2017 and December 2020. We used March 2020 as the intervention month to determine if there were any significant changes in the national rate of antidepressant and benzodiazepine tablets dispensed as the result of the COVID-19 pandemic.

Results: There was a temporary reduction in the dispensing rate of antidepressants in April 2020 (from 489 tablets per 100 in March 2020 to 356 tablets per 100 in April 2020; $p \leq .0001$); however, the rate returned to its previous level by August 2020. There were no detectable deviations in benzodiazepine dispensing after the declaration of the state of emergency in Ontario.

Conclusions: Despite the increased reporting of depressive and anxious symptoms during the COVID-19 pandemic, there have been no changes in the dispensing trends of medications used to treat these disorders. As the pandemic continues to evolve, future research is needed to monitor the prevalence of depression and anxiety, and associated medication use, in the Canadian population.

KEYWORDS

antidepressant, anxiety, benzodiazepine, COVID-19, depression, medication, pandemic

1 | INTRODUCTION

Since the World Health Organization declared severe acute respiratory syndrome coronavirus 2 (i.e., COVID-19) as the cause of a worldwide pandemic in March 2020 (World Health Organization, 2021), there has been concern that fear of infection, increased social isolation, and the economic impacts of lockdowns would lead to rising prevalence of depression and anxiety (Brooks et al., 2020). Furthermore, a pandemic could lead to restricted accessibility to primary care and other healthcare services including treatment and supports for mental health diagnoses, which could potentiate depression and/or anxiety especially for patients who have limited access to virtual care (Centre for Addiction and Mental Health, 2020). Indeed, studies conducted in the population over the course of the pandemic suggest that the prevalence of depressive and anxious symptoms have increased (McGinty et al., 2020; Rajkumar, 2020;

Salari et al., 2020; Vindegaard & Benros, 2020; Xiong et al., 2020). In Canada, the proportion of Canadians reporting having "excellent" or "very good" mental health decreased from 68% in 2019 to 55% in July of 2020 (Statistics Canada, 2020), while in the United States, symptoms of anxiety or depression rose to 42% in December 2020 from 11% between January and June 2019 (Nature, 2021). So far, it has been unclear whether the increases in symptom reporting have translated to increased depression and anxiety diagnoses at the population level.

The treatment options for depression and anxiety include pharmacological and psychological approaches that can be used alone or in combination. Antidepressants are often prescribed first-line for the chronic treatment of both depression and anxiety, whereas benzodiazepines can be used as short-term treatment options for acute anxiety (Katzman et al., 2014; Kennedy et al., 2016). Because there exists a body of literature that suggests an increase in the prevalence of depressive and anxious symptoms during the COVID-19 pandemic, our focus was to determine whether this has had an impact on patient access to antidepressant and anxiolytic medications in the Canadian context. This is an important measure because quantifying the pharmacological treatment of depression and anxiety is a highly specific way of measuring access to treatment for these disorders at a population level. Moreover, very few existing studies on the topic of pandemic-related mental health dysfunction have focused on Canadian populations. Because the impact of and public response to COVID-19 varies from country to country, we sought to analyze trends in the dispensing rates of antidepressants and benzodiazepines in Canada over the past 4 years to determine whether the COVID-19 pandemic, and its associated public health responses, have led to changing rates of access to pharmacological treatment for depression and anxiety.

2 | MATERIALS AND METHODS

2.1 | Settings and design

We conducted a population-based, cross-sectional time-series analysis of antidepressants and benzodiazepines dispensed monthly by Canadian community pharmacies between January 1, 2017 and December 31, 2020.

2.2 | Sources of data

We obtained medication dispensing data from the IQVIA database which uses a representative sample of more than 6100 community pharmacies across Canada that captures approximately 78% of total prescriptions dispensed nationally to create projections for the total quantity dispensed nationally [based on 2020 data]. The sampling error is typically ~3%, although data from 2016 suggests it can be as high as ~5%–10% for monthly estimates at the provincial level. These data are monitored and validated by IQVIA and are commonly used for research purposes (Gomes et al., 2014). The data obtained for this study consisted of prescriptions paid for by cash, third-party insurers, and provincial/national drug programs, and was stratified by province, month, age group, and drug product. We did not require research ethics approval because the data was deidentified and obtained in aggregate form. We used Statistics Canada census data from 2017 to 2020 (Statistics Canada, 2021) to obtain population estimates overall and by age nationally and provincially over the study period to calculate population-standardized dispensing rates. Because Statistics Canada only provided annual population estimates, we used linear interpolations to estimate the monthly population sizes.

