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

Bharat C[1], Gisev N[1], Barbieri S[2], Dobbins T[3], Larney S[4], Buizen L[1], Degenhardt L[1]

[1] National Drug and Alcohol Research Centre, UNSW Sydney, Sydney, Australia, [2] Centre for Big Data Research in Health, UNSW Sydney, Sydney, Australia, [3] School of Population Health, UNSW Sydney, Sydney, Australia, [4] Université de Montréal and Centre de Recherche du CHUM, Montreal, Canada

Presenter's email: c.bharat@unsw.edu.au

Introduction: Studies investigating mortality risk associated with use of opioid analgesics, benzodiazepines, gabapentinoids, and OAT among people with opioid dependence (PWOD) are lacking. This study addresses this gap using a cohort of 37,994 PWOD initiating opioid analgesics between July 2003 and July 2018 in New South Wales, Australia.

Method: Linked administrative records provided data on dispensings, sociodemographics, clinical characteristics, OAT, and mortality. Cox proportional hazards models assessed associations between time-varying measures of individual and concurrent medicine use and OAT with all-cause mortality, accidental opioid overdose, non-drug induced accidents, and non-drug-induced suicide. Opioid analgesic dose effects, expressed as oral morphine equivalents (OMEs) per day, were also examined.

Results: During the study period, 3,167 individuals died. Compared with no use, all medicines of interest were associated with increased accidental opioid overdose risk; hazard ratios (HR) ranged from 1.33 (95% CI: 1.05-1.68) for opioid analgesic use to 6.10 (95% CI: 4.11-9.06) for opioid analgesic, benzodiazepine and gabapentinoid use. Benzodiazepine use was associated with increased non-drug-induced accidents and non-drug-induced suicides. For all-cause mortality, all combinations of benzodiazepines and gabapentinoids with opioid analgesics were associated with increased risk (aHRs ranged from 1.35-2.73). For most medicines/medicine combinations, all-cause mortality risk was reduced when in OAT compared to out of OAT. Higher opioid analgesic doses were associated with increased all-cause mortality (e.g., 90-199mg vs 1-49mg OME per day: HR 1.90 [95% CI: 1.52-2.40]).

Discussions and Conclusions: Among PWOD, benzodiazepines and gabapentinoids appear to increase mortality risk when used in combination with opioid analgesics, although the risk may be reduced when engaged in OAT.

Implications for Practice or Policy: These findings provide much needed insights for clinicians in assessing the benefit-risk ratio when prescribing these medicines, as well as guiding strategies aimed at reducing mortality and related harms.

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