

Dispensing patterns of mental health medications before and during the COVID-19 pandemic in Alberta, Canada: An interrupted time series analysis

The International Journal of
Psychiatry in Medicine
2022, Vol. 0(0) 1–13
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DOI: 10.1177/00912174221084818

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Abstract

Background: The COVID-19 pandemic has negatively impacted the general population in all aspects of life. Estimates of mental health medication dispensing in Alberta were investigated to elucidate areas of need within mental health and pharmacy practice during the pandemic.

Methods: We employed an interrupted time series analysis using linear regression models to estimate community and outpatient medication dispensing trends of 46 medications used to treat mental health disorders. Three parameters were examined. The first was the medication dispensing slope before COVID-19. The second was the immediate effect of COVID-19 on dispensing (i.e., the difference in dispensing rate

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between the month before and after the first case of COVID-19) and the third was the medication dispensing slope during COVID-19.

Results: Dispensing rates of 61% ($n = 34$) of the examined medications remained similar before and during the COVID-19 pandemic. However, eight medications (i.e., amitriptyline, escitalopram, fluoxetine, paroxetine, bupropion, desvenlafaxine, venlafaxine, and oxazepam) showed an immediate and significant increase in dispensing rate following the onset of the pandemic that was sustained over the first 13-months of the pandemic.

Conclusion: Initial increases in dispensing patterns of antidepressants may be attributed to a “stockpiling phenomenon” but the sustained higher levels of dispensing suggest an unfavorable shift in the population’s mental health. Monitoring of medication dispensing patterns during COVID-19 may serve as a useful indicator of the population’s mental health during the current pandemic and better prepare community pharmacists in future pandemic planning, medication dispensing strategies, and care of chronic medical conditions.

Keywords

COVID-19, SARS-CoV-2, psychotropics, drug dispensing, trends

Introduction

The COVID-19 pandemic has infected more than 370 million people worldwide, and 480,000 people in Alberta from March 2020 until January 2022, resulting in negative consequences for the general population.¹ The uncertainty of COVID-19, coupled with financial stresses, resource shortages, misinformation, and conflicting messages from authorities, are all sources of stressors that have the potential to negatively influence the population’s mental and physical wellbeing. Lockdowns and self-isolation practices have also made it difficult for people to access in-person services including individual and group counseling, therapy groups, addiction services, chronic pain interventional clinics, physiotherapy, and massage therapy. Patients that were using these services for maintenance therapy or treatment may experience anxiety from navigating this ambiguous new uncharted territory. Furthermore, studies have shown an increased reliance on community pharmacies for general medical advice, and COVID-19 information throughout the pandemic, as lockdown measures make accessing usual healthcare services difficult.²

Several studies have been published looking at the mental health impact of COVID-19 on the general population as well as healthcare workers. A study looking at the initial phase of the COVID-19 outbreak in China and psychological impact reported that 53.8% of the respondents reported moderate to severe depressive symptoms, and 28.8% reported moderate to severe anxiety symptoms.³ In the United States, data from the Census Bureau showed that there was an increase in reporting of anxiety and

depressive symptoms from 1 in 10 to 4 in 10 adults.⁴ In Alberta alone, there has been an increase in COVID-19 related calls to the different mental health helplines. Prior to the pandemic Alberta's Mental Health Line was receiving on average 30 calls per day, and during the pandemic that number increased to 110 calls per day.⁵

The global pandemic has changed everyone's lives in a short amount of time, affecting finances, social security, physical and mental health. This is supported by evidence of an 11% increase in Canada-wide claims for antidepressants between January and June 2020 compared to 2019.⁶ However, similar estimates of mental health medication dispensing in Alberta, the province with one of the highest rates of COVID-19 cases in Canada, are not available. Since the pandemic, the largest numbers of COVID-19 cases have been seen in Ontario and Quebec, followed by Alberta.⁷ To address this gap, this study examined medication dispensing patterns in Alberta community and outpatient pharmacies before and during COVID-19, focusing specifically on medications used to treat mental health disorders.

