3RD ANNUAL EMERALD CONFERENCE

A REVIEW OF PRELIMINARY DATA TRENDS IN THE DOSING PROJECT™, A NOVEL APPROACH TO CANNABIS CLINICAL STUDY

John S Abrams, PhD

Session III: Regulatory Certification, Accreditation, & Standardization and Novel Clinical Development Paradigms

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Why is The Dosing Project Needed?

Current State: Many of the current efforts lack scientific and clinical rigor

We are proposing a web-based, crowd-sourced

observational study designed to establish baseline dosing standards

Use Initial Results to:

- Establish initial Dose & Mode of Administration (MOA) recommendations
- ID commercially viable indications at today's COGs
- Provide sourcing opportunities for patients as well as Manufacturers & Dispensaries

Logistic Regression: Whole Model Test Mining for a significant χ^2

Stratified by Indication; Grouped by: Agent, MOA
~~**Additional Regressors: Gender, Age, & Ethnicity (?)**~~

Full

Partial

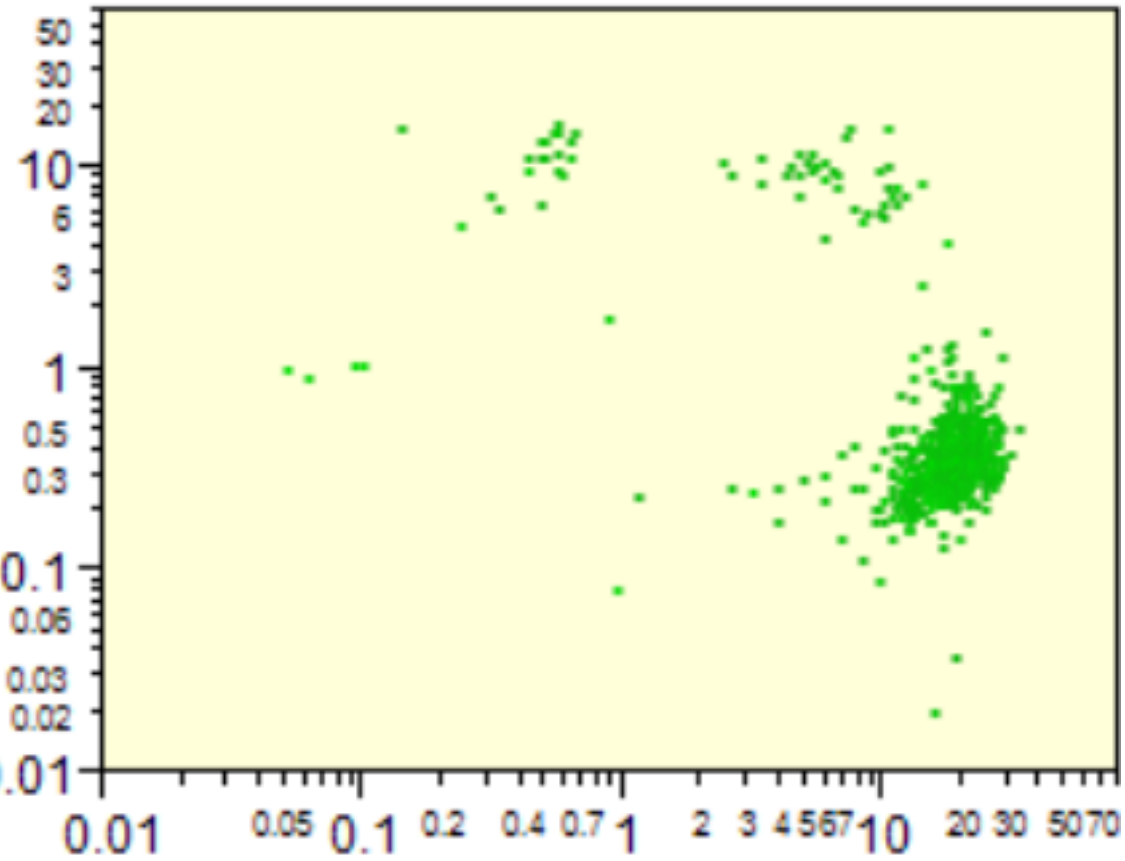
None

Continuous Scale
0.5 5.0

3

Scatterplot: Cannabis Flower Samples – CBD vs THC

Approximately Equal CBD : THC



High CBD : Low THC
10 : 0.5
(20:1)

n=686

flower)
10 : 8
(1.25 : 1)

High THC : Low CBD
20 : 0.4
(50 : 1)

Weight % THC (per dry

The Dosing Project™

Sign up at http://dosing.thecesc.org

It's simple!

Describe your strain…

Smell the flower…

High THC | THC ≈ CBD | High CBD | Floral | Earth | Fuel

How much did you puff?

Rate your experience.

The Dosing Project: Overview of Proof of Concept (POC) Phase

1. Self-reporting of symptom relief on 4 part categorical scale
2. Self-reporting of Cannabinoid Chemotype group (High CBD, Equivalent CBD:THC, or High

THC)

3. Self-reporting of Terpenoid Chemotype group ("Floral", "Earth", or "Fuel")

4. Self-reporting of indication

5. MOA limited to Smoking or Vaping of Flower 

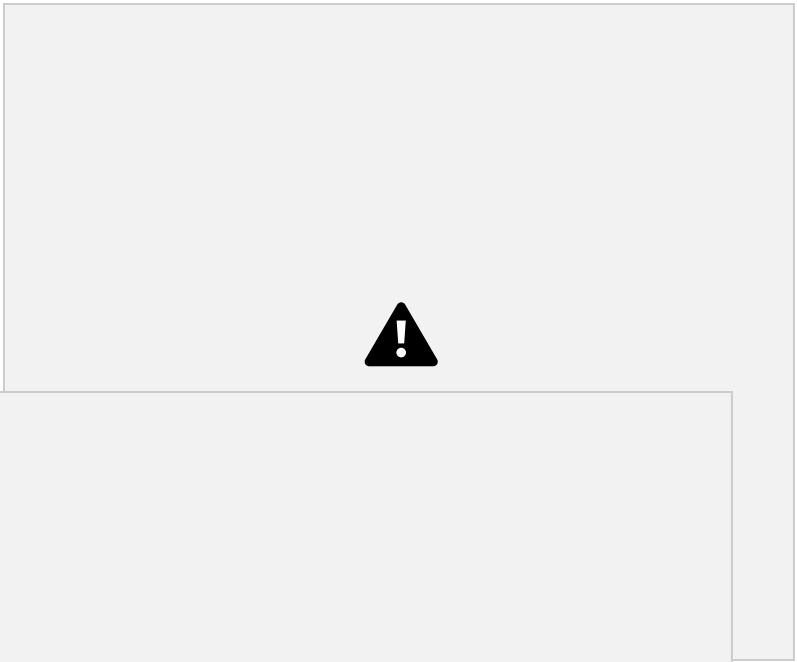
The Dosing Project: Overview of Proof of Concept (POC) Phase

Questions to be answered in this Phase: 1. Does the app work?

