

The Dosing Project:

An Explorative Analysis of Cannabis Products for Adverse Events & Effective Dosages

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CESC

Safe Cannabis Experience

Why Does Marijuana Make Some People Faint?

JOURNAL OF THORACIC DISEASE

Symptomatic Sinus Arrest Induced by
Acute Marijuana Use

BENZINGA

Uncontrollable Vomiting Due to
Marijuana Use on the Rise



CBD in Marijuana May Worsen Glaucoma

ScienceDaily

Bad actors to blame for inaccurate
cannabis labels? Not so fast



Women With Cancer Awarded Billions in Baby Powder Suit

An appellate court in Missouri upheld more than \$2 billion in damages against Johnson & Johnson, saying the company knew there was asbestos in its baby powder.

Johnson & Johnson Lawsuits Raise Fears Over Baby Powder

Johnson & Johnson to End Talc-Based Baby Powder Sales in North America

The company has faced thousands of lawsuits from cancer patients who claim that its talc was contaminated with asbestos, a known carcinogen, and that the company knew of the risks.

All products have liabilities, even Baby Powder

The Dosing Project

Non-Interventional Surveillance Study Investigating the Acute Effects of Cannabis Use in a Naturalistic Setting

Study Rationale

- Lack of FDA oversight for Safety
- Cannabis Consumer Dosage occurs through Trial and Error
- Over 3,000 CBD Brands Marketed w/o Validation
- Over 700 Cannabis Flower Names w/o Validation
- New Product Additives/Fillers/Base – Vape Pen Illness 2019
- De-Convolute Cannabis using Multi-Agent Pharmacology

After using Cannabis, Participants respond to a brief online survey

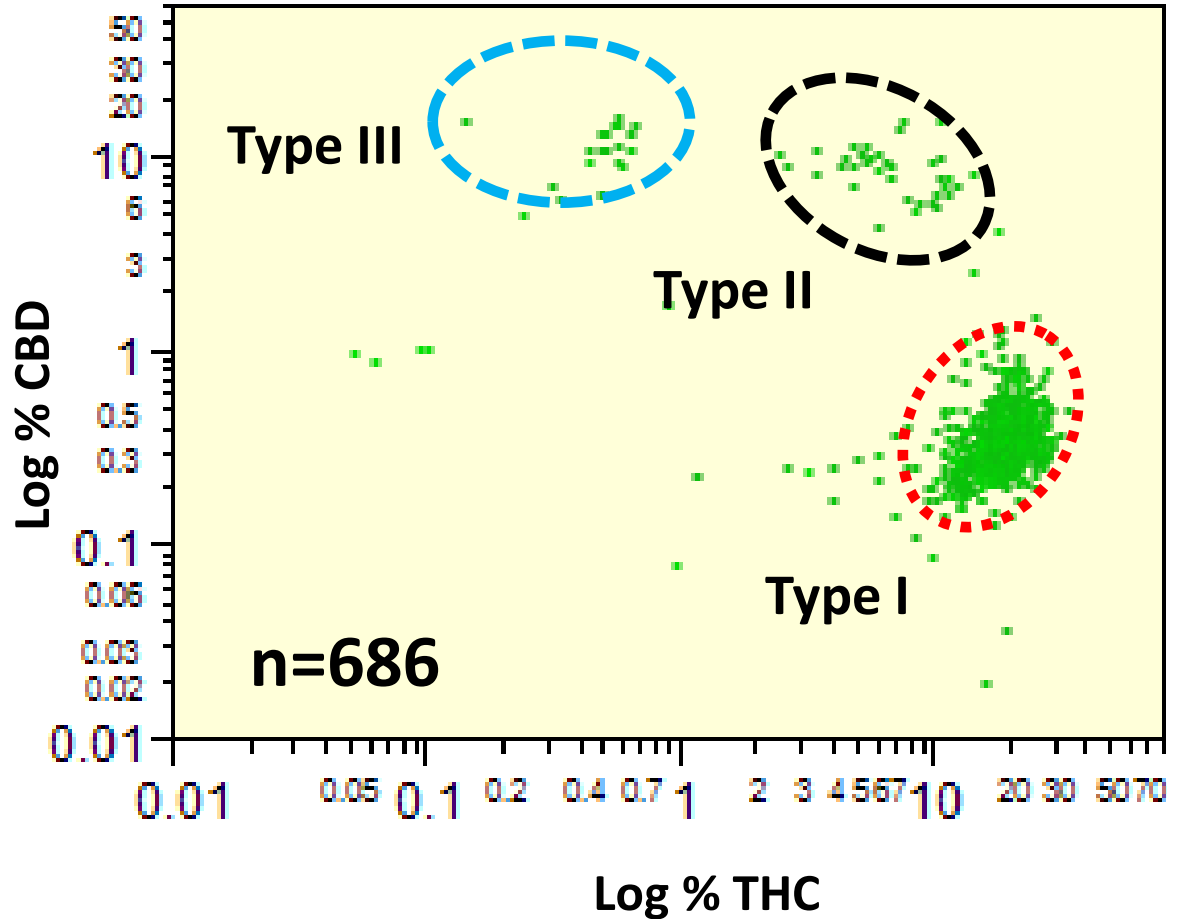
Study Hypothesis: Surveillance Studies of Community Accessible Cannabis Products can identify beneficial Dosages and Adverse Events (AE)

Primary Objective: Improve the Safe and Efficacious Use of Community-Accessible Cannabis Products

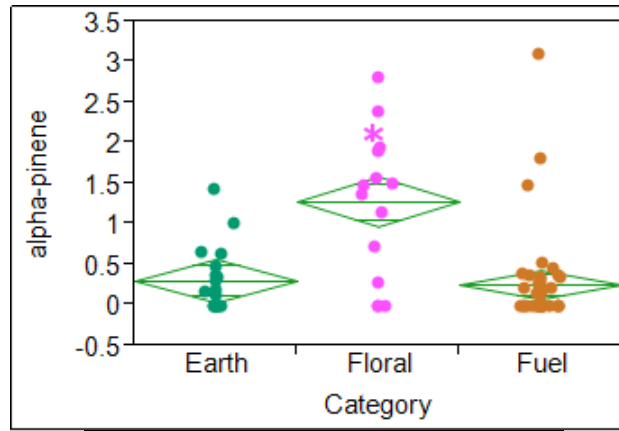
5-Step Analysis

1. **Characterization** of Cannabis products.
2. **Categorization** by dosage and routes of administration
3. **Stratification** of respondents
4. **Correlation** to therapeutic benefit and adverse events
5. **Certification** of Safety and Efficacy using newly derived Effect Index for comparisons

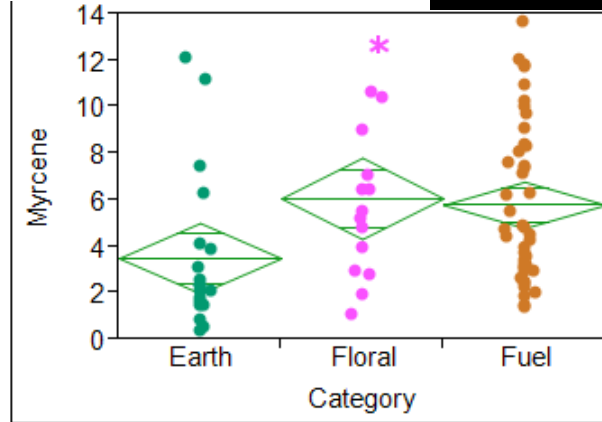
**Dominant
Cannabinoid
Type I, II, III**