Methods

Data sources

Dispensing data for 46 medications (Table 1) used to treat mental health disorders were requested from Alberta Health's Pharmaceutical Information Network for 13 months before the first COVID-19 case in Alberta (i.e., December 2018 to January 2020) and 13 months after (i.e., February 2020 to March 2021). For each drug, the Pharmaceutical Information Network provided distinct monthly dispensing counts for the 26-month observation period of this study. Drugs and drug combinations were defined using the World Health Organization's Anatomical Therapeutic Chemical codes.⁸ The Pharmaceutical Information Network collects greater than 95% of all drug dispensing events submitted by community and outpatient pharmacies in Alberta.⁹ Alberta population estimates were obtained from the Alberta Office of Statistics and Information website.¹⁰ This study was exempted by the University of Calgary Conjoint Health Research Ethics Board.

Statistical analysis

The dispensing rate for each of the drugs was calculated for each month for the total population. In these calculations, monthly dispensing counts (numerator) were divided by the number of inhabitants in Alberta (denominator) and then multiplied by 10,000 to derive a monthly dispensing rate per 10,000 Alberta inhabitants. To examine differences in dispensing patterns of each drug before and during COVID-19, we conducted 46 interrupted time series analyses using the following segmented linear regression model

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t$$

Table 1. Psychiatric medications dispensed according to category.

| SSRI | TCA | Stimulant |
|----------------|-----------------------|------------------------|
| Citalopram | Amitriptyline | Dexamfetamine |
| Escitalopram | Clomipramine | Lisdexamfetamine |
| Fluoxetine | Desipramine | Methylphenidate |
| Paroxetine | Doxepin | <i>Antipsychotic</i> |
| Sertraline | Imipramine | Aripiprazole |
| <i>SNRI</i> | Nortriptyline | Asenapine |
| Desvenlafaxine | Trimipramine | Clozapine |
| Duloxetine | <i>Anxiolytic</i> | Haloperidol |
| Venlafaxine | Bupirone | Loxapine |
| Atomoxetine | <i>Benzodiazepine</i> | Olanzapine |
| <i>NDRI</i> | Alprazolam | Paliperidone |
| Bupropion | Clobazam | Quetiapine |
| <i>NaSSA</i> | Clonazepam | Risperidone |
| Mirtazapine | Diazepam | Chlorpromazine |
| <i>SARI</i> | Lorazepam | Zuclopenthixol |
| Trazodone | Midazolam | <i>Mood stabilizer</i> |
| | Oxazepam | Carbamazepine |
| | Temazepam | Lithium |
| | | Valproic acid |

NaSSA, noradrenergic and specific serotonergic antidepressant; NDRI, norepinephrine dopamine reuptake inhibitor; SARI, serotonin antagonist and reuptake inhibitor; SNRI, serotonin norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

where Y_t represents the dispensing rate of a drug at time t , T is the time (months) elapsed since the start of the observation period, and X_t is a dummy variable indicating before COVID-19 period (coded 0) or during COVID-19 period (coded 1). β_0 represents the dispensing rate at $T = 0$ (intercept), β_1 is interpreted as the monthly change (slope) in dispensing rate before COVID-19, β_2 is the immediate change in dispensing rate following the onset of the COVID-19 pandemic in Alberta, and β_3 indicates the monthly change (slope) in dispensing rate during the first 13-months of the COVID-19 using the interaction between time and COVID-19 period (TX_t). All statistical analyses were conducted using Jamovi 1.2.27, an R based statistical software.

Results

The top five dispensed psychiatric medications in the 13-months before the pandemic were quetiapine (1774 per 10,000 Alberta inhabitants), escitalopram (1738 per 10,000), trazodone (1455 per 10,000), venlafaxine (1427 per 10,000), and sertraline (1312 per 10,000), whereas the top five dispensed medications in the 13-months following the pandemic were escitalopram (2005 per 10,000), quetiapine (1858 per 10,000),

trazodone (1590 per 10,000), sertraline (1564 per 10,000), and venlafaxine (1532 per 10,000).

