Research Paper

Evaluating interventions to facilitate opioid agonist treatment access among people who inject drugs in Toronto, Ontario during COVID-19 pandemic restrictions

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ABSTRACT

Background: In March 2020, following a provincial COVID-19 emergency declaration, modifications to opioid agonist treatment (OAT) were introduced in Ontario, Canada to promote treatment access amid the pandemic and ongoing opioid overdose crisis. Modifications included federal exemptions to facilitate OAT prescription re-fills, extensions, and deliveries and interim treatment guidance emphasizing take-home (non-observed) doses and reduced urine drug screening for OAT patients.

Methods: We conducted an interrupted time series study using health administrative data from September 17th, 2019–September 21st, 2020, on 359 people who inject drugs with suspected opioid use disorder in Toronto, Ontario. We used segmented regression analyses to evaluate the joint effects of the provincial COVID-19 emergency declaration, federal OAT exemptions, and interim treatment guidance—all implemented between March 17th–23rd, 2020—on the weekly proportion of participants enrolled in OAT (i.e., ≥1 day(s) covered with methadone or buprenorphine/naloxone), with an opioid-related overdose (based on emergency department visits and hospitalizations), and who died (all-cause), and the weekly proportion of OAT-enrolled participants receiving take-home doses (i.e., ≥1 day(s) covered) and undergoing urine drug screening.

Results: Post-implementation, the interventions were associated with immediate absolute changes in OAT enrollment (+1.95%; 95% CI=0.04%–3.85%), receipt of take-home doses (+18.3; 95% CI=13.2%–23.4%), and urine drug screening (-22.4%; 95% CI=[-26.9%]–[-17.9%]) and a gradual absolute increase of 0.56% in urine drug screening week-to-week (95% CI=0.27%–0.86%) beyond the pre-implementation trend. At 26 weeks post-implementation, OAT enrollment and urine drug screening approached pre-implementation levels whereas the increase in take-home doses was largely sustained (+15.0%; 95% CI=4.33%–25.6%). No post-implementation increases in opioid-related overdoses were observed. Death was not modelled (low event frequency).

Conclusion: Changes to OAT provision following provincial COVID-19 restrictions were associated with an immediate and sustained increase in take-home dose coverage among OAT-enrolled participants, without corresponding increases in opioid-related overdoses among all participants.

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Introduction

To curb the transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and incidence of coronavirus disease 2019 (COVID-19), the Government of Ontario, Canada declared a provincial state of emergency on March 17th, 2020 and implemented associated measures to close non-essential services, mandate mask-wearing in indoor spaces, and facilitate physical distancing (Lawson et al., 2021; Ontario Agency for Health Protection and Promotion (Public Health Ontario), 2020). The COVID-19 pandemic emerged amidst an ongoing opioid overdose crisis in Canada, which has resulted in 20,470 hospitalizations for opioid poisoning and 15,820 opioid-related deaths from January 2016 through March 2020, with approximately 41% and 35% of these hospitalizations and deaths occurring in the province of Ontario (Public Health Agency of Canada, 2021a,b). Over the six months preceding the COVID-19 emergency declaration in Ontario, the provincial rate of opioid-related deaths increased steadily month-to-month from 5.2 per 100,000 population in September 2019 to 11.2 per 100,000 population in February 2020 (Public Health Ontario, 2021).

Opioid agonist treatment (OAT) with methadone or buprenorphine/naloxone is the recommended first-line therapy for moderate to severe opioid use disorder across Canada due to its effectiveness in reducing the risk of overdose-related mortality and morbidity in treated patients, and thus represents a key intervention in the opioid overdose crisis response (Bruneau et al., 2018; Centre for Addiction and Mental Health, 2021; Eibl et al., 2017; Government of Ontario, 2018). In Ontario, as in most of Canada, OAT is primarily dispensed daily for observed ingestion in community pharmacies (Eibl et al., 2017; Government of Ontario, 2018). Before the COVID-19 pandemic, only stabilized OAT patients who regularly attended daily observed doses over a sufficient period (typically ≥2 months) and routinely cleared urine drug screening (to rule out other opioid use) could receive days' to weeks' worth of take-home (non-observed) methadone or buprenorphine/naloxone doses per dispensation (Eibl et al., 2017; Government of Ontario, 2018). However, during the pandemic, compliance with provincial COVID-19 emergency orders and public health guidelines by OAT dispensaries could result in reduced operating hours, reduced capacity, or temporary closures (e.g., due to outbreaks), thereby hindering treatment access at these sites (Canadian Centre on Substance Use and Addiction, 2020; Friesen et al., 2021; Nguyen & Buxton, 2021). Even without such service interruptions, Ontarians with opioid use disorder may be deterred from initiating or maintaining OAT during the pandemic to mitigate their risk of SARS-CoV-2 infection or transmission, as treatment requires regular in-person clinical encounters (Eibl et al., 2017; Government of Ontario, 2018). In response to anticipated pandemic-related barriers to treatment access and continuity of care, which might further exacerbate the opioid overdose crisis, several modifications to OAT practices were introduced shortly after the provincial COVID-19 emergency declaration (Centre for Addiction and Mental Health et al., 2020).

First, Health Canada implemented temporary federal exemptions to the *Controlled Drugs and Substances Act* on March 19th, 2020 (presently effective through September 30th, 2026) (Health Canada, 2020). These exemptions allowed prescribers across Canada to refill or extend OAT prescriptions by phone, pharmacists to extend and transfer OAT prescriptions, and pharmacy employees to deliver OAT prescriptions to patients self-isolating at home or other locations (Health Canada, 2020). Second, on March 22nd, 2020, interim guidance on providing OAT during the COVID-19 pandemic was released for Ontario prescribers and pharmacists (Centre for Addiction and Mental Health et al., 2020). To maintain treatment access while minimizing OAT patients' risk of SARS-CoV-2 infection, the COVID-19 OAT guidance recommended scheduling virtual versus in-person visits (where possible), reducing the frequency of urine drug screening, and facilitating take-home doses, primarily by re-evaluating patients deemed ineligible under pre-pandemic guidelines using a relaxed set of eligibility criteria (Centre for Addiction and Mental Health et al., 2020; College of

Physicians & Surgeons of Ontario, 2011). Specifically, the interim guidance recommended that OAT patients who continue to use substances (including opioids) can receive take-home doses during the pandemic unless they meet 'high-risk' criteria: (1) intoxicated or sedated at clinical assessment; (2) unstable psychiatric comorbidity (acutely suicidal or psychotic); (3) recent overdose; or (4) current high-risk use of illicit substances (e.g., injecting high-dose intravenous illicit opioids) (Centre for Addiction and Mental Health et al., 2020). Both the exemptions and interim guidance were intended to mitigate pandemic-related barriers to OAT access in Ontario without contradicting provincial COVID-19 emergency orders and physical distancing recommendations. However, whether or to what degree these interventions facilitated OAT access among structurally vulnerable people with opioid use disorder during the pandemic is largely unknown.

