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SYNOPSIS

Review of "Effect of Risk Mitigation Guidance for Opioid and Stimulant Dispensations on Mortality and Acute Care Visits during Dual Public Health Emergencies"

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One-Minute Summary

- This retrospective cohort study explores the association between receiving prescription opioids through British Columbia's (BC) Risk Mitigation Guidance (RMG) program (i.e., safer supply) and all-cause or overdose-related mortality and acute care utilization in the week following dispensation. The study also examines these outcomes in relation to stimulant medication prescribed through the RMG program during the same period: March 2020 to August 2021.
- Among adults ≥18 years old in BC diagnosed with opioid and/or stimulant use disorder(s), receiving prescription opioids at least one day per week had a dose-responsive association with reduced all-cause (adjusted hazard ratio [aHR] 0.39, 95% confidence interval [CI] 0.25 to 0.60) and overdose-related (aHR 0.45, 95% CI 0.27 to 0.75) mortality in the subsequent week, but no significant associations were seen with the odds of acute care visits.
- In contrast, receiving prescription stimulant at least one day per week was not significantly associated with mortality in the subsequent week, but was associated with reduced odds of acute care visits for any cause (aOR 0.82, 95% CI 0.72 to 0.95).
- These findings suggest that prescribing opioids to people diagnosed with opioid use disorder could reduce mortality on a population level in the short-term, perhaps by circumventing exposure to potentially toxic unregulated drugs. The benefit of prescribing stimulants to people with stimulant use disorder is less clear, but was associated with reduced acute healthcare visits.

Additional Information

Drug overdose is a growing public health concern in North America, worsening during the COVID-19 pandemic. The province of BC had been particularly affected by a toxic unregulated drug supply, driven by fentanyl and fentanyl analogues, which can cause respiratory depression and subsequently, death.[1]

RMG was introduced by the BC government and the BC Centre on Substance Use shortly after the COVID-19 pandemic (i.e., March 2020) and was intended to provide guidance to clinicians on prescribing pharmaceutical alternatives to people at risk of overdosing or experiencing withdrawal from opioid, alcohol, benzodiazepine, and/or stimulant use.[1]

Cohorts in this study were identified through case-finding algorithms that were applied to pre-linked administrative databases (e.g., Medical Services Plan, PharmaNet, Discharge Abstract Database, National Ambulatory Care Reporting System) to find individuals who had an indication of opioid and/or stimulant use disorder(s) between January 1996 and August 2021. The algorithms examined International Classification of Diseases (ICD) codes and drug identification numbers (DIN) that indicate the use of opioid agonist therapy (OAT) for the opioid cohort and used ICD codes to identify stimulant use disorder for the stimulant cohort. Another set of algorithms identified RMG dispensations using prescription data from PharmaNet, as unique DIN were not assigned to RMG medications at the time of the study. This formed the study's exposure groups of those who received RMG opioid (n=5356) or RMG stimulant (n=1061) dispensations during the follow-up period March 27, 2020 to August 31, 2021. Then, using nearest neighbour high dimensional propensity score matching, exposure group participants from each cohort were matched 1-to-1 with unexposed controls.

Approximately 60% of the study population were male and the median age was 38 years old. Slightly over half of participants were based in Vancouver or South Central Vancouver Island and approximately 10% of participants were from rural areas. Roughly 80% of people who accepted RMG opioid and/or stimulant dispensation during the study period received income assistance and nearly 40% were precariously housed in the prior year.

The main study outcomes were 1) all-cause mortality, 2) overdose-related mortality, and 3) acute healthcare visits, measured in the week following initial dispensation through RMG. Mortality was ascertained through examining BC vital statistics and Coroners' records data. Acute care utilization was informed by the National Ambulatory Care Reporting System and Discharge Abstract Databases. Participants were followed up until loss to follow up (e.g., death), incarceration, or the end of the study period in August 2021.

The authors attempted to account for time-varying confounding through marginal structural models and used weighted regression to measure the key associations.

In the high dimensional propensity score matched cohort, RMG opioid dispensation was associated with lower all-cause and overdose-related mortality, with more days per week of dispensation having a stronger inverse association, similar to a dose-response relationship. However, RMG opioid dispensations were not significantly associated with the odds of acute healthcare visits for overdose or for any cause. Conversely, there was not a significant association between increasing days per week of RMG stimulant dispensation and mortality, but there was a significant decrease in healthcare visits.

Several sensitivity analyses were conducted:

- Upon including all individuals in the cohort without matching, RMG opioid dispensation showed a protective effect on mortality that was stronger with more days per week of RMG, similar to the results from the matched cohort. Unlike the matched cohort, RMG opioid dispensation in the unmatched cohort was significantly associated with an increase in acute care visits.
- The association between RMG opioid dispensation and mortality was no longer significant in a subgroup analysis of individuals who did not receive OAT for at least 30 days leading up to RMG initiation.
- To account for variations in daily dosing in the RMG opioid cohort, the authors expressed the exposure of RMG opioid dispensation in terms of weekly morphine equivalent (ME), and they observed a dose-sensitive protective effect of higher ME on all-cause mortality.

PHO Reviewer's Comments

This represents one of the earliest published population-level observational studies assessing the impact of opioid and stimulant pharmaceutical alternatives on mortality and acute healthcare utilization in a dual emergency (i.e., COVID-19 pandemic and drug toxicity) setting. Methodologically, it used a combined longitudinal and survival data model for analysis.

Results align with a recent international scoping review (which did not include the study discussed here) published in February 2024, that examined the outcomes and reflections of participants of safer opioid supply programs. The findings revealed that opioid toxicity rates were reduced and overall, participants perceived these programs favourably, reporting improved quality of life and physical and mental health. Concerns of diversion risk were linked to inadequate program offerings, such as insufficient access to required opioid doses or types.[2]

In contrast, a more recently-published ecological study investigating opioid prescribing and opioid-related hospitalization and mortality trends in the two years following launch of BC's Safer Opioid Supply policy found that opioid prescription rates and poisoning-related hospitalizations increased, without significant mortality rate change.[3] The study's limited sample size of people receiving safer opioid supply prescriptions, along with its ecological study design and the multitude of factors influencing opioid-related hospitalizations—some addressed but others not—call for caution in applying these results for decision making.

In applying the Critical Appraisal Skills Programme (CASP) quality appraisal tool to the Slaunwhite et al. retrospective cohort study, we identified multiple strengths and limitations.

Strengths include 1) using population-based information from numerous pre-linked administrative databases, 2) posing focused yet generalizable research inquiries, especially relevant to Ontario, and 3) rigorously controlling for confounding variables using multiple methods.

Limitations include 1) potential misclassifications in exposure and control group assignments due to the absence of validated methods for ascertaining RMG participation using PharmaNet data, DIN, or ICD codes, 2) residual confounding by pre-study OAT usage patterns, including adherence, duration, and dosages, and 3) due to limited publications on this topic, it is challenging to determine fit with other literature.

Limiting outcome measurement to only one week post-exposure prevented the authors from evaluating long-term or cumulative effects of participating in the RMG program on health or societal outcomes.

Connecting with prescribers through the RMG program likely offered opportunities for diagnostic evaluations and linkages to social and health services for participants, addressing their comorbidities. Given that over half of the participants at baseline lacked a primary care provider and many faced socioeconomic hardships, improving primary care accessibility may have alleviated reliance on emergency health services for similar support needs.

References

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