Dispensing slopes/trends in the 13-months prior to COVID-19 were stable for 61% ($n = 34$) of the examined medications. However, in the month following the first case of COVID-19, significant increases in dispensing rates were seen for several tricyclic antidepressants (i.e., amitriptyline, clomipramine, and trimipramine), selective serotonin reuptake inhibitors (SSRIs) (i.e., escitalopram, fluoxetine and paroxetine), serotonin norepinephrine reuptake inhibitors (i.e., desvenlafaxine and venlafaxine), NDRIs (i.e., bupropion), and anxiolytics (i.e., alprazolam and oxazepam) (Figure 1 and Table 2). None of these medications continued to increase over the first 13 months of the pandemic but eight (i.e., amitriptyline, escitalopram, fluoxetine, paroxetine, bupropion, desvenlafaxine, venlafaxine, and oxazepam) sustained the higher dispensing rate established immediately following the onset of the pandemic. A significant immediate decrease in dispensing rate was seen in loxapine, a typical antipsychotic medication, which then returned to before COVID-19 dispensing rates in the following

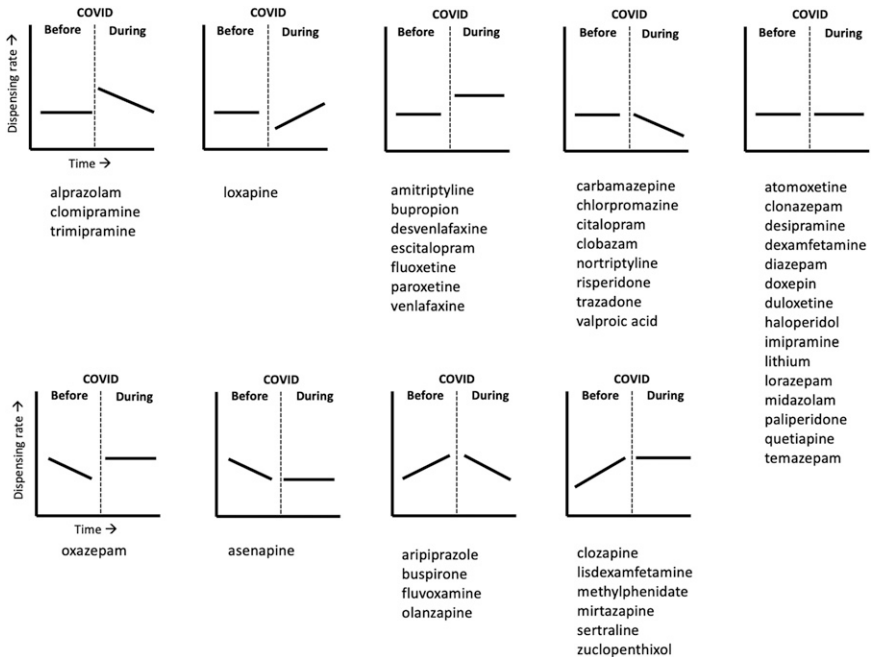


Figure 1. Summary of dispensing patterns 13-months before and 13-months during the COVID-19 pandemic in Alberta, Canada. Dispensing patterns were inferred from the intercept, slope estimates, and p -values in Table 2. The dispensing pattern of the medication was shown to have increased if the estimate was positive with a p value <0.05 , decreased if the estimate was negative with a p value <0.05 , and no change if the p value was >0.05 . The different medications were then separated into the different graphical trends.