2.3 | Medication trends

Our primary measure of interest was the population-adjusted rate of units (i.e., tablets) dispensed per 100 population on a monthly basis between January 1, 2017 and December 31, 2020. The antidepressants included in the study were bupropion, desvenlafaxine, duloxetine, monoamine oxidase inhibitors, mirtazapine, selective serotonin reuptake inhibitors, tricyclic antidepressants, trazadone, vilazodone, vortioxetine, and venlafaxine, and the benzodiazepines included were alprazolam, bromazepam, chlordiazepoxide, clorazepate, diazepam, lorazepam, and oxazepam. We only included oral solid dosage forms of medications because it would be difficult to quantify units of oral liquids and injectable dosages; the latter dosage forms are also much less commonly used in the population. The specific antidepressant and benzodiazepine drugs used in our analysis as well as our grouping of drugs into drug classes are shown in the Supporting Information Appendix. Although antipsychotics can be used as adjunctive therapies for the treatment of depression and anxiety, we did not include them in our analysis because of their primary use for other disorders not covered by this study, such as bipolar disorder and schizophrenia. For each antidepressant and benzodiazepine in our study, we calculated monthly dispensing rates nationally and stratified our analyses by province and patient age group to determine if patterns differed geographically or demographically. We also calculated relative changes (i.e., percent increase/decrease) in the monthly dispensing rates of antidepressants and benzodiazepines compared to March 2020 (Supporting Information Appendix).

In a post-hoc exploratory analysis, we examined the distribution of each antidepressant and benzodiazepine type in the 6 months before and following March 2020 to determine whether there had been any changes in the composition of antidepressants and benzodiazepines dispensed during the pandemic.

2.4 | Statistical analysis

We used interventional autoregressive integrated moving average (ARIMA) models to examine the impact of several interventions on monthly units of antidepressant and benzodiazepine dispensations

nationally across Canada overall and stratified by patient age group (i.e., ≤18, 19–29, 30–49, 50–64, and ≥65 years). We differenced the time series to achieve stationarity and adjust for seasonality which was confirmed using the augmented Dickey–Fuller test. We selected model parameters using the residual autocorrelation function, partial autocorrelation function, and inverse autocorrelation function correlograms. Lastly, we chose the final model using the autocorrelation plots and the Ljung–Box χ^2 test for white noise.

Different intervention functions were added to each model to account for the impact of COVID-19, including a pulse intervention function to test for a temporary change in dispensing in April 2020 and a ramp intervention function to test for gradual changes in trends from March 2020 to the end of the study period. We used the *t*-statistic from the maximum likelihood estimation to determine if the intervention functions were significant parameters in the ARIMA model and thus had a significant impact on the time series. We used a type 1 error rate of 0.05 and conducted the analyses using SAS statistical software (v 9.4, EG 8.2; SAS Institute) and the SAS/ETS Time Series Forecasting System.

3 | RESULTS

3.1 | Antidepressants

A total of 7.904 billion tablets of antidepressants were dispensed nationally across Canada from January 2017 to December 2020, with the rate of dispensing rising 31.4% over the course of this 4-year period (from 400 tablets per 100 to 526 tablets per 100 nationally in January 2017 and December 2020, respectively; Figure 1). Overall, there was considerable provincial variation in the rate of antidepressant dispensing. The ranking from highest to lowest antidepressant dispensing province in March 2020 was Newfoundland and Labrador, Nova Scotia, New Brunswick, Prince Edward Island, Quebec, Saskatchewan, British Columbia, Alberta, Manitoba, Ontario (Supporting Information Appendix). There was a 1.8-fold difference between the highest dispensing province (Newfoundland and Labrador, 792 tablets per 100 population) and the lowest dispensing province (Ontario, 445 tablets per 100 population) for this month. Predictably, increasing patient age group was associated with increasing rate of antidepressant dispensing. For example, the national dispensing rate for seniors ≥65 years in March 2020 was more than double that of young adults aged 19–29 (800 vs. 361 tablets per 100 population, respectively; Figure 2). There was no change in the types of antidepressants dispensed in the 6 months before March 2020 and the 6 months following (Supporting Information Appendix). Relative changes in monthly dispensing rates of antidepressants compared to March 2020 are displayed in the Supporting Information Appendix.

