CRL Testing Experience for Fentanyl in Oral Fluid

Michael Clark, Melissa Beals, Martin Jacques, Rebecca Henkhaus, David Kuntz; CRL, Lenexa, KS.

INTRODUCTION

The evolution of fentanyl from effective analgesic to national abuse crisis has been a well-documented tragedy over the last decade. Fentanyl is used in pure form, combination drug cocktails, counterfeit prescription pills, and in drugs covertly spiked to increase potency. With strength 100-fold greater than morphine and 50-fold more powerful than heroin, fentanyl has contributed to well over 200,000 overdose deaths in the United States since 2021.

CRL began testing for fentanyl and its metabolite norfentanyl in oral fluid in 2018. As opioid abuse has grown to epidemic proportions, employers have added fentanyl to routine drug testing panels for increased workplace safety.

OBJECTIVE

Evaluate the CRL workplace drug testing experience for fentanyl in oral fluid specimens, from screening to confirmation, including reasons for test and polydrug positive results.

METHODS

A retrospective analysis was performed on reported results and demographic data for oral fluid workplace drug testing samples analyzed at CRL from January 2022 to 2024. Sample collection was performed using OraSure Intercept devices, which provide a 1.2mL total specimen volume through the combination of 400µL of oral fluid collected onto the device pad and 800µL of buffer in the device tube. Because of this combined specimen/buffer composite, oral fluid confirmation results are reported as diluted values and results require multiplication by 3 to attain neat values.

Oral fluid specimens requiring fentanyl testing are prepared for screening by dilution with aqueous mobile phase, while the confirmation assay requires a liquid-liquid extraction preparation. Samples are screened and confirmed by separate LC-MS/MS analytical methods using Shimadzu Nexera UHPLC systems and API6500+ Mass Spectrometers.

RESULTS & DISCUSSION

Using a 1.0 ng/mL fentanyl cutoff concentration for both screening and confirmation, 97.9% of samples screening positive were confirmed.