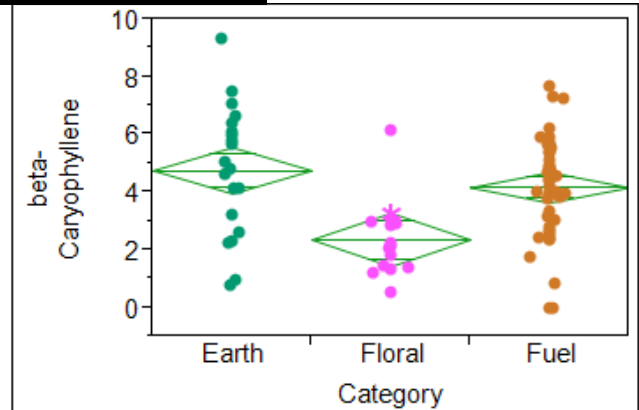
Aroma-Type Earth, Floral, Fuel



alpha-pinene



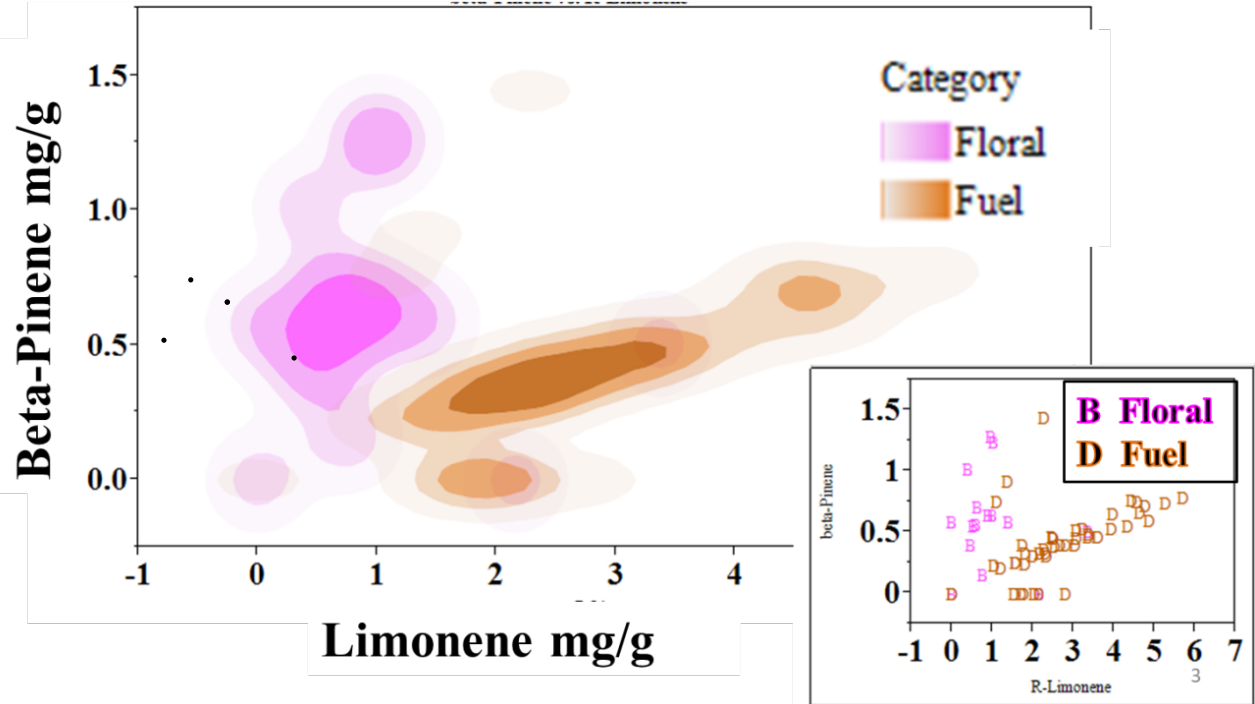
myrcene



beta-caryophyllene

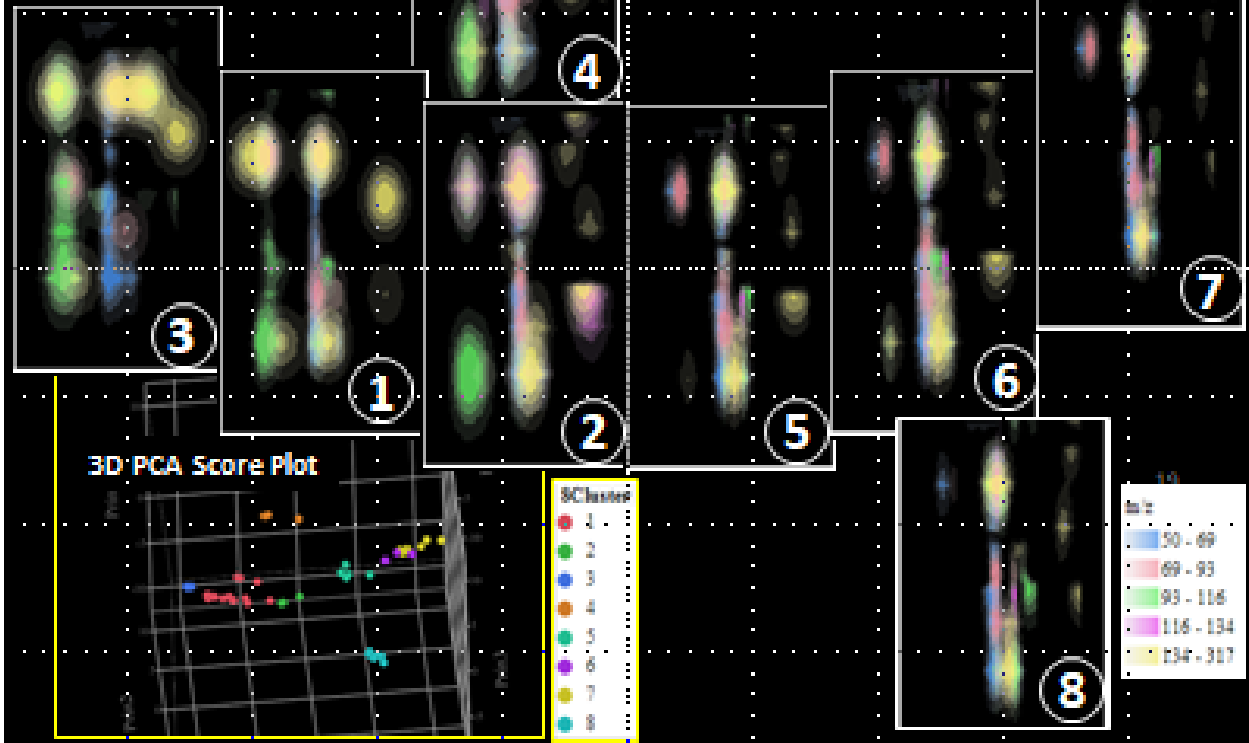
The Beta-Pinene / Limonene Ratio-Group Defines Cannabis Aroma Categories

Terpene Ratio
Beta Pinene
Limonene-
Ratio



Untargeted Discovery Features Chemical “Fingerprint”

Untargeted Discovery Features



**Industry
Product Types**

Categorization - I



Flower

Pre-Rolls/Joints
Pipes/Water-Pipes
Vaporizers
Capsules

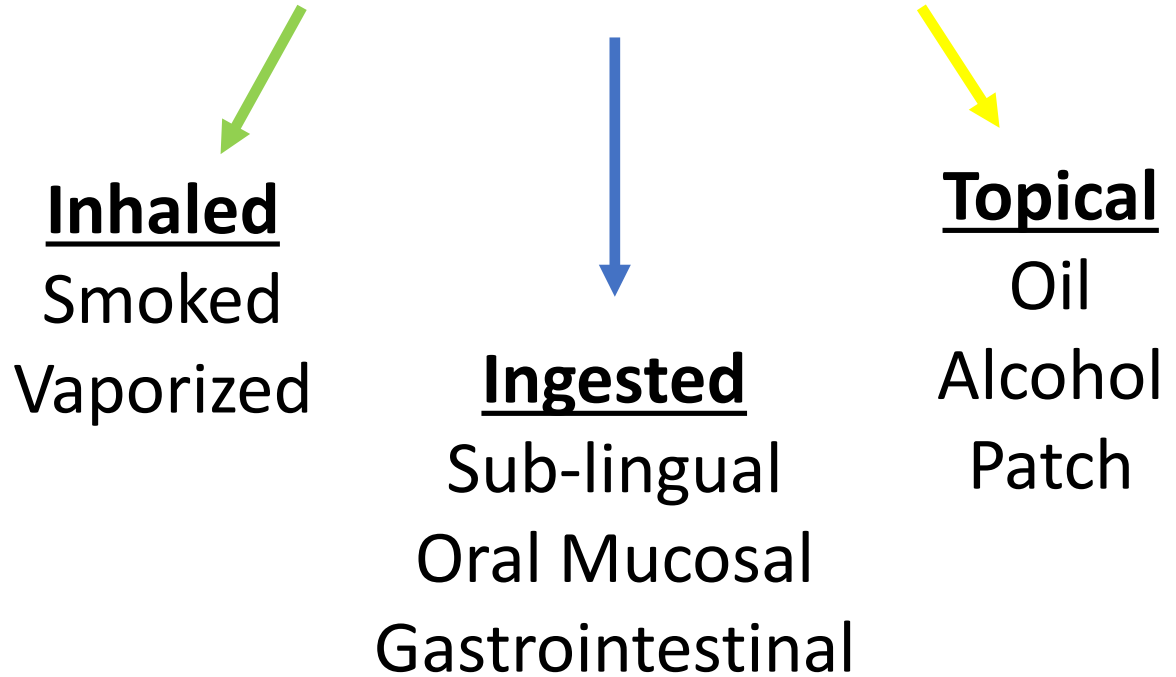


Concentrate

Cartridges
Oral Liquid/Tincture
Gummy, Capsule, Tablet
Hash/Wax/Shatter/etc.
Baked Goods/Candy

