



Overview of Clinical Research on Kratom Use in the United States

Arkansas Health Services Subcommittee of Public Health

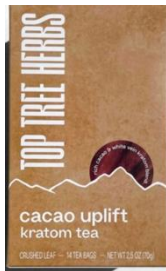
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Disclosures

- I am an Assistant Professor at Johns Hopkins University School of Medicine in the Department of Psychiatry and Behavioral Sciences.
- All of my kratom research is supported by NIDA (K99DA055571, R00DA055571-02) or my JHU departmental startup funds.
- Within the past year, I have served as a paid scientific advisor to the International Plant and Herbal Alliance and The Kratom Coalition. I also serve as an expert witness in legal cases involving kratom.
- The views expressed today are my own and do not necessarily reflect the views or positions of the Johns Hopkins School of Medicine.

Product Diversity¹



Kratom in the United States: 2007-2017²⁻¹¹

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Self-Treatment of Opioid Withdrawal with a Dietary Supplement, Kratom

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Addiction

CASE REPORT

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Self-treatment of opioid withdrawal using kratom (*Mitragynia speciosa korth*)

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Please note: An erratum has been published for this issue. To view the erratum, please click here.
Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 65 / No. 1
March 18, 2016

CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016



Continuing Education Examination available at <http://www.cdc.gov/mmwr/mmwr/continuing>

50 million

adults have **chronic pain**
daily or almost daily.



www.cdc.gov/mmwr

U.S. Recorded Nearly 110,000 Overdose Deaths in 2022

The number leveled off after two years of sharp increases, according to new data from the Centers for Disease Control and Prevention.

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U.S. Suicides Reached a Record High Last Year

Older men are at highest risk, while suicide rates among young people have declined

2024: Who is Using Kratom in the US?²⁻¹⁴

Prevalence Estimates¹⁵:

- Past year use ranges from 2.6-10 million adults.
- Unknown how many regularly monthly/daily consumers.

Age: 20s to mid-70s; mean age **mid-30s**

~55% male

High-school educated to advanced degrees

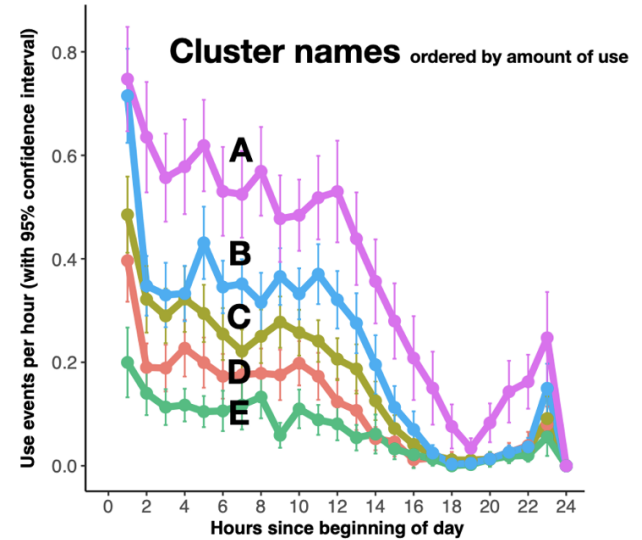
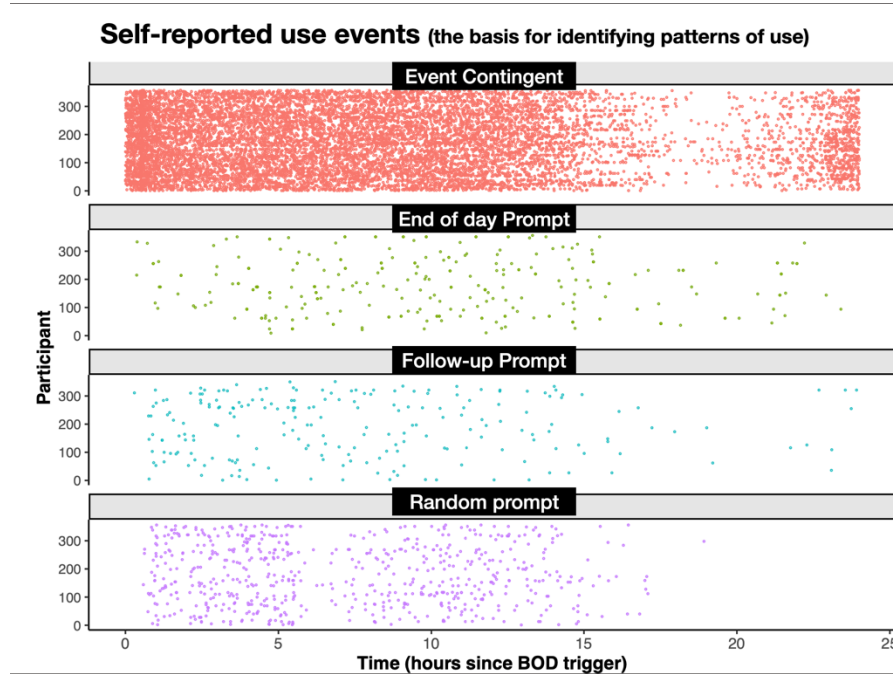
~85% Non-Hispanic White