Figure A: Fentanyl and Norfentanyl Confirmation Status

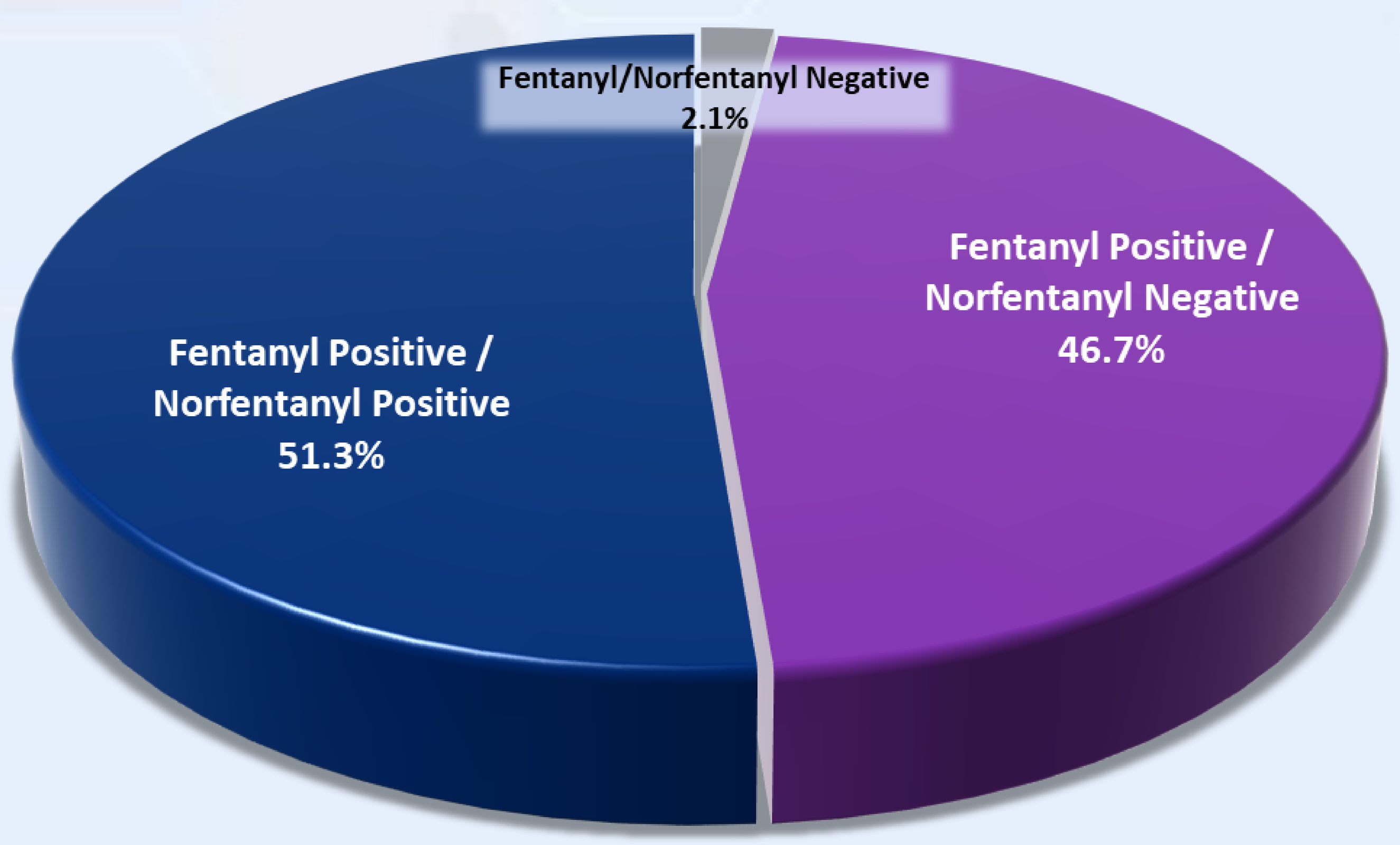
