Risk of overdose higher when opioid agonists are prescribed with other medicines

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Patients prescribed medicines to replace illicit drugs are at higher risk of overdose resulting in hospital admission when taking other medicines which treat mental health conditions or pain, University of Manchester

researchers have found.

The authors of the study, published in the journal *Addiction* on August 3, say doctors should avoid co-prescription of opioid agonists, with benzodiazepines, gabapentinoids, antipsychotics or Z-drugs if harm is greater than the benefit to patients.

Opioid agonists, medicines which include methadone or buprenorphine, are used as a substitute for illicit drugs when treating people who are dependent on drugs like heroin.

In the patient records of 20,898 recipients of opioid agonist treatment that were analyzed by the researchers, patients prescribed benzodiazepines, which are commonly used sedatives, were 1.45 times more likely to have a hospital admission for overdose compared to patients who were not prescribed them.

Gabapentinoids, which are used to treat a range of disorders including neuropathic pain, epilepsy and anxiety disorders, prescribed in combination with opioid agonists, were 2.2 times more likely to result in hospital admission for overdose.

Z-drugs, which are also sedatives, were 1.6 times more likely and antipsychotics—used to treat psychosis were 1.85 times more likely to result in overdose.

There was no evidence for increased risk linked with antidepressant co-prescription.

The research team studied primary care patients in England with opioid use disorder aged between 18 and 64 years, 15,155 of whom were prescribed methadone and 5,743 buprenorphine between January 1998 and December 2017.

Opioid use disorder is characterized by cravings for opioids, continued use despite physical or psychological deterioration, increased tolerance, and withdrawal symptoms.

The data was obtained from the Clinical Practice Research Datalink GOLD and Aurum databases and linked to data from the Hospital Episode Statistics and Office for National Statistics.

Scientists already know that methadone, as a full opioid agonist, can trigger overdose at high doses; buprenorphine, a partial opioid agonist, appears safer.

However, both treatments may interact with other medications that are commonly prescribed for patients with opioid use disorder.

Lead author Dr. Eleni Domzaridou, a research associate at The University of Manchester said, "We found an elevated risk of non-fatal overdose among patients who were prescribed opioid agonists together with medication prescribed for other reasons.

"A non-fatal overdose often precedes subsequent drug-poisoning death. Therefore informing clinicians to help them prescribe medication to these patients as safely as possible is paramount.

"Our findings highlight the importance of joint working between GPs and mental health professionals when caring for the complex health needs of patients with opioid use disorder."

Co-investigator Professor Tim Millar added, "This is another part of the jigsaw in our understanding of how we might reduce overdose risk in this complex and marginalized patient population."

More information: Eleni Domzaridou et al, Non-fatal overdose risk

associated with prescribing opioid agonists concurrently with other medication: Cohort study conducted using linked primary care, secondary care and mortality records, *Addiction* (2023).

Provided by University of Manchester