Very wide income range.

Some using >15 years.

Many (not all) use daily 2-4 times/day.

What we know from ecological momentary assessment (N=357)^{16,17}:



Clusters analyses based on dosing frequency.

A = "Most Frequent" kratom use
E = "Least Frequent" kratom use

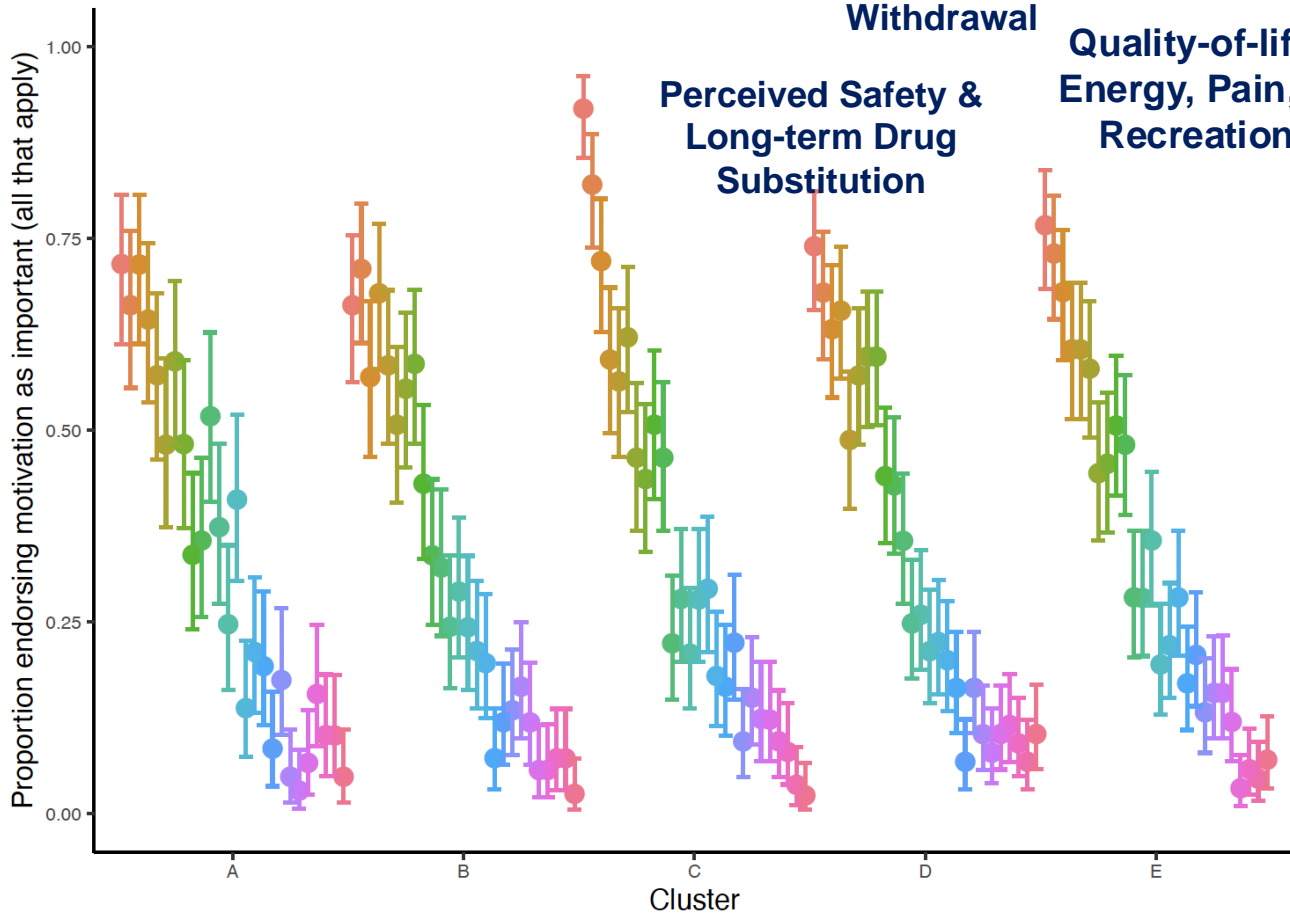
13,401 unique kratom use events reported in real time.

