# The evidence for cannabis in Tourette syndrome: where are we?

May 19, 2023


**Presented By**:

Elia Abi-Jaoude, MSc, MD, PhD, FRCPC

SickKids Tics and Tourette's Clinic

UHN Tourette Syndrome Clinic

Assistant Professor, University of Toronto

# DISCLOSURE

No financial conflicts of interest

Acknowledgment: Tourette Association of America

# TEAM

- Tracy Bhikram, PhD
- Ferdous Parveen, MBBS
- Jody Levenbach, PhD C Psych
- Myriam Lafreniere-Roula, PhD
- Paul Sandor, MD FRCPC

# LEARNING OBJECTIVES

1. To describe the current evidence for cannabinoids in the management of tics
2. To know when to consider cannabis in the management of tics for adults with Tourette syndrome (TS)
3. To advise patients with TS on the potential benefits and harms of cannabinoids, and on practicalities around administration

# MEDICATIONS FOR TICS

- $\alpha_2$-Agonists – Level B, low-moderate confidence
- Antipsychotics – Level C, moderate confidence
- Adverse effects – Level A
- Other
  - THC, *adults* – Level C, low confidence

*Pringsheim et al, 2019*

# Reason for Referral

# Cannabis for tics

# BRIEF HISTORY OF CANNABIS IN CANADA

- 1923: Cannabis criminalized
- 2001: Medical Marihuana Access Regulations – medical cannabis
- 2013: Marihuana for Medical Purposes Regulations – plethora of options
- 2015: Definition of medical cannabis expanded – cannabis oil, fresh buds
- 2018: Cannabis Act - recreational
- 2019: Cannabis edibles, topicals, concentrates*

# Commonly Treated Conditions*:

Conditions we see:

- Chronic Pain
- Multiple Sclero
- Fibromyalgia
- Palliative Care
- HIV / AIDS
- Cancer
- Degenerative
- Neuropathy
- Arthritis, Oste
- Endometriosis
- Gastrointestin
- Spinal Cord D

- Anxiety
- PTSD
- ADD/ADHD
- Depression
- Insomnia
- Stress
- Panic Disorder
- Bipolar Disorder (Type 2)
- Borderline Personality Disorder

(PTSD)

isorder (ADHD)

OPINION

# Why We Need to Press Pause on Any Kind of Cannabis Promotion

## Many companies are selling marijuana as if the drug is totally harmless. It's not

November 25, 2018 | By Ruth Ross

If you talk to your friends or peruse the Internet, you will hear a lot about the wonders of cannabis. It makes you high, it makes you happy. It relieves pain, it curbs nausea, it reduces anxiety, it helps with depression and it aids sleep.

https://magazine.utoronto.ca/opinion/why-we-need-to-press-pause-on-cannabis-promotion/

# CANNABIS COMPOUNDS

- THC – partial agonist $CB_1R$ & $CB_2R$
- CBD – negative allosteric modulator $CB_1R$ & $CB_2R$
- Hundreds of compounds
- Terpenes

# CANNABINOID PRODUCTS

- Pharmaceutical
  - Nabilone
  - Dronabinol
  - Nabiximols
  - Cannabidiol
- Inhaled cannabis
  - Smoking
  - Vaporizing
  - Vaping
- Oral cannabis
  - Oil
  - Capsules
  - Edibles

# EFFECTS

## Benefits

- Antiemetic
- Appetite stimulation
- Decr pain
- Anti-spastic
- Anti-seizure

## Harms

- Dizziness
- Sedation
- Fatigue
- Psychomotor slowing
- “high”
- Amotivation
- Depression
- Irritability
- Anxiety
- Derealization/ depersonalization
- Altered perception
- Psychosis
- Dry mouth
- Red eyes

