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81. Benzodiazepine co-exposure among patients treated in the emergency department with suspected opioid overdose

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Background: Simultaneous exposure to both benzodiazepines and opioids can lead to synergistic respiratory depression and sedation, increasing the likelihood of overdose. Co-exposure of benzodiazepines with opioids may complicate the effectiveness of antidotal treatment and result in the need for further medical care. Our objective was to report on the detection of prescription and illicit benzodiazepine co-exposures among patients treated in emergency departments with suspected opioid overdoses. We aimed to compare the demographic characteristics, clinical manifestations, treatments, outcomes, and regional differences of patients with opioid overdose who were also exposed to benzodiazepines, versus those without benzodiazepine co-exposure.

Methods: The Toxicology Investigators Consortium (ToxIC) Fentalog Study is an ongoing, cohort study of patients presenting to 10 emergency departments across the US with suspected opioid overdose. Discarded blood/serum were analyzed using liquid chromatography quadrupole time-of-flight mass spectrometry for over 1,100 drugs of abuse, novel psychoactive substances, and pharmaceutical drugs. As of 18 April 2023, 1,264 cases met inclusion, and 735 cases had complete data including analytes. The analytic sample was restricted to only cases with opioids present (n . 670). A central IRB approved this study. All analyses were conducted in R v4.2.1.

Results: Among the cases with opioids present, 33.4% of cases tested positive for benzodiazepines. 28% of cases tested positively for prescription benzodiazepines, and 9% of cases tested positively for illicit benzodiazepines. The most commonly detected prescription benzodiazepine was alprazolam (42.2% of prescription benzodiazepines); the most common illicit benzodiazepine was clonazolam (72.9% of illicit benzodiazepines). One third of patients had either an illicit or prescription benzodiazepine present alongside at least one opioid. Fentanyl was the most frequently detected opioid in patients with opioid and benzodiazepine co-exposure (74.1%), followed by methadone (29.5%). No statistically significant differences were found for age, sex, and race/ethnicity between the benzodiazepine group and the no benzodiazepine group. A higher percentage of benzodiazepines were found alongside opioids in the Northeast (68.8%) compared to opioids alone (59.9%) (2 . 9.61, df . 2, P . 0.01). While a higher percentage of patients with only opioids received naloxone (80.7%) compared to patients with both opioids and benzodiazepines (71.7%, P . 0.01), there was no statistically significant difference between

the total naloxone dosage in mg between the two groups. The benzodiazepine group had double the prevalence of intubation (10.3%) compared to the opioid only group (4.9%) (2 . 5.95, df . 1, P . 0.01). No patient received flumazenil. There were no statistically significant differences in other clinical outcomes between those with benzodiazepines present and those without (e.g., cardiovascular events, neurological events, medical outcome, and length of stay).

Conclusion: We identified a high rate of benzodiazepine and opioid co-exposure, suggesting concomitant use or addition to the opioid supply. A higher percentage of benzodiazepines were found alongside opioids in the Northeast. Patients in the benzodiazepine/opioid group had significantly higher rates of intubation, suggesting greater severity of overdose.