2. How robust is recruiting?

3. How easily can a statistically significant dose-response model be obtained for either indication?

Recruiting for The Dosing Project™



Pain

Sleep

Summary: Recruiting I

<u>Google AdWords potent marketing force to drive recruiting:</u>

- **Started campaigns in late June 2017**

- **Increased recruiting ~ 10 X over baseline rate • ~ 3 % CTR and 10 % of CTRs result in a valid TDP response**
- **Implies ~ 1/300 search page views (Impressions) will result in a valid TDP response**
- **Able to drive recruiting into targeted responder cohorts**

Summary: Recruiting II

<u>20161115 Thru 20180206</u>:

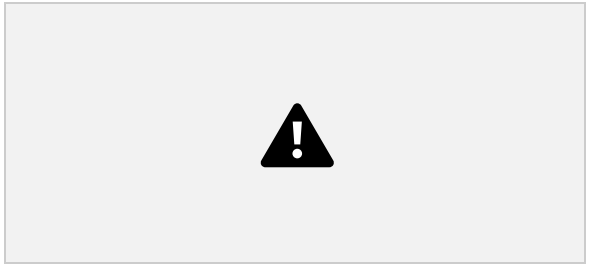
- **730 have initially logged into the app •**

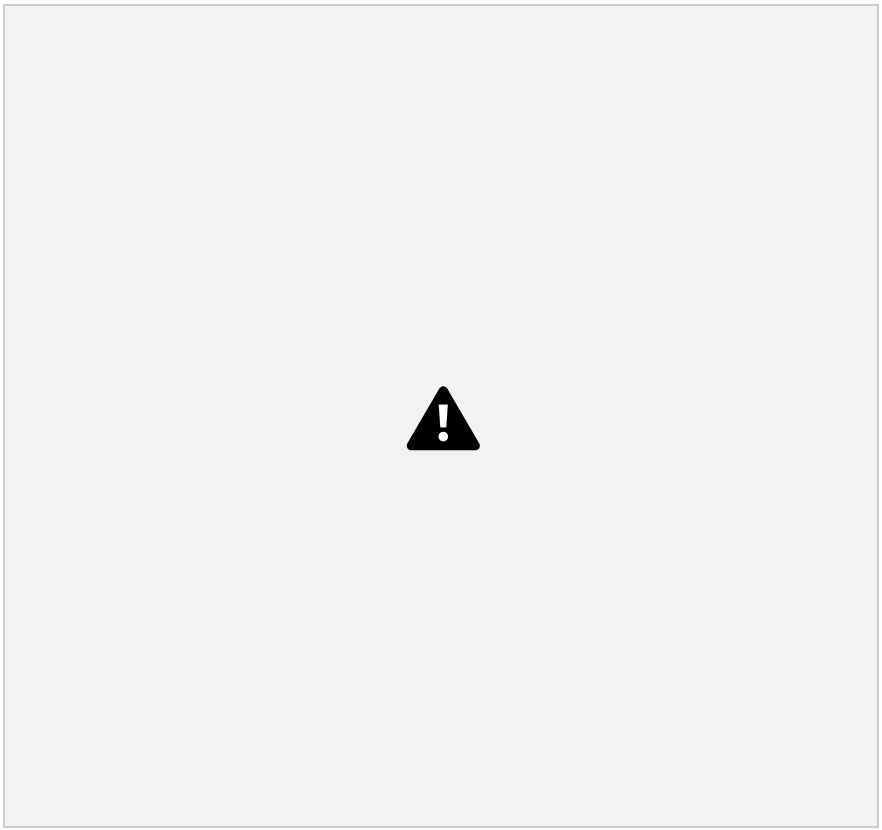
377 have completed valid responses •

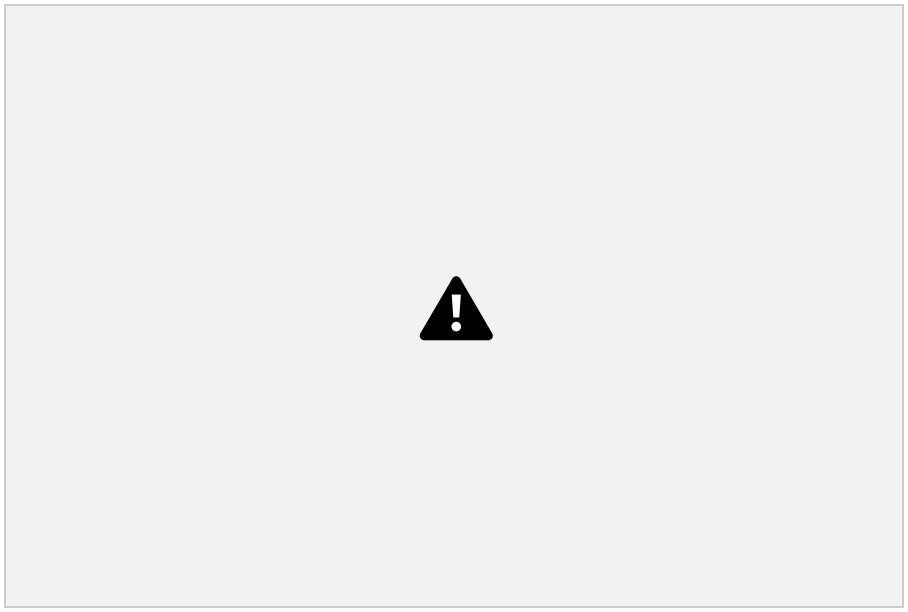
Principal reason for failure to complete a response is study ineligibility

- **Almost universally single, individual responders. Virtually no repeat responders currently.**