Table 2. Interrupted time series analyses using segmented linear regression models for 46 mental health medications.

| Drug dispensed | Drug class | B ₀ (Intercept, baseline dispensing ^a) | B ₁ (Pre-COVID slope) | | B ₂ (Immediate effect of COVID) | | B ₃ (Post-COVID slope) | |
|----------------|----------------------|---|----------------------------------|--------|--|-------|-----------------------------------|--------|
| | | | Estimate | p | Estimate | p | Estimate | p |
| Citalopram | SSRI | 85.133 | -0.124 | 0.806 | 10.790 | 0.054 | -1.485 | 0.047 |
| Escitalopram | SSRI | 125.890 | 1.120 | 0.236 | 24.410 | 0.020 | -2.630 | 0.054 |
| Fluoxetine | SSRI | 46.894 | 0.464 | 0.106 | 6.960 | 0.026 | -0.788 | 0.055 |
| Fluvoxamine | SSRI | 4.695 | 0.091 | 0.004 | 0.600 | 0.058 | -0.120 | 0.007 |
| Paroxetine | SSRI | 26.659 | -0.015 | 0.933 | 4.741 | 0.020 | -0.513 | 0.054 |
| Sertraline | SSRI | 92.060 | 1.260 | 0.037 | 12.540 | 0.050 | -1.370 | 0.104 |
| Desvenlafaxine | SNRI | 13.080 | 0.036 | 0.758 | 3.406 | 0.010 | -0.343 | 0.044 |
| Duloxetine | SNRI | 73.925 | 0.533 | 0.188 | 8.013 | 0.068 | -0.865 | 0.133 |
| Venlafaxine | SNRI | 107.181 | 0.372 | 0.612 | 18.067 | 0.028 | -2.117 | 0.050 |
| Bupropion | NDRI | 73.273 | 0.654 | 0.192 | 12.563 | 0.024 | -1.399 | 0.054 |
| Mirtazapine | NaSSA | 62.685 | 0.671 | 0.027 | 1.317 | 0.665 | -0.762 | 0.069 |
| Trazodone | SARI | 105.748 | 0.885 | 0.074 | 8.558 | 0.102 | -1.390 | 0.049 |
| Amitriptyline | TCA | 48.258 | 0.326 | 0.327 | 7.873 | 0.033 | -0.951 | 0.051 |
| Clomipramine | TCA | 2.952 | -0.005 | 0.707 | 0.316 | 0.025 | -0.058 | 0.003 |
| Desipramine | TCA | 0.508 | -0.007 | 0.088 | 0.063 | 0.131 | 0.004 | 0.455 |
| Doxepin | TCA | 7.207 | 0.004 | 0.889 | 0.329 | 0.303 | -0.068 | 0.114 |
| Imipramine | TCA | 1.527 | -0.008 | 0.474 | 0.221 | 0.067 | -0.019 | 0.238 |
| Nortriptyline | TCA | 9.516 | 0.070 | 0.218 | 1.027 | 0.095 | -0.188 | 0.025 |
| Trimipramine | TCA | 1.253 | 0.012 | 0.233 | 0.288 | 0.014 | -0.060 | <0.001 |
| Bupirone | Azapirone anxiolytic | 9.689 | 0.218 | <0.001 | 0.220 | 0.551 | -0.144 | 0.007 |
| Alprazolam | Benzodiazepine | 8.930 | -0.032 | 0.316 | 0.728 | 0.038 | -0.100 | 0.033 |
| Clobazam | Benzodiazepine | 6.812 | 0.052 | 0.097 | 0.567 | 0.088 | -0.138 | 0.004 |
| Clonazepam | Benzodiazepine | 80.588 | -0.219 | 0.373 | 4.307 | 0.107 | -0.341 | 0.328 |

(continued)

Table 2. (continued)

