

EXHIBIT A

Case Control study of mitragynine induced fatalities vs all cause deaths with mitragynine found on autopsy



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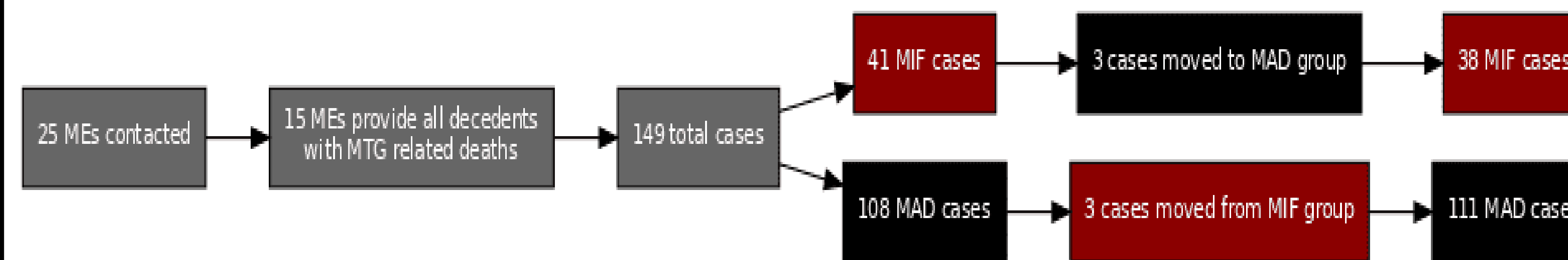
Background

- **Mitragynine (MTG)** is the primary active compound in kratom, a widely available but unregulated herbal supplement in the U.S.
- MTG is described to **have stimulant effects at low doses with opioid-like effects at higher concentrations**
- MTG was labeled as a Schedule I drug by the DEA in 2016. After significant backlash, this decision was revoked in October 2016.
- Advocates site analgesia, mood enhancement, and **role as an aid in quitting illicit narcotics**. However, therapeutic effects largely anecdotal with few clinical trials
- MTG increasingly implicated in overdose deaths, yet limited data exist on specific risk factors
- **All cause overdose mortalities are frequently found to have MTG on autopsy**, calling into question MTG's efficacy in quitting or as an alternative to other illegal substances

Objective

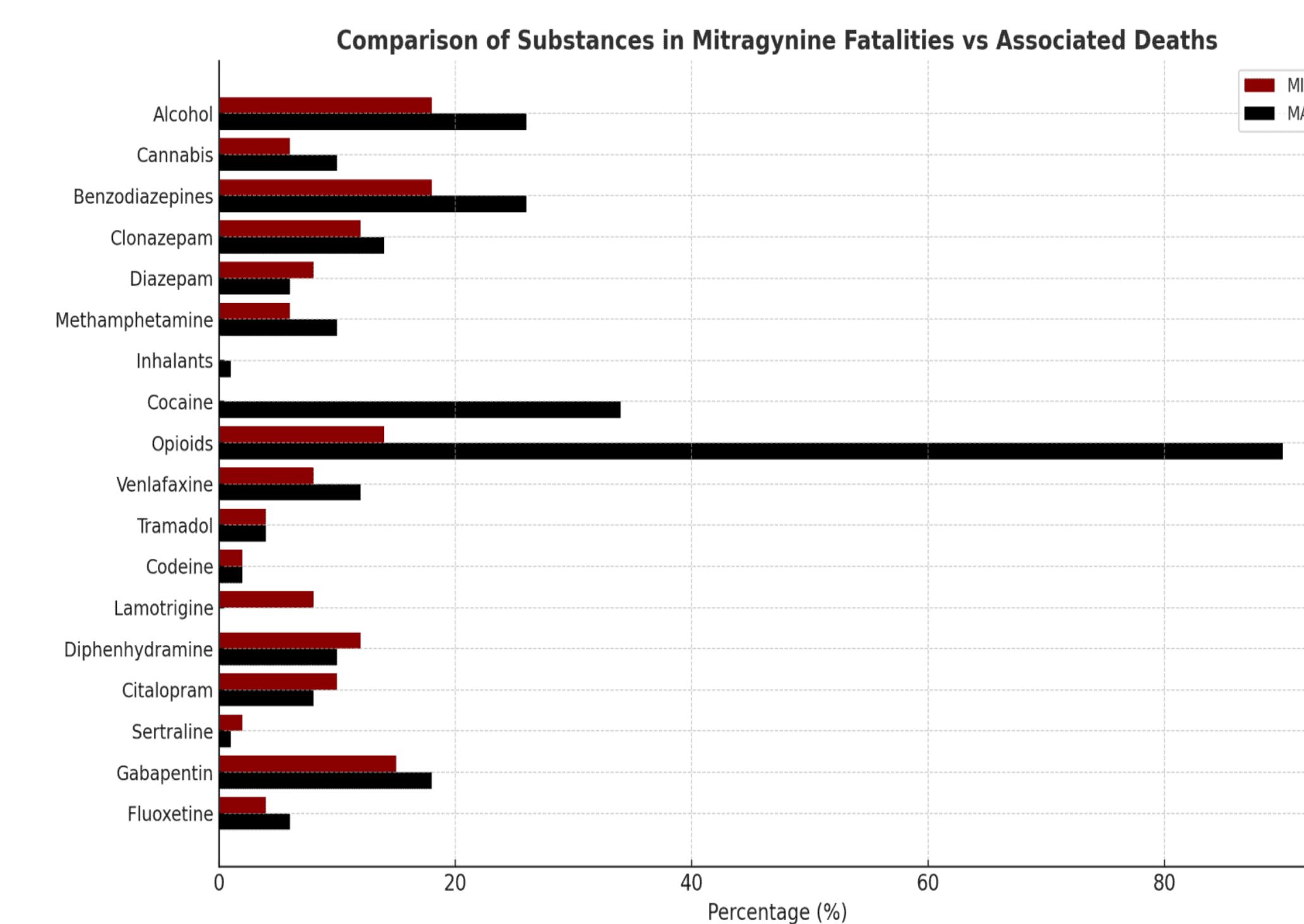
To better understand risk factors for mitragynine toxicity and death by comparing isolated cases of toxicity with polysubstance deaths and to better gauge the use of MTG as a tool to greater opioid use