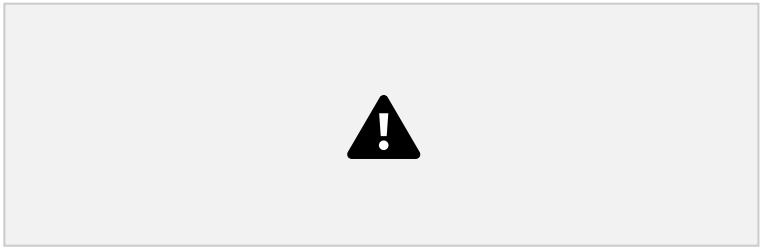
INDICATION



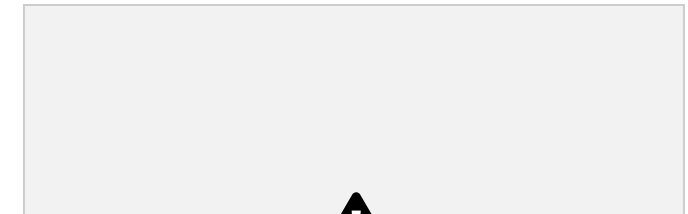




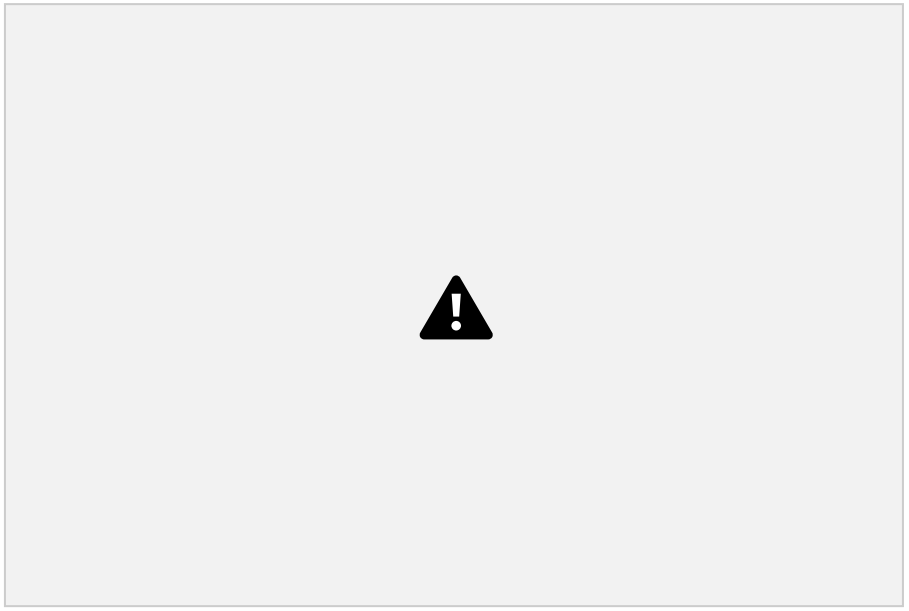
MOA

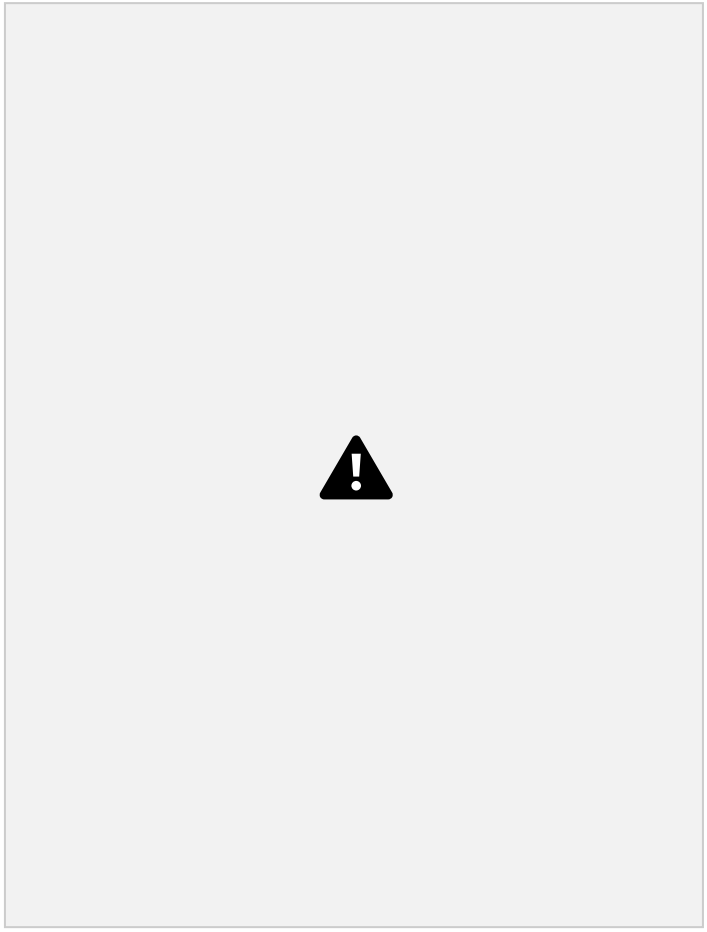


CANNABINOID



RATIO GROUP

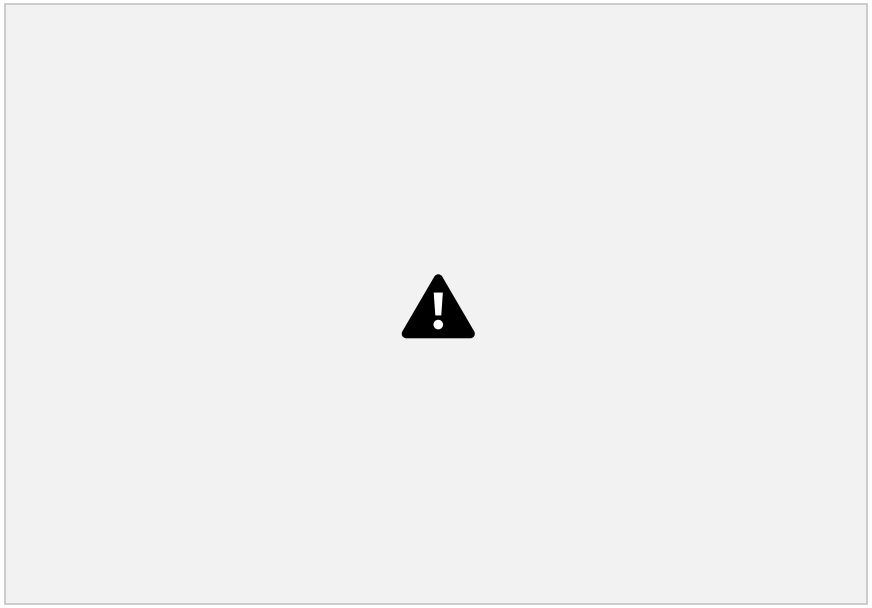


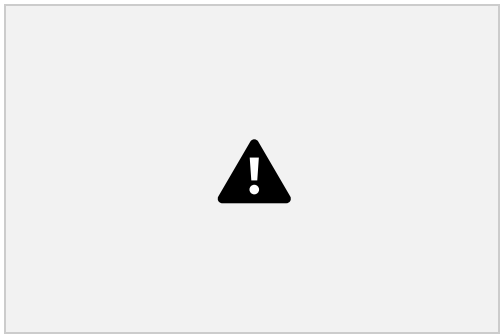


Dataset Cohort Counts Through 20180206

HI THC HI CBD THC EQUIV CBD 33 7

9 3 11 1





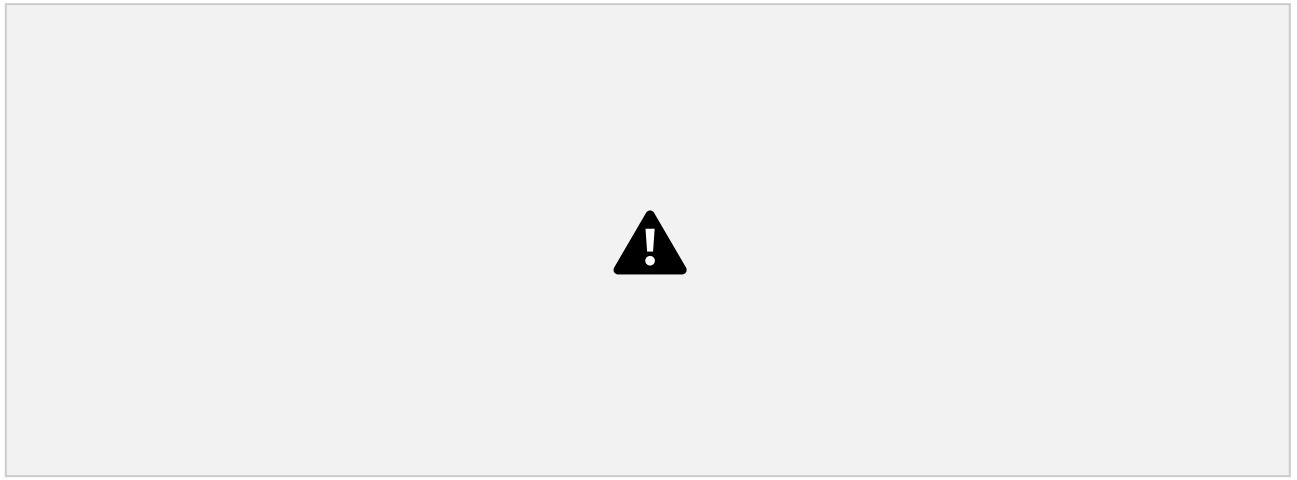
19 22 26 15

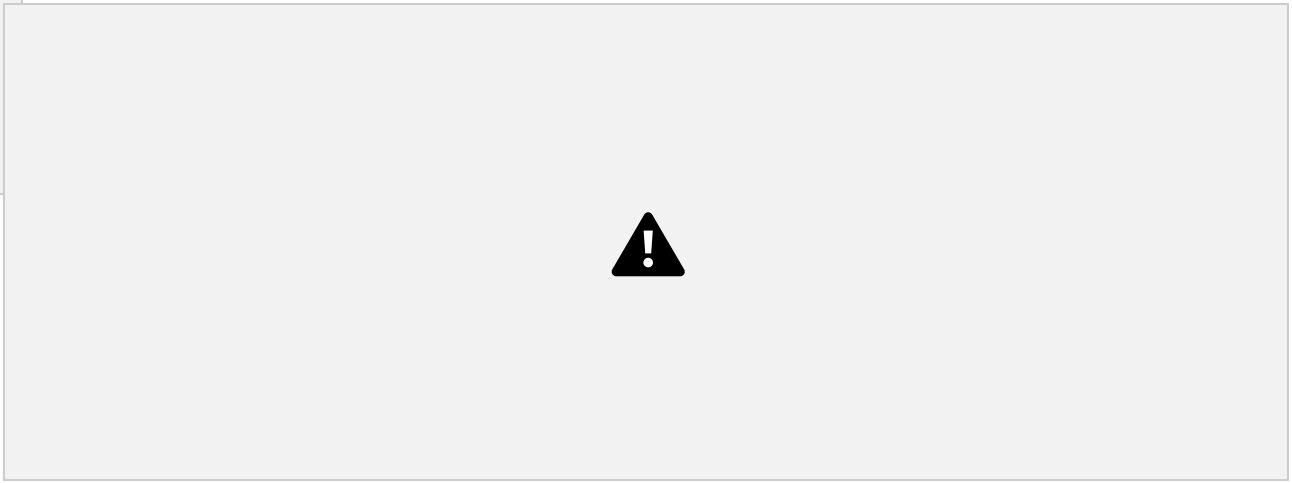
104 19

TOTAL N = 269

Timing of Reporting *

PAIN





SLEEP

*** 20171026 Dataset**

Dosage

PAIN

Puffs

SLEEP

0.5 1.0

16

1-2 3-4 5-6

Puffs