E: Broad motivations for use

Manage Psychiatric
Symptoms & Drug
Withdrawal

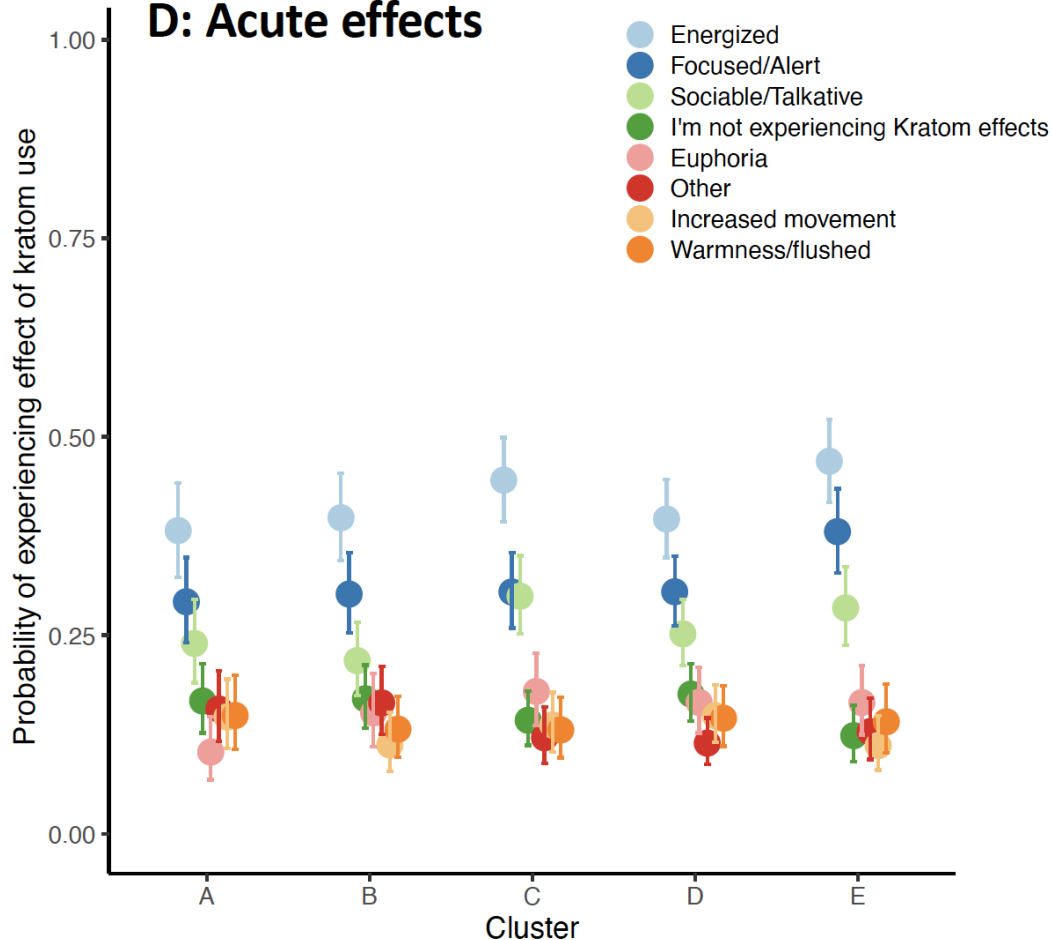
Perceived Safety &
Long-term Drug
Substitution