**Route of
Administration**

Categorization - II



Stratification by Indication

Chart Review of Medical Cannabis Use

Disorders of:	Medical Cannabis Patients	
Pain	16,753	52%
Mood	10,931	34%
Sleep	2,943	9%
Appetite	226	1%
Other	1,205	4%
Total	32,058	100%

Cannabis Specialty Clinics 2015- California

Characterization + Categorization + Stratification



Correlation



“Blue Tart” Pre-Roll

Type I “Floral” Inhaled Flower used for Pain

How Much Do You Use? Dosage

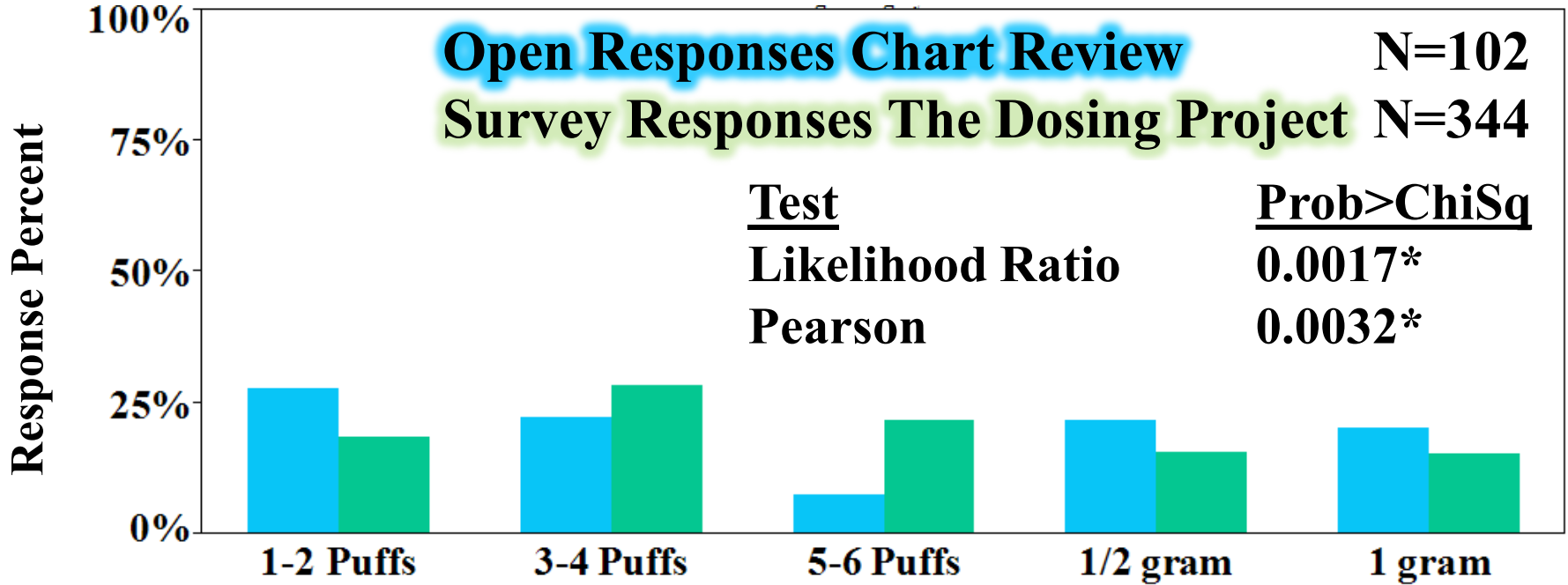
1-2 Puffs 3-4 Puffs 5-6 Puffs ½ Gram 1 Gram

Does it Work? Therapeutic Responses

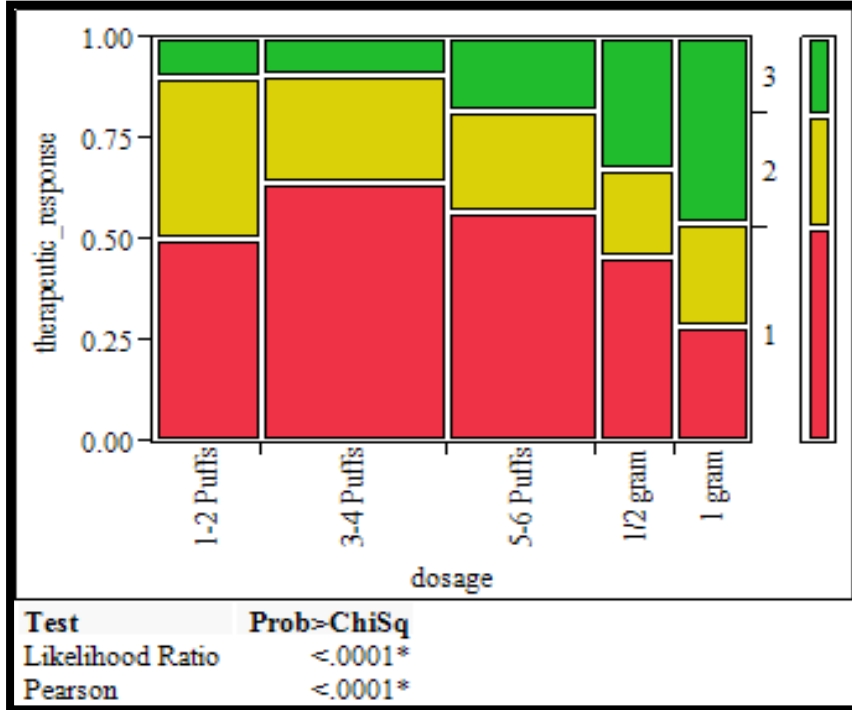
Completely Almost Completely Somewhat Not Much