The COVID-19 state of emergency led to a statistically significant temporary (i.e., pulse) reduction in the overall dispensing rate of antidepressants in April 2020 (from 489 tablets per 100 in March 2020 to 356 tablets per 100 in April 2020; $p \leq .0001$) but no change in slope from March 2020 until the end of the study period ($p = .236$; Table 1). By August, the rates stabilized, and there were no detectable deviations from the trends in antidepressant dispensing that had been observed before COVID-19. Results were consistent by age group, with statistically significant temporary reductions in antidepressant dispensing rates for age groups ≤18 years (68–50 tablets per 100; $p \leq .0001$), 19–29 years (361–262 tablets per 100; $p \leq .0001$), and 30–49 years (508–360 tablets per 100; $p \leq .0001$; Table 1). Models for age groups 50–64 years and ≥65 years could not be fit because requirements for the white noise test were not met.

3.2 | Benzodiazepines

A total of 1.442 billion tablets of benzodiazepines were dispensed nationally across Canada from January 2017 to December 2020, with

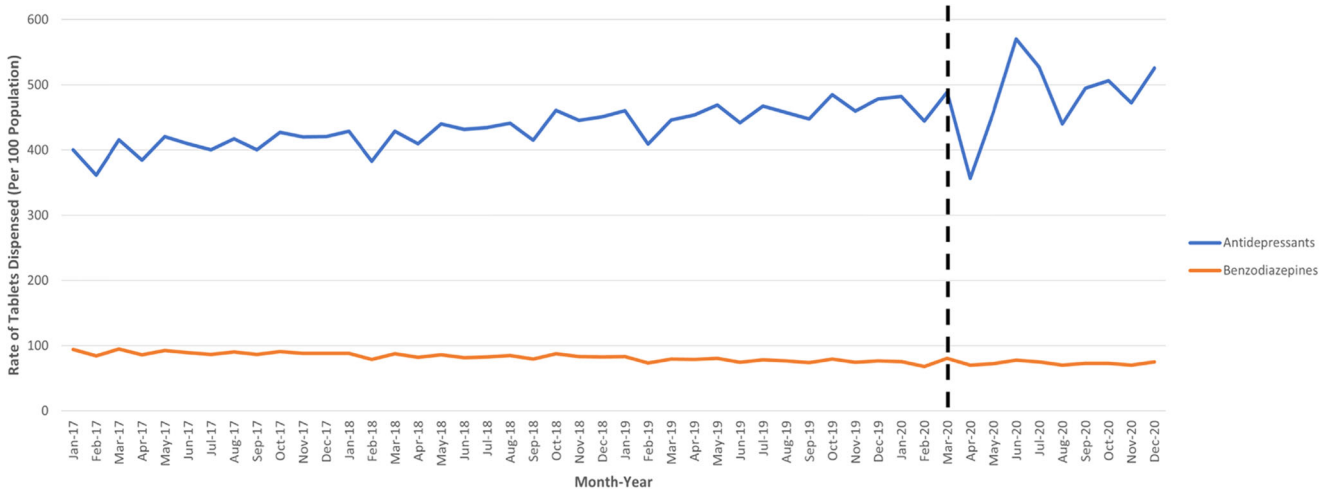

FIGURE 1 Rate of antidepressant and benzodiazepine tablets dispensed (in number of tablets per 100 population) nationally between January 2017 and December 2020