Quality-of-life,
Energy, Pain, &
Recreation



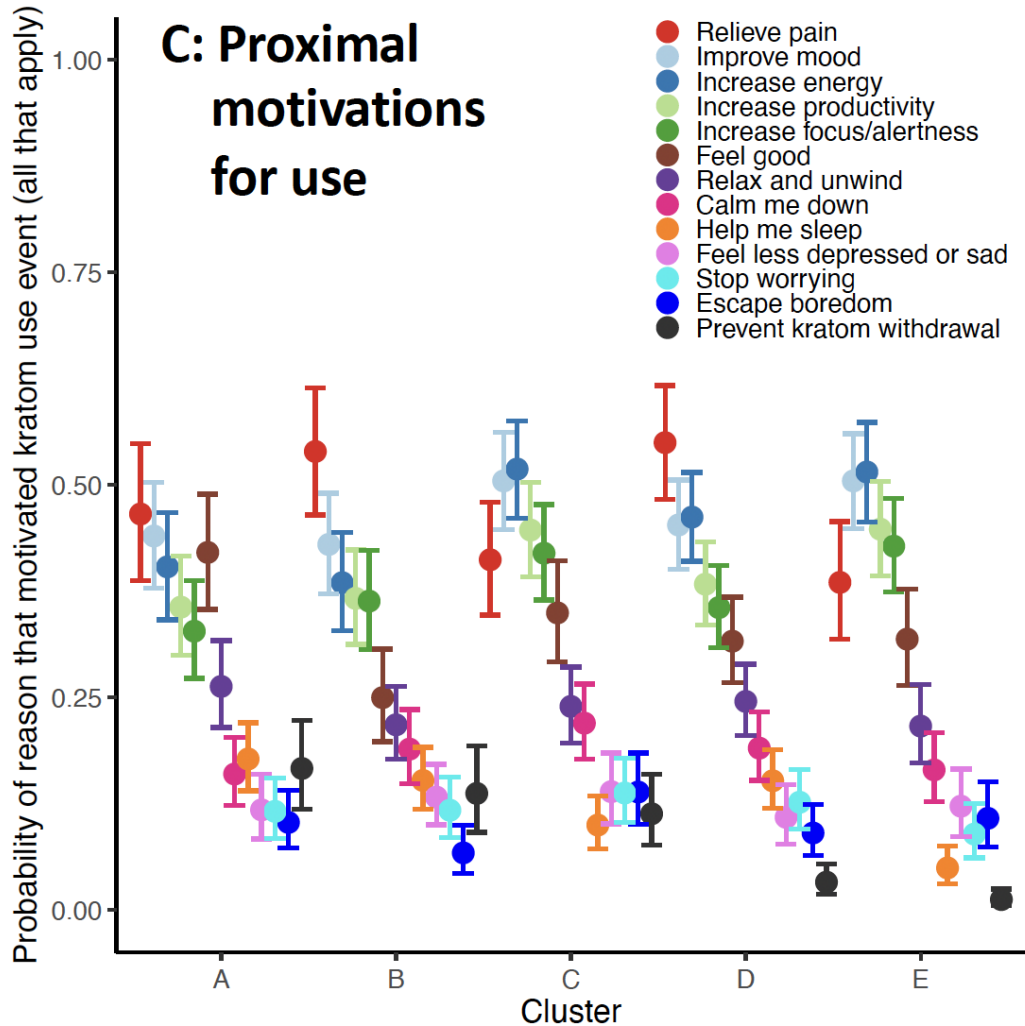
- Just to feel less crappy, improve quality of life
- Boost energy/stamina/endurance for work/exercise
- Kratom is safer than other substances
- Self-treat anxiety symptoms
- Self-treat depression symptoms
- Reduce social anxiety
- Relieve short term pain
- Treat long term pain
- Recreation, fun, relaxation
- Address occasional sleepiness or low energy
- Sleep aid
- Self-treat chronic fatigue syndrome
- Self-treat ADD/ADHD symptoms
- Long-term substitute for opioids
- Euphoric high
- Self-treat post-traumatic stress symptoms
- Self-treat headaches/migraines
- Prefer kratom high to highs from other drugs
- Long-term substitute for alcohol
- Doctors won't prescribe the drugs I need
- Self treat irritable bowel syndrome
- Self-designed stack of drugs to feel good
- Relieve withdrawal from Rx opioids
- Relieve withdrawal from NonRx opioids
- Relieve withdrawal from a variety of drugs
- As a study drug