1-2 3-4 5-6

g

0.5 1.0

Summary: Use Patterns I

- **Amount of smoked Cannabis varies depending on indication:**
  - **For Pain: ~ 35 % are using 3-4 puffs per**

session
  - For Sleep: ~ 42 % are using 0.5 – 1 g per session
- Smoking or Vaping?
  - 75 % of Respondents are <u>SMOKING</u> Cannabis flower

Summary: Use Patterns II

- THC / CBD Ratio-Type:

- 3/5 use HI THC
- 1/5 use HI CBD
- 1/5 use HI THC EQUIV CBD

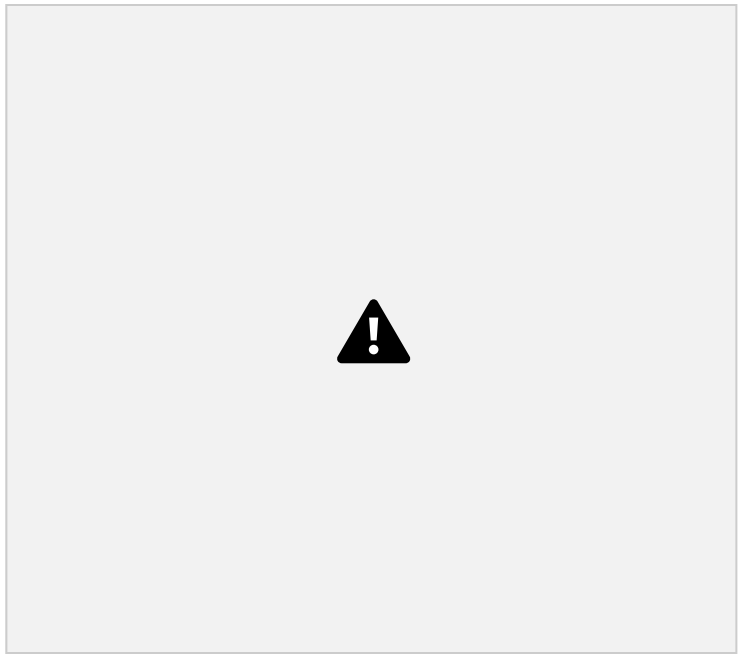
- **Response time interval since dosing:**
  - For Pain: > 60 % respond either immediately or within 1 hour after dosing
  - For Sleep: ~ 55 % respond after 8 - 16 hours of dosing