Is it Safe? Adverse Events: Yes or No

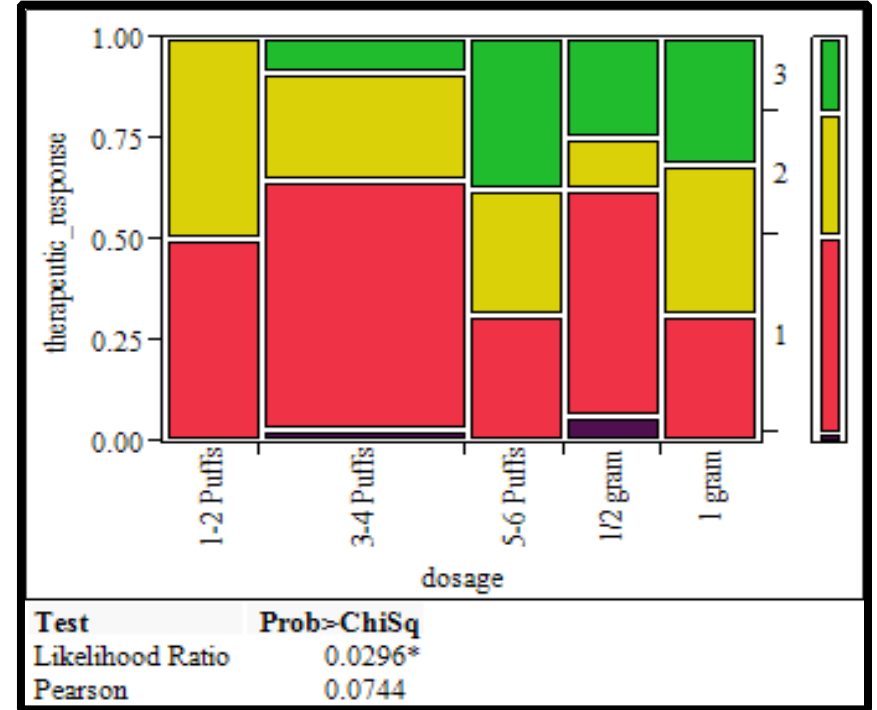
Dosage Categories



Inhaled Flower Dose - Effect

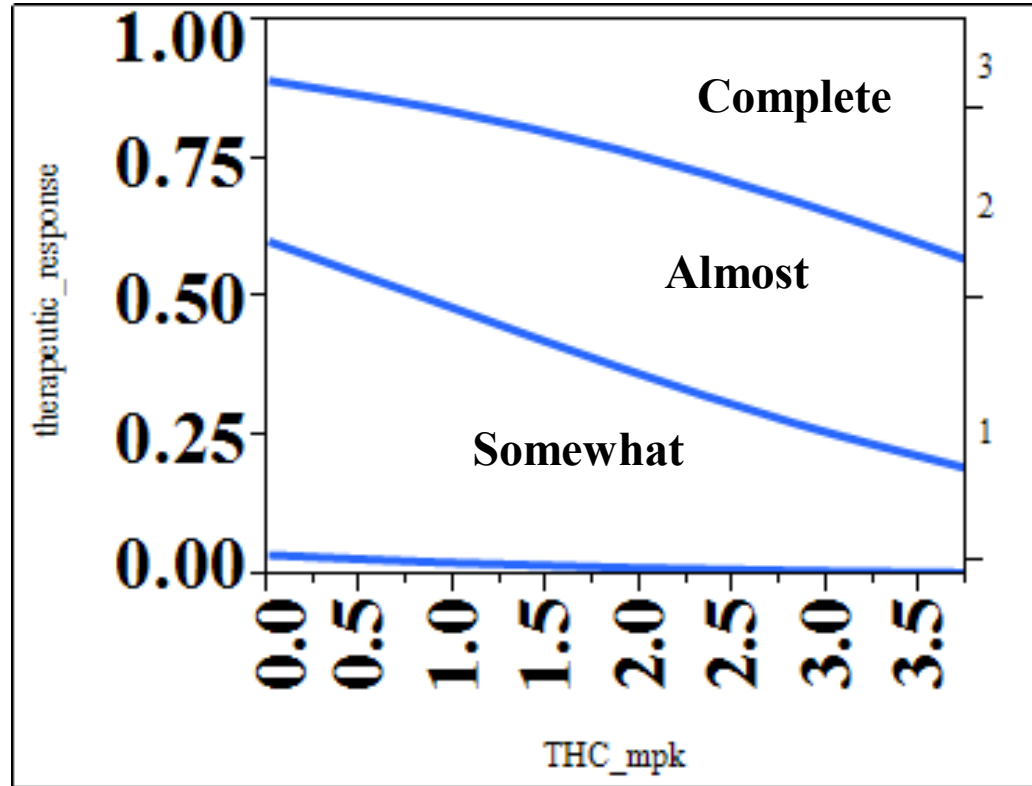


All Types



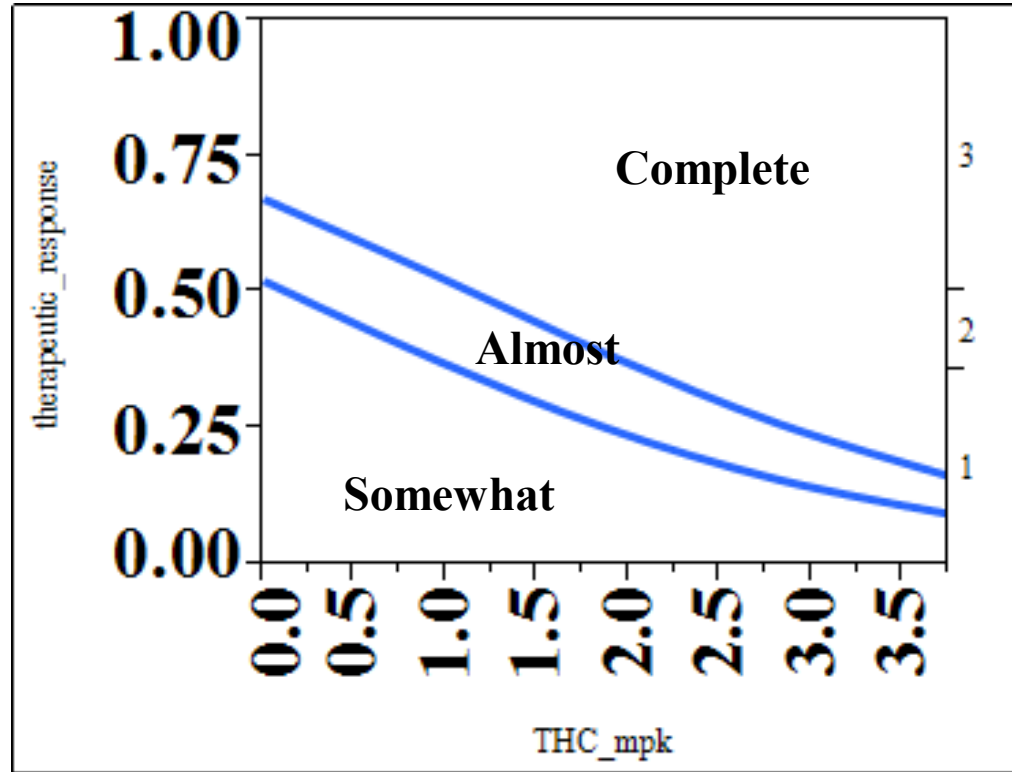
Type I for Pain

**Inhaled Type I
Dose
Response
THC mg/kg
For Pain**



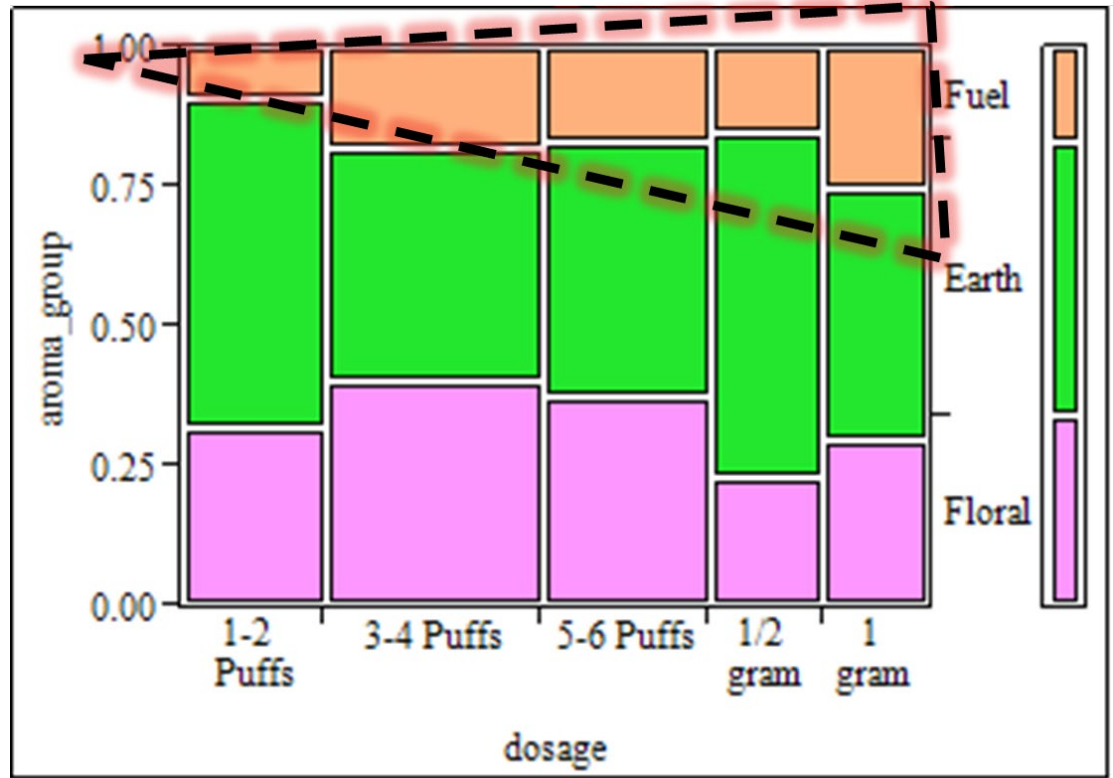
Prob>ChiSq
0.0477*

Inhaled Type I Dose Response THC mg/kg For Sleep



Prob>ChiSq
0.0694

Inhaled Flower Dose Categories by Aroma-Type



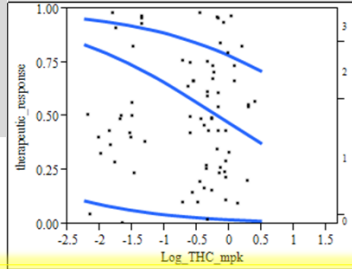
N	DF	-LogLike	RSquare (U)
341	8	6.5413598	0.0189