D: Acute effects



**Stimulatory *and*
 Analgesic effects at
 low *and* high
 serving sizes.** ^{16,18}

*Reported via Follow-up prompts
 Randomized to 15-120 minutes post kratom
 use entry.*



Top 10 most reported reasons during real-time use entries:

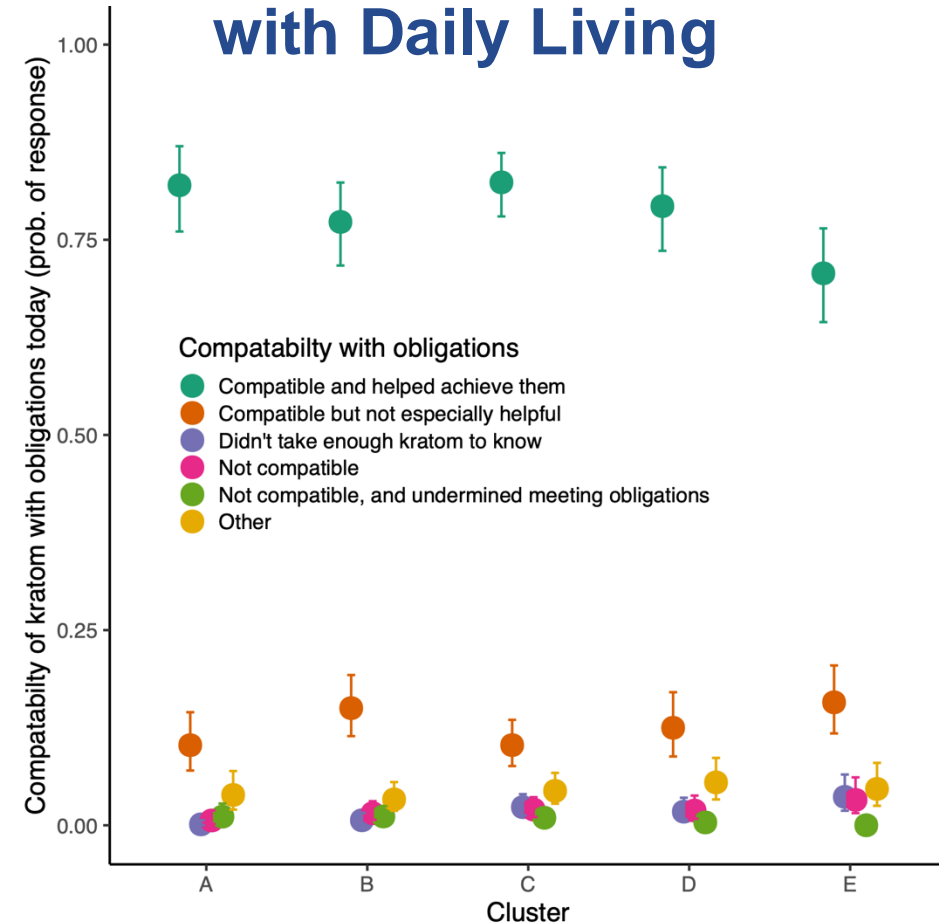
~50% used for **analgesia**.

