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## **8. Clinical and demographic correlates of confirmed xylazine and levamisole exposure among ED patients with acute fentanyl overdose**

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**Background:** Previous research on opioid overdose (OD) patients in the emergency department (ED) with xylazine suggests decreased severity of some cardiovascular and CNS-related clinical outcomes. We examined predictors of xylazine positivity detected by liquid chromatography quadrupole time-of-flight mass spectroscopy (LC-QTOF-MS) among ED opioid overdose patients.

**Methods:** The Toxicology Investigators Consortium (ToxIC) Fentalog Study is a multicenter, prospective cohort study enrolled adult (> 18) patients with suspected opioid OD who presented to one of ten participating EDs in the US between September 2020 and December 2022. Waste serum from each patient was analyzed via LC-QTOF-MS to detect all current opioids, fentanyl analogues, and adulterants. Medical record data was abstracted, de-identified, and entered into a REDCap database. The study was approved by a central IRB with waiver of informed consent. Chi-square analysis and t-tests were performed using SAS.

**Results:** Out of 755 patients who had blood analytes confirmed at the time of data extraction, xylazine was detected in 152 (20.2%). Xylazine positive patients were primarily localized in the Northeast/Mid-Atlantic regions (73.7%), male (76.8%), white (46.7%), and non-Hispanic (81.6%). Bivariate analysis revealed a significant relationship between xylazine positivity and region of the US (73.7% of cases in Northeast/MidAtlantic vs. 26.3% of cases in Midwest/West Coast, P. 0.0031). Additionally, males had a significantly higher prevalence of xylazine (76.8%) compared to females (23.2%) (P. 0.0225). Midwest/West regions (OR 0.589, 95% CI 0.389–0.892) and female sex (OR 0.635, 95% CI 0.414–0.975) were associated with significantly lower odds of xylazine positivity, after adjusting for age, race, and ethnicity. Goodness of fit testing revealed a chi-square value of 4.35 (P.0.8240) and AUC of 0.6078.

**Conclusion:** In this prospective, multi-center cohort study, patients from non-Northeast regions of the United States had lower odds of xylazine positivity, which is consistent with current surveillance reports. Female patients also had lower odds of xylazine positivity. Future studies should investigate potential explanations for gender differences in xylazine positivity including substance use patterns, xylazine physiologic effects, and xylazine metabolism.