Due to the brief time elapsed between the implementation of the provincial COVID-19 emergency declaration (March 17th, 2020), federal OAT exemptions (March 19th, 2020), and interim COVID-19 OAT guidance (March 22nd, 2020), we cannot estimate and compare the independent effects of each intervention on OAT access (Penfold & Zhang, 2013). Therefore, our primary objective was to evaluate the joint effects of these co-occurring interventions on OAT enrollment (i.e., the proportion actively receiving treatment) within a cohort of structurally vulnerable people who inject drugs (PWID) with suspected opioid use disorder in Toronto, Ontario. We additionally assessed whether the interventions affected receipt of take-home doses and the frequency of urine drug screening among OAT-enrolled participants—targets of the interim treatment guidance—which might influence overall enrollment. Lastly, we investigated concurrent pre- and post-implementation trends in opioid-related overdoses and all-cause mortality within the study population.

Methods

Design and setting

We conducted an interrupted time series study between September 17th, 2019, and September 21st, 2020, to assess the effects of the provincial COVID-19 emergency declaration (and associated public health measures), federal OAT exemptions, and provincial COVID-19 OAT guidance on OAT enrollment and treatment-related outcomes within a prospective community-based cohort of PWID living in Toronto, Ontario with suspected opioid use disorder. The study was divided into two 26-week-long periods—pre-implementation (September 17th, 2019–March 16th, 2020) and post-implementation (March 24th, 2020–September 21st, 2020)—around the non-calendar week in which the interventions were consecutively implemented (March 17th–23rd, 2020) (Centre for Addiction and Mental Health et al., 2020; Health Canada, 2020; Ontario Agency for Health Protection and Promotion (Public Health Ontario), 2020). Study conduct and reporting were guided by published recommendations for interrupted time series designs (Ramsay et al., 2003; Turner et al., 2020b).

For context, eFigure 1 displays the daily incidence of COVID-19 cases reported in Toronto during the study period. Within our pre-implementation period, a total of 117 COVID-19 cases were reported, with the first cases reported in Toronto on January 23rd, 2020 (Public Health Ontario, 2022). From January 23rd through March 16th, 2020, a median of 0 COVID-19 cases were reported daily in the city (interquartile range = 0 to 1 cases/day) (Public Health Ontario, 2022). In contrast, our post-implementation period encompasses the majority of "Wave 1" of the COVID-19 pandemic in Toronto (exponential increase in daily case counts beginning late March 2020) as well as the start of "Wave 2" in September 2020 (Ontario Agency for Health Protection and Promotion (Public Health Ontario), 2020, 2021; Public Health Ontario, 2022). Within the post-implementation period, a total of 16,223

COVID-19 cases were reported (median [interquartile range]=71 [32 to 136] cases/day) (Public Health Ontario, 2022).

Data sources

Data were drawn from the ongoing Ontario integrated Supervised Injection Services study in Toronto (OiSIS-Toronto), which aims to evaluate how supervised consumption services influence health care service use and clinical outcomes among local PWID (Scheim et al., 2021a,b). At recruitment, all OiSIS-Toronto participants are ≥18 years old, live in Toronto, report injection drug use in the past six months, provide written informed consent, and complete a baseline questionnaire that collects data on their sociodemographic information, drug use behaviours, and history of treatment for substance use disorders (Scheim, Sniderman, et al., 2021). Recruitment, which began November 5th, 2018, is achieved through self-referral, snowball sampling, and community or street outreach (Scheim et al., 2021b).

We identified OiSIS-Toronto as a suitable source cohort for this study for several reasons. First, the high baseline prevalence of self-reported overdose and frequent (i.e., daily or near daily) opioid injection drug use among OiSIS-Toronto participants suggests that many cohort members may be eligible for, and benefit from, OAT (Scheim et al., 2021a). Second, most OiSIS-Toronto participants are experiencing structural vulnerabilities that pose serious challenges to OAT initiation and retention. For example, over 90% of participants reported recent homelessness or unstable housing at baseline (Scheim et al., 2021b), a structural vulnerability that has been previously associated with difficulty accessing OAT (Prangnell et al., 2016). Third, OiSIS-Toronto participants are asked at baseline for additional consent to having their questionnaire data transferred and linked at ICES—a non-profit research institute authorized under Ontario's health information privacy law to collect and analyze health care and demographic data for health system evaluation and improvement (Bouck et al., 2022; Scheim et al., 2021b). The linkage process has been summarized previously in greater detail (Bouck et al., 2022). Briefly, 74% (521/701) of OiSIS-Toronto participants recruited by March 19th, 2020, consented to and were successfully linked at ICES. For these linked participants, we can access their routinely collected health care administrative data (e.g., prescription medication claims and hospitalization records) and demographic data at ICES, which enables repeated assessment of OAT enrollment and treatment-related outcomes at more regular intervals (e.g., weekly) and potentially with greater accuracy versus cohort questionnaires (completed semi-annually after baseline, all data participant-reported) (Bouck et al., 2022; Scheim et al., 2021b).