~50% used to increase **energy** or to improve mood.

Instrumental Use & Compatibility with Daily Living

Regardless of how often participants were taking kratom, most reported that kratom was a **help** to meeting their daily roles & obligations.

Even when not perceived as helpful, kratom was perceived as **compatible**, *not* as a hindrance.^{10,16,18,19}

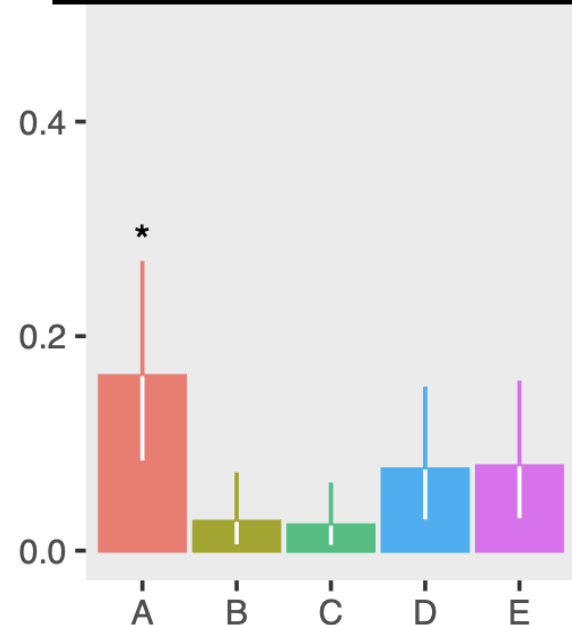


Instrumental Use: Harm Reduction



Over 1/3 of the 357 participants reported *initiating* kratom use as a substitute for opioids, alcohol, or stimulants.¹⁶