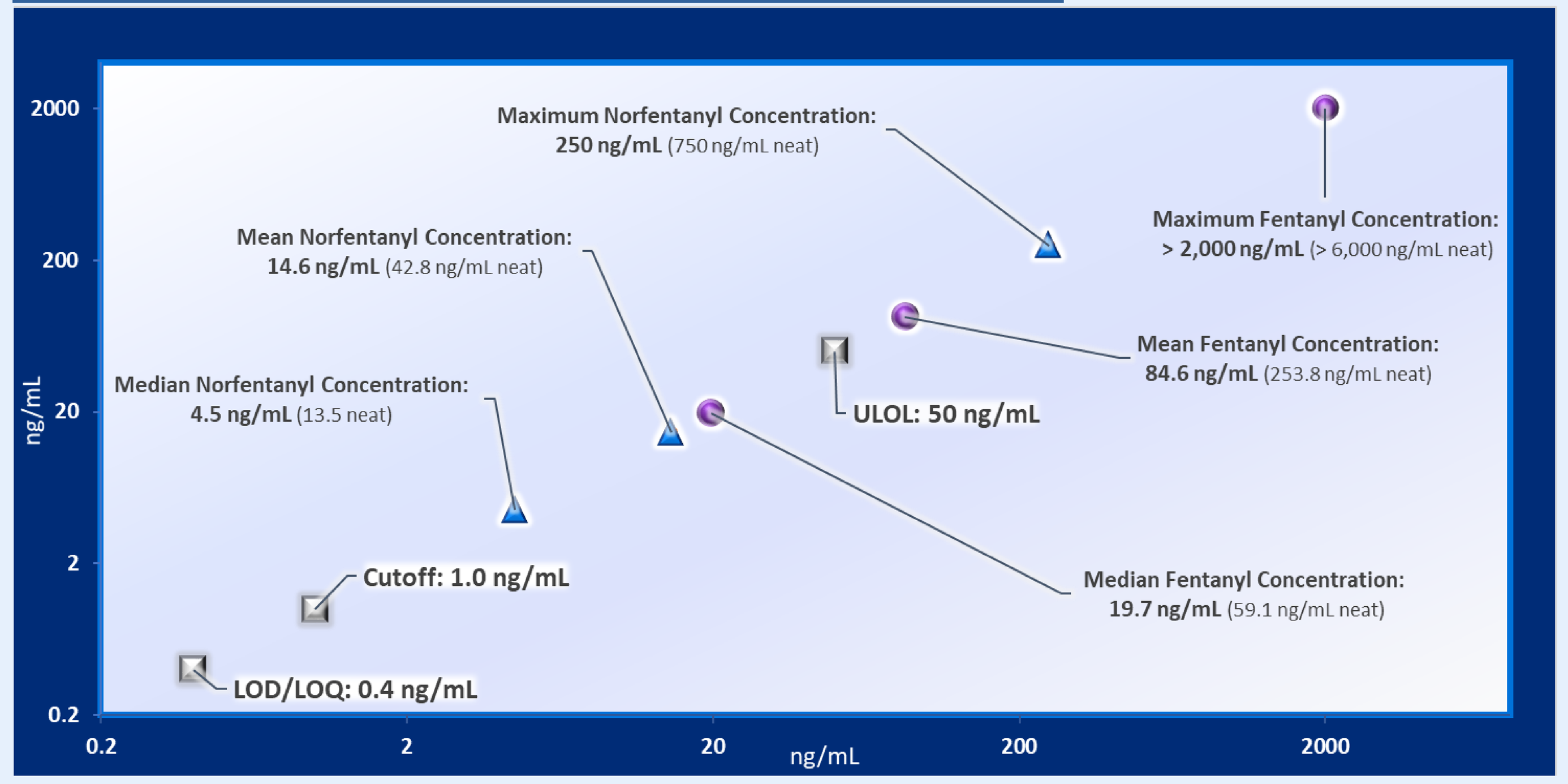
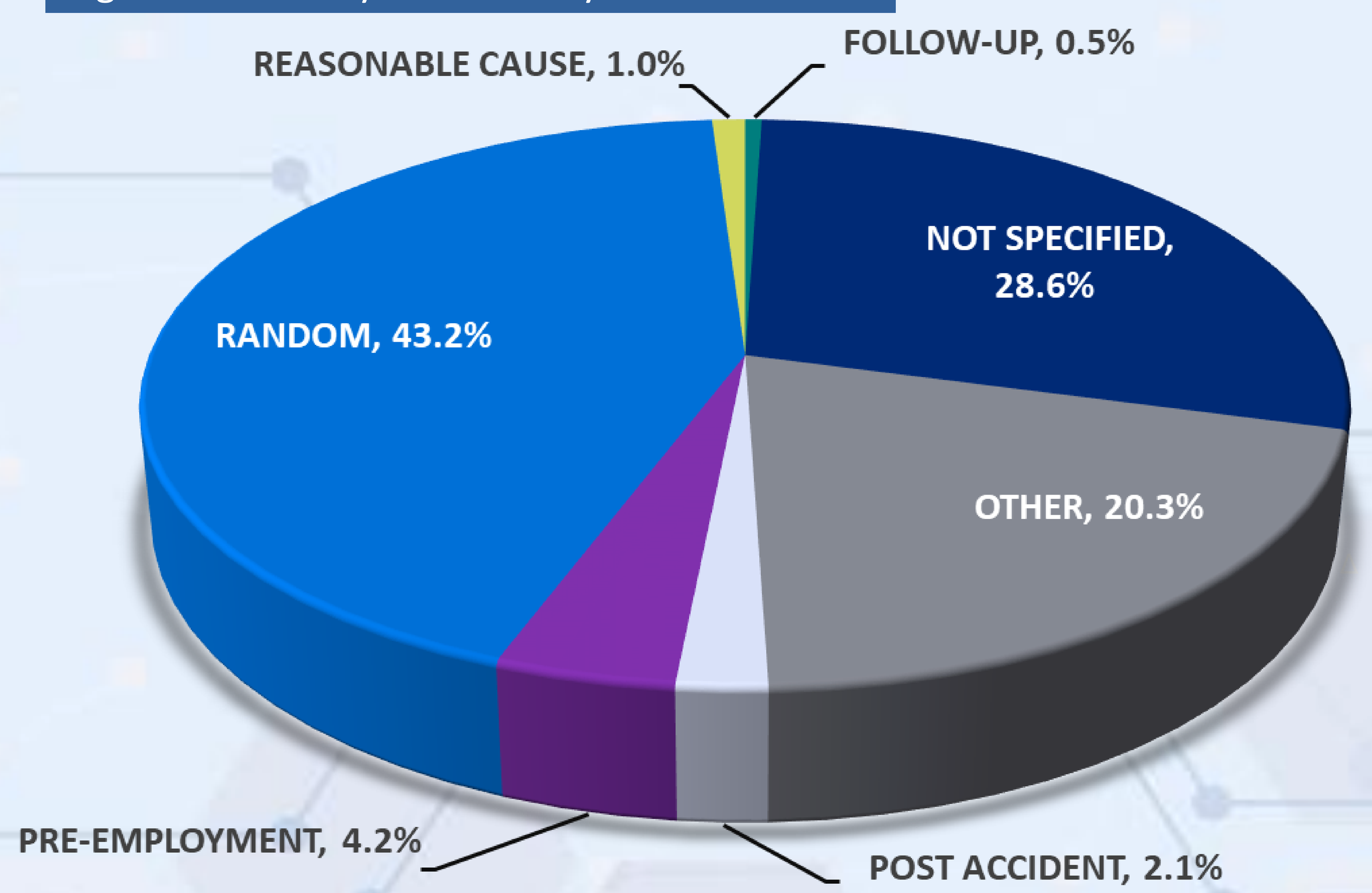