We used OiSIS-Toronto participant data from the following health care administrative and demographic databases, which were linked using encoded identifiers and analyzed at ICES: the Registered Persons Database, which includes sociodemographic information and vital statistics on anyone ever issued an Ontario Health Insurance Plan (OHIP) number (OHIP is the province's publicly-funded health insurance plan); the OHIP database, which captures billing claims submitted to OHIP by physicians in Ontario; the Ontario Drug Benefit database, which captures dispensation claims for prescription medications covered, fully or partially, under Ontario's public drug insurance plan; the National Ambulatory Care Reporting System, which captures diagnoses and procedures during emergency department visits in Ontario; the Discharge Abstract Database, which captures diagnoses and procedures during inpatient hospitalizations in Ontario; the Ontario Mental Health Reporting System, which captures inpatient mental health services received by Ontarians; and the Narcotics Monitoring System, which captures all dispensations for controlled substances (including methadone and buprenorphine/naloxone) from community pharmacies across Ontario, irrespective of payer. This study was approved by Research Ethics Boards at Unity Health Toronto and Toronto Public Health.

Participants

We constructed a cohort comprising all OiSIS-Toronto participants who: (1) consented to and had their baseline questionnaire data linked at ICES (required for outcome measurement); (2) completed their baseline questionnaire by September 16th, 2019 (i.e., the day before our study period began); (3) self-reported non-medical opioid use in the past six months on their baseline questionnaire (taken to suggest a potential opioid use disorder); and (4) were alive as of September 16th, 2019 (according to the Registered Persons Database). Participants were followed until death or September 22nd, 2020, whichever came first.

Outcomes

Over the 53-week study period (September 17th, 2019–September 21st, 2020), we collected health administrative data to measure the following outcomes on a weekly basis among all remaining participants (i.e., all participants alive at the end of the preceding week): (1) OAT enrollment, defined as having ≥1 day(s) that week covered with methadone or buprenorphine/naloxone based on prescription dispensation records (eligible formulations listed in eTable 1) from that week and the prior 30 days (Fig. 1); (2) opioid-related overdose, defined as ≥1 emergency department visit (any diagnosis type) or inpatient hospitalization (pre-admission diagnosis) for opioid poisoning (ICD-10-CA codes T40.0 to T40.4 or T40.6) in that week (Gomes et al., 2018; Gomes et al., 2021a); and (3) death (all-cause). Among OAT-enrolled participants in a given week, we additionally measured: (1) receipt of take-home doses, defined as having ≥1 day(s) in that week covered with a take-home dose of methadone or buprenorphine/naloxone based on prescription dispensation records from that week and the prior 30 days and (2) urine drug screening, defined as ≥1 OHIP billing claim with fee code G040 to G043 that week (Morin et al., 2020; Moss et al., 2018).

Characteristics

To describe the study cohort over time, we measured several characteristics using administrative data on the day before the study period commenced and the day before the provincial COVID-19 emergency declaration: age (in years); sex (male or female); Ontario Drug Benefit plan coverage, defined as age≥65 years (i.e., eligible due to age) or ≥1 prescription dispensation claim in the past 180 days in the Ontario Drug Benefit database; acute psychiatric comorbidity, defined as ≥1 emergency department visit in the past 30 days for schizophrenia (including delusional disorders) or deliberate self-harm (Gomes et al., 2021a); alcohol use disorder, defined as ≥1 emergency department visit, hospitalization, or OHIP billing claim in the past 180 days indicating alcohol use disorder (Gomes et al., 2021a); and recent opioid-related overdose, defined as ≥1 emergency department visit or hospitalization for opioid poisoning in the past 7 days (eAppendix 1). Many of these characteristics were selected as they approximate 'high-risk' criteria that could disqualify patients from receiving take-home doses, even under the relaxed COVID-19 OAT guidance (Centre for Addiction and Mental Health et al., 2020).

Statistical analysis

For each outcome, we pooled weekly data among participants and analyzed the resulting weekly proportions (expressed as percentages) using a segmented linear regression model with first-order autoregressive errors and terms for time (t [in weeks]; treated as a continuous variable), implementation ($I=1$ if post-implementation, $I=0$ if pre-implementation), and time since implementation (t-26 if post-implementation and 0 if pre-implementation; in weeks, treated as a continuous variable) (Wagner et al., 2002). Model parameters were estimated using restricted maximum likelihood estimation (Turner et al., 2020a). Week 27 (March 17th–23rd, 2020) was excluded from analysis
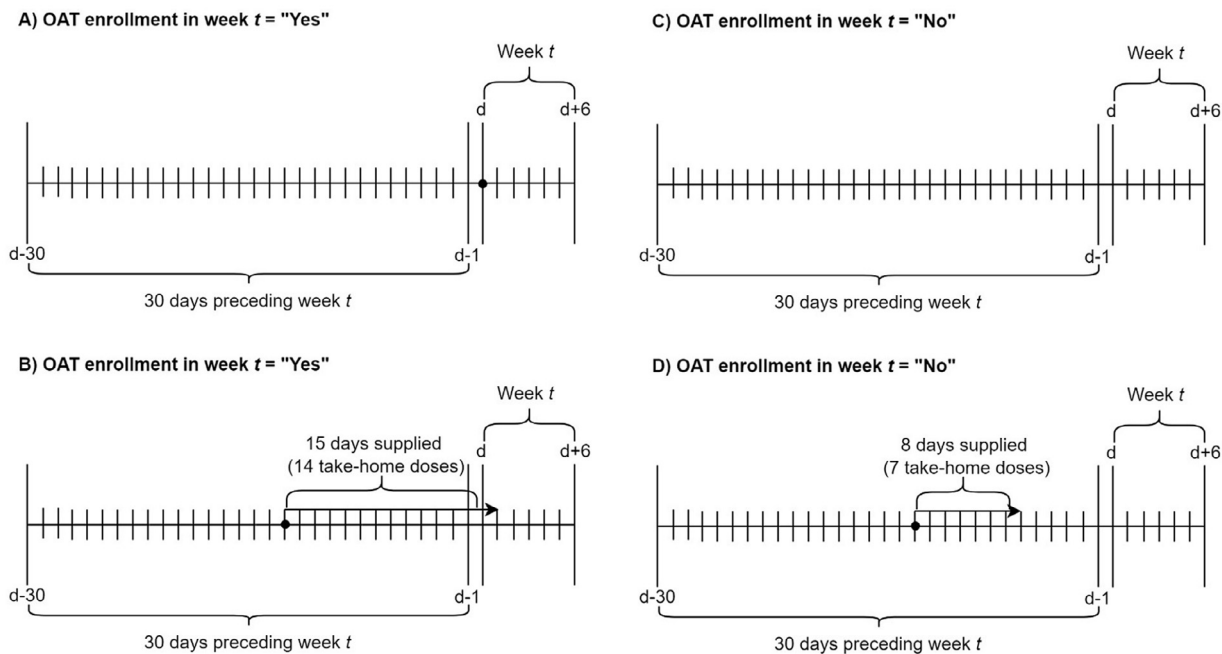
A) OAT enrollment in week *t* = "Yes"