Test	ChiSquare	Prob>ChiSq
Likelihood Ratio	13.083	0.1090
Pearson	12.873	0.1163

Inhaled Type I Dose Response THC mg/kg

Pain

Logistic Fit of therapeutic_response By
Log_THC_mpk aroma_group=Floral, for_symptom=P



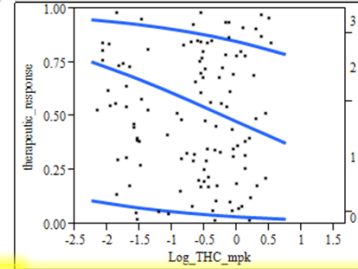
Prob>ChiSq

0.0209*

n=76

Earth

Logistic Fit of therapeutic_response By
Log_THC_mpk aroma_group=Earth, for_symptom=Pain



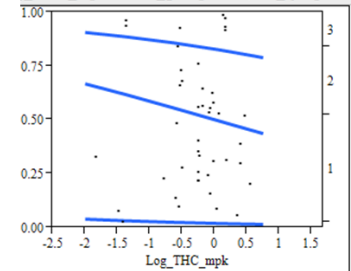
Prob>ChiSq

0.0318*

n=113

Fuel

Logistic Fit of therapeutic_response By
Log_THC_mpk aroma_group=Fuel, for_symptom=Pain



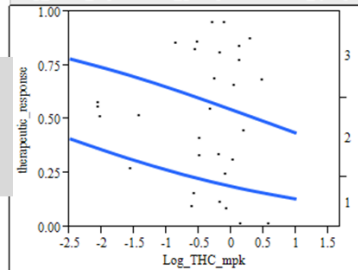
Prob>ChiSq

0.5685

n=44

Sleep

Logistic Fit of therapeutic_response By
Log_THC_mpk aroma_group=Floral, for_symptom=S

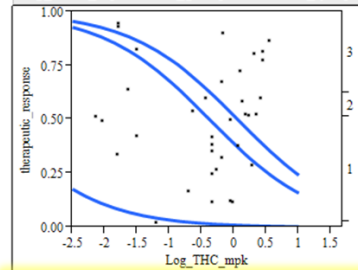


Prob>ChiSq

0.3253

n=30

Logistic Fit of therapeutic_response By
Log_THC_mpk aroma_group=Earth, for_symptom=Sleep

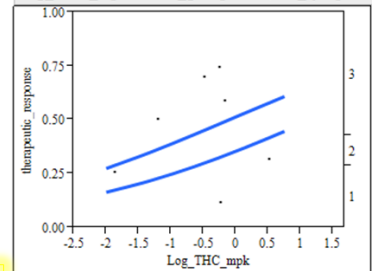


Prob>ChiSq

0.0077*

n=37

Logistic Fit of therapeutic_response By
Log_THC_mpk aroma_group=Fuel, for_symptom=Sleep



Prob>ChiSq

0.5907

n=7

Is it Safe?

National Poison Data System
January 2017- December 2019
N=28,630

Adverse Events of Industry Product Types

Exposures

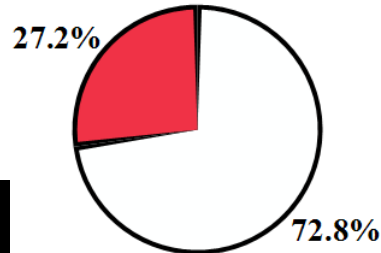
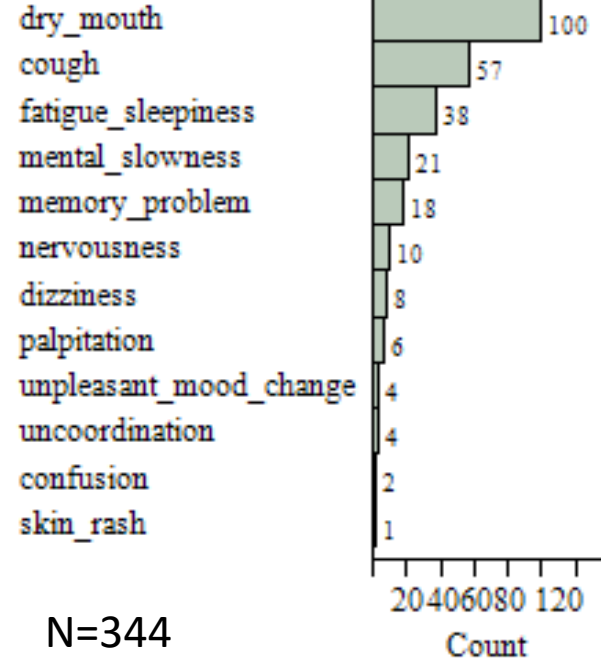
- Flowers (65.5%)
- Manufactured Edibles (19.3%)
- Concentrates (9.6%)
- Vaporized liquids (3.8%)
- Other Cannabis products (1.8%)

Adverse Events Inhaled Flower

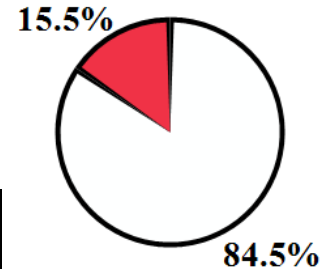
 24K

I experienced the following side effects: cough

- none
- confusion
- cough
- dizziness
- dry mouth
- fatigue or sleepiness
- memory problems
- mental slowness
- nervousness
- heart palpitation (fast heart beat)
- skin rash
- uncoordinated movement
- unpleasant change in mood/perception