Figure B: Fentanyl and Norfentanyl Confirmation Values



Using a 1.0 ng/mL fentanyl cutoff concentration for both screening and confirmation, 97.9% of samples screening positive were confirmed. Median positive fentanyl and norfentanyl concentrations were 19.7 ng/mL and 4.5 ng/mL, or 59.1 and 13.5 ng/mL as neat values. Mean positive fentanyl and norfentanyl levels were 84.6 and 14.6 ng/mL, or 253.8 and 42.8 ng/mL neat. Maximum fentanyl concentrations was over 2,000 ng/mL, or 6,000 ng/mL neat; maximum norfentanyl concentration was 250 ng/mL, or 750 ng/mL neat value.

Figure C: Fentanyl Positives By Reason for Test



Categorized by reason for test indicated on sample requisitions, 43.2% of oral fluid fentanyl positives were a result of workplace “Random” tests. While pre-employment drug screens account for more than 50% of testing, this category attributed to a mere 4.2% of fentanyl positives.

More than 70% of oral fluid fentanyl positives also confirmed positive for at least one other drug. Methadone was most prevalent in these polydrug combinations, appearing in 29.2% of positive fentanyl samples. Stimulants such as methamphetamine and cocaine were also frequently found in fentanyl positives; fentanyl and methamphetamine/amphetamine combinations made up 26.7% of the concurrent positives, while fentanyl and cocaine combinations occurred in 24.4% of concurrent positives.