# CASE SERIES

- 14 of 17 patients decr tics & related Sx (*Müller-Vahl et al, 1998*)
- 17 of 18 patients very much or much improved (*Abi-Jaoude et al, 2017*)
- 38 of 42 any kind of benefit (*Thaler et al, 2018*)
  - hallucinations (4), irritability and confusion (6), cognitive decline (7), acute psychotic episode (1)
  - 10 of the 42 patients stopped after one year
- 98 patients: preference for THC-rich medical cannabis (*Milosev et al, 2019*)
- Pediatric age: 7 cases *(reviewed by Szejko et al, 2022)*

# CLINICAL TRIALS

- 12 adults, single dose cross-over RCT: oral THC > placebo (TSSL -14 vs -5, p=0.015) *(Müller-Vahl et al, 2002)*
- 24 adults, 6-wk RCT oral THC vs placebo: TSSL overall significant (p=0.037), but inconsistent *(Müller-Vahl et al, 2003)*
- 16 adults, 12-wk open-label THC/palmitoylethanolamide: YGTSS-TTS 20% improvement *(Bloch et al, 2021)*
- 49 adults, 12-wk RCT monoacylglycerol lipase inhibitor: YGTSS-TTS p=0.04 in favor of placebo *(Müller-Vahl et al, 2021)*
- 18 adults, 12-wk open-label cannabis: YGTSS 38% improvement *(Anis et al, 2022)*

# CANNABIS RCT

Efficacy and tolerability of three vaporized medical cannabis products and placebo for tics

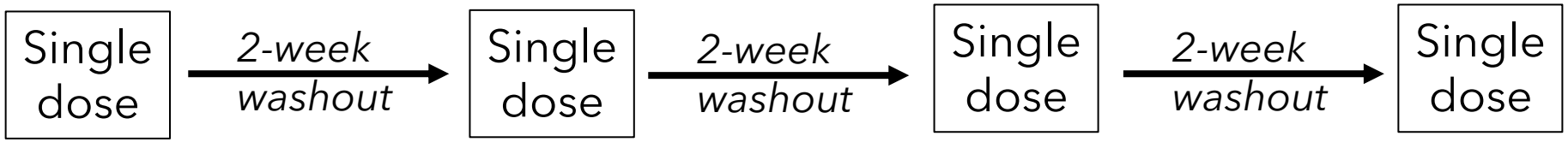
- Primary efficacy endpoint: MRVTRS
- Secondary efficacy endpoints: PUTS, SUDS, CGI-I
- Correlation with cannabinoid plasma levels
- Tolerability

