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### 13. “Tranq dope” opioid overdose: clinical outcomes for emergency department patients with illicit opioid overdose adulterated with xylazine

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**Background:** Illicit opioids, now consisting primarily of fentanyl and a variety of adulterants, are the primary cause of drug overdose (OD) fatality in the US. Xylazine, or "Tranq," is an alpha-2 agonist used as a veterinary tranquilizer that is being increasingly detected among decedents after an OD of illicit opioids; however, clinical outcomes in non-fatal OD involving xylazine are unclear. We compared clinical outcomes for emergency department (ED) patients with illicit opioid OD who were positive for xylazine to those who were negative for xylazine.

**Methods:** This multicenter, prospective cohort study enrolled adult (>18) patients with suspected opioid OD who presented to one of nine participating EDs in the US over 1 year. Waste serum from each patient was analyzed via liquid chromatography quadrupole time-of-flight mass spectroscopy (LC-MS) to detect all current illicit opioids, fentanyl analogues, adulterants, and xylazine. Patients without available waste serum or without illicit opioids detected were excluded. Medical record data were abstracted and entered into a REDCap database for analysis. The OD severity outcomes of interest were: (a) cardiac arrest requiring CPR (primary); and (b) coma within 4 h of arrival (secondary). Univariate analysis and multivariable logistic regression were performed using Stata v17. Central IRB approval was granted with waiver of consent.

**Results:** Out of 1166 patients screened, 845 were excluded, leaving 321 patients for analysis (90 xylazine, 231 non-xylazine), who were 69.5% male and median age 39. The primary outcome occurred in 37 patients, and the secondary outcome occurred in 111 patients. Most patients received at least one dose of naloxone (77.8% xylazine, 84.4% non-xylazine). CNS-related clinical outcomes were more common in both groups compared to cardiovascular-related clinical outcomes. Univariate analyses comparing clinical outcomes for xylazine and non-xylazine patients are summarized in. After controlling for multiple confounders (age, sex, race, prior psychiatric history, initial ED blood pressure, naloxone received), patients with xylazine had a significantly lower odds of cardiac arrest (OR 0.30, 95% CI 0.10–0.92) and coma (OR 0.52, 95% CI 0.29–0.94).

**Conclusions:** In this large multicenter cohort study, clinical outcomes for ED patients with illicit opioid OD were significantly less severe in those testing positive for xylazine. Because quantitative serum

concentrations were not evaluated in this study, future studies should focus on the relationship between relative xylazine and illicit opioid serum concentrations.