

<b>Title</b>	Evaluating the effects of Risk Mitigation Guidance opioid and stimulant dispensations on mortality and acute care visits during dual public health emergencies
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## Key messages

- Risk Mitigation Guidance (RMG) opioid prescribing was associated with a significant reduction in the likelihood of death among people with an opioid use disorder.
- Risk Mitigation opioid prescribing was associated with a 61% reduction in death from any cause in the subsequent week. A prescription for 4 or more days was associated with a 91% reduction in death in the subsequent week.
- Prescribing pharmaceutical alternatives to illicit drugs are a promising intervention to reducing drug poisoning deaths among people with opioid use disorder.

## Introduction

**Primary research question:** What was the impact of RMG opioid and stimulant medications on death and acute care visits for people with an opioid or stimulant use disorder?

**Background:** The toxicity of the unregulated drug supply is the primary contributor to drug poisoning (overdose) deaths in British Columbia (BC) and across Canada. The Province of BC first introduced Risk Mitigation Guidance (RMG) in March of 2020 to support physicians and nurse practitioners to prescribe

pharmaceutical alternatives to unregulated drugs. This guidance aimed to help people who use drugs to self-isolate and quarantine if needed during the COVID-19 pandemic. In July of 2021, the Province of BC released a provincial Prescribed Safer Supply policy to decouple pharmaceutical alternatives from the COVID-19 pandemic.

**Study objective:** There is limited evidence to date that describes the outcomes associated with prescribing pharmaceutical alternatives to the unregulated drug supply and no evidence at the population level. The objective of this study was to determine what effect RMG prescribing had on all-cause and overdose-related mortality, and acute care visits.

## Study Design and Methods

This study analyzed administrative health information for all persons who received RMG opioid or stimulant dispensations from March 27, 2020 to August 31, 2021.

### Data sources

Population-level administrative health data was used to identify a cohort of BC residents with an opioid use disorder (OUD) or a stimulant use disorder (StUD). A total of 5,882 people with OUD or StUD were dispensed RMG. Individual-level sources of connected administrative health data was then used to analyze the cohort. These data sources included: Medical Services Plan (MSP), PharmaNet, National Ambulatory Care Reporting Systems, Discharge Abstract Database from hospitals, and the BC Coroner's Service and Vital Statistics. These databases provided information such as physician billing records, community pharmacy dispensations, emergency department visits, hospitalizations, and mortality.

### Outcome measures

The main outcomes were mortality and acute care visits because they are among the most severe outcomes associated with substance use during the unregulated drug poisoning crisis.

### Cohort matching

A non-exposure group (people with an OUD or StUD who were not given RMG medications) was created to compare the persons with an OUD or StUD who received RMG medication (the exposure group). Each person in the exposure group was carefully matched with a person in the non-exposure group who shared a similar set of demographic, socio-economic, healthcare service utilization, and health status characteristics. Matching was conducted using both investigator-selected variables and high-dimensional propensity scoring methodology. This approach helps balance confounding factors between the groups to more accurately evaluate the effect of RMG prescribing on death and acute care visits.

## Analysis

Marginal structural models were used to determine the effect of RMG prescribing on each of the primary outcomes in the subsequent week. Sensitivity analyses were conducted to assess the robustness of the results relating to the control group composition, exposure and outcome classifications, and statistical model specifications.

## Findings & Interpretations

### People given a prescribed opioids had a significantly reduced likelihood of dying

Findings:

- Receipt of RMG opioids for 1 day or more in one week was associated with a 61% reduction in the likelihood of death from any causes in the subsequent week.
- Receipt of RMG opioids for 1 day or more in one week was associated with a 55% reduction in overdose death in the subsequent week.
- The protective effects increased with longer prescribing: Receipt of 4 or more days of opioid RMG was associated with a 91% reduction in death in the subsequent week. Receipt of 4 days or more of opioid RMG was also associated with a 89% reduction in overdose death.
- The protective effects were also dose dependent: the higher the dose of opioids prescribed in a week the less likely a person may die from a toxic drug poisoning.

Interpretations:

- People who have access to prescribed pharmaceutical alternatives may rely less on the unregulated toxic drug supply, which may contribute to the reduction in mortality.
- The protective effects could also be because of the increased interactions with health care providers who can provide care for many health conditions that contribute to mortality.
- Because longer prescribing was associated with higher protection, additional research and quality improvement interventions are needed to examine RMG opioid retention.

### Prescribing stimulants was not associated with a significant reduction in the likelihood of death

Findings:

- Prescriptions of one day or more of stimulant RMG was associated with a 50% reduction in death from any causes, however the results were not statistically significant.
- Prescriptions of 4 days or more of stimulant RMG was associated with a 61% reduction in death from any causes, however the results were not statistically significant.

Interpretations:

- Several clinical trials have demonstrated the safety and effectiveness of prescribed stimulant medication, however, these studies have been conducted in controlled clinical settings. There may be other confounding factors that influence health outcomes for people accessing stimulants from the unregulated toxic drugs supply.