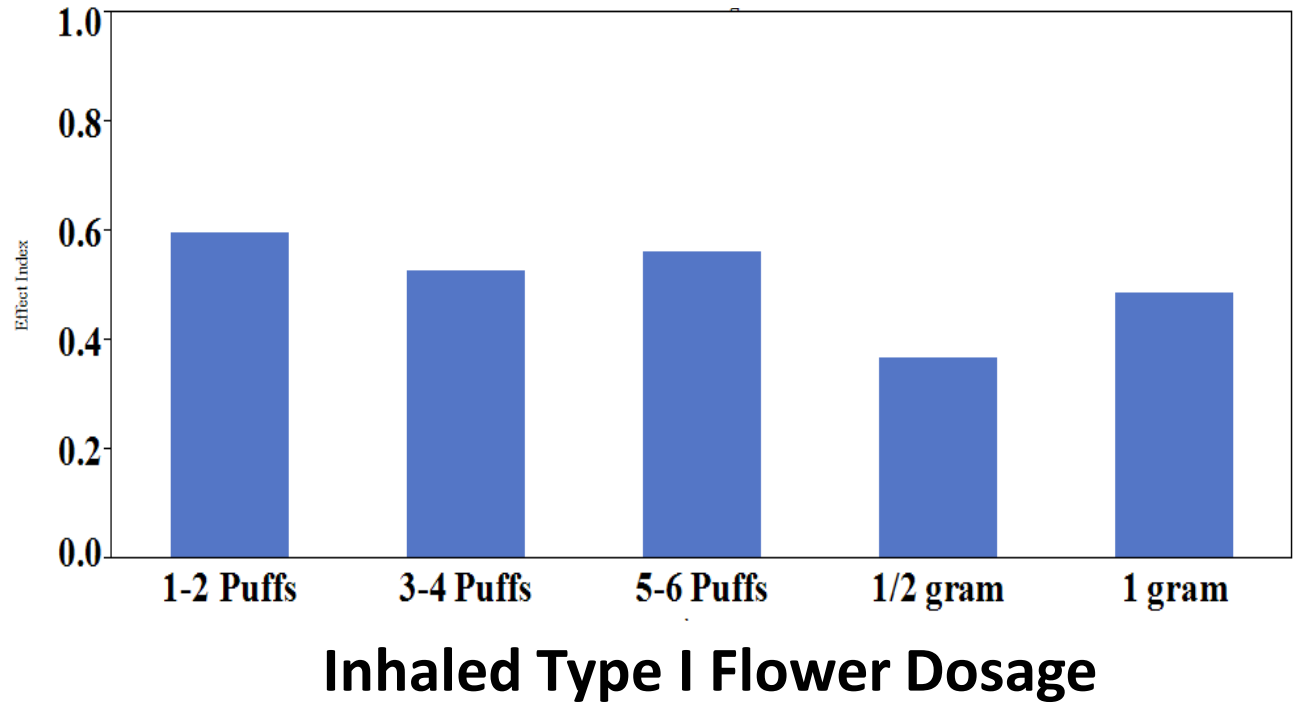
Dry Mouth



Cough

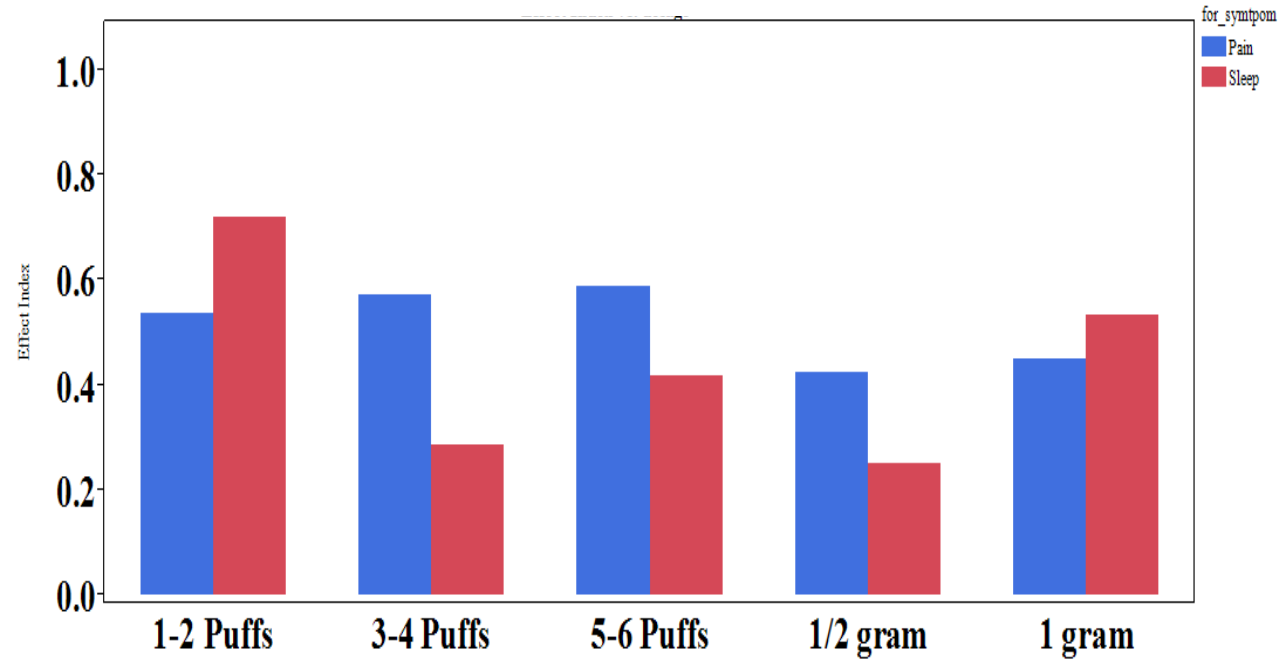
Safety Index

**Responses
without AE**
Divided by
**Total
Responses**



Safety Index by Indication

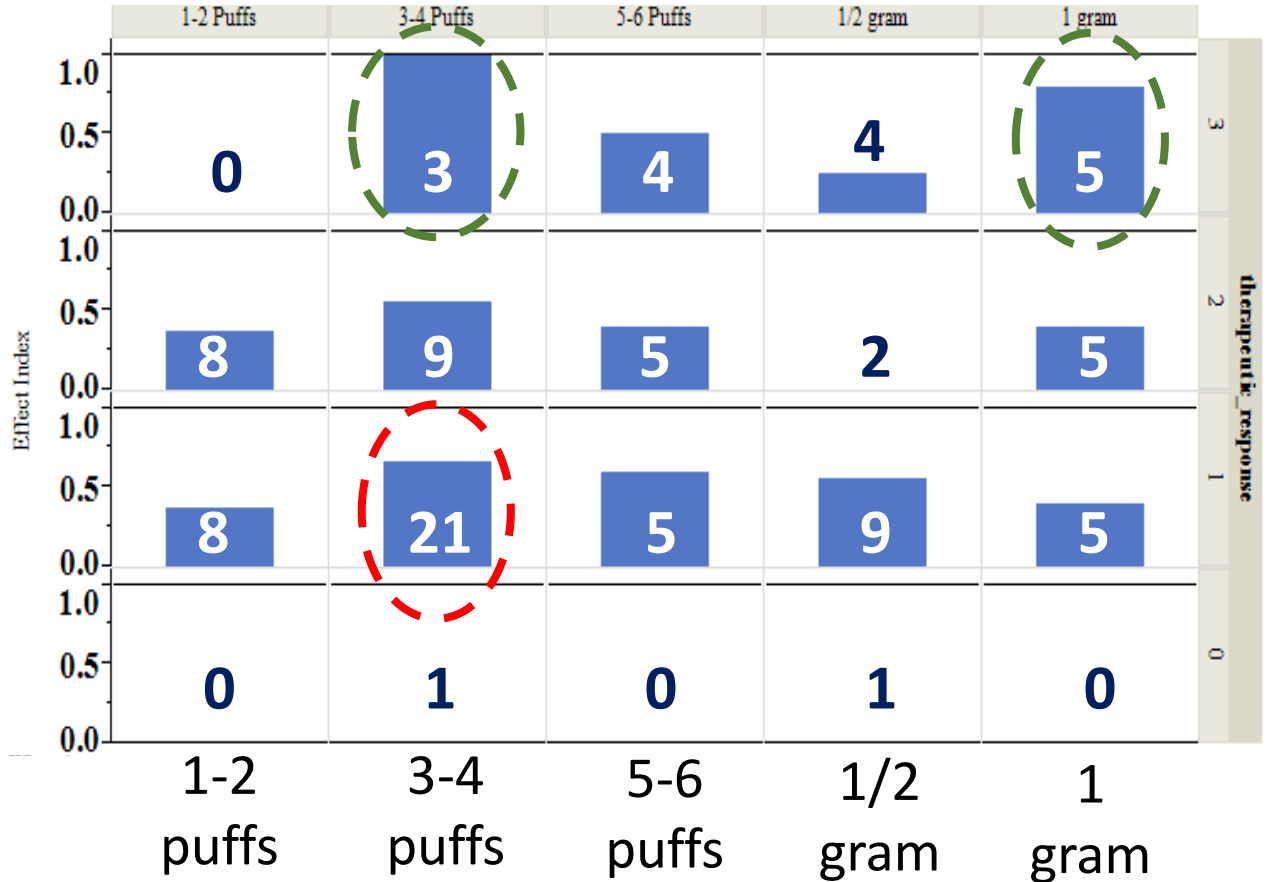
**Inhaled
Type I Flower
Pain vs. Sleep**