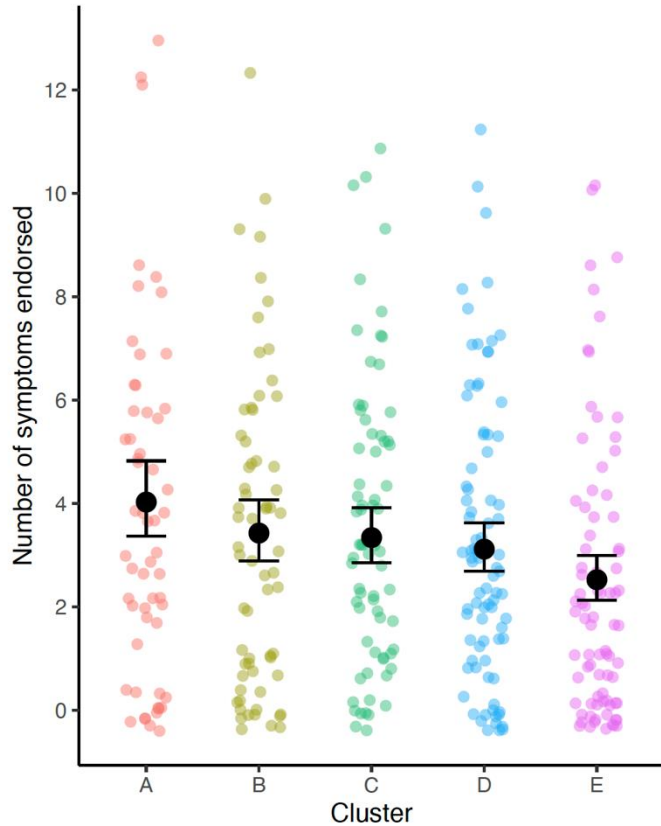
Long-term Opioid Substitute



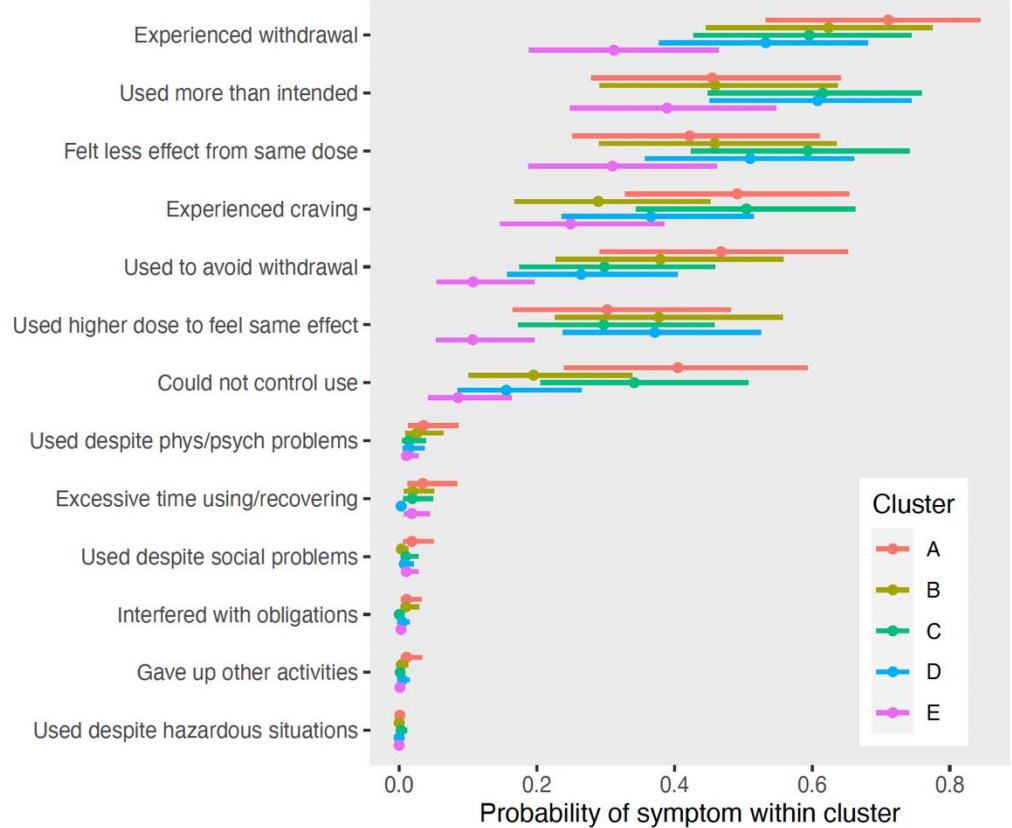
*Harm-reduction was more likely among those taking kratom more often & on a more regimented schedule but also who conceptualized kratom as “life-saving” (Group A).

Kratom Physical Dependence & Addiction 7,16,20-27

A: Number of DSM symptoms endorsed



B: Prevalence of specific symptoms



Safe or Dangerous?

- Few published clinical case reports on kratom-related morbidities/mortalities.²⁸
- Small PK studies: No adverse events other than some GI upset.²⁹⁻³¹

FDA Single Ascending Dose (SAD) study:³²

-1 g, 3g, 8g, 10g, 12 g well-characterized whole leaf kratom encapsulated administered to healthy volunteers (N=40; 8 subjects/cohorts).

-No serious adverse events; no vitals outside normal parameters.

-Only vomiting occurred at a frequency greater than placebo, among 5 participants at $\geq 8g$ dose (may be due to the volume of plant material).

-No doses showed strong indicator of subjective ratings related to abuse potential and did not significantly differ from placebo.

-Subjective ratings for feeling “high” or “drunk” were highest at 12g but still low at 33.7/100 and 15.7/100, respectively.

-FDA concluded that under study conditions, kratom was well-tolerated.

-FDA plans to move forward with HAP.

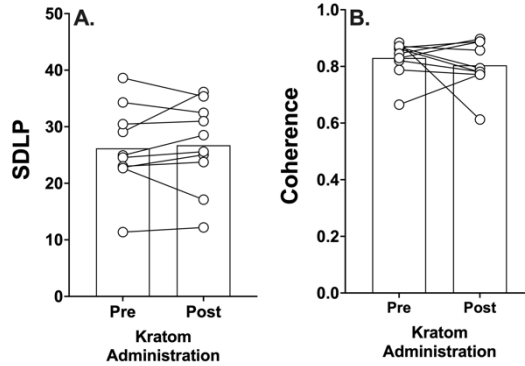
Safe or Dangerous?