C) OAT enrollment in week *t* = "No"

B) OAT enrollment in week *t* = "Yes"

D) OAT enrollment in week *t* = "No"

Fig. 1. Ascertainment of participant enrollment in opioid agonist treatment per week. *Notes*: OAT = opioid agonist treatment. A participant was deemed enrolled on OAT in week *t* if they had ≥1 eligible dispensation(s) in that week (i.e., between [d, d+6]) (e.g., panel A) or if they had a dispensation in the 30-day window preceding week *t* (i.e., between [d-30, d-1]) where the quantity (i.e., days supplied) dispensed on the most recent dispensation date provided coverage minimally through the first day of week *t* (d) (e.g., panel B). Participants were considered to not be enrolled in OAT in week *t* if they had no eligible dispensations during week *t* and (i) had no dispensation in the prior 30 days (e.g., panel C) or (ii) had a dispensation in the prior 30 days but the quantity dispensed on the most recent dispensation date did not provide coverage through the first day of week *t* (d) (e.g., panel D).

as all interventions (provincial COVID-19 emergency declaration, federal OAT exemptions, and interim COVID-19 OAT guidance) were implemented that week on different dates. Estimated coefficients for the implementation and time since implementation terms were respectively interpreted as the collective immediate effect (level change) and gradual effect (slope change) of the interventions on the modelled outcome, expressed as absolute differences with 95% confidence intervals (CI) (Wagner et al., 2002). We additionally estimated the overall effect (i.e., the combined immediate and gradual intervention effects) on each outcome at 26 weeks post-implementation, expressed as an absolute difference with 95% CI, by comparing the predicted outcome response for the last week of observation (week 53: September 15th–21st, 2020) with the extrapolated response for that same week assuming no interventions occurred (Wagner et al., 2002). We performed all analyses using SAS V9.4 software (SAS Institute Inc.; Cary, NC).

Results

Of the 701 OiSIS-Toronto participants recruited by March 19th, 2020, 521 (74.32%) had their baseline questionnaire and administrative data linked at ICES. Of these participants, 359 (68.91%) met our remaining eligibility criteria and were included in the study cohort (Fig. 2). On the day before the study period commenced, the mean (standard deviation [SD]) age of these 359 participants was 41.27 (SD, 10.62) years, 66.57% were male, 77.44% had Ontario Drug Benefit coverage, 14.48% had a recent alcohol use disorder diagnosis, and 1.95% had an emergency department visit or hospitalization for an opioid-related overdose in the past week (Table 1). Compared to the day before the study commenced (September 16th, 2019), the distribution of these characteristics was largely similar among participants on the day before the provincial COVID-19 emergency declaration (March 16th, 2020), except a larger proportion (6.53% vs 1.95%) had an opioid-related overdose in the past week. Over the 26 weeks between these two dates, 7 participants died. Over the remainder of the study period (week 27–53), an additional

≤5 participants died (exact number of post-implementation deaths suppressed to prevent re-identification of individual participants per ICES policies). Due to the low number of events, death was not subsequently modelled.

OAT enrollment and opioid-related overdoses

Our measures of weekly OAT enrollment and opioid-related overdoses share a common denominator, i.e., the number of participants remaining (still alive) in the cohort at the end of the preceding week. The average weekly denominator for these outcomes was 353 participants (SD, 2.99).

Fig. 3 plots the observed and predicted weekly proportions of participants enrolled in OAT.

Overall, 36.49% (131/359) of participants were enrolled in OAT the first week. Based on the fitted model, there was a non-statistically significant decrease of 0.08% per week in OAT enrollment (95% CI -0.23% to 0.07%) during the pre-implementation period. Comparing the first full week post-implementation (week 28: March 24th–30th, 2020) and the last week pre-implementation (week 26: March 10th–16th, 2020), the interventions were associated with an immediate increase of 1.95% in OAT enrollment (95% CI 0.04% to 3.85%). Furthermore, post-implementation, OAT enrollment gradually declined an additional 0.17% week-to-week over and above the pre-implementation trend (95% CI -0.42% to 0.08%). At 26 weeks post-implementation, the interventions were not associated with a statistically significant difference in OAT enrollment compared to if they had not been implemented (-2.57% difference; 95% CI -9.23% to 4.09%).

The weekly number of participants that experienced an opioid-related overdose (based on emergency department visit and hospitalization records) was low throughout the study period. We observed that ≤5 participants had an opioid-related overdose for 50 of 53 weeks measured (including week 1: ≤5/359 or ≤1.39% with an opioid-related overdose that week), with a maximum weekly value of 11 participants. Corre-

Table 1

Characteristics of participants on day before study period commenced and day before provincial COVID-19 state of emergency declaration – the Ontario integrated Supervised Injection Services study in Toronto.

Characteristic	Day before study period commenced (September 16th, 2019)	Day before provincial COVID-19 emergency declaration (March 16th, 2020)
No. of remaining participants	359	352
Age (y), mean (SD)	41.27 (10.62)	41.83 (10.66)
Male, n (%)	239 (66.57)	234 (66.48)
ODB coverage[a], n (%)	278 (77.44)	273 (77.56)
Acute psychiatric comorbidity[b], n (%)	≤5 (NR)	≤5 (NR)
Alcohol use disorder[c], n (%)	52 (14.48)	46 (13.07)
Recent opioid-related overdose[d], n (%)	7 (1.95)	23 (6.53)

Notes: SD = standard deviation; ODB = Ontario Drug Benefit; NR = not reported. Cell counts between 1-5 were suppressed (reported as '≤5') and corresponding proportions were not reported in accordance with ICES policies to prevent back calculation of these values and possible identification of individual participants.

