Association of opioid analgesics, benzodiazepines, gabapentinoids, and opioid agonist treatment with mortality among individuals with opioid dependence

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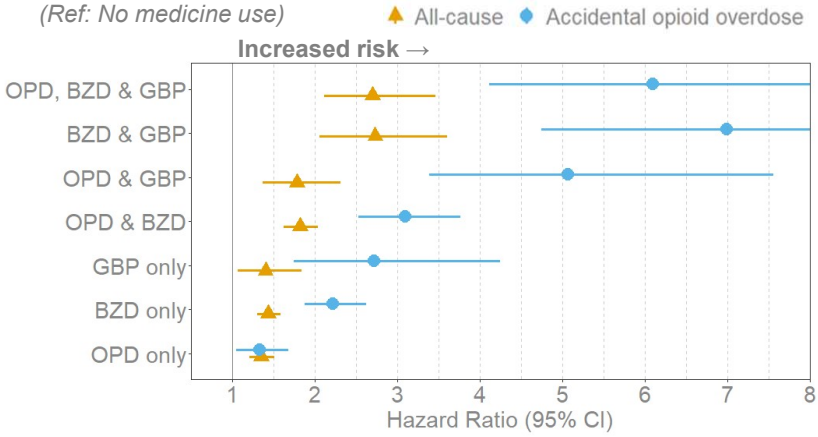
The Difference is Research

Q1: What is the effect of concurrent use of opioid analgesic (OPD), benzodiazepine (BZD) and gabapentinoid (GBP) use on all-cause and cause-specific mortality?

Concurrent use of opioids with benzodiazepines and/or gabapentinoids was associated with a substantial increase in accidental opioid overdose risk; lesser extent for all-cause mortality

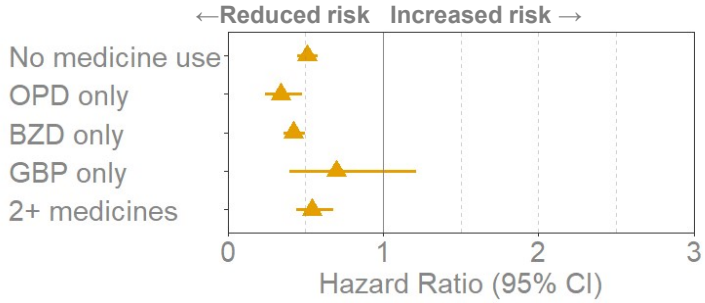
(Ref: No medicine use)



Q2: Do these medicine effects vary depending on whether someone is receiving opioid agonist treatment (OAT)?

For most exposure combinations, all-cause mortality risk was reduced when in versus out of opioid agonist treatment

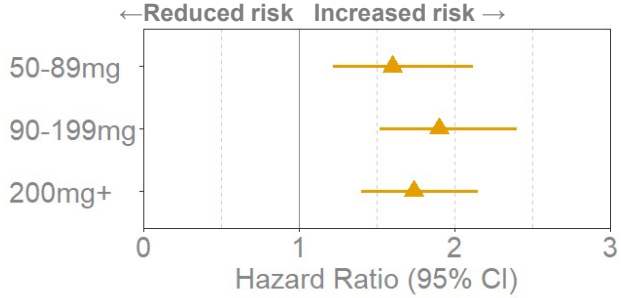
(Ref: Out of OAT for the same medicine exposure)



Q3: Do these medicine effects vary according to the amount of opioid analgesic used?

Higher opioid analgesic doses were associated with increased mortality risk

(Ref: 1-49mg oral morphine equivalent/day)



Background

- People with opioid dependence have high rates of comorbidity and therefore, a high likelihood of polypharmacy.
- They may be prescribed opioids through opioid agonist treatment (OAT) programs for managing their opioid dependence and may also be prescribed opioid analgesics (OPD) for pain management.
- Although the combined use of opioid analgesics with benzodiazepines (BZD) and gabapentinoids (GBP) may add to mortality risk, no study has comprehensively examined this medicine use pattern during periods in and out of OAT.
- Quantifying these effects would provide much needed insights to clinicians assessing the benefit-risk ratio when prescribing these medicines.

Methods

Data come from the POPPY II study [1], a cohort of all adult residents who initiated a new opioid analgesic dispensing episode between July 2003 and Dec 2018 in New South Wales, Australia.

Study cohort included 37,994 people in POPPY II with either (1) an opioid dependence diagnosis during a health service contact or (2) receipt of OAT (+ no prior history of cancer or palliative care).

Outcomes: all-cause mortality and accidental opioid overdose; 12% (n=3,176) died during follow-up, of which 31.1% (n=987) were accidental opioid overdoses.

Exposure to medicines (OPD, BZD, & GBP) defined by applying the IDP method [2] to records of medicine dispensings.

Methods: Cause-specific Cox proportional hazard models adjusted for baseline demographics, time-varying OAT status and clinical comorbidities.

Limitations: Unable to capture non-subsidized medicines, actual medicine use and non-prescribed drugs; potential confounding by indication.

Implications

When co-prescription is necessary, a greater focus on OAT engagement, overdose prevention education, and overdose antidotes is necessary to minimise the unintended consequences.

References: [1] Gisev, N et al. (2018) PMID: 30518593; [2] Bharat, C et al. (2023) PMID: 36345837

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