Methods

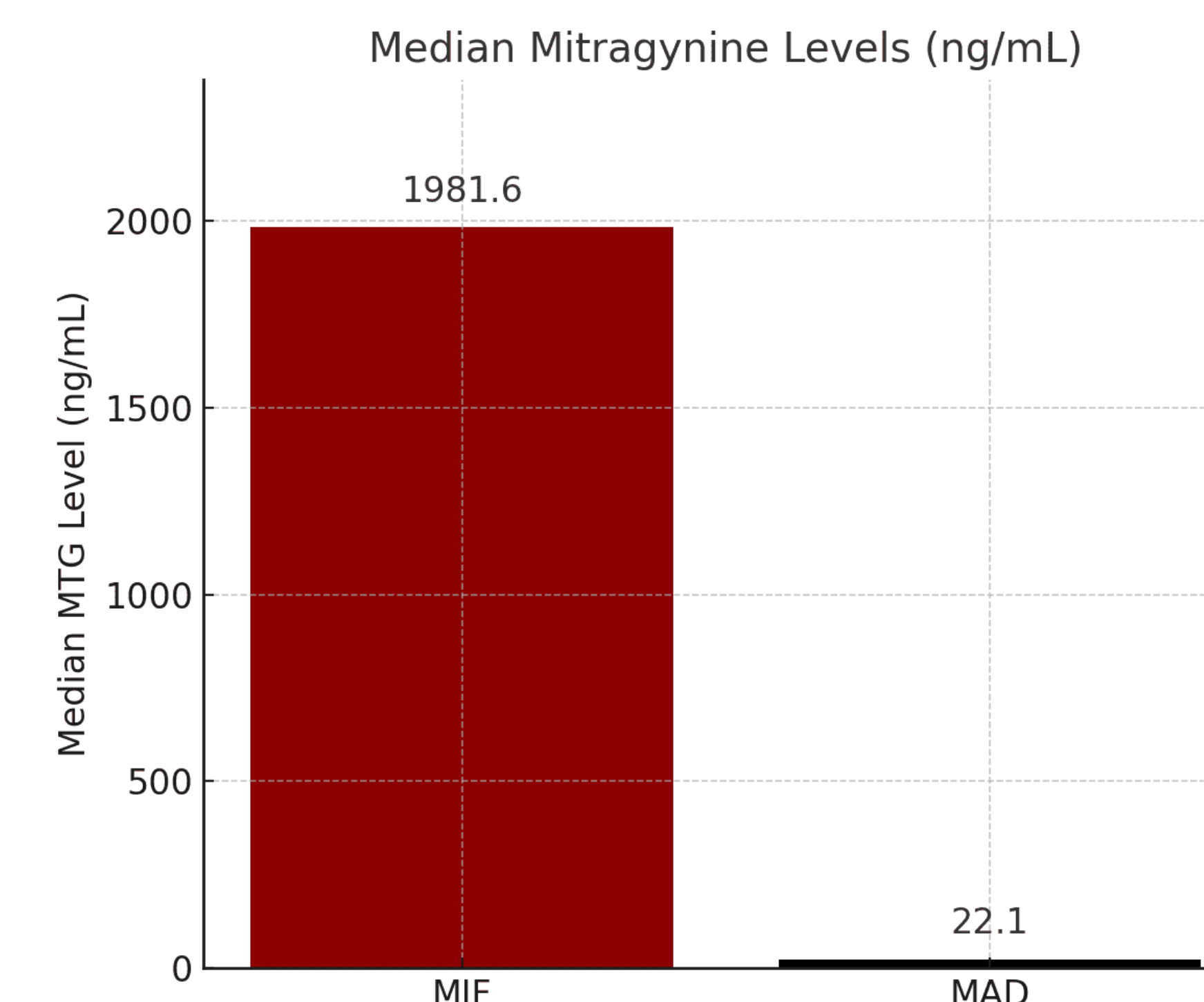
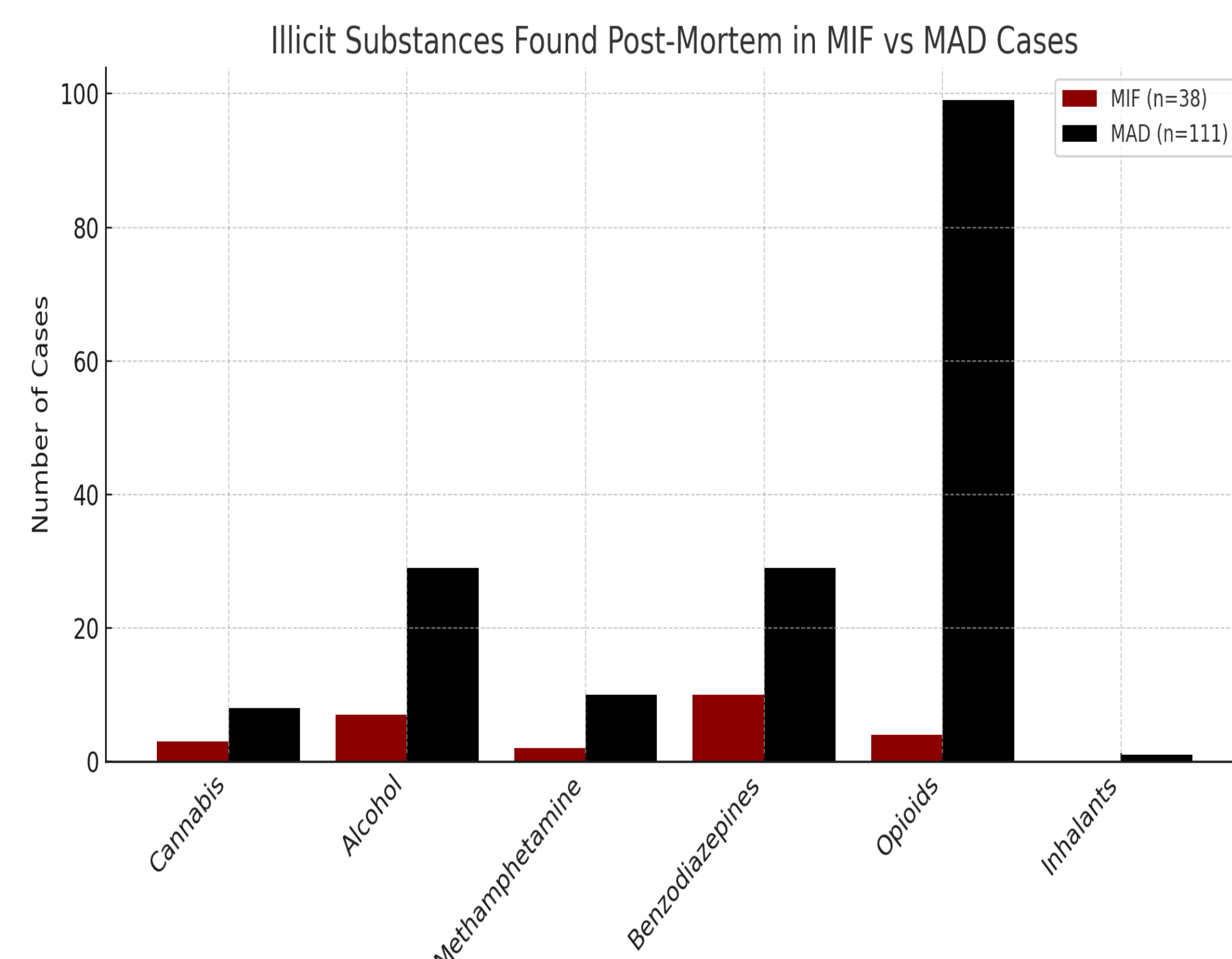


- Study period: 2017 – 2022
- Four researchers evaluated all ME determined causes of death using WHO-UMC and Liverpool Causality tool
- Documented ME autopsy findings on private RedCap database
- Evaluated trends amongst demographics, gross autopsy findings, toxicology reports

Results



- Demographics were similar in terms of age, race, BMI
- Median MTG level 1900 in MIF cases and 23 in MAD cases
- 66% of all cases had opioids on autopsy
- Most common opioid was fentanyl, 14% had multiple opioids
- MIF cases had more pulmonary edema, cerebral edema, and cardiomegaly



Conclusions

Key Takeaway

The effectiveness of kratom as a tool for addiction management may be overestimated

- Mitragynine is playing an increasingly popular role in overdose deaths
- Many of these deaths feature toxic doses of fentanyl
- Subjects who die from MTG alone, often have significantly higher levels than polysubstance deaths
- Gross autopsy findings in MTG induced fatalities are analogous to those found in MTG associated deaths

References

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Acknowledgments

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