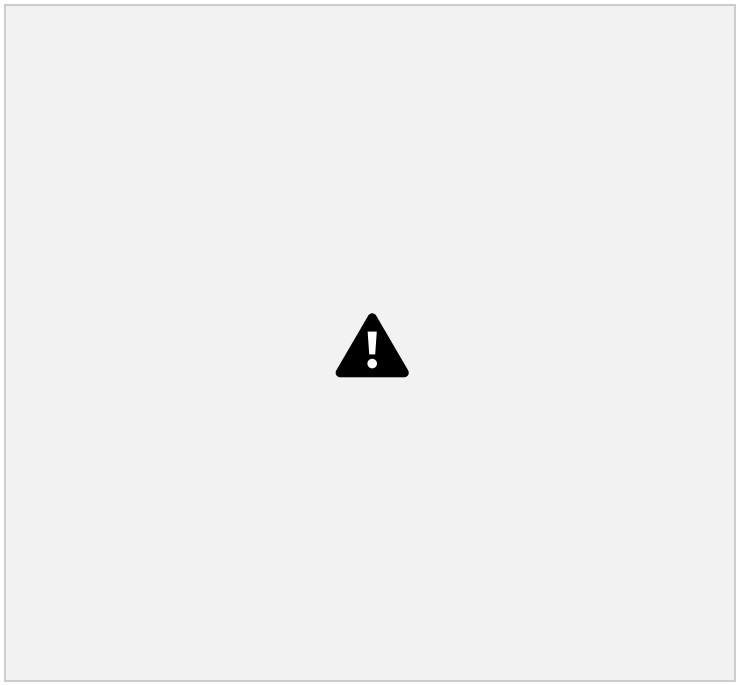
DATA TRANSFORM & ORDINAL

LOGISTIC REGRESSION MODELS

Need to Log Transform the THC_MPK

Data



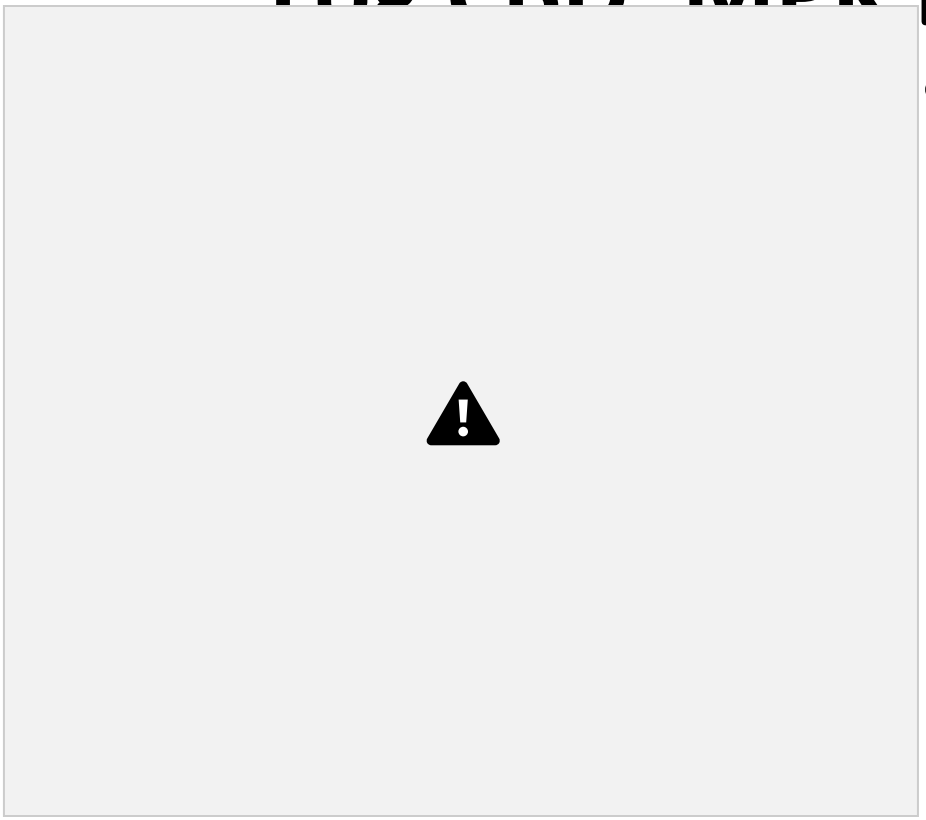


Shapiro-Wilk W Test Prob<W
<.0001

Prob<W
0.5896

Kolmogorov's D
Prob>D
> 0.1500
Shapiro-Wilk W Test

Log CBD_MPK Data Is Normally ibuted



Shapiro-Wilk W Test

Prob<W 0.9177

Ordinal Logistic Regression for Therapeutic Response

Indication **Whole Model Test Effect Likelihood Ratio Tests**

Source
Log_THC_mpk
Log_CBD_mpk
administration_type

Log_CBD_mpk*Log_THC_mpk Log_THC_mpk
Log_CBD_mpk
administration_type

N Prob>ChiSq Prob>ChiSq 0.037

Pain 205 0.0042 Sleep 0.2427

0.9252

0.0102

0.4145

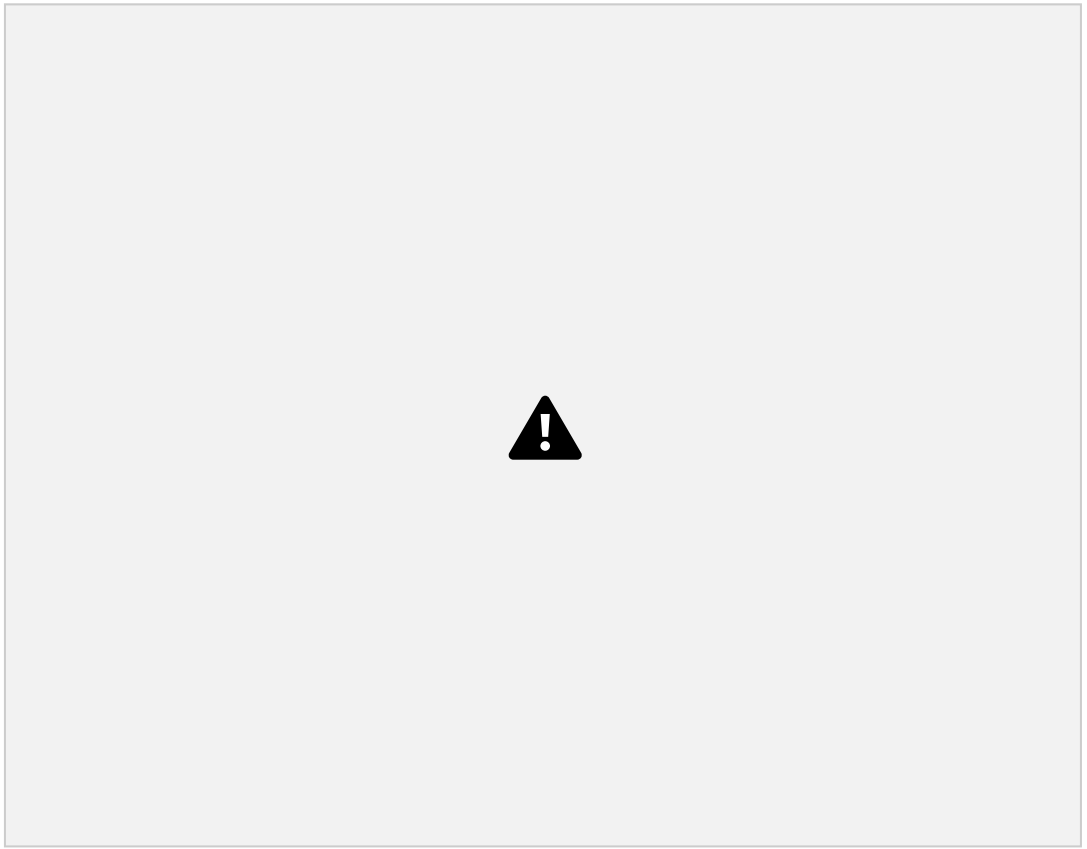
63 0.0272 0.1475

Log_CBD_mpk*Log_THC_mpk 0.0749

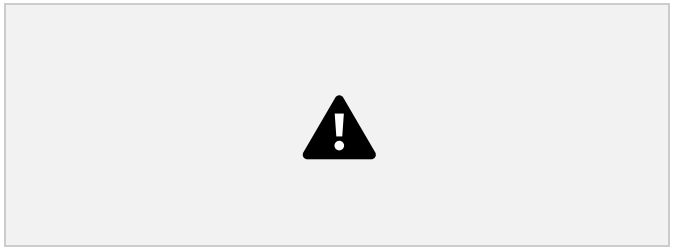
0.8693

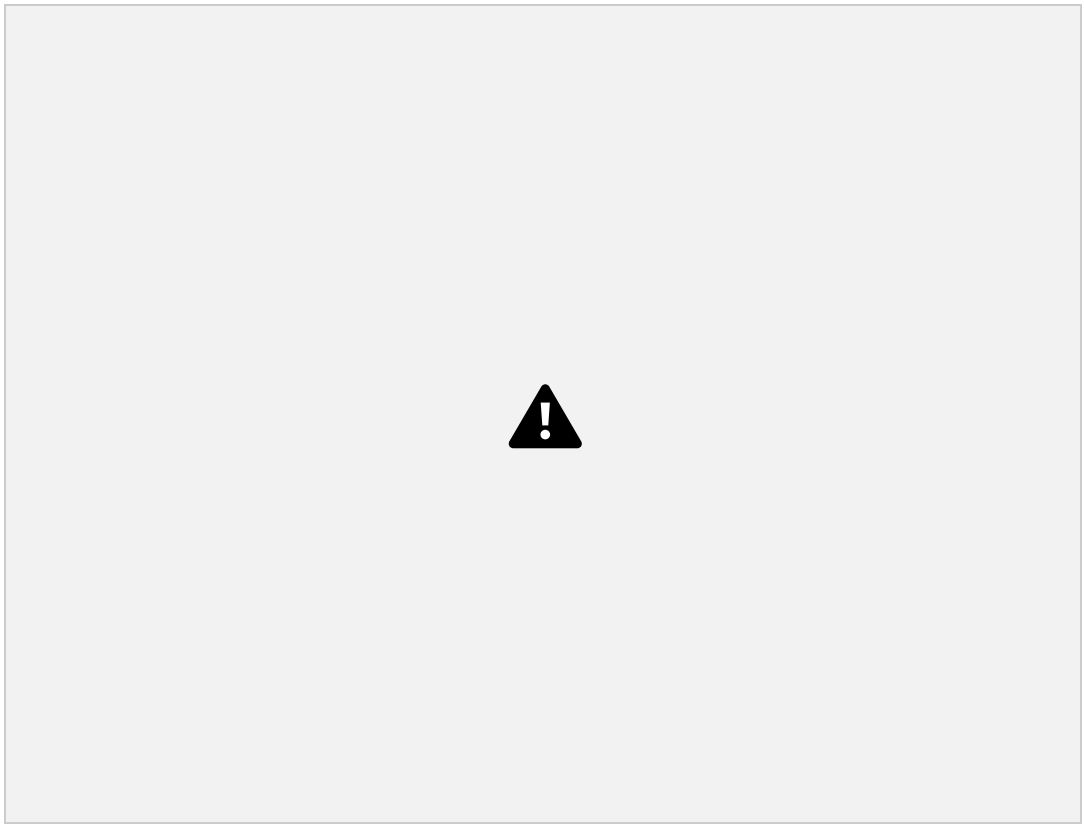
* P < 0.05

Pain: Ordinal Logistic Regression of Therapeutic Response vs Log_THC_MPK



Sleep: Ordinal Logistic Regression of Therapeutic Response vs Log_THC_MPK





Pain: Plot of Therapeutic Response vs Log_THC_MPK

Sleep: Plot of Therapeutic Response vs Log_THC_MPK

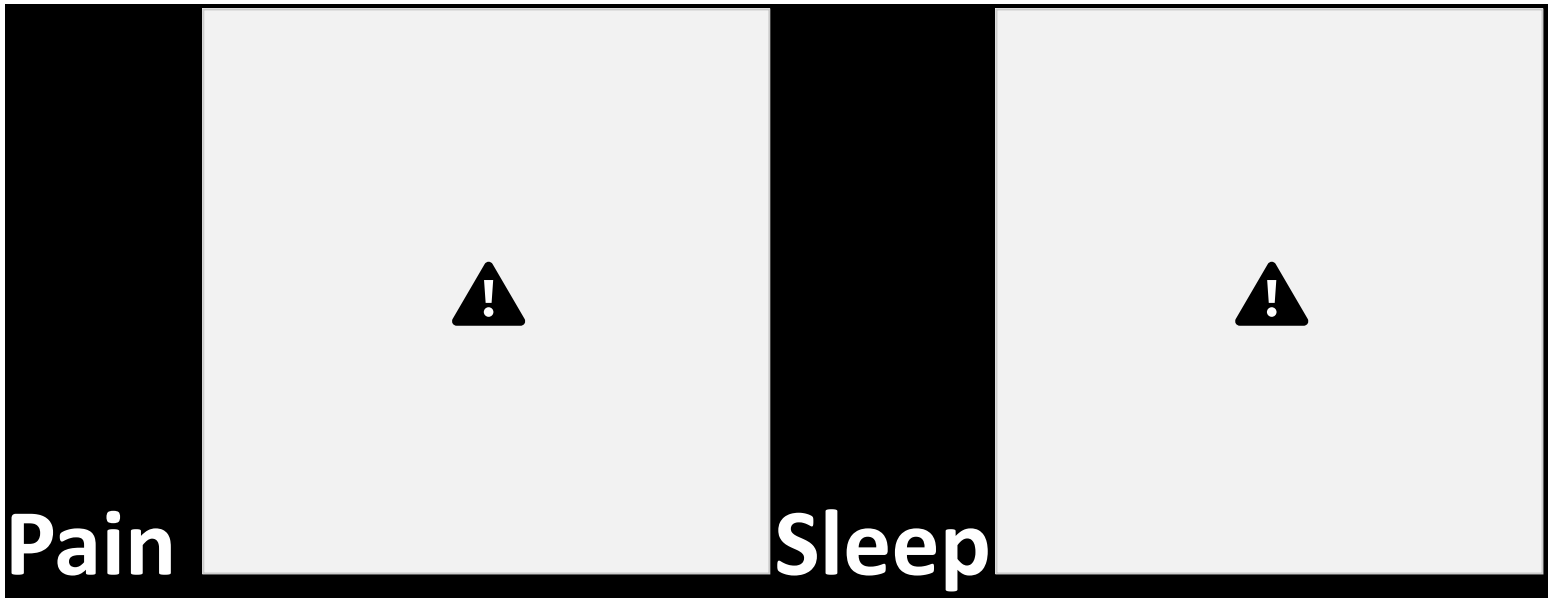
Response – Dose for Pain

Complete Response: Median Dose = 0.94 mpk

e – Dose for Sleep

Complete Response:
Median Dose = 1.22 mpk

Prediction Profiler



@ 1 mpk THC (inhaled)

For Pain: **57 % probability** of “Complete” or “Almost Complete” response

For Sleep: **80 % probability** of “Complete” or “Almost Complete” response

The Dosing Project:

Logistic Regression with Effect Likelihood Ratio Tests and Profiler Prediction to Determine Optimal Dosing

Completely improved

Almost completely improved

Somewhat improved

No

"Complete Response"

- Sleep: 1.22

Cohort median mpk

dose: •

Pain: 0.94 mpk

Continuous

improvement

0.5 5.0

1.0

The Dosing Project:

Logistic Regression with Effect Likelihood Ratio Tests and Profiler Prediction to Determine Optimal Dosing

Completely improved

Almost

"Almost Complete" outcome @ 1 mpk THC

Achieving a "Complete" or (inhaled) has a:

Pain: 57 % Probability

completely improved

Somewhat improved

No

Sleep: 80 %
Probability

Continuous

improvement

0.5 5.0

1.0

The Dosing Project:

Logistic Regression with Effect Likelihood Ratio Tests and Profiler Prediction to Determine Optimal Dosing Ordinal Logistic Regression

Completely improved

Almost completely improved

Somewhat improved

No improvement

Curve: for Sleep

- Steeper
- Different pharmacologic mechanisms ?
- Lack of stratification in Pain cohort ?

