

# Co-prescription of opioids and gabapentin substantially increases the risk of accidental opioid overdoses

## Background

- Gabapentin is a drug that is used to treat chronic pain and is often used together with opioids.
- Despite gabapentin being generally perceived as safe, co-prescription of opioids and gabapentin is known to increase the amount of these drugs absorbed by the body and the way in which these drugs affect the central nervous system. This can potentially lead to dangerous risks of overdose when these drugs are used together.



## What were we investigating?

The study examined whether co-prescription of gabapentin and opioids was associated with an increased risk of accidental opioid-related death.

## Study Details

### How was the study conducted?

- We conducted a population-based matched nested case-control study among residents of Ontario between the ages of 15 to 104 who were eligible for public drug coverage and who were dispensed an opioid between April 1, 1997 and December 31, 2013.
- Cases were defined as an opioid user who died of an opioid-related cause. Opioid overdoses that were caused by a suicide or homicide were excluded and we limited our inclusion criteria to patients who received opioids for non-cancer and non-palliative care pain. Eligible cases were matched with up to four controls.
- The primary exposure was concomitant gabapentin use in the 120 days before the index date.
- In a secondary analysis we stratified gabapentin use into low dose (<900mg daily), moderate dose (900 to 1799 mg daily) and high dose ( $\geq 1800$  mg daily). A sensitivity analysis explored the association between very high dose ( $\geq 2500$  mg daily) gabapentin use.
- Conditional logistic regression was used to compare the odds of dying of opioid-related causes among opioid recipients co-prescribed gabapentin relative to those prescribed opioids alone.

## Key Points

- Moderate and high dose gabapentin use was associated with a nearly 60% increase in the odds of accidental opioid-related death relative to opioid use alone.
- This risk is nearly doubled in patients who are co-prescribed opioids and very high dose ( $\geq 2500$  mg daily) gabapentin.
- Combined use of opioids and gabapentin is common. In this study, approximately 8% of patients receiving opioids were co-prescribed gabapentin, and in 2013, nearly half of all gabapentin users were co-prescribed an opioid.

## What did we find?

- During our study period we identified 1,256 cases that were matched to 4,619 controls and included in our analysis.
- Overall, 12.3% of cases (n=155) and 6.8% of controls (n=313) were co-prescribed gabapentin.
- The odds of an opioid-related death was 49% higher among individuals recently exposed to gabapentin and opioids (adjusted OR [aOR] 1.49, 95% CI 1.18 to 1.88) compared to those exposed to opioids alone.
- Exposure to moderate or high doses of gabapentin was associated with a nearly 60% increased odds of opioid-related deaths compared to exposure to opioids alone (aOR 1.56, 95% CI, 1.06 to 2.28 for moderate doses and aOR 1.58, 95% CI 1.09 to 2.27 for high doses).
- In a sensitivity analysis, exposure to very high dose gabapentin was associated with a two-fold increased odds of opioid-related deaths (aOR 1.83, 95% CI 1.04 to 3.22) compared to use of opioids alone.

## Recommendations

### Clinicians

Clinicians should consider carefully whether prescribing this combination of drugs is absolutely necessary. In cases where co-prescription of opioids and gabapentin is needed, clinicians should closely monitor patients and adjust opioid and gabapentin doses accordingly.

### Patients and Caregivers

It is important to be aware of the potential respiratory risks of taking both gabapentin and opioids at the same time. If you are prescribed both of these drugs, speak to your doctor and pharmacist about the risks of combining these products and ways to safely adjust your doses.

## For More Information

Gomes et al. Gabapentin, opioids and the risk of opioid-related death: A population-based nested case-control study. PLoS Medicine, 2017.