**Prescribed stimulants reduced acute health care visits for any cause**

Findings:

- Prescribed opioids had no significant reduction in acute health care visits for overdose-related reasons or any reasons.
- RMG stimulants were associated with a statistically significant reduction in acute health care visits for overdose-related reasons or any reasons.

Interpretations:

- People prescribed RMG medications may be accessing acute health care facilities for reasons unrelated to the unregulated substance use. Many people prescribed RMG medications have existing chronic conditions and experience higher rates of unstable housing and poverty. These factors contribute to poor health outcomes and increase the likelihood of acute health care services.
- Interventions for StUD in BC are very limited. The reduction in acute health care visits for people receiving dispensations of RMG stimulations could be related to the identification of new or emerging illnesses or conditions (i.e., skin infections).

## Limitations

- Two algorithms were used to identify RMG opioid and stimulant dispensations in PharmaNet. It is still possible that some dispensations were misclassified and prescriptions were for other purposes such as cancer or palliative care.
- Data on RMG dispensations does not include dispensations from programs or sites where data is not entered into PharmaNet such as hospitals.
- It is not possible to determine from administrative data whether a person used their medication as prescribed.
- This study specifically focused on people diagnosed with OUD or StUD. These results may not be generalizable to other settings or populations, such as people not diagnosed with an OUD or StUD.

## Supporting Information

### Document citation

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### Data steward(s) disclaimer

All inferences, opinions, and conclusions drawn in this Knowledge Update are those of the authors and do not reflect the opinions or policies of the Data Steward(s), affiliated agencies or funders.