[a] Defined as age≥65 or ≥1 dispensation(s) in the ODB database in the past 180 days.

[b] Defined as ≥1 emergency department visit for schizophrenia (including delusional disorders) or deliberate self-harm in the past 30 days.

[c] Defined as ≥1 emergency department visit, hospitalization, or physician claim with an alcohol use disorder diagnostic code in the past 180 days.

[d] Defined as ≥1 emergency department visit or hospitalization for opioid poisoning in the past 7 days.
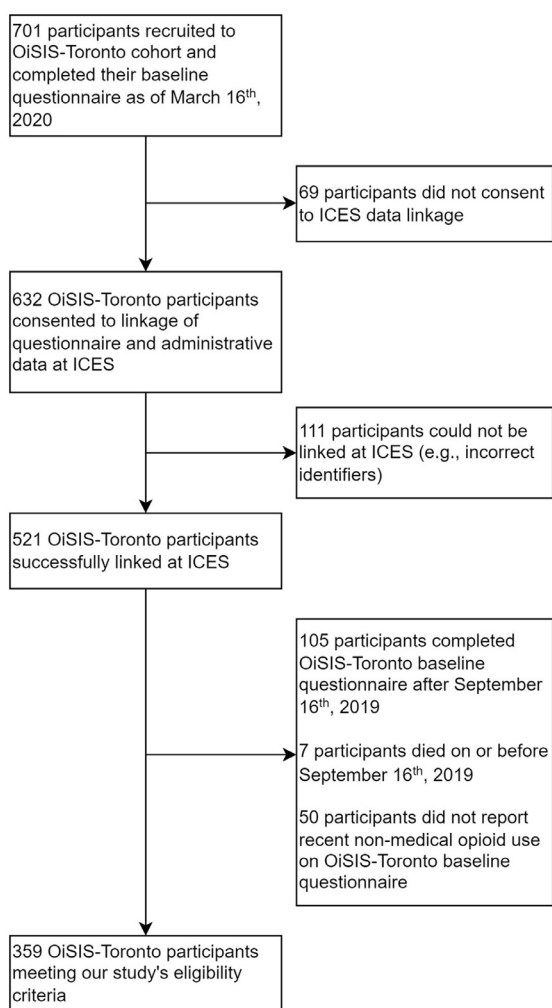

Fig. 2. Flow of participants into the study. *Notes:* OiSIS-Toronto = Ontario integrated Supervised Injection Services Toronto.

spondingly, we did not plot the observed data for this outcome to prevent possible re-identification of individual participants based on small cell sizes (i.e., numerator values between 1 to 5) in accordance with ICES policies; however, we fit a segmented linear regression model to the observed data. Based on the fitted model ($Y_t = 0.33 + 0.03t - 0.32I - 0.05[t - 26]I + \varepsilon_t$, where $\varepsilon_t = 0.29\varepsilon_{t-1} + w_t$ and $w_t \sim N(0, 0.44)$, the pro-

portion of participants with an opioid-related overdose remained relatively constant during the pre-implementation period (0.03% increase per week; 95% CI -0.01% to 0.08%). Post-implementation, the proportion experiencing an opioid-related overdose immediately decreased by 0.32% (95% CI -1.24% to 0.60%) and gradually decreased by an additional 0.05% per week beyond the pre-implementation trend (95% CI -0.11% to 0.02%); however, neither change was statistically significant. At 26 weeks post-implementation, the interventions were not associated with a statistically significant change in the proportion of participants experiencing an opioid-related overdose versus had the interventions not been implemented (-1.53% difference; 95% CI -3.42% to 0.36%).

Take-home doses and urine drug screening

Fig. 4 plots the observed and predicted weekly proportions of OAT-enrolled participants who received take-home doses and underwent urine drug screening. The average weekly denominator was 116 OAT-enrolled participants (SD, 7.89) for both outcomes. On average, 90.07% of OAT-enrolled participants each week were last dispensed methadone (range = 87.10% to 92.86%).

Overall, 18.32% (24/131) of OAT-enrolled participants received take home doses in week 1. Based on the fitted model, this proportion remained relatively unchanged during the pre-implementation period (0.04% increase per week; 95% CI -0.21% to 0.29%) (Fig. 4a). Post-implementation, the interventions were associated with a statistically significant immediate increase of 18.31% in the proportion of OAT-enrolled participants receiving take-home doses (95% CI 13.21% to 23.40%); however, no gradual effect was observed post-implementation (0.13% decrease per week beyond the pre-implementation trend; 95% CI -0.49% to 0.24%). At 26 weeks post-implementation, the interventions were associated with a statistically significant increase of 14.98 additional OAT-enrolled participants receiving take-home doses per 100 (95% CI 4.33% to 25.62%) versus if the interventions were never implemented.