Figure D: Most Common Concurrent Drugs in Oral Fluid Fentanyl Positive Samples

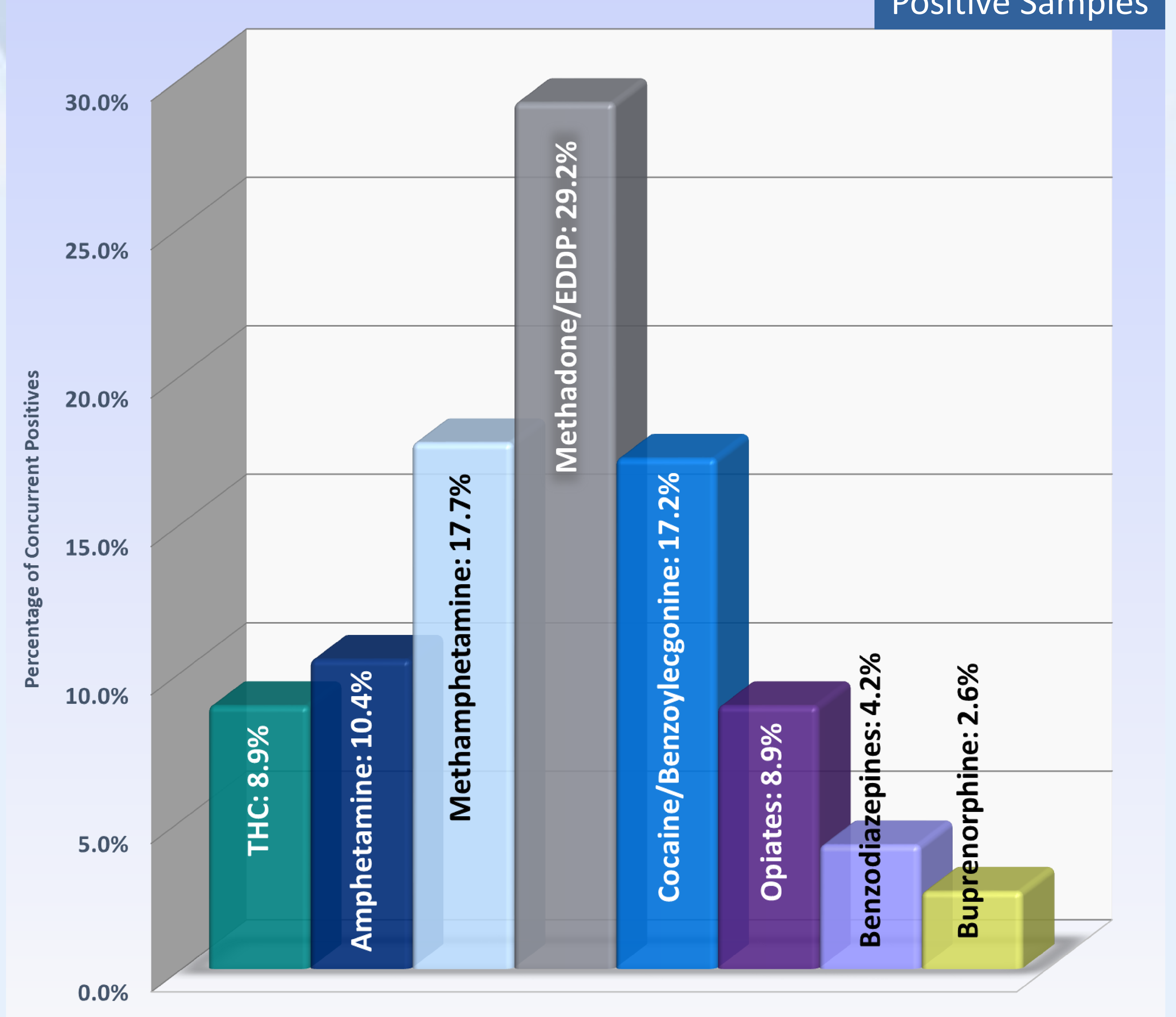