**Inhaled
Type I Flower
for
Pain**

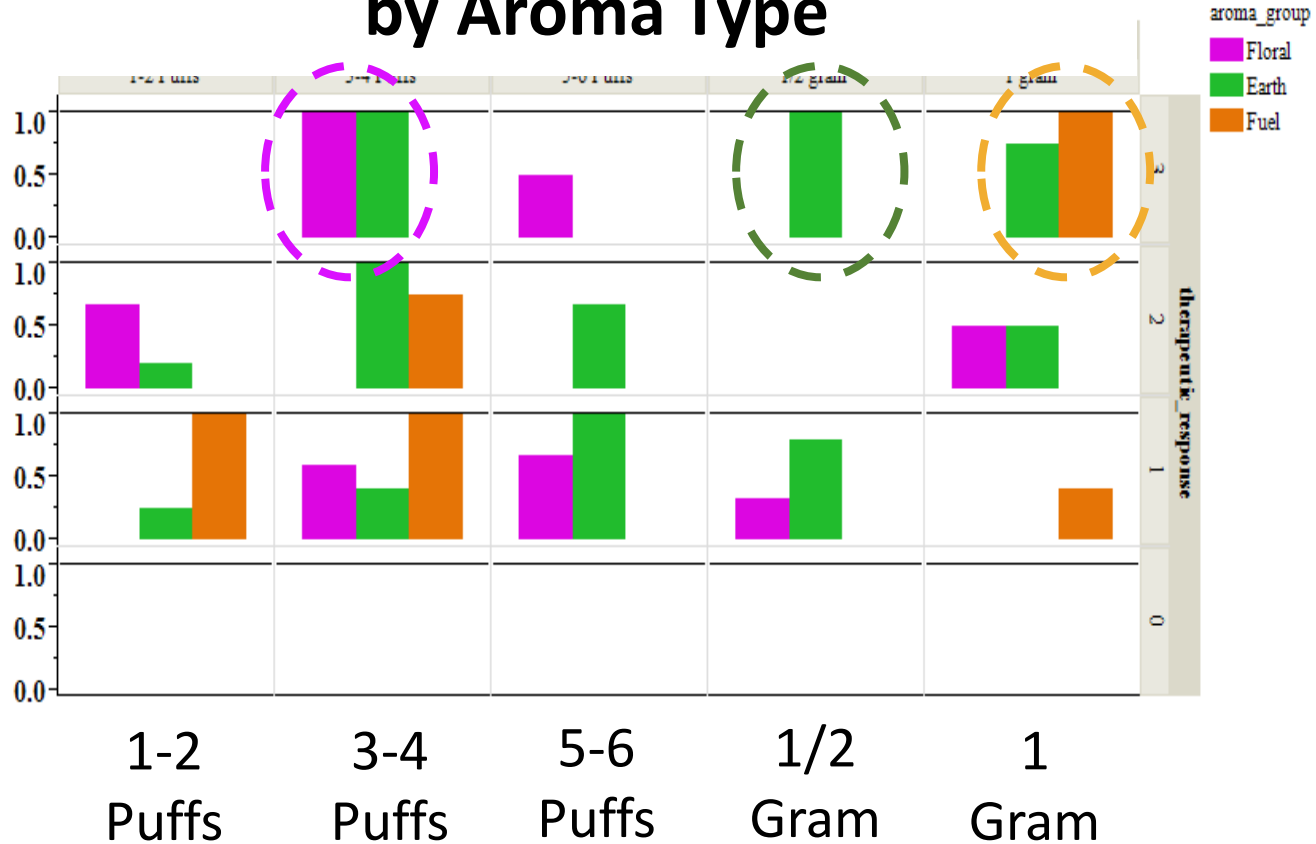
N = 94

**Safety Index
by Therapeutic Response**



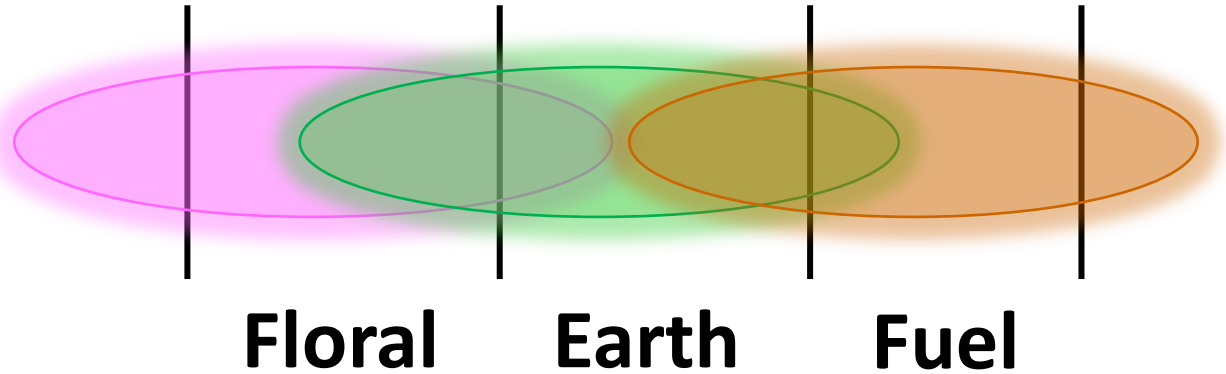
Safety Index by Aroma Type

Inhaled
Type I Flower
for
Pain



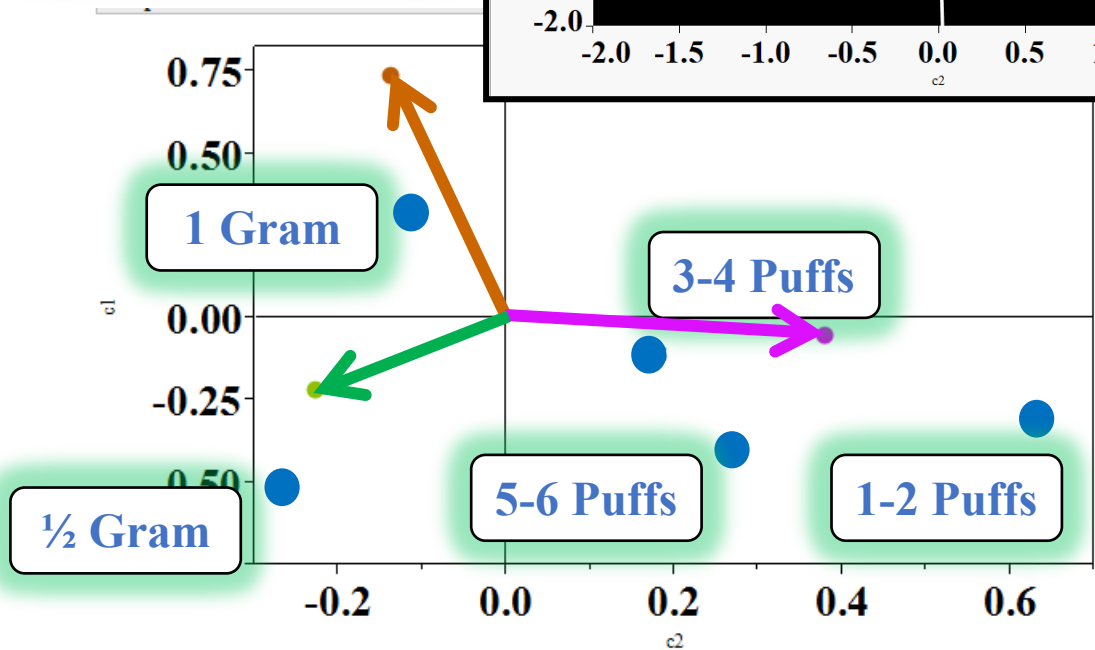
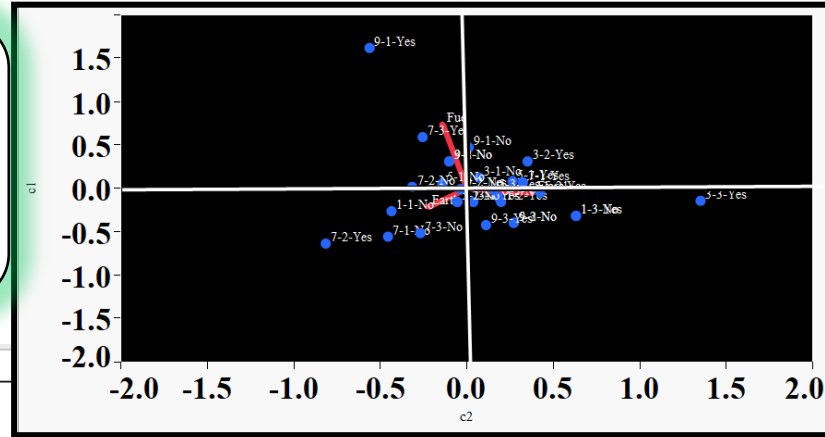
**Testable
Hypothesis:
Optimizing
Safety and Effect**
Inhaled Type I
Aroma Flower
for Pain

