Background: Novel psychoactive substances (NPS) use trends continue to evolve yearly and regionally.

Research Question: What are the temporal trends and regional characteristics of NPS among suspected opioid overdose patients presenting to the emergency department?

Methods: The Toxicology Investigators Consortium Fentalog Study is a prospective multicenter cohort of suspected opioid overdoses among eight medical centers across the U.S. Blood from these patients underwent qualitative toxicological analyses using liquid chromatography quadrupole time-of-flight mass spectrometry for the presence of over 900 psychoactive substances. NPS yearly trends and regional patterns were compared using Chi-square tests and Fisher’s exact tests.

Results: Among the total cases (n=537), 170 cases (31.7%) tested positive for ≥ 1 NPS. NPS opioids increased >500% from 4.8% of all opioids in 2020 to 25.5% of all opioids in 2021. In 2022, NPS opioids comprised 20.5% of all opioids. These differences in NPS opioids by year were significant (p<0.001). The highest percentage of NPS opioids among all opioids was in the Midwest (28.7%), followed by the Northeast (18.0%) and West (15.3%) (p=0.01). NPS benzodiazepines comprised 1/3 of all benzodiazepines in 2020 (32.3%) and 2021 (35.2%) before decreasing to 16.0% in 2022 (p=NS). The West had the highest percentage of NPS benzodiazepines (18.6%) among all benzodiazepines (p=0.04). The majority (93.3%) of NPS cannabinoids (n=15) were found in the Northeast (p=0.02).

Conclusion: In this large multicenter cohort with NPS serum confirmation, NPS opioids have surged dramatically over the past 2 years. NPS opioids were highest in the Midwest, NPS benzodiazepines were highest in the West, and NPS cannabinoids were highest in the Northeast.