Figure E: Oral-Fluid Fentanyl Polydrug Positives

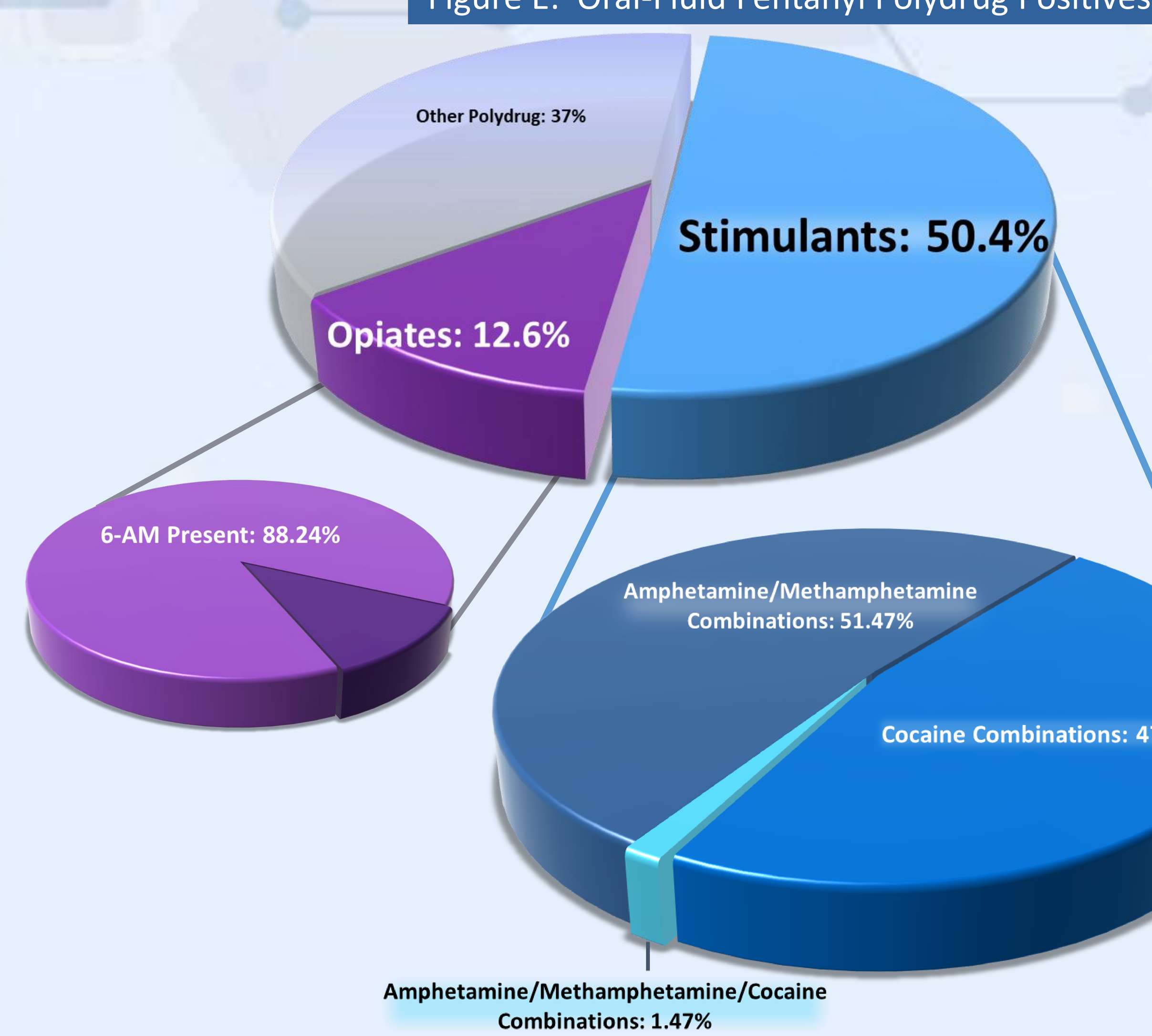
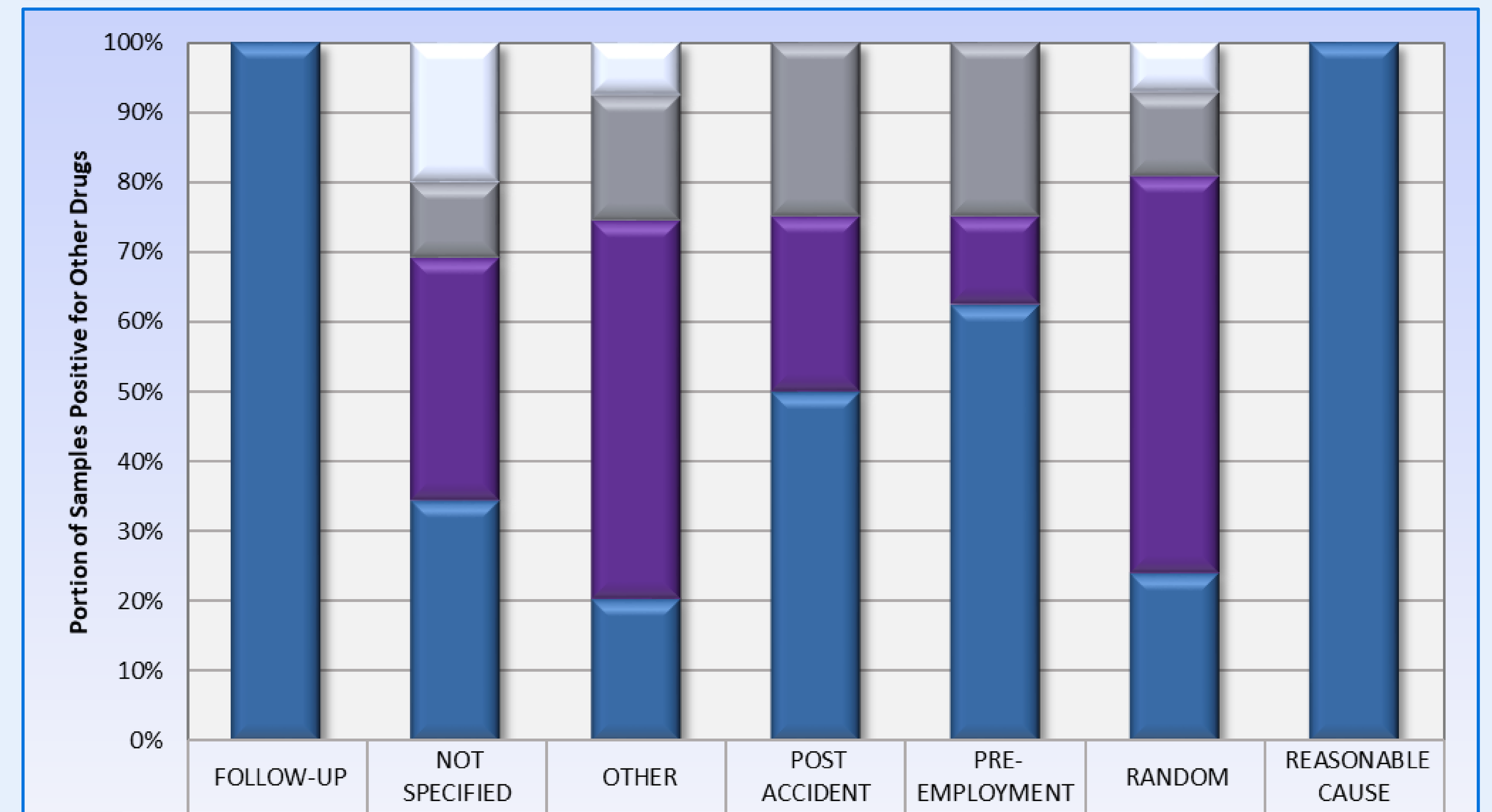


