Impact of opioid agonist therapy in individuals with opioid use disorder who experience an overdose in Ontario, Canada

Introduction

- Opioid agonist therapies (OATs) including methadone, transmucosal buprenorphine (TM-BUP), buprenorphine extended-release (BUP-XR), and sustained-release oral morphine (SROM) are effective established medications for opioid use disorder (MOUD).[1,2]
- However, the overdose (OD) risk for patients with opioid use disorder (OUD) using various OATs remains insufficiently characterized.[3]
- **Aim:** To evaluate the impact of different OATs on opioid-related non-fatal and fatal ODs in Ontario, Canada.

Methods

- A retrospective, nested case-control study using Ontario's health administrative data held at ICES (formerly Institute for Clinical and Evaluative Sciences).
- Treatment-naïve patients with OUD initiating their first OAT between January 1, 2022, and June 30, 2024, were included.
  - Cases (patients with fatal or non-fatal OD events) and controls (no OD events) were matched (1:10) on age, sex, and time at risk for OD.
  - Fatal OD events were identified by opioid-related deaths recorded in the Drug and Drug/Alcohol Related Death Database.
  - Non-fatal OD events were identified by an ICD-10-CA code for "opioid toxicity" recorded at an emergency department (National Ambulatory Care Reporting System) or hospital (Discharge Abstract Database).
- **Analysis period**: The 24-month period after cohort entry until censoring to assess study outcomes. **Lookback period**: Back to 2002 to assess baseline characteristics and medical history.
- **Index date**: Cases: Date of OD event in the analysis period.
  Controls: Cohort entry date plus days to matched case's OD event.
  Patients could be controls in either cohort prior to the relevant OD event.
  Patients with a non-fatal OD and subsequent fatal OD were included in both non-fatal and fatal OD case cohorts. Patients with multiple non-fatal ODs were indexed in the non-fatal OD case cohort only once, at time of first non-fatal OD.
- **OAT exposure** was defined as having a prescription for an OAT at OD event date. Patients with coinciding prescriptions for different OATs at OD event were classified in the "multiple OATs" group. This study only reported OAT use at the time of index OD event; however, patients may have used other OATs between Base Cohort entry and their index date, or anytime following a non-fatal OD.

Results

- Among 45,243 patients in the Base Cohort, 4,109 (9%) had at least one non-fatal OD and 770 (2%) had a fatal OD (**Figure 1**).
- Patients with higher OAT coverage (≥80%) at index experienced less non-fatal and fatal OD compared to those with lower OAT coverage (<80%) (**Table 1**).
- BUP-XR had the lowest proportion of patients with non-fatal and fatal OD compared to other OATs or no OAT (**Figure 1**).

Acknowledgement: This study contracted ICES Data & Analytic Services (DAS) and used de-identified data from the ICES Data Repository, which is managed by ICES with support from its funders and partners: Canada's Strategy for Patient-Oriented Research (SPOR), the Ontario SPOR Support Unit, the Canadian Institutes of Health Research, and the Government of Ontario. The opinions, results and conclusions reported are those of the authors. No endorsement by ICES or any of its funders or partners is intended or should be inferred.

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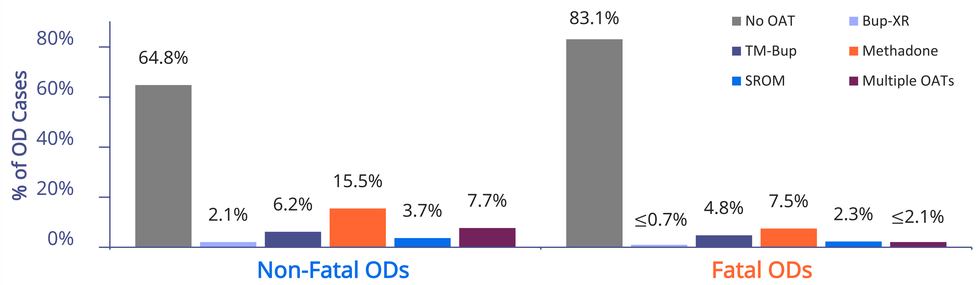
Buprenorphine-prescribed patients have a lower proportion (BUP-XR) (Figure 1) and lower odds (BUP-XR, TM-BUP) (Figure 2) of non-fatal and fatal OD events compared to no OAT.

Figure 1. Proportion of OD events experienced by patients using various OATs



All patients (N = 45,243)	No OAT at OD event	BUP-XR	TM-BUP	Methadone	SROM	Multiple OATs
Non-Fatal Cases (n = 4,109)	2,664 (64.8%)	85 (2.1%)	254 (6.2%)	636 (15.5%)	152 (3.7%)	318 (7.7%)
Total patients on OAT‡	22,311	1,438	10,523	7,439	1,300	2,188
Fatal Cases (n=770)	640 (83.1%)	*1-5 (≤0.7%)	37 (4.8%)	58 (7.5%)	18 (2.3%)	*12-16 (≤2.1%)
Total patients on OAT‡	4,426	*253-257	1,911	1,245	251	*380-384

‡ Count of patients and their matched controls on an OAT at index.
An asterisk (*) denotes a range resulting from ICES privacy regulations, applied when cell counts are <6. Other counts may also be suppressed to prevent back-calculation.

Conclusions

- Findings suggest that sustained exposure to OAT and OAT type were important determinants of OD risk, with effects varying by OAT.
- Limitations include potential misclassification in administrative data, incomplete or inaccurate capture of opioid-related non-fatal and fatal OD events and OAT use, and absence of a direct measure of OAT adherence.

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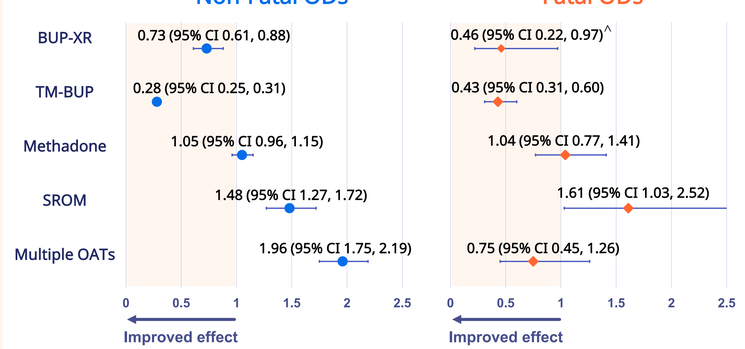
Additional Information

Table 1. Demographic and clinical characteristics

	Non-Fatal OD Cases (n=4,109)	Fatal OD Cases (n=770)
Age, mean (SD)	37.0 (10.5)	39.5 (11.4)
Sex, male n (%)	2,780 (67.7%)	538 (69.9%)
Income quintile, Q1 (lowest) n (%)	1,907 (46.4%)	318 (41.3%)
Comorbidities		
Substance use disorders	3,296 (80.2%)	580 (75.3%)
Anxiety disorders	2,230 (54.3%)	374 (48.6%)
Mood disorders	1,628 (39.6%)	271 (35.2%)
Schizophrenia	993 (24.2%)	158 (20.5%)
No comorbidities	373 (9.1%)	85 (11.0%)
Total time on any/all OAT		
Less than 80% of time on OAT, n (%)	3,120 (75.9%)	654 (84.9%)
80-100% of time on OAT, n (%)	989 (24.1%)	116 (15.1%)

Figure 2. Unadjusted odds ratios for OD events by OAT, compared to no OAT at OD event



^ This odds ratio should be interpreted with caution because there were so few fatal OD while prescribed BUP-XR (Figure 1).

Authors and Disclosures

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