Complete Response Increasing Dose →



**Safe & Effective Dosage:
Complete Response,
No AE**

Multiple Correspondence Analysis
Inhaled Aroma-type Flower



**Floral
Earth
Fuel**

Effect Index (EI) for Safety

- Comparative Measure of Cannabis Safety & Efficacy
- Analogous to a Therapeutic Index

$$\textit{Effect Index (EI)} = \frac{\textit{AE}_{50}}{\textit{ED}_{50}}$$

AE₅₀ = Dose (mg/kg) 50% probability of an Adverse Event

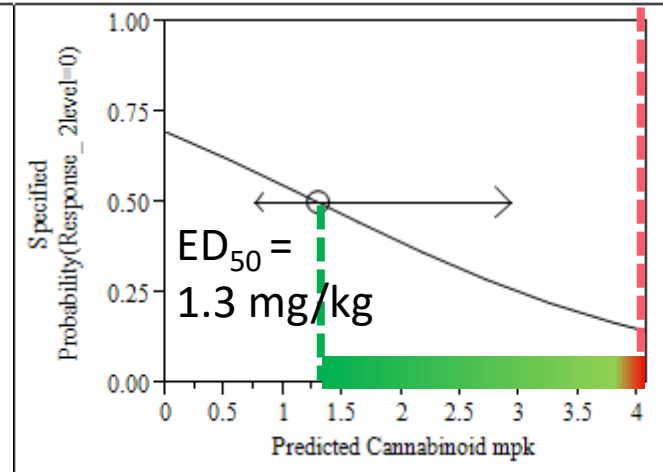
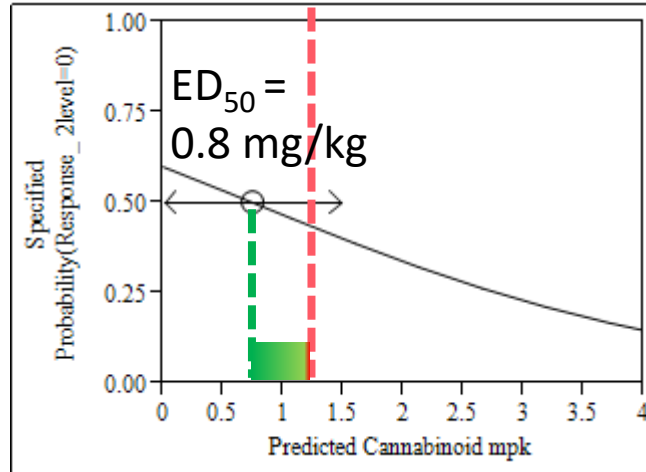
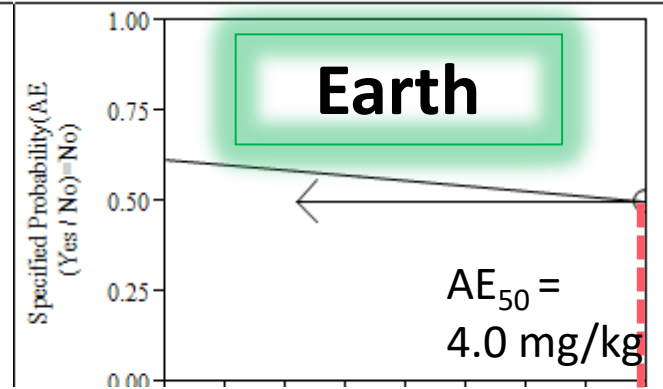
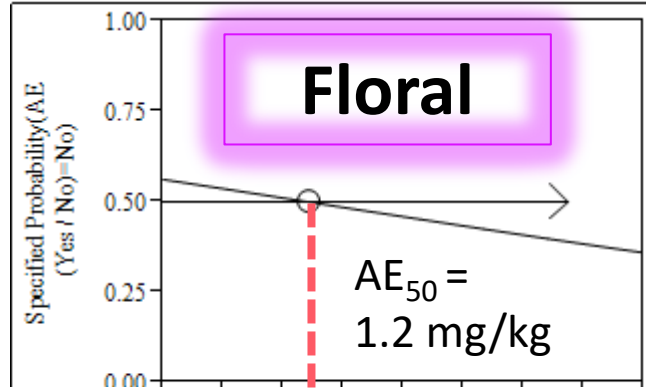
ED₅₀ = Dose (mg/kg) 50% probability of either a Complete or Almost Complete Response

Logistic Fit

Adverse Events and Effective Dose

Floral
Effect Index =
1.5

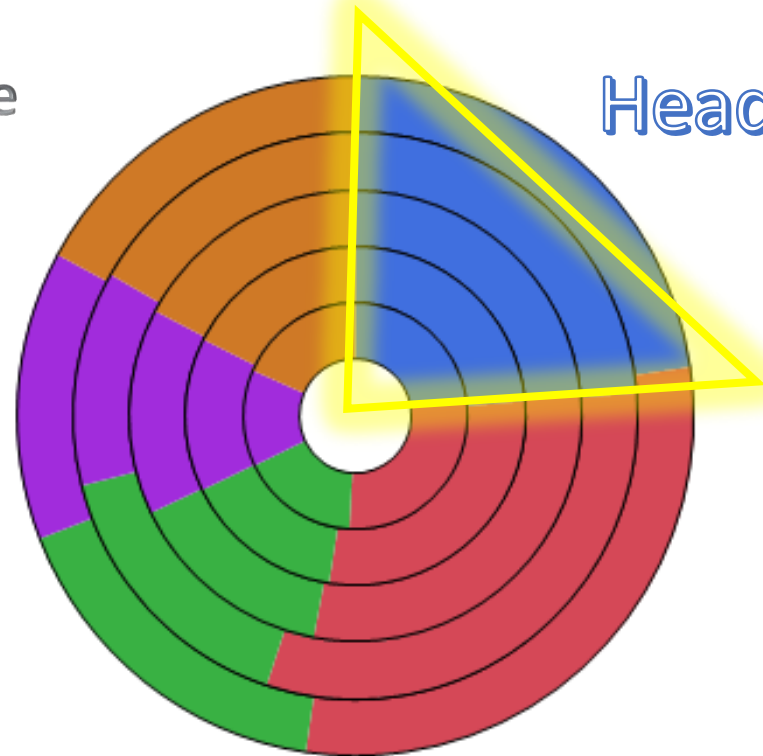
Earth
Effect Index =
3.1



α -Pinene cluster includes Sabinene . . . May explain narrow Effect Index (EI)

Acetylcholinesterase
Inhibitors: Nausea,
Muscle Cramps,
Insomnia

Headaches



ID + Feature

- Sabinene-13.540_2.700_93-13.54(0.045)
- α -Pinene-12.420_0.375_105-12.42(0.0062)
- α -Pinene-12.420_2.700_110-12.42(0.045)
- α -Pinene-12.420_2.700_135-12.42(0.045)
- α -Pinene-12.740_2.700_121-12.74(0.045)

The Dosing Project Report

“Blue Tart” Pre-Roll

Characterization: **Type I “Floral”**
Categorization: **Inhaled Flower**
Stratification: **Pain**
Correlation: **Effective Dosage “3-4 puffs”**
Certification: **Effect Index = 1.5**

Narrow Effect Index

For Pain, recommend “Earth” Aroma-types



Acknowledgements

Divergence Neuro – Clinical Trials Information Technology

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MediCann – Participant recruitment

NeuroMeditation Institute – QEEG and Survey Scales

Scientific Cell - Sponsor

SepSolve Analytical – Analytical Algorithms

Veda Scientific – Laboratory Analysis

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