Figure F: Polydrug Fentanyl Positives by Reason for Test



	FOLLOW-UP	NOT SPECIFIED	OTHER	POST ACCIDENT	PRE-EMPLOYMENT	RANDOM	REASONABLE CAUSE
3+	0%	20.0%	7.7%	0.0%	0.0%	7.2%	0%
2	0%	10.9%	17.9%	25.0%	25.0%	12.0%	0%
1	0%	34.5%	53.8%	25.0%	12.5%	56.6%	0%
0	100%	34.5%	20.5%	50.0%	62.5%	24.1%	100.0%

A common misconception is that fentanyl and norfentanyl are unable to be detected in oral fluid, but the testing experience at CRL proves quite the opposite. Specimens from professional monitoring programs, rehabilitation, and probation parole groups were eliminated from the data pool; though requests for fentanyl in oral fluid workplace drug testing were relatively low, the positivity rate was 3-5%. The number of polydrug positives including fentanyl was unsurprising, with cases of stimulant-fentanyl combinations in sync with current trends in overdoses; it was unexpected, however, that among fentanyl polydrug positives, fewer than 15% included opiates. The prevalence of fentanyl in random drug tests suggests high potential for workplace impairment, as detection period of fentanyl in oral fluid is 24-48 hours depending on dosage and frequency of use.

CONCLUSION

Employers must be vigilant regarding the pervasiveness of fentanyl in the workplace, and oral fluid testing allows for non-invasive collection with a detection period relevant to present-time impairment. Analysis of oral fluid samples for fentanyl at CRL offers employers an important tool to help maintain a safe work environment.