Continuous

0.5 5.0

1.0

Based on Analysis of 20171026 Dataset

SIDE EFFECTS / ADVERSE EVENTS (AE'S}

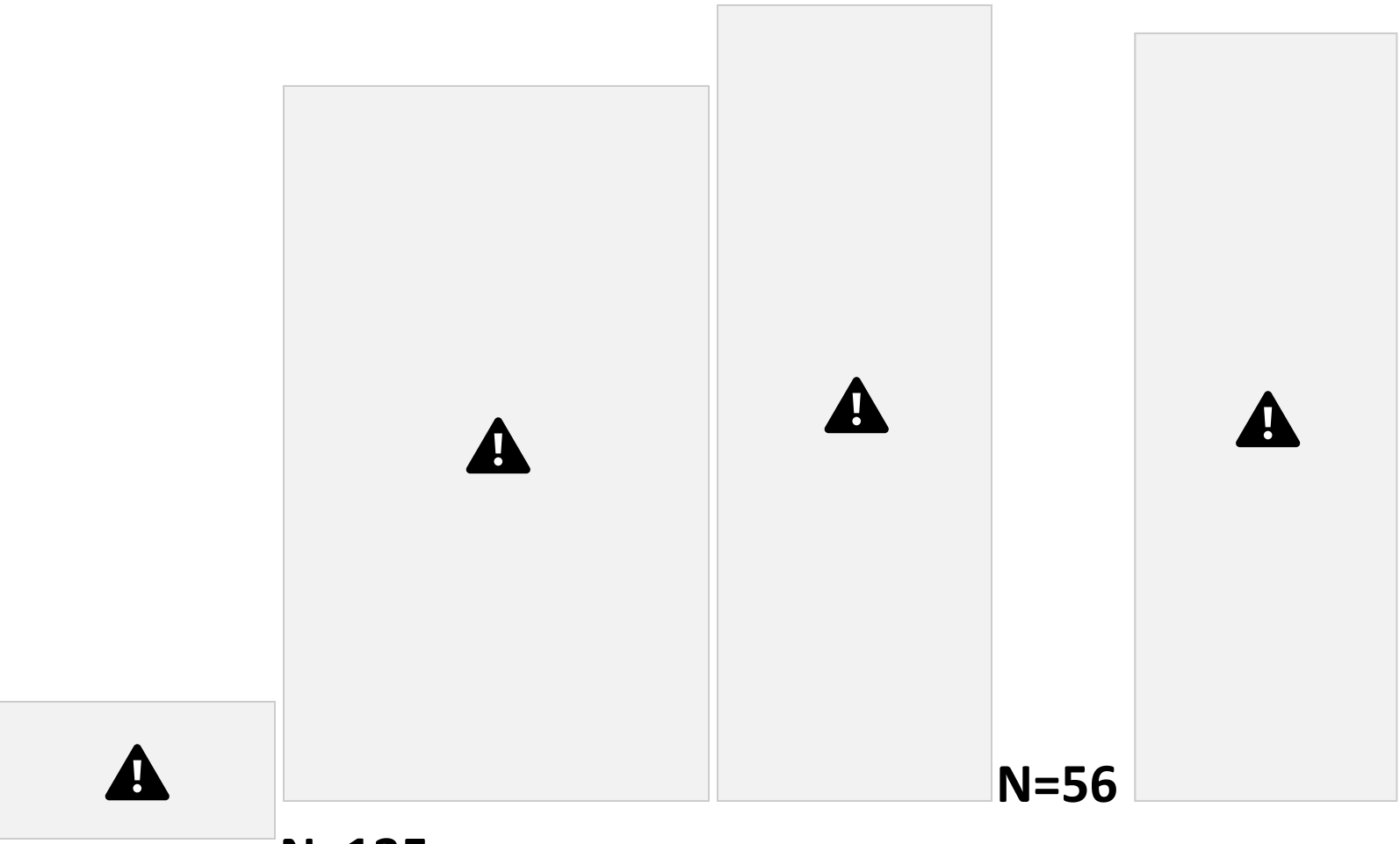
E’s: THC – Pain & Sleep

AE’s: CBD – Pain & Sleep

Dosages: Combined Pain & Sleep

Reported Side Effect Frequencies for Smoking or Vaping Cannabis Flower

Side Effect Vaping Smoking



Normalized Incidence of Most

Frequent AE's by Dose

Dry Mouth Cough Incidence Incidence

Puffs
1-2 3-4 5-6
g
0.5 1.0

N = 234

Puffs

1-2 3-4 5-6

g

AE's: Summary & Conclusions

- Major AE'S likely reflect act of smoking or vaping rather than THC or CBD C API's. • Side Effect incidence profile is very similar between smoking and vaping flower • Dry Mouth > Cough > Fatigue / Sleepiness • Incidence by Dose for "Dry Mouth" & "Cough" is different for Smoking vs Vaping •

SYFT – MS collaboration to identify different components in the air stream from Smoked vs Vaped Cannabis Flower.

The Dosing Project: Overview of Proof of Concept (POC) Phase

<u>Questions to be answered in this Phase</u>:

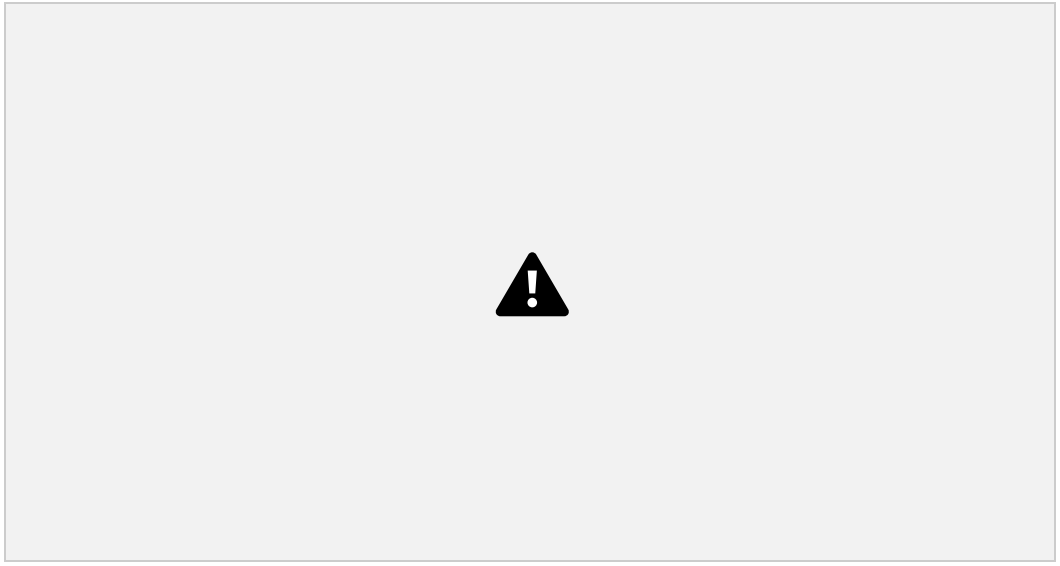
1. Does the app work?

