Objective: In 2017, psychostimulant deaths involving cocaine and methamphetamine both increased by more than 30% from the years prior. Opioid co-exposure with psychostimulants is a major driver of this increase in overdose deaths. Furthermore, the prevalence of fentanyl analog (fentalog) positivity among urine drug test results positive for cocaine or methamphetamine in non-fatal exposures is becoming increasingly more common. Characterization of clinical outcomes in patients with exposure to fentanyl/fentalogs and psychostimulants is critical but few studies have examined outcomes in this patient population. This study aims to investigate outcomes in patients with exposure to fentanyl and psychostimulants and compare outcomes in patients with fentanyl/psychostimulants to those with fentanyl/fentalogs only.

Methods: This was a secondary analysis of a prospective consecutive cohort of emergency department (ED) patients with opioid overdose presenting to 9 participating sites within the ToxIC network from 6 October 2020 to 17 August 2021. ED patients age 18+ with presumed opioid overdose and available waste blood specimens for analysis were enrolled. Exclusion criteria included age < 18 years, non-toxicological diagnosis, prisoners and trauma/burn patients. Waste blood specimens from enrolled patients were sent to the Center for Forensic Science Research and Education and liquid chromatography quadrupole time-of-flight mass spectrometry were paired with clinical data for analysis. The primary study outcome was total naloxone bolus dose administered. Secondary outcomes included endotracheal intubation, cardiac arrest and troponin elevation within 4 hours of ED arrival and presenting vital signs. We performed t-test and chi-squared analyses to compare demographics and outcomes between groups.

Results: Of 378 patients enrolled, 207 (51.8%) were found to have both psychostimulants and fentanyl present on assay. Patients in the fentanyl only group were significantly older than the fentanyl/stimulant group (mean 45.2 years versus 40.6 years, p < 0.01). Patients in both groups were predominantly male. Patients in the fentanyl/stimulant group had significantly higher total naloxone dose requirements (mean total dose 3.56 mg versus 2.85 mg, p = 0.01). There was no significant difference in presenting vital signs or rates of intubation, cardiac arrest, and troponin elevation.

Conclusion: We identified a high rate of co-exposure to psychostimulants and fentanyl. Patients in the fentanyl/stimulant group had significantly higher naloxone dose requirements, suggesting potential greater severity of overdose. Fentanyl/stimulant patients and fentanyl only patients had similar rates of endotracheal intubation, cardiac arrest, and myocardial injury. Further, powered studies are needed to fully evaluate the impact of psychostimulant co-exposure on outcomes in fentanyl/fentalog overdose.