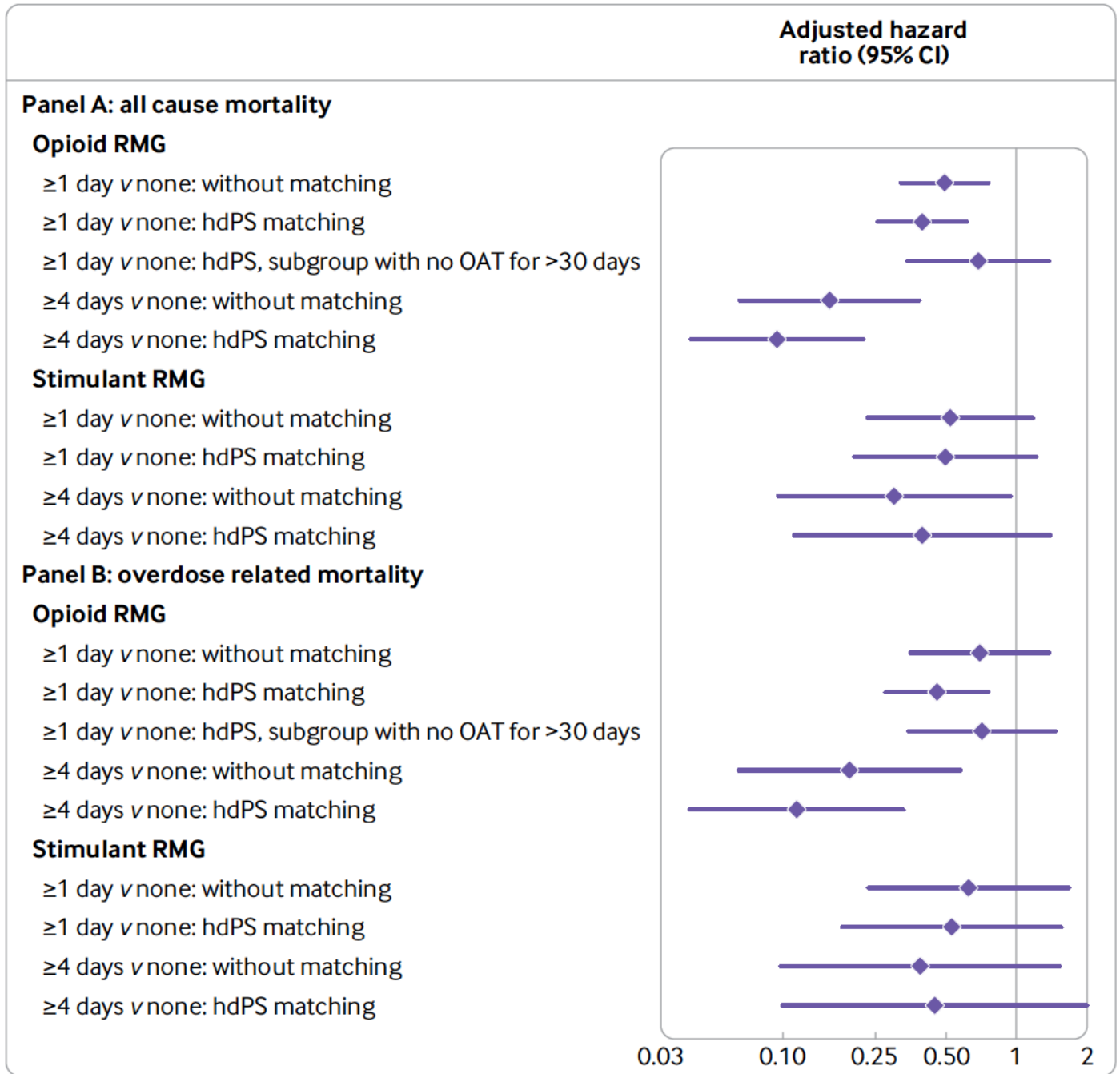
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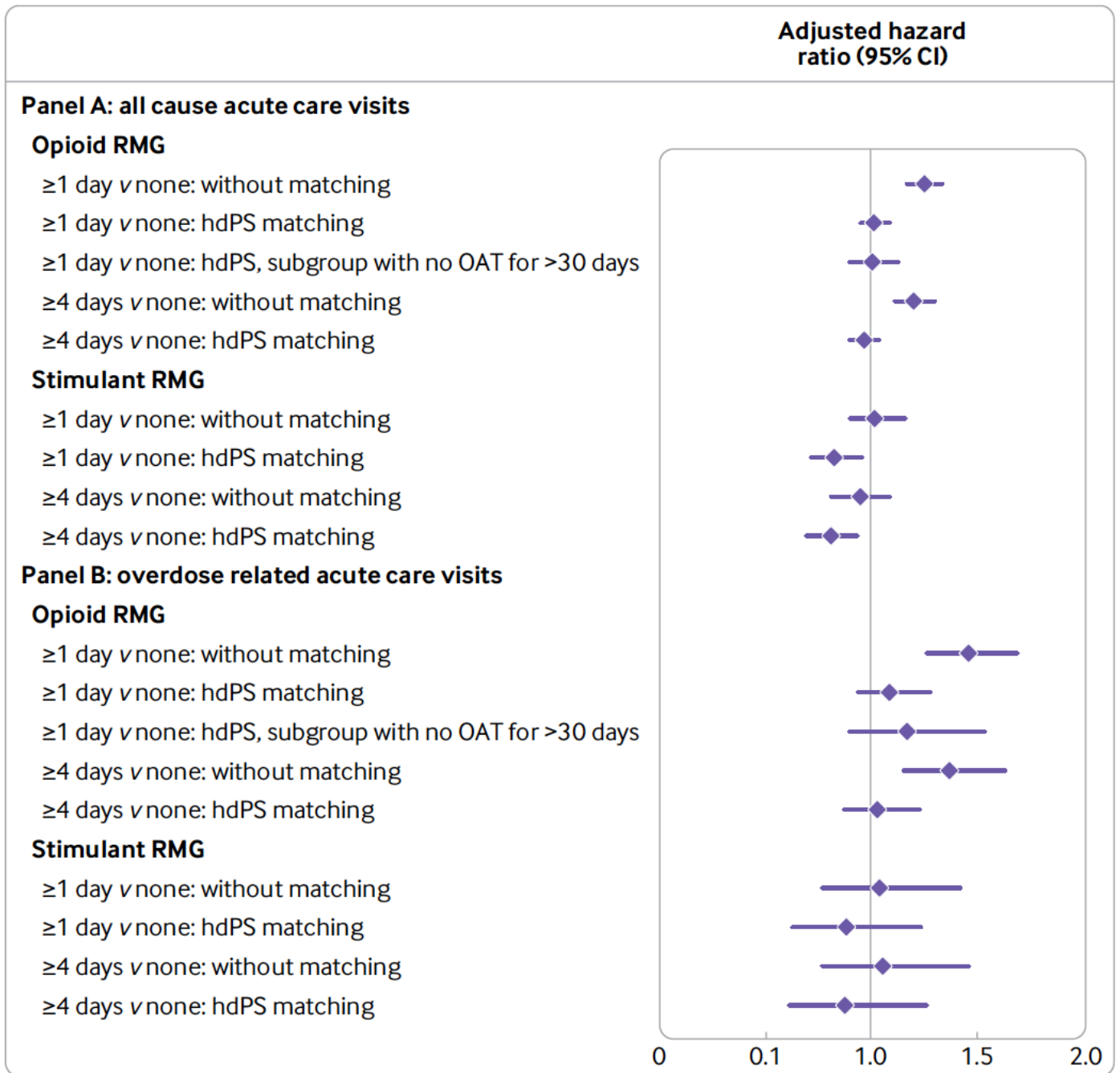
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## Figures

**Figure 1. Results of marginal structural models on primary mortality outcomes. Hazard ratios plotted on log scale. hdPS=high dimension propensity score matching; OAT=opioid agonist treatment; PS=propensity score.**



**Figure 2. Results of marginal structural models on secondary outcomes. hdPS=high dimension propensity score matching; OAT=opioid agonist treatment; PS=propensity score.**



**Figure 3. Results of marginal structural models on mortality outcomes – dose sensitivity analysis. hdPS=high dimension propensity score matching; OAT=opioid agonist treatment; PS=propensity score.**