We observed that 68.70% (90/131) of OAT-enrolled participants underwent urine drug screening in the first week. Based on the fitted model, this proportion was relatively stable during the pre-implementation period (0.15% decrease per week; 95% CI -0.36% to 0.06%) (Fig. 4b). Post-implementation, the interventions were associated with a statistically significant immediate decrease of 22.38% in the proportion of OAT-enrolled participants undergoing urine drug screening (95% CI -26.89% to -17.88%) and a statistically significant gradual increase of 0.56% in urine drug screening per week beyond the pre-implementation trend (95% CI 0.27% to 0.86%). At 26-weeks post-implementation, the interventions were associated with 7.72 fewer OAT-enrolled patients per 100 undergoing urine drug screening (95%
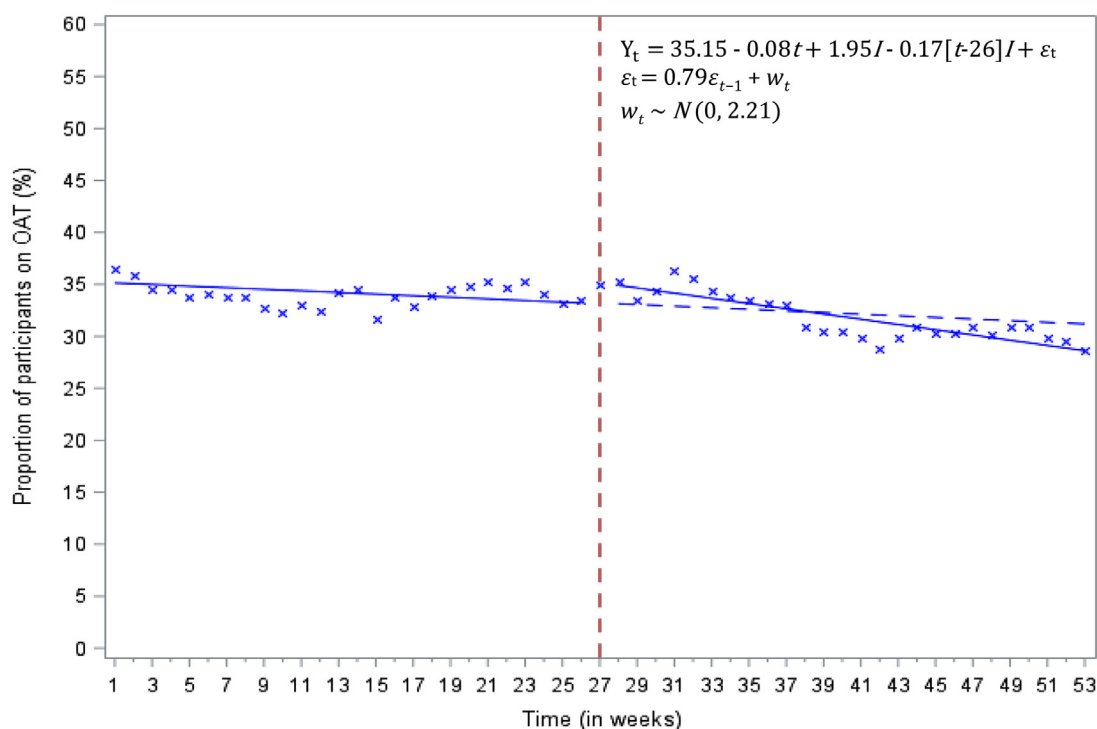
$$Y_t = 35.15 - 0.08t + 1.95I - 0.17[t\text{-}26]I + \varepsilon_t$$
$$\varepsilon_t = 0.79\varepsilon_{t-1} + w_t$$
$$w_t \sim N(0, 2.21)$$

Fig. 3. Weekly proportion of participants enrolled in OAT between September 17th, 2019 and September 21st, 2020 – Ontario integrated Supervised Injection Services study in Toronto. Notes: Observed proportions represented by blue 'x's, the solid blue lines are the fitted regression pre- and post-implementation trendlines, and the hatched blue line represents the projected trend had the interventions not been implemented (i.e., counterfactual). The fitted trendlines and counterfactual were obtained from a segmented linear autoregressive error regression model (equation provided in figure). The vertical hatched red line indicates the week in which the interventions were implemented (week 27: March 17th–23rd, 2020), which was excluded from all analyses.

CI -16.53% to 1.10%) compared to if the interventions were never implemented; however, this difference was not statistically significant.

Discussion

We evaluated the effects of a provincial COVID-19 emergency declaration, federal exemptions, and interim treatment guidance on OAT enrollment and related outcomes—measured weekly from September 17th, 2019 through September 21st, 2020—among 359 Toronto-based PWID with suspected opioid use disorder. Post-implementation, the interventions were collectively associated with a slight immediate increase in OAT enrollment among all participants (1.95%) and substantial immediate changes in receipt of take-home doses (any quantity; 18.31% increase) and urine drug screening (22.38% decrease) among OAT-enrolled participants. By the final week of observation, OAT enrollment and urine drug screening reverted towards expected levels had the interventions never occurred whereas the increase in receipt of take-home doses was largely sustained (14.98% increase). The interventions were not associated with any changes in opioid-related overdoses among all participants. Due to the low number of deaths, we could not evaluate the joint impact of the interventions on all-cause mortality (outcome not modelled).

These findings suggest that rapid modifications to OAT delivery at the beginning of the COVID-19 pandemic in Ontario may have helped mitigate anticipated pandemic-related barriers to treatment access within the study cohort. Although OAT enrollment did not meaningfully increase among participants, the absence of post-implementation decreases in enrollment is arguably a success of the COVID-19-related OAT modifications (federal exemptions and interim treatment guidance), as pandemic restrictions (including provincial emergency orders) were expected to worsen OAT access and thereby enrollment in this population (Centre for Addiction and Mental Health et al., 2020). The relatively static level of OAT enrollment post-implementation is likely

owed to the immediate and sustained increase in the proportion of OAT-enrolled participants receiving take-home doses and the immediate, albeit temporary, decrease in the proportion undergoing weekly urine drug screening. Specifically, the increased likelihood of receiving take-home doses following the OAT modifications and corresponding decreased likelihood of routine urine drug screening (at least initially) may have facilitated treatment retention despite pandemic restrictions by reducing OAT patients' in-person clinical encounters and affording greater flexibility in their dosing schedules (Corace et al., 2022; Haasen & Brink, 2006; Sarasvita et al., 2012; Schaub et al., 2010). These post-implementation changes are likely attributable to the provincial interim treatment guidance, which explicitly recommended that prescribers and pharmacists reduce the frequency of urine drug screening and observed doses for OAT patients during the COVID-19 pandemic (Centre for Addiction and Mental Health et al., 2020).