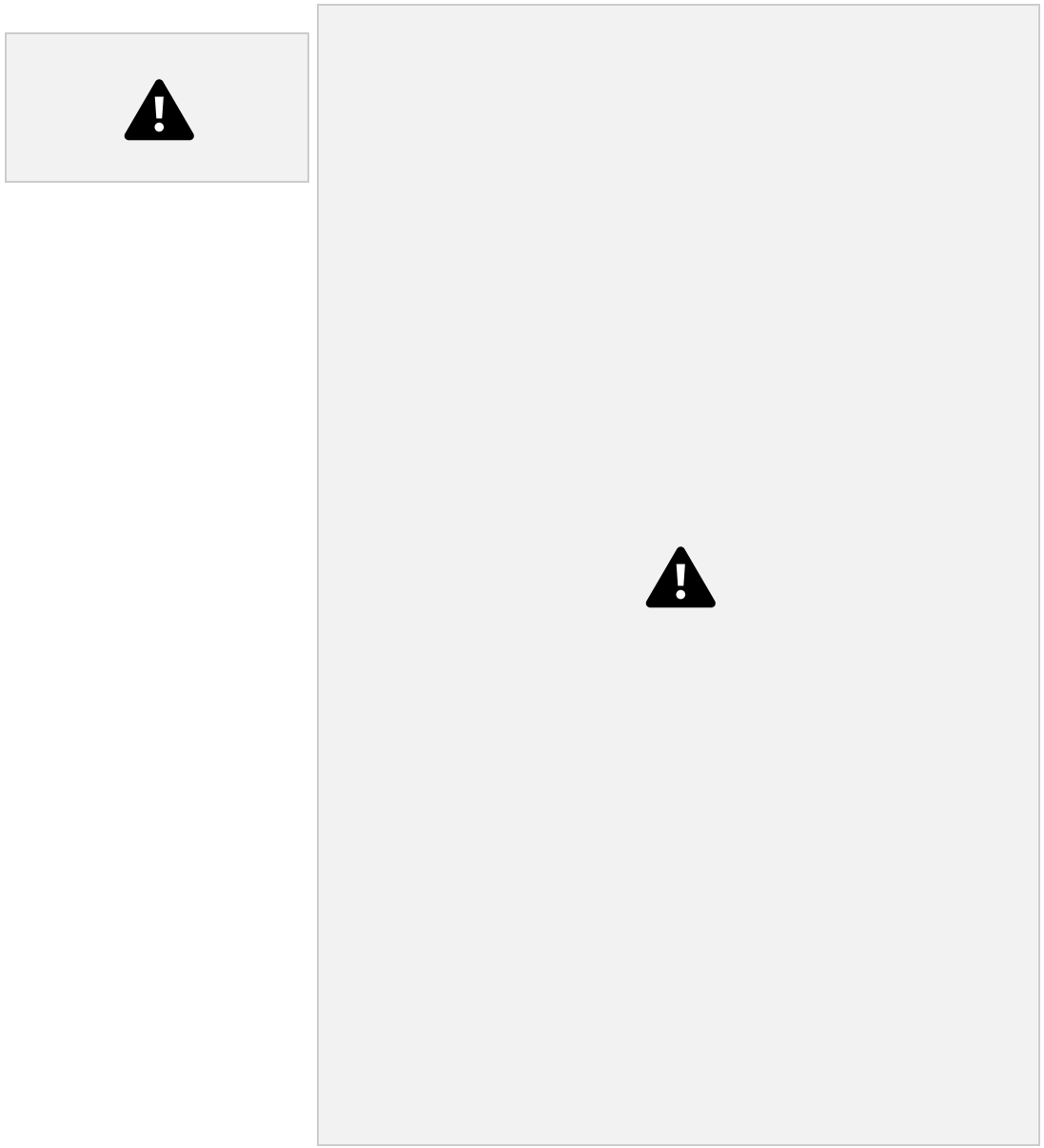
YES – Needs some minor additions

2. How robust is recruiting?

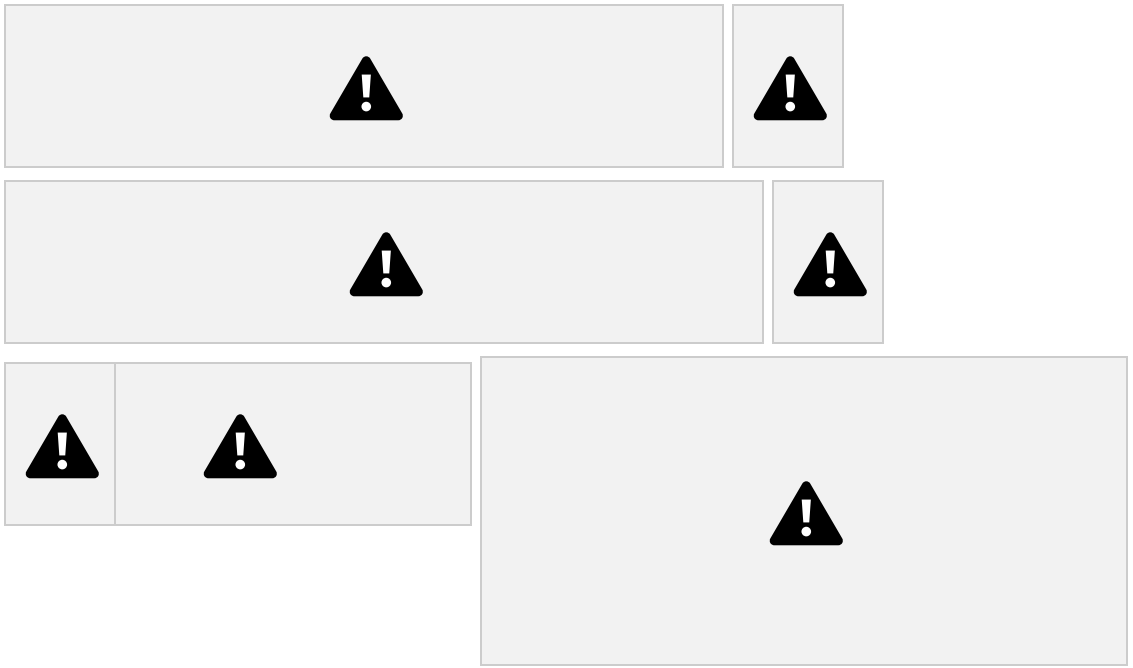
Works well when ad driven; exploring other options too. Need to expand to additional MOAs. 3. How easily can a statistically significant dose response model be obtained for either indication? Needs N > 60; More as additional Factors are added for Effect Likelihood Ratio Tests 

The Dosing Project™





Calculator Page



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