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**Background**: Opioids contribute a major proportion of all agents in the Toxicology Investigators Consortium case registry. In 2015, opioids accounted for nearly 9% of all agent fields; however, the relative contribution of both the overall opioid class and individual agents has varied over time. The relative class contribution, which includes all natural, semisynthetic, and synthetically derived opioid agonists/antagonists, appears to have declined.

**Research Question**: What changes in toxic events involving individual opioids have occurred over the initial 6 years of reporting to the ToxIC Registry?

**Methods**: This descriptive analysis included all ToxIC Registry cases reported from January 1, 2010 through December 15, 2015. Analysis based cases with at least one agent (N = 37,558, 87.1% cases). Summary statistics included testing of the difference of proportion statistics (prtest) and modeled proportions for trend (ptrend) using Bcase/total cases^ metric (STATA/SE, Statacorp LP).

**Results**: An average of 915 cases involved exposure to >1 opioid annually over the 6 years (range 541–1137), representing 12.5% to 21.1% (5- year average 14.6%). Linear tests for trend showed a consistent down- ward absolute value (4.2% AAPC). A positive versus negative trend was observed for single (+3.3% AAPC, 3.848 chi-squared p = 0.05) versus multiple agent poisonings (-3.2% AAPC, 15.95 p < 0.0001).

Heroin, methadone, oxycodone and tramadol were common in all years (four of top five opioids in single and multiple). Relative rank differences appeared including for heroin 31.6% single (rank #1) and 14.6% of multiple (rank #3) poisonings. Agent-specific trends varied in direction, magnitude, and significance. In single-agent events, positive trends were observed for buprenorphine, morphine, heroin, and opioid-unspecified, while negative trends appeared for methadone and fentanyl. Multiple agent poisonings had significant increases (p < 0.0001) for heroin, hydrocodone, and oxycodone.

**Discussion**: During this period, cases involving >1 opioid demonstrated variation in their relative contribution to the ToxIC registry by specific drug and single/multiple exposure. It is important to parse out the relative influence of polydrug exposures, as well as other factors that influence reporting over time.

**Conclusion**: As the Registry continues to increase in size and accumulated years, the ability to identify stable estimates of trend will continue to improve.