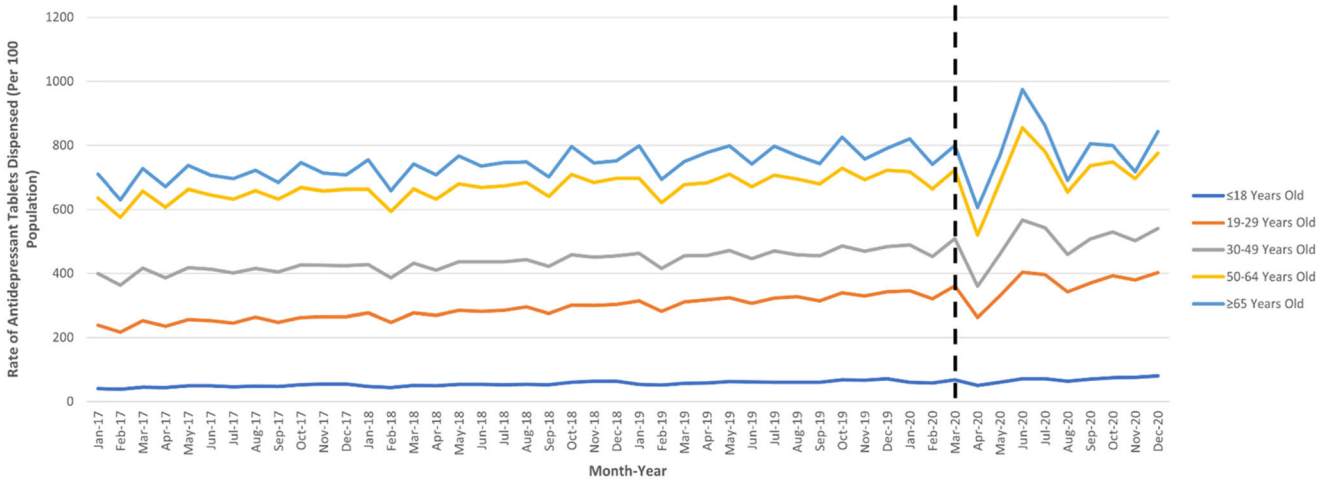

FIGURE 2 Rate of antidepressant tablets dispensed (in number of tablets per 100 population) nationally based on patient age group, between January 2017 and December 2020

TABLE 1 ARIMA model parameters for the rate of antidepressant and benzodiazepine units dispensed nationally overall and stratified by patient age group

Models	Model specification	Pulse intervention: April 2020		Ramp intervention: March 2020	
		Estimate (standard error)	*p*-Value	Estimate (standard error)	*p*-Value
Antidepressant rate (units per 100 population)	(7,1,12,0)	−58.5 (±11.3)	<.0001*	1.6 (±1.3)	.236
Age stratification					
≤18 years	(4,1,12,0)	−12.6 (±1.8)	<.0001*	0.2 (±0.2)	.439
19–29 years	(5,1,12,0)	−66.1 (±9.2)	<.0001*	2.1 (±1.1)	.058
30–49 years	(5,1,12,0)	−88.2 (±13.5)	<.0001*	1.7 (±1.7)	.322
50–64 years	Models could not be run since the white noise test was not met				
≥65 years	Models could not be run since the white noise test was not met				
Benzodiazepine rate (units per 100 population)	(2,1,12,0)	−3.3 (±1.8)	.063	0.0 (±0.3)	.916
Age stratification					
≤18 years	(2,1,12,0)	−0.2 (±0.2)	.297	−0.2 (±0.2)	.998
19–29 years	(2,1,12,0)	0.1 (±0.6)	.909	0.0 (±0.1)	.848
30–49 years	(4,1,12,0)	−0.9 (±1.6)	.595	−0.1 (±0.4)	.801
50–64 years	(2,1,12,0)	−3.1 (±2.3)	.170	−0.1 (±0.4)	.718
≥65 years	(4,1,12,0)	−10.4 (±5.7)	.067	0.1 (±0.7)	.896

Abbreviation: ARIMA, autoregressive integrated moving average.
*Significance (<.05).

the rate of dispensing declining 19.9% over the course of this 4-year period (from 94 tablets per 100 to 75 tablets per 100 nationally in January 2017 and December 2020, respectively; Figure 1). Overall, there was a high degree of provincial variation in prescribing, with a 5.2-fold difference in rates between the highest dispensing province (New Brunswick, 222 tablets per 100 population) and the lowest dispensing province (Saskatchewan, 43 tablets per 100 population) in March 2020 (Supporting Information Appendix). As seen with the antidepressant data, increasing patient age was associated with increasing rates of benzodiazepines dispensed; the national

dispensing rate for seniors ≥65 years in March 2020 was almost 12 times higher than that of young adults aged 19–29 (230 and 19 tablets per 100 population, respectively; Figure 3).

The ARIMA model did not detect a statistically significant temporary change ($p = .063$) or change in slope ($p = .916$) in the overall dispensing rate of benzodiazepines as the result of the COVID-19 state of emergency (Table 1). Similarly, statistically significant changes were not seen in benzodiazepine dispensing rates when analyzed individually by age group (Table 1). In other words, there were no detectable deviations in the trends of benzodiazepine dispensing over the study period. Similar to the antidepressant analysis, there was no change in the types of benzodiazepines dispensed before and after March 2020 (Supporting Information Appendix). Relative changes in monthly dispensing rates of benzodiazepines compared to March 2020 are displayed in the Supporting Information Appendix.

