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The risk of fatal opioid overdose associated with the concurrent use of opioid analgesics and psychotropic medicines: a retrospective population-based cohort study

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Abstract

Background and Aims: Opioids and psychotropic medicines are often concurrently prescribed, despite an increased risk of adverse events, including fatal overdose. This study examined the risk of fatal opioid overdose associated with the concurrent use of opioids and psychotropic medicines.

Design and Methods: A retrospective population-based cohort study (POPPY II) of all adult residents in NSW who initiated prescription opioids between 1st July 2003 and 31st December 2018. Pharmaceutical Benefits Scheme dispensing records were linked to six other datasets to provide information on socio-demographic and clinical characteristics, health service use, and adverse outcomes. Cox proportional hazards models were used to assess the association between time-dependent medicines exposure (opioid use only vs concurrent use with psychotropic medicines) and the risk of fatal opioid overdose.

Results: Of the 2,936,299 individuals in the cohort, there were 1,944 fatal opioid overdoses. Over one-third (36.6%) used an opioid and psychotropic medicine concurrently, most frequently antidepressants (23.3%) and benzodiazepines and Z-drugs (18.3%). Compared to exposure with opioids or psychotropic medicines alone, mortality was highest during periods of concurrent opioid and psychotropic medicine exposure. This was highest among those using benzodiazepines and Z-drugs concurrently (adjusted hazard ratio (aHR) 3.84, 95% confidence interval (CI) 3.29-4.49), and gabapentinoids (aHR 2.91, 95% CI 2.41- 3.52). Risk of fatal overdose increased as the number of concurrent psychotropic medicines used increased: aHR 3.40, 95% CI 2.71-4.26 for 1 psychotropic medicine; aHR 6.12, 95% CI 4.85-7.71 for 2 psychotropic medicines; and aHR 11.63, 95% CI 9.28-14.58 for ≥3 psychotropic medicines.

Conclusions: The risk of fatal opioid overdose is elevated among people using opioids and psychotropic medicines concurrently, and varies by medicine class, and the number of medicines used. Given the frequent use of these medicine combinations in practice, greater efforts are needed to improve the quality use of these medicines to reduce potential overdose risk.