These inferences are supported by analogous findings from the broader OAT patient population in Ontario. A study by Kitchen et al. observed that the number of Ontarians actively being treated with methadone or buprenorphine/naloxone was unchanged following the provincial COVID-19 emergency declaration and interim OAT guidance (Kitchen et al., 2022). Though enrollment remained stable, as in our study, the interim treatment guidance was associated with immediate increases in the weekly proportions of OAT patients receiving extended supplies of take-home methadone or buprenorphine/naloxone doses (i.e., ≥7 days' worth per dispensation) (Kitchen et al., 2022). Another population-based analysis of OAT-enrolled Ontarians found that individuals who received increased take-home doses in the first 30 days following the interim treatment guidance (e.g., transitioned from daily observed dosing to any take-home doses) were significantly less likely to pause or discontinue treatment in the next six months versus those without increased take-home doses (Gomes et al., 2022). Taken together with our findings, these results suggest that, as intended, the provincial interim treatment guidance led to increased provision of take-home
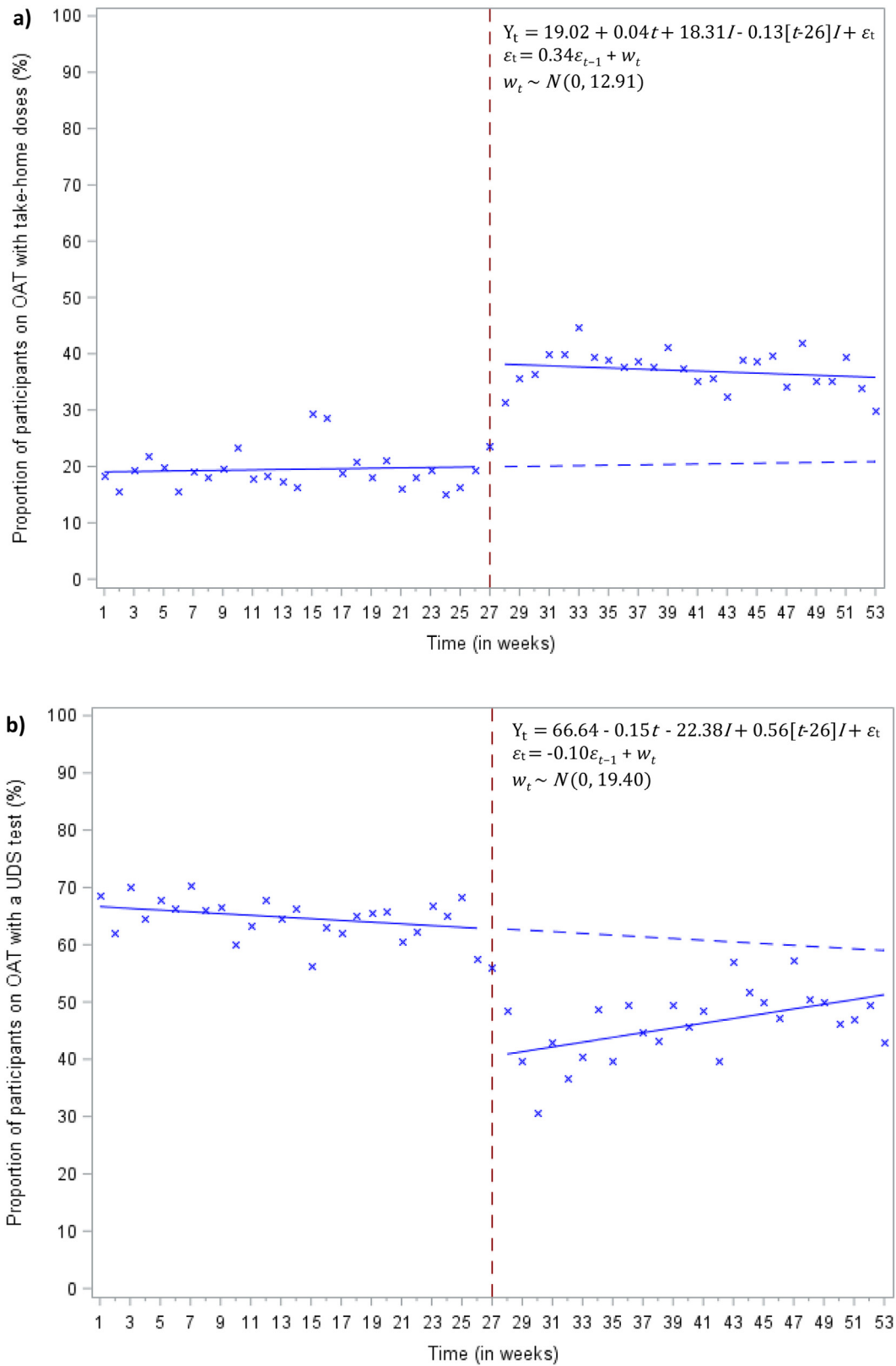
Fig. 4. Weekly proportion of participants enrolled in OAT that received take-home OAT doses (panel a) and underwent urine drug screening (panel b) between September 17th, 2019 and September 21st, 2020 – Ontario integrated Supervised Injection Services study in Toronto. Notes: Observed proportions represented by blue 'x's, the solid blue lines are the fitted regression pre- and post-implementation trendlines, and the hatched blue line represents the projected trend had the interventions not been implemented (i.e., counterfactual). The fitted trendlines and counterfactual were obtained from segmented linear autoregressive error regression analyses (model equation provided in each figure). The vertical hatched red line indicates the week in which the interventions were implemented (week 27: March 17th–23rd, 2020), which was excluded from all analyses.

doses to OAT patients both in the general population and our study co-hort of structurally vulnerable PWID, which facilitated treatment reten-tion in the early stages of the COVID-19 pandemic (Gomes et al., 2022; Kitchen et al., 2022).