NIDA IRP Study:³³

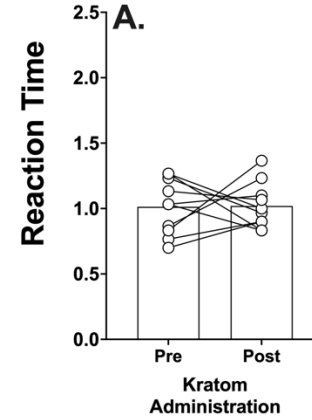
- 1.1-10.9g kratom self-administered (N=10). Ecological validity.
- **No adverse events.**
- Vitals, including respiration) within normal parameters.
- Mild subjective euphoria detected among 3 participants.
- Similar to FDA's findings subjective ratings for feeling "high" were very low at 15.2/100 & feeling "intoxicated" (4.8/100).
- No objective psychomotor impairment or intoxication detected.
- Participant interviews indicated serotonin excess might occur at high doses. Unclear if this is occurring, but highlights the fact that kratom is not "an opioid"¹⁸
- None had ever sought medical care for kratom-related events.¹⁸



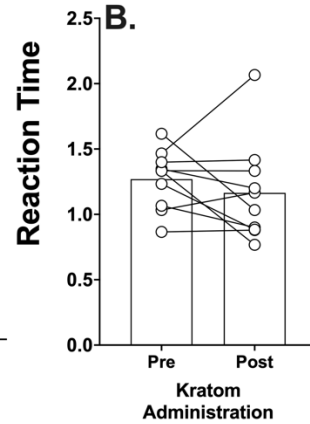
Car Following Task



Crash Avoidance



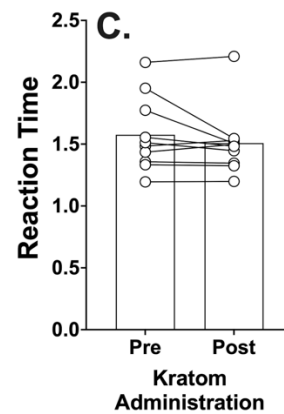
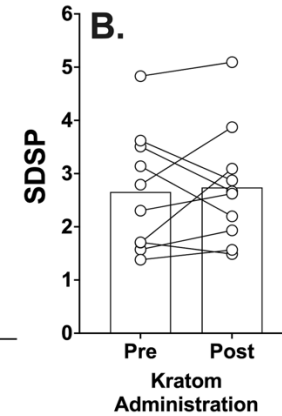
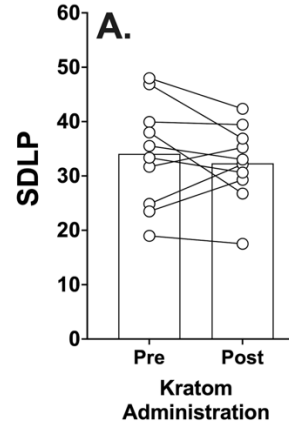
Stop Light



No significant changes across driving simulator outcomes:³⁴

Only one participant showed a modest increase in SDLP and a decrease in coherence score (indicating impairment); remaining participants showed stable performance pre to post-kratom self-administration.

Divided Attention Task



Takeaways:

- Kratom continues to be used for harm-reduction and chronic pain, but also now for mood, quality-of-life, energy, productivity, and recreation/socializing.
- Kratom doses up to 12g are well tolerated & have not resulted in serious adverse events or acute impairment.
- Abuse potential of kratom remains unknown, but data indicate low abuse potential of mitragynine, kratom's major alkaloid.
- Kratom may cause physical dependence, but does not appear to result in moderate or severe SUD based on clinical case reports & research.
- Consumers who participate in research report kratom as compatible or helpful in meeting daily roles & responsibilities.

Investments in scientific research must be made to inform kratom regulation.

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