4 | DISCUSSION

The declaration of the COVID-19 pandemic and its associated public health responses in March 2020 appear to have contributed to a temporary destabilization in antidepressant dispensing across the country. Specifically, the rate dropped considerably from March to April, before rising again between April and June. This fluctuation was short-lived, only lasting for 4 months before restabilizing. On the other hand, the onset of COVID-19 did not appear to have any effect on the rate of benzodiazepine dispensing across Canada. These findings for antidepressant and benzodiazepine dispensing rates were similar across all patient age groups.

Many people around the world have reported declining mental health as the result of the COVID-19 pandemic (McGinty et al., 2020; Nature, 2021; Rajkumar, 2020; Salari et al., 2020; Statistics Canada, 2020; Vindegaard & Benros, 2020; Xiong et al., 2020), suggesting that rates of antidepressant and benzodiazepine dispensing would potentially increase during the pandemic. However, our findings suggest that this is not the case. Antidepressants are commonly used first-line options for the treatment of moderate to severe depression and anxiety (Katzman et al., 2014; Kennedy et al., 2016), whereas benzodiazepines are often used for short-term, acute management of anxiety while antidepressant medications start to take effect (Katzman et al., 2014). The absence of a sustained increase in the dispensing of these drugs indicates that, although more people reported depressive and anxious symptoms, this has not directly translated to increases in the pharmacological treatment of their symptoms. This finding is similar to the results of a US study that showed a significant decline in new starts of antidepressants, anxiolytics, and antipsychotics during the initial months of the COVID-19 pandemic (Nason et al., 2021). It may be that the increases in symptoms reported in population-level studies represent psychological distress and adjustment disorders due to the COVID-19 pandemic that did not require pharmacological treatment. Another possible explanation could be that people sought alternative, nonpharmacological treatment for their symptoms, such as psychological therapy. For instance, Google Trends data showed a relative increase in search interest for "online counselling" and "online therapy" in and around the months when COVID-19 was declared (Google Trends, 2021a; 2021b) and a study conducted in the United States showed a significant increase in psychiatric visits from 2019 to 2020 (Ridout et al., 2021). However, it is possible that with increasing demand, individuals did require treatment but were unable to access it due to shortages of accessible mental health professionals, long wait times, cultural and language barriers, stigma, geographic and demographic inequities, and costs associated with therapy (Moroz et al., 2020). Although virtual care emerged rapidly across Canada with the advent of the COVID-19 pandemic (Bhatia et al., 2021), evidence shows that there was an initial reduction in mental health referrals early in the pandemic followed by a rapid acceleration in urgent and emergency referrals after lockdown (Chen et al., 2020).

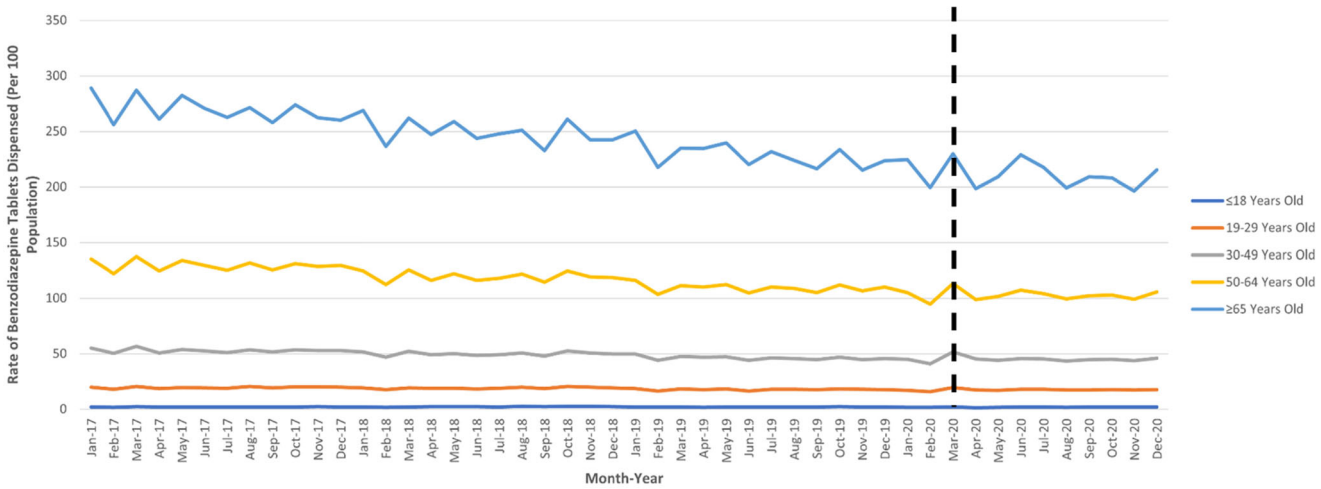

FIGURE 3 Rate of benzodiazepine tablets dispensed (in number of tablets dispensed per 100 population) nationally based on patient age group, between January 2017 and December 2020