Increases in take-home doses for OAT patients have also been observed in other jurisdictions that released similar guidance de-emphasizing observed doses during the COVID-19 pandemic. In the United States, a federal exemption and national guidelines were imple-mented in March 2020 to allow prolonged take-home doses of ≤28 days for stable patients or ≤14 days for less stable patients on methadone for opioid use disorder (Substance Abuse and Mental Health Services Ad-ministration (SAMHSA), 2020). A pre-post analysis of 194 methadone patients in Spokane, Washington found that patients received, on aver-age, an additional 41.4 days' worth of take-home doses over the three months following the guidelines versus the preceding three months (Amram et al., 2021). Similar to Ontario, the Australian government re-leased national guidelines emphasizing virtual visits, less frequent urine drug screening, and reducing observed dosing for OAT patients during the pandemic (Lintzeris et al., 2021). Based on three public treatment services in Sydney, Australia, Lintzeris and colleagues found that the proportion of OAT patients receiving any take-home methadone or sub-lingual buprenorphine doses increased considerably in the four months after guideline-based service changes (67% or 210/314) versus the pre-ceding four-month period (23% or 86/378) (Lintzeris et al., 2021). Lastly, in Ukraine, the national Ministry of Health released interim guid-ance in March 2020 relaxing an existing requirement of six months of sobriety for OAT patients to receive take-home doses (Meteliuk et al., 2021). As in our study, OAT enrollment increased negligibly post-guidance but the proportion of OAT patients in Ukraine receiving take-home doses increased substantially in the first 60-days post-guidance (82.2% or 10,766/13,097) versus the last 60-days pre-guidance (57.5% or 7,381/12,837) (Meteliuk et al., 2021). While the impact of interim treatment guidance promoting take-home doses on opioid-related over-doses was not evaluated in the preceding international studies, annu-alized mortality among OAT patients in Ukraine was comparably low between the post- and pre-guidance periods (Meteliuk et al., 2021).

We found no evidence of immediate or gradual increases in opioid-related overdoses within the overall cohort following the provincial COVID-19 emergency declaration and corresponding OAT modifica-tions. This important result is somewhat surprising given the elevated overdose risk in the source cohort (i.e., 38.6% of OiSIS-Toronto partic-ipants reported a recent non-fatal overdose at baseline) (Scheim et al., 2021a) and our restriction to participants with a suspected moder-ate or severe opioid use disorder. In contrast with our findings, prior analyses have demonstrated significant increases in the rate of fa-tal opioid-related overdoses in Toronto and Ontario during the first months of the pandemic overlapping with our post-implementation pe-riod (Gomes et al., 2021b; Toronto Public Health, 2021). These con-flicting trends may be because most OiSIS-Toronto participants—all of whom were PWID—did not qualify for take-home OAT doses un-der pre-pandemic guidelines (College of Physicians & Surgeons of On-tario, 2011). In other words, compared to the average OAT patient in Ontario, cohort members may have been more likely to initiate take-home doses following the relaxed, interim treatment guidance, as evi-denced by the drastic post-guidance increase in take-home dose cover-age among OAT-enrolled participants. Relatedly, Gomes and colleagues found that Ontarians who transitioned from daily dispensed methadone to any quantity of take-home doses in the 30 days after the interim guidance were 27% less likely to experience an opioid-related over-dose over the next six months of the pandemic versus methadone pa-tients who did not initiate take-home doses (Gomes et al., 2022). Given this protective association and the prominence of methadone (versus buprenorphine/naloxone) dispensing in our study, the absence of post-implementation increases in opioid-related overdoses for the overall co-hort could be due to increases in take-home dose provision among OAT-enrolled participants (with corresponding increases in treatment reten-

tion and decreases in overdose risk) (Gomes et al., 2022), which offset increases in overdose risk within the non-OAT-enrolled subset over time.

Limitations

Several limitations of our study merit discussion. First, our opioid-related overdose measure relied on data from emergency departments and inpatient hospital stays, and therefore does not capture overdoses attended to in the community or confirmed opioid-related deaths where the individual was not transported to hospital (Gomes et al., 2018). Therefore, this outcome underestimates the true incidence of these events. Second, our findings may not be generalizable to the broader population of PWID in Toronto, as the source cohort (OiSIS-Toronto) is a convenience sample primarily composed of supervised consump-tion service clients (Scheim et al., 2021b). Third, the health admin-istrative databases used in this study lack information on participant characteristics that might influence their access to OAT and eligibil-ity for take-home doses even under relaxed pandemic criteria (e.g., homeless and unable to safely store take-home doses). Fourth, in us-ing self-reported non-medical opioid use at OiSIS-Toronto baseline to identify participants with a suspected opioid use disorder, some indi-viduals may have ceased non-medical opioid use before the study pe-riod began; including these non-OAT-eligible participants would under-estimate overall treatment enrollment. Fifth, due to the global nature of the COVID-19 pandemic and similar public health responses under-taken elsewhere, we could not identify a concurrent, external control group for analysis, which could have strengthened (or challenged) our attribution of post-implementation outcome changes to measured inter-ventions (Jandoc et al., 2015; Lopez Bernal et al., 2016).

Conclusions

Although provincial COVID-19 emergency measures were expected to worsen treatment access in Toronto, Ontario, it appears that rapid changes to OAT provision (via federal exemptions and interim treatment guidance) resulted in an immediate and lasting increase in take-home dose coverage among OAT-enrolled participants in our study, without corresponding increases in opioid-related overdoses among all partici-pants. Therefore, it may be worthwhile to consider long-term adoption of these OAT modifications beyond the COVID-19 pandemic in popula-tions that are comparable to our study cohort (i.e., structurally vulner-able people who inject drugs).

Data availability

The dataset used in this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (e.g., healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet pre-specified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset cre-ation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

Declarations of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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on which we conducted this research is the traditional territory of many nations including the Mississaugas of the Credit, the Anishnabeg, the Chippewa, the Haudenosaunee, and the Wendat Peoples, and home to many diverse First Nations, Inuit, and Métis Peoples. This study was supported by ICES, which is funded by an annual grant from the Ontario Ministry of Health (MOH) and the Ministry of Long-Term Care (MLTC). This study also received funding from a COVID-19 Rapid Research–Social Policy and Public Health Responses Operating Grant (application year: 2020; application #: 447989) awarded by the Canadian Institutes of Health Research. Parts of this material are based on data and information compiled and provided by Ontario Ministry of Health (MOH) and the Canadian Institute for Health Information. The analyses, conclusions, opinions, and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred. We thank IQVIA Solutions Canada Inc. for use of their Drug Information File.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2022.103680.

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