REFERENCES

U.S. Department of Justice, Drug Enforcement Administration. Drug Enforcement Administration National Drug Threat Assessment 2024. Feb/May 2024. DEA-DCT-DIR-010-24. https://www.dea.gov/sites/default/files/2024-07/2024%20NDTA-updated%207.5.2024.pdf
Spencer M.R., Miniño A.M., Warner M. Drug overdose deaths in the United States, 2001–2021. NCHS Data Brief, no 457. Hyattsville, MD: National Center for Health Statistics. 2022. DOI: https://dx.doi.org/ 10.15620/cdc:122556.
Spencer M.R, Warner M., Cisewski J.A., Miniño A., Dodds D., Perera J., Ahmad F.B. Estimates of drug overdose deaths involving fentanyl, methamphetamine, cocaine, heroin, and oxycodone: United States, 2021. Vital Statistics Rapid Release; no 27. Hyattsville, MD: National Center for Health Statistics. May 2023. DOI: https://dx.doi.org/ 10.15620/cdc:125504.
QuickStats: Age-Adjusted Drug Overdose Death Rates, by State — United States, 2022. MMWR Morb Mortal Wkly Rep 2024; 73:708. DOI: http://dx.doi.org/10.15585/mmwr.mm7332a4
National Center for Health Statistics. CDC WONDER. Provisional mortality data. 2022.
Ahmad FB, Cisewski JA, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2023. Available at https://www.cdc.gov/nchs/nvss/ vsrr/drug-overdose-data.htm
Friedman, J., Bourgois, P., Godvin, M., Chavez, A., Pacheco, L., Segovia, L.A., Beletsky, L., Arredondo, J. The introduction of fentanyl on the US–Mexico border: An ethnographic account triangulated with drug checking data from Tijuana. International Journal of Drug Policy, Volume 104, 2022, 103678, ISSN 0955-3959, https://doi.org/10.1016/j.drugpo.2022.103678.
Shover, C.L., Falasinnu, T.O., Dwyer, C.L., Benitez Santos, N., Cunningham, N.J., Freedman, R.B., Vest, N.A., Humphreys,K. Steep increases in fentanyl-related mortality west of the Mississippi River: Recent evidence from county and state surveillance. Drug and Alcohol Dependence, Vol 216, 2020, 108314, ISSN 0376-8716, https://doi.org/10.1016/j.drugalcdep.2020.108314.
Shover, C.L., Friedman, J.R., Ruby Romero, R., Jimenez, S., Beltran, J., Garcia, C., Goodman-Meza, D. Leveraging pooled medical examiner records to surveil complex and emerging patterns of polysubstance use in the United States. International Journal of Drug Policy, 2024, 104397, ISSN 0955-3959, https://doi.org/10.1016/j.drugpo.2024.104397
Huhn, A.S., Hobelmann, J.G., Oyler, G.A., Strain, E.C. Protracted renal clearance of fentanyl in persons with opioid use disorder. Drug and alcohol dependence, Vol 214, September 2020, 108147. https://doi.org/10.1016/j.drugalcdep.2020.108147
Kiefer, M.K., Cowen, J., Hinely, K.A., Rood, K.M. Prolonged detection of urine norfentanyl in individuals enrolled in a medication for opioid use disorder in pregnancy and postpartum program: a case series. AJOG Global Reports, Vol 4, Issue 2, 2024, 100313, ISSN 2666-5778, https://doi.org/10.1016/j.xagr.2024.100313.
Uljon, S. Chapter One - Advances in fentanyl testing, Ed(s): Makowski, G.S. Advances in Clinical Chemistry, Elsevier, Vol 116, 2023, Pages 1-30, ISSN 0065-2423, ISBN 9780443192920, https://doi.org/10.1016/bs.acc.2023.05.004.
Stanley, T.H. The History and Development of the Fentanyl Series. Journal of Pain and Symptom Management Vol 7 No. 3 (Suppl.) April 1992, Pages S3-S7, ISSN 0885-3924, https://doi.org/10.1016/0885-3924 (92)90047-L.
Fentanyl and analogues. LverTox. 16 Oct 2017. Archived from original 7 Jan 2017. Ret 14 Dec 2017 https://web.archive.org/web/20170107002718/https://livertox.nlm.nih.gov/FentanylAndAnalogues.htm
Overdose deaths from fentanyl laced stimulants have risen 50-fold since 2010. https://www.uclahealth.org/news/overdose-deaths-fentanyl-laced-stimulants-have-risen-50-fold
Friedman J., Shover C.L. Charting the fourth wave: Geographic, temporal, race/ethnicity and demographic trends in polysubstance fentanyl overdose deaths in the United States, 2010–2021. Addiction. 2023; 118(12): 2477–2485. https://doi.org/10.1111/add.16318
Substance Abuse and Mental Health Services Administration. SAMHSA Overdose Prevention and Response Toolkit. Publication No. PEP23-03-00-001. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2023. https://store.samhsa.gov/sites/default/files/overdose-prevention-response-kit-pep23-03-00-001.pdf
Maucione, S., WYPR, KFF Health News. Fentanyl mixed with cocaine or meth is driving the '4th wave' of the overdose crisis. (2023). https://www.npr.org/sections/health-shots/2023/09/14/1199396794/fentanyl-mixed-with-cocaine-or-meth-is-driving-the-4th-wave-of-the-overdose-cris
Arditi, L. Stimulant users caught up in fatal 'fourth wave' of opioid epidemic. (2024). https://www.npr.org/sections/shots-health-news/2024/07/09/nx-s1-5015243/stimulant-users-meth-cocaine-coke-in-overdose-fourth-wave-opioid-epidemic
Payer, D.E., Young, M.M., Maloney-Hall, B., Mill, C., Leclerc, P., Buxton, J., the Canadian Community Epidemiology Network on Drug Use, & the National Drug Checking Working Group. (2020). Adulterants, contaminants and co-occurring substances in drugs on the illegal market in Canada: An analysis of data from drug seizures, drug checking and urine toxicology. Ottawa, Ont.: Canadian Centre on Substance Use and Addiction. https://www.ccsa.ca/sites/default/files/2020-04/CCSA-CCENDU-Adulterants-Contaminants-Co-occurring-Substances-in-Drugs-Canada-Report-2020-en.pdf
Spencer M.R., Miniño A.M., Garnett M.F. Co-involvement of opioids in drug overdose deaths involving cocaine and psychostimulants, 2011–2021. NCHS Data Brief, no 474. Hyattsville, MD: National Center for Health Statistics. 2023. DOI: https://dx.doi.org/10.15620/cdc:129733 https://www.cdc.gov/nchs/products/databriefs/db474.htm
Bazazi, A.R., Low, P., Gomez, B.O. et al. Overdose from Unintentional Fentanyl Use when Intending to Use a Non-opioid Substance: An Analysis of Medically Attended Opioid Overdose Events. J Urban Health, Vol 101, 245–251 (2024). https://doi.org/10.1007/s11524-024-00852-0
American Medical Association. AMA Overdose Epidemic Report 2023. https://www.ama-assn.org/system/files/ama-overdose-epidemic-report.pdf
Ciccarone D. The rise of illicit fentanyls, stimulants and the fourth wave of the opioid overdose crisis. Current opinion in psychiatry, Vol 34(4), 2021, 344–350. https://doi.org/10.1097/YCO.0000000000000717

DISCLOSURE

No relevant financial or nonfinancial relationships to disclose.