# RCT OF CANNABIS FOR ADULTS WITH TS

vaporized cannabis, 0.25 g

- THC 10%
- THC/CBD 9%/9%
- CBD 13%
- placebo THC <0.3%, CBD <0.3%

# DESIGN



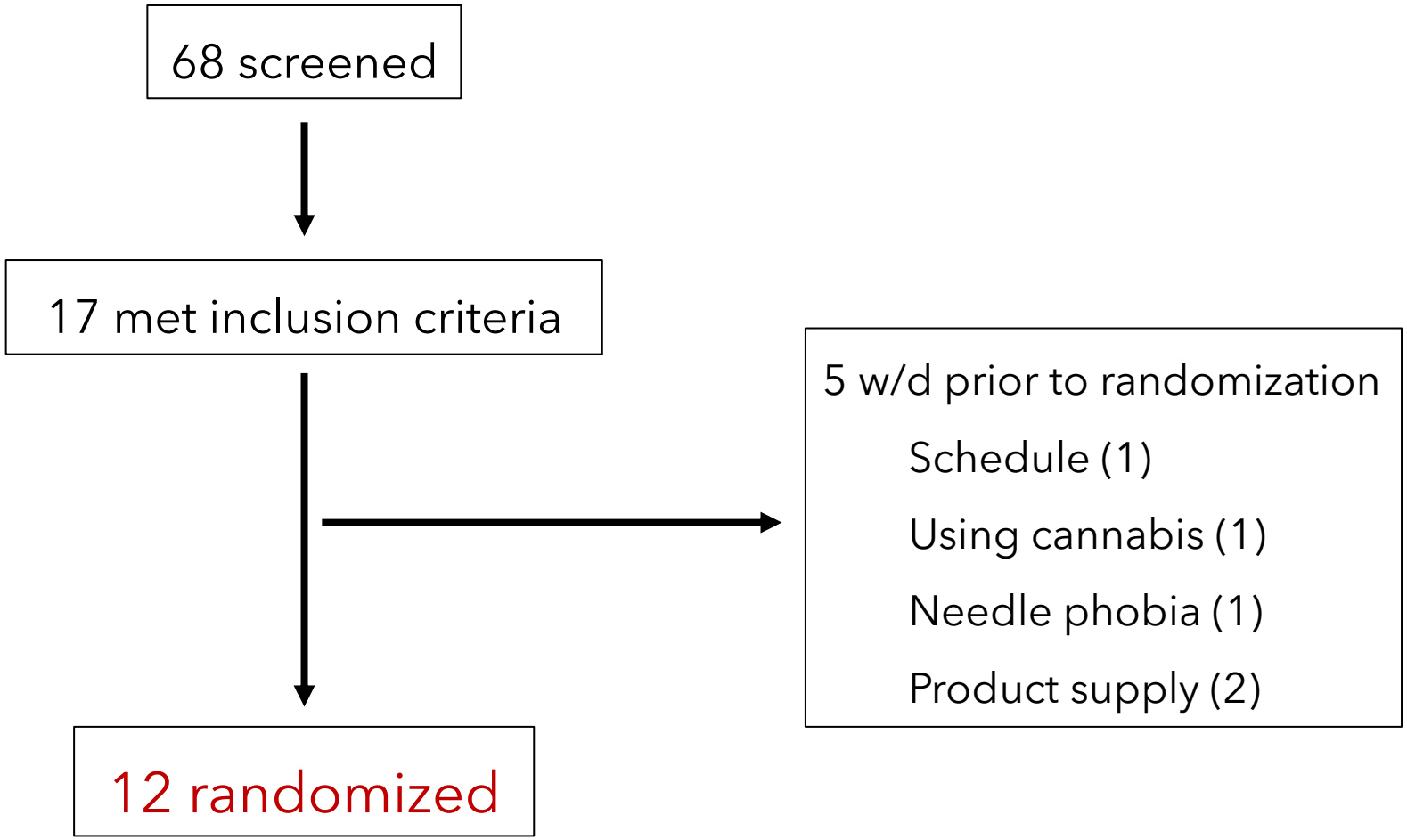

0, 0.5, 1, 2, 3, 5 hours

- MRVTRS, PUTS, SUDS, CGI-I
- Blood sampling: THC, OH-THC, COOH-THC, CBD

# ANALYSIS

- Nonlinear mixed effects modelling
- Repeated measures
- Adjusted for baseline score
- Treatment order effects
- Correlation with cannabinoid plasma levels
- Adjusted for multiple comparisons

# PARTICIPANTS



# DEMOGRAPHICS & CLINICAL HX

- 11 males, 1 female; 38 yo (22-54)
- OCD (7), ADHD (6), anxiety (4), depression (3), ASD (1)
- YGTSS-TTS 28.7 (15-44)
- Concurrent meds – 7 participants

  - Antipsychotic (3)
  - SSRI (3)
  - Stimulant (2)
  - Benzodiazepine (3)
  - Benztropine (2)
  - Bupropion (1)
  - Anticonvulsant (1)
  - Other (4)

- Past cannabis use (3)

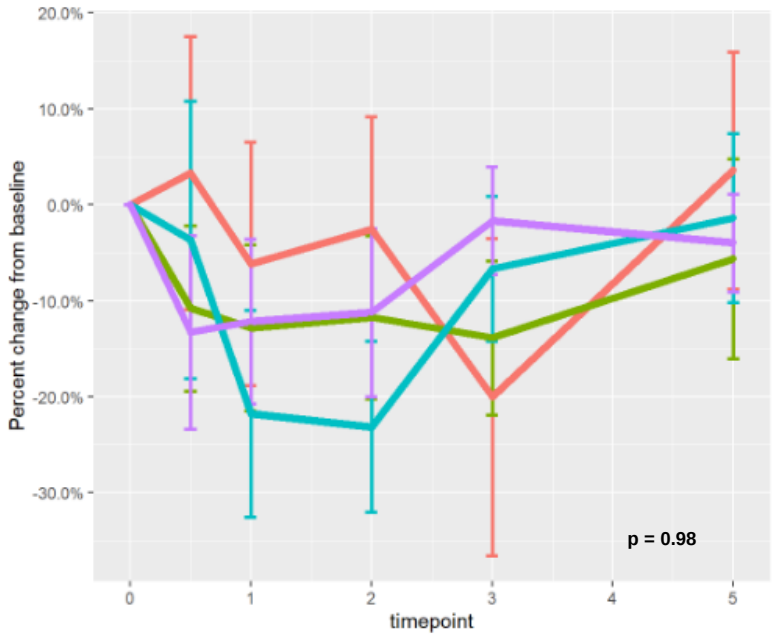
# DROPOUTS

3 dropouts

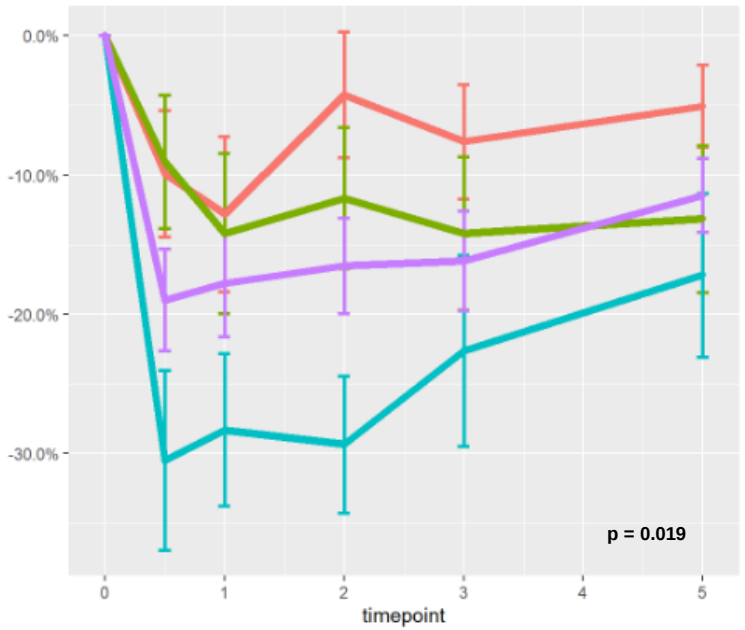
- Adverse event – syncope/seizure (1)
- Unable to draw blood (1)
- Schedule (1)

# EFFICACY...

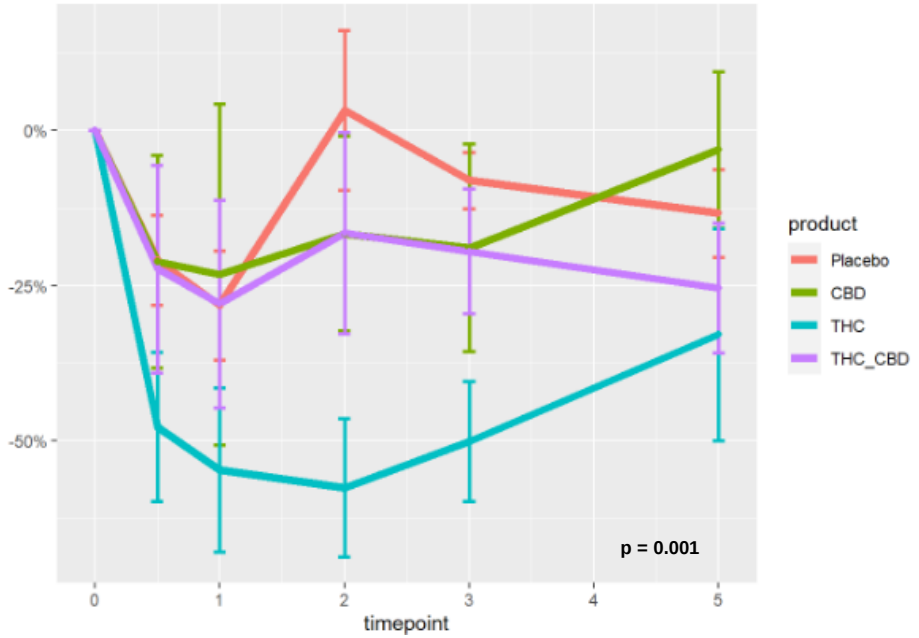
## MRVTRS




## PUTS

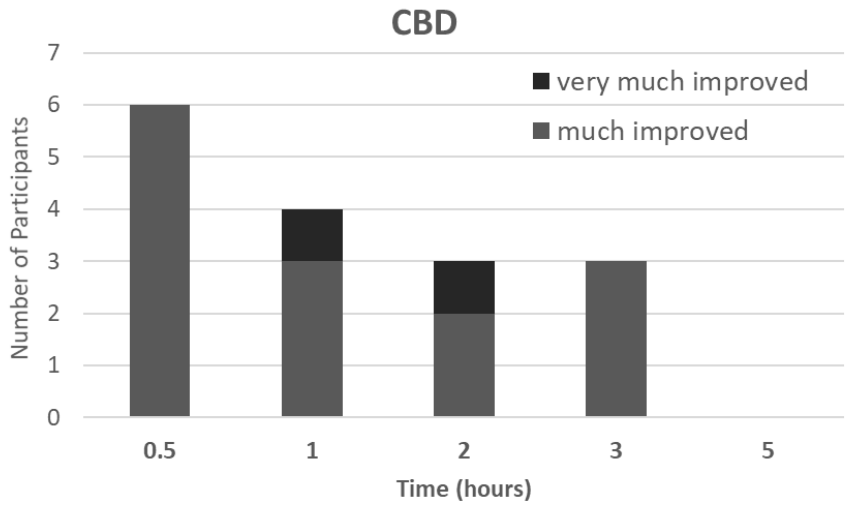


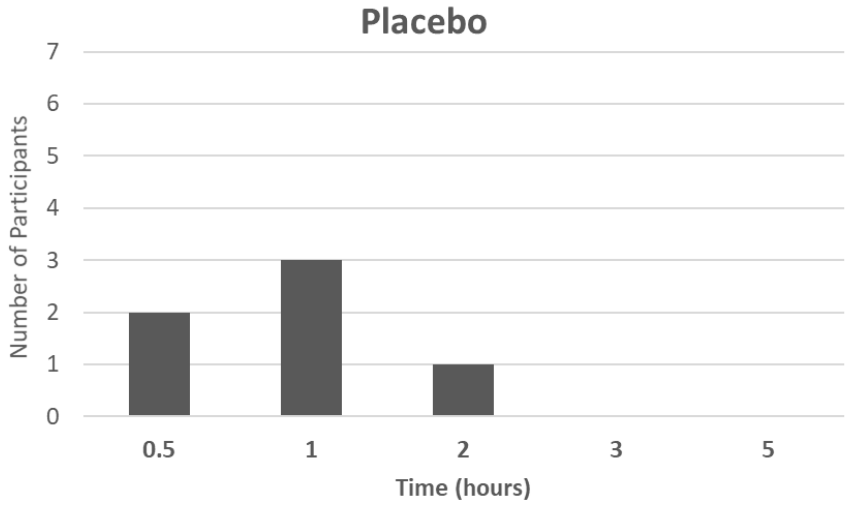

## SUDS

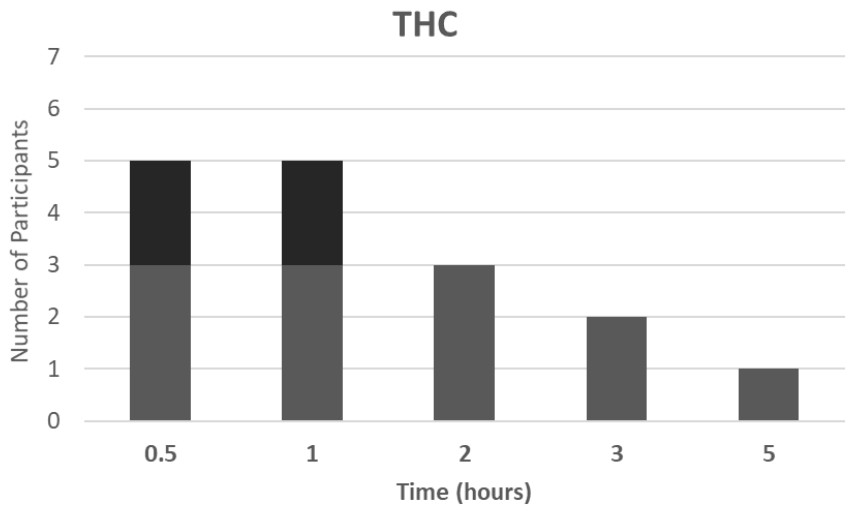


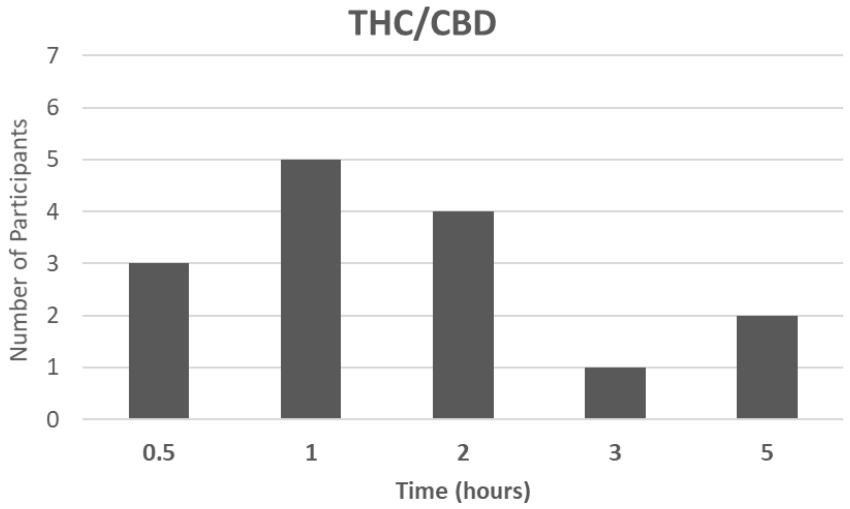
# ...EFFICACY...

## CGI-I

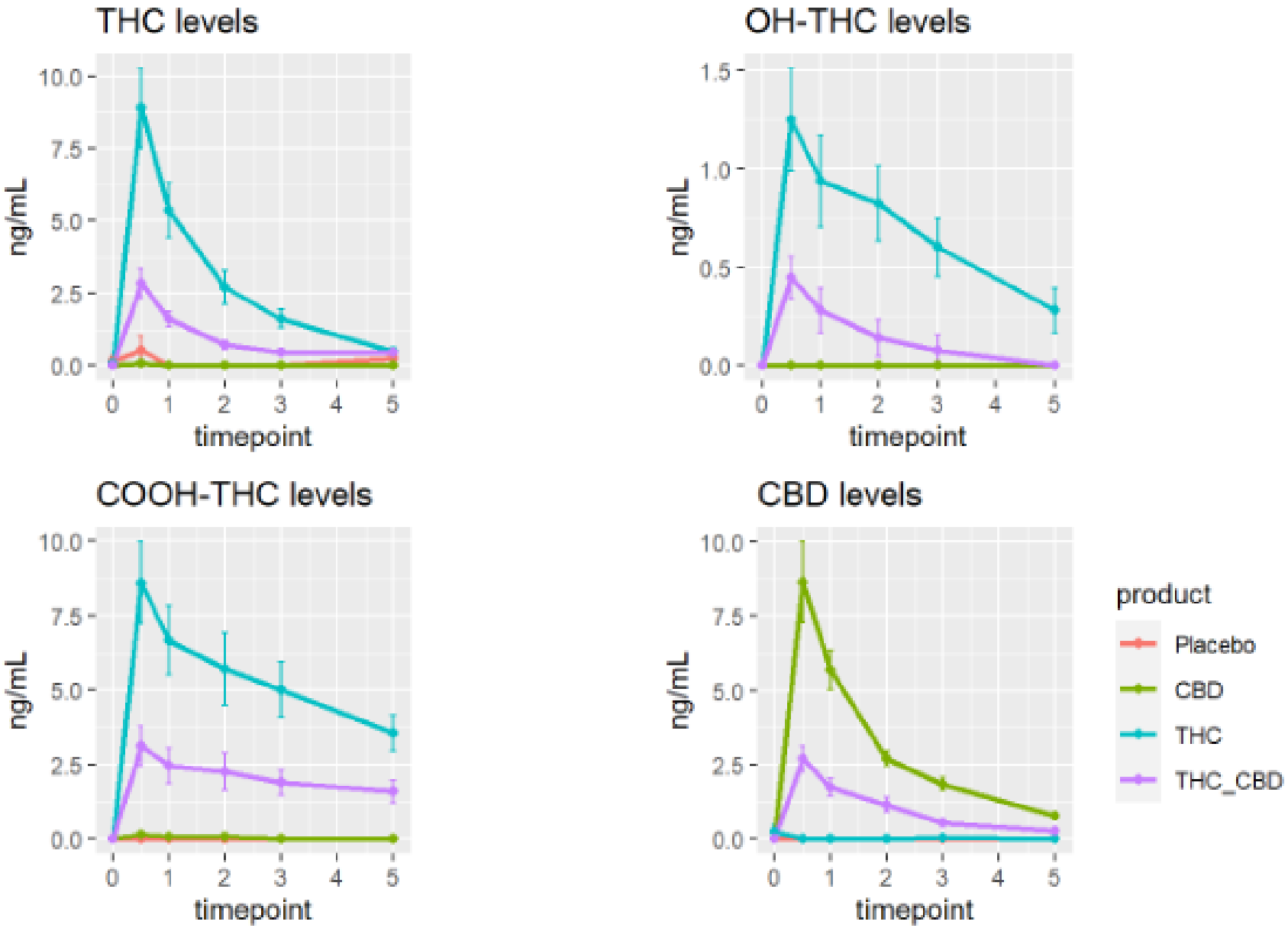


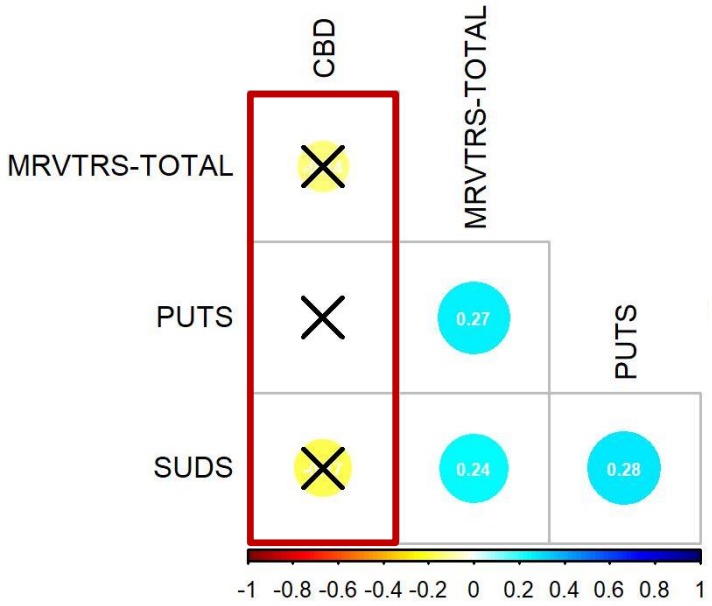
# PLASMA LEVELS



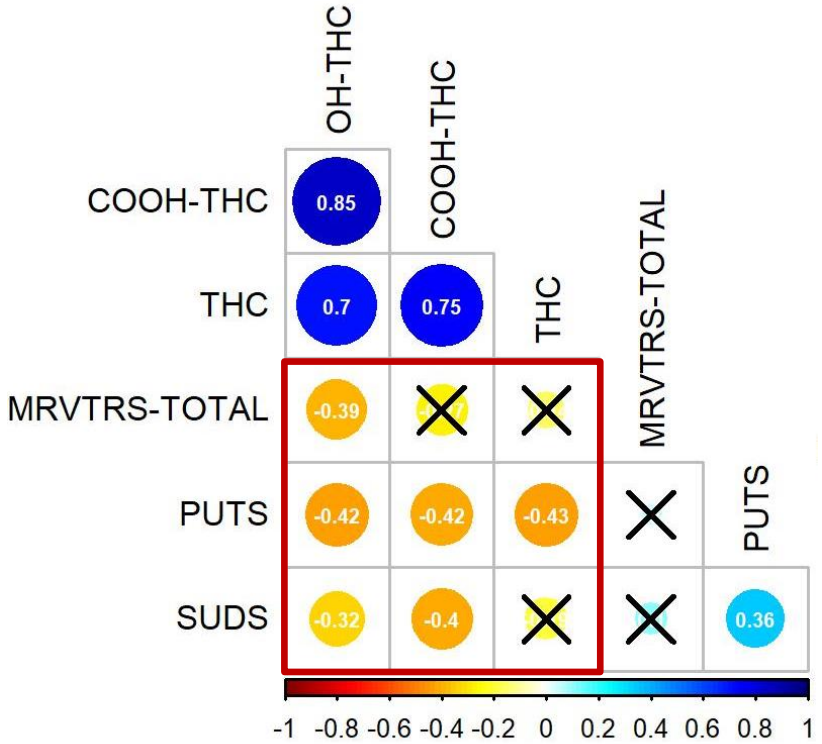
# ...EFFICACY

Correlations with cannabinoid plasma levels across all time points

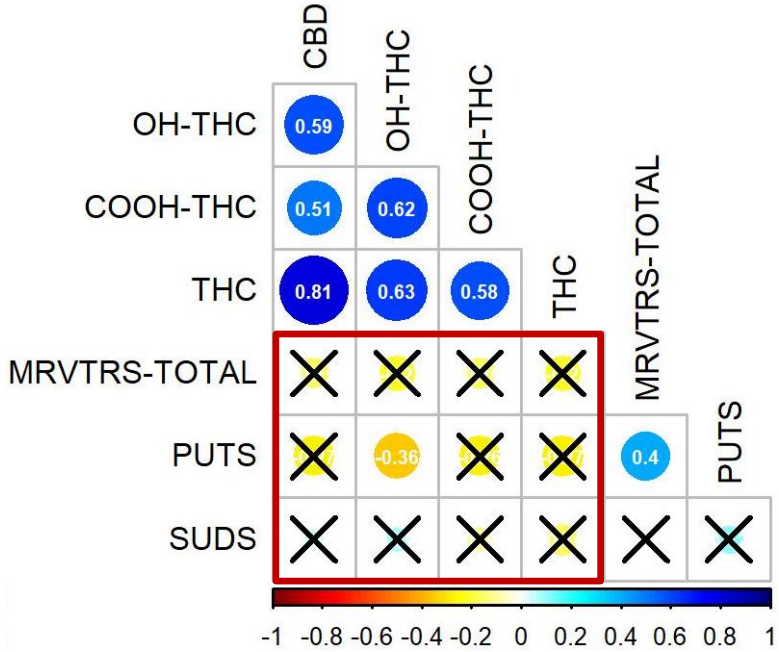
## CBD 13%