Therefore, limited access to technology, unaffordable costs, and privacy and security issues—which may increase the risk for mental health destabilization due to COVID-19 containment efforts—might have negatively impacted access to timely care (Moreno et al., 2020). Future research is needed to properly assess longer-term trajectories of treatment patterns and access to care as the pandemic progresses.

The temporary fluctuation seen with antidepressant dispensing in the months following March 2020 can be explained by restrictions on prescription durations that were imposed by regulatory bodies in Canada to prevent drug shortages (Canadian Pharmacists Association, 2020). In March 2020, many provinces announced that they would be limiting the dispensing of chronic medications to 30 days to deter patients from stockpiling and disrupting the drug supply (Ontario Ministry of Health Drugs and Devices Division, 2020a). This policy change would explain the noticeable drop in antidepressant dispensing rate from March to April and the subsequent increases in dispensing rate over the next 2 months (i.e., May and June), when patients on chronic antidepressant therapy would require refills on their prescriptions. Many provincial restrictions were lifted in June 2020 (Ontario Ministry of Health Drugs and Devices Division, 2020b), and the rates of antidepressant dispensing re-stabilized after this. A similar destabilization was not seen with the benzodiazepine dispensing rate because, unlike antidepressants, benzodiazepines are controlled substances prescribed in smaller quantities and are not often used for chronic treatment of anxiety. Instead, they are meant to be prescribed for the short-term treatment of acute anxiety, and therefore, prescription durations are often much shorter. Future studies will be needed to evaluate the impact of these policy changes on patient adherence to antidepressant therapy as visiting the pharmacy monthly to access medications (as opposed to once every three months) may reduce patient adherence to treatment, particularly during a pandemic.

This study is not without its limitations. Perhaps the most evident limitation is that we are unable to determine indications for medication use. For example, we are unable to distinguish whether an antidepressant drug is being used to treat depression or anxiety. We also had to exclude antipsychotic medications from our analysis, despite their adjunctive use to treat depression and anxiety, because of their more common use to treat bipolar disorder and schizophrenia. Furthermore, our study only analyzed dispensing data from the first two waves of COVID-19 in Canada, thus further research is required as data from subsequent waves become available. Third, our study looks at the dispensing rates of medications but not their consumption; the two are not necessarily equivalent. We also did not have access to individual-level data, and therefore were unable to determine whether the COVID-19 pandemic impacted medication initiation rates in Canada, a phenomenon that has been described elsewhere (Ridout et al., 2021) and could be reflective of particular barriers to accessing care among people newly diagnosed with mental health disorders. Finally, because we did not have access to individual-level data, we used the number of tablets dispensed as proxy measures of access to treatment for depression and anxiety in the population. However, the number of tablets is preferred over a measure such as the number of prescriptions dispensed because the former accounts for changes in medication strength as well as for variances in prescription duration. Furthermore, post-hoc analyses showed that the composition of therapeutics remained similar throughout the pandemic, lending further support to our finding that there were no major sustained changes in pharmacological treatment over time.

5 | CONCLUSION

Our study suggests that despite the increased reporting of depressive and anxious symptoms in the population during the COVID-19 pandemic, there have been no changes in the dispensing trends of medications commonly used to treat these conditions in Canada. Future research is needed to monitor the prevalence of depression and anxiety and associated medication use in the Canadian population as a result of the COVID-19 pandemic.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

DATA AVAILABILITY STATEMENT

The statements, findings, conclusions, views, and opinions expressed in this report are based in part on data obtained under license from IQVIA Solutions Canada Inc. concerning the following information service (s): GPM, data period January 1, 2017 to December 31, 2020. All Rights Reserved. The statements, findings, conclusions, views, and opinions expressed herein are not necessarily those of IQVIA Inc. or any of its affiliated or subsidiary entities. The data that support the findings of this study are available from IQVIA (www.iqvia.com). Restrictions apply to the availability of these data, which were used under license for this study.

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SUPPORTING INFORMATION

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