| Drug dispensed | Drug class | B ₀ (Intercept, baseline dispensing ^a) | B ₁ (Pre-COVID slope) | | B ₂ (Immediate effect of COVID) | | B ₃ (Post-COVID slope) | |
|------------------|-----------------------------|---|----------------------------------|--------|--|-------|-----------------------------------|-------|
| | | | Estimate | p | Estimate | p | Estimate | p |
| Diazepam | Benzodiazepine | 16.571 | 0.036 | 0.446 | 0.123 | 0.806 | 0.049 | 0.463 |
| Lorazepam | Benzodiazepine | 85.832 | -0.082 | 0.797 | 4.637 | 0.180 | -0.224 | 0.620 |
| Midazolam | Benzodiazepine | 0.413 | 0.003 | 0.435 | -0.005 | 0.916 | 0.007 | 0.249 |
| Oxazepam | Benzodiazepine | 2.341 | -0.041 | <0.001 | 0.290 | 0.007 | 0.001 | 0.947 |
| Temazepam | Benzodiazepine | 23.367 | -0.079 | 0.357 | 1.828 | 0.053 | -0.149 | 0.224 |
| Atomoxetine | SNRI | 4.713 | 0.026 | 0.181 | 0.000 | 0.999 | -0.028 | 0.317 |
| Dexamfetamine | Stimulant | 22.771 | 0.095 | 0.230 | 1.566 | 0.067 | -0.165 | 0.141 |
| Lisdexamfetamine | Stimulant | 43.762 | 1.160 | <0.001 | 0.451 | 0.845 | -0.281 | 0.362 |
| Methylphenidate | Stimulant | 47.105 | 0.645 | 0.009 | -1.588 | 0.514 | -0.067 | 0.834 |
| Aripiprazole | Atypical antipsychotic | 40.592 | 0.443 | 0.007 | 1.585 | 0.332 | -0.448 | 0.047 |
| Asenapine | Atypical antipsychotic | 0.308 | -0.007 | 0.024 | 0.039 | 0.219 | 0.001 | 0.728 |
| Chlorpromazine | Phenothiazine antipsychotic | 1.756 | 0.005 | 0.634 | -0.020 | 0.840 | -0.028 | 0.048 |
| Clozapine | Atypical antipsychotic | 16.988 | 0.162 | 0.038 | -0.156 | 0.844 | -0.187 | 0.085 |
| Haloperidol | Typical antipsychotic | 3.636 | 0.037 | 0.104 | 0.105 | 0.654 | -0.025 | 0.426 |
| Loxapine | Typical antipsychotic | 1.967 | -0.011 | 0.291 | -0.279 | 0.019 | 0.032 | 0.040 |
| Olanzapine | Atypical antipsychotic | 47.610 | 0.374 | 0.034 | 0.761 | 0.669 | -0.503 | 0.042 |
| Paliperidone | Atypical antipsychotic | 7.698 | 0.023 | 0.456 | 0.331 | 0.325 | 0.042 | 0.352 |
| Quetiapine | Atypical antipsychotic | 131.257 | 0.744 | 0.111 | 3.890 | 0.423 | -1.018 | 0.122 |
| Risperidone | Atypical antipsychotic | 49.980 | 0.288 | 0.130 | 0.835 | 0.672 | -0.514 | 0.060 |
| Zuclopenthixol | Typical antipsychotic | 2.816 | 0.045 | 0.004 | -0.117 | 0.437 | -0.035 | 0.089 |
| Carbamazepine | Mood stabilizer | 21.050 | 0.021 | 0.836 | 1.872 | 0.089 | -0.301 | 0.043 |
| Lithium | Mood stabilizer | 12.383 | -0.014 | 0.765 | 0.691 | 0.161 | -0.055 | 0.397 |
| Valproic acid | Mood stabilizer | 39.117 | 0.204 | 0.191 | 1.065 | 0.514 | -0.528 | 0.022 |

NaSSA, noradrenergic and specific serotonergic antidepressant; SARI, serotonin antagonist and reuptake inhibitor; TCA, tricyclic antidepressant. ^aper 10,000 Alberta inhabitants.

13 months. A delayed decrease in dispensing was observed for some tricyclic antidepressants (i.e., nortriptyline), SSRIs (i.e., citalopram), SARI (i.e., trazodone), anti-epileptics (i.e., clobazam), and antipsychotics (i.e., chlorpromazine and risperidone), whereas fluvoxamine (SSRI), two antipsychotics (i.e., aripiprazole and olanzapine), and buspirone (anxiolytic) showed an increase in their dispensing slopes before COVID-19, did not change immediately after COVID-19 began, and then decreased during COVID-19 back to their initial baseline dispensing rates.

Discussion

During the initial stages of COVID-19 in Alberta, we saw an increase in dispensing patterns in several commonly prescribed antidepressants. This may have reflected a “hoarding and stockpiling” phenomenon where pharmacies ordered more stock of the medication in response to rising pressure from the public to dispense more than their usual duration of medications.¹¹ Many news outlets reported on the stockpiling of essential supplies including toilet paper, hand sanitizer, and masks, and our results suggest this was also true for medications. A cross sectional study done in Germany showed that there were surges in pharmacy purchasing behavior for psychotropic, neurologic, and cardiovascular drugs dubbed as “panic buying” associated with the COVID-19 lockdown.¹² Furthermore, to decrease face-to-face time, pharmacies also increased medication refills to monthly amounts for medications that were typically dispensed weekly.¹³ In March 2020, the Alberta Pharmacists’ Association announced that prescriptions should not exceed a 30-day supply to prevent medication shortages.¹⁴ Along with the announcement, the Alberta Blue Cross (Alberta’s largest prescription drug benefits carrier) suspended approvals for medication in excess of 30 days for travel.¹⁴

Our findings suggest that most of the mental health medication dispensing patterns in Alberta remained at the same dispensing rate before and during the first two waves of the COVID-19 pandemic. However, several antidepressants did show an initial increase in dispensing patterns that remained steady at the higher rate in the following months. This contrasts with some of the tricyclic antidepressants such as clomipramine and trimipramine, which showed an initial increase in dispensing followed by a regression back to pre-COVID-19 dispensing rates. The sustained increased dispensing rate of some antidepressants during the COVID-19 pandemic may reflect the population’s mental health as a whole. The World Health Organization had expressed concern that there would be “elevated rates of stress or anxiety,” and that quarantine measures and the interruption to normal life routines may have an effect on “levels of loneliness, depression, harmful alcohol and drug use, and self-harm or suicidal behavior.”¹⁵ Indeed, multiple global studies have examined the negative impact of COVID-19 on the population’s mental health. A national sample of the mental health of adults in the first 6 weeks of lockdown in the United Kingdom demonstrated increased suicidal ideation, especially in the younger adult population.¹⁶ In China, a nationwide survey of 56,679 participants revealed that 34.1% of the participants reported at least one psychological

symptom (i.e., depression, anxiety, insomnia, and acute stress) during quarantine, especially in vulnerable groups.² Although others have stated: “a psychiatric epidemic is co-occurring with the COVID-19 pandemic,” with the general population suffering from an increased epidemiological burden of mental health problems.¹⁷

In contrast to antidepressants, carbamazepine and valproic acid had a delayed decrease in dispensing patterns following the onset of the COVID-19 pandemic. These medications are used as antiepileptics and mood stabilizers for mental health and neurological conditions. We speculate the delayed decrease in dispensing pattern may reflect difficulty in obtaining antiepileptic medications during the first two waves of the COVID-19 pandemic. A multi-country online study looking at 399 persons with epilepsy showed that 19.6% of the participants had difficulty obtaining antiepileptics during the pandemic.¹⁸ In Italy, during the COVID-19 surge, outpatient examinations of persons with epilepsy were postponed in 95% of cases, and a third of the 456 persons with epilepsy reported issues with epilepsy management.¹⁹ Furthermore, when valproic acid and carbamazepine are used as antiepileptics, serum concentrations are followed clinically for therapeutic effect. In mental health conditions, serum concentrations are ordered both for therapeutic drug monitoring and to rule out toxicity.²⁰ We speculate that with the ongoing COVID-19 pandemic, it was more difficult for individuals to access laboratories or specialist appointments in order for them to have their blood drawn or their therapeutic levels followed. In fact, two of the major providers of laboratory services in Alberta (i.e., Alberta Precision Laboratories and DynaLIFE) temporarily reduced or eliminated outpatient and walk-in appointments to curb the spread of COVID-19.²¹ Although telehealth filled some of these treatment gaps, much of the population’s care delivery remained impacted.²²

During COVID-19, many people have turned to community pharmacists as they are the most accessible primary care providers when patients have questions about their medications or medical conditions.²³ Previous research has shown a positive effect of clinical pharmacist interventions in the general population. Clinical pharmacist interventions decreased the number of polypharmacy medications in geropsychiatric patients with sustained effect.²⁴ Future collaboration of patients with mental health concerns with community clinical pharmacists may help alleviate pressures on the healthcare system.

The results from this study should be interpreted in the context of these acknowledged limitations. First, the dispensing rate data comes from community and outpatient pharmacies, and therefore does not account for in-hospital dispensing patterns. As such, medications that are commonly initiated and titrated in hospital (e.g., clozapine) could be underestimated. Second, dispensing rates are not equivalent to medication consumption rates. Although, previous work has shown high concordance (~80%) between dispensing and consumption rates.²⁵ Third, we were not able to determine from our data the origin of the prescription that led to the dispensing event. In Alberta, pharmacists can prescribe Schedule 1 drugs but typically prescribe by adapting an ongoing prescription or in emergency cases. Fourth, our data only captured dispensing during the first and second waves of the pandemic. The impact of subsequent

waves on our results will require future analysis. Finally, we did not have access to individual level dispensing data, and as such, we were unable to determine the underlying reason/indication for the observed dispensing rates.

In summary, we found that dispensing rates for most mental health medications were stable before and remained stable during the first two COVID-19 waves in Alberta. Although initial increases in dispensing rates were seen for many medications, most returned to pre-COVID dispensing levels during the 13-month observation period. There were, however, several medications (mostly antidepressants) that maintained a higher dispensing rate, suggesting an unfavorable shift in the population's mental health. As such, monitoring of medication dispensing patterns as COVID-19 continues to unfold in Alberta and elsewhere, may serve as a useful indicator of the population's mental health during the current pandemic and better prepare community pharmacists in future pandemic planning, medication dispensing strategies, and care of chronic medical conditions.

Knowledge Into Practice

What was known about this topic?

- COVID-19 has had a detrimental impact on the public's mental health and pharmacies are often the first point of contact for individuals to obtain information about COVID-19, and to continue their medical care. During the pandemic, the Alberta College of Pharmacy has recommended guidelines to ensure continuity of patient care, and to help alleviate health burdens.

What does this study add to existing knowledge?

- This study estimated the trends in mental health medication dispensing rates in Alberta before and during the COVID-19 pandemic. The increased dispensing rates of some antidepressants suggest a worsening of mental health concerns during the pandemic and provide insight into trends that we may expect if additional waves or future pandemics were to occur.

What are the implications for pharmacy practice?

- The initial increased dispensing rates of mental health medications likely reflected a "stockpiling phenomenon" by pharmacies in the face of the many unknowns of how the pandemic may unfold. For future pandemic preparedness, similar behavior may be expected, and policies to combat "panic buying" may be necessary.

- Medication dispensing data have the potential to serve as one indicator of the population's mental health and can inform pharmacy and mental health interventions, practices, and policies during pandemics.

Acknowledgments

We would like to acknowledge Michael Cooley at the Government of Alberta for his assistance with obtaining aggregate data housed in Alberta Health's Pharmaceutical Information Network database.

Authors' contributions

Lisa Ying: Data curation, Investigation, Formal analysis, and Writing- Original draft preparation. Mark Yarema: Writing- Reviewing and Editing. Chad Bousman: Conceptualization, Methodology, Writing- Reviewing and Editing, and Supervision

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This research was supported in part by the University of Calgary Cumming School of Medicine, and the Alberta Children's Hospital Research Institute.

Research ethics

This study was exempted by the University of Calgary Conjoint Health Research Ethics Board.

Data availability

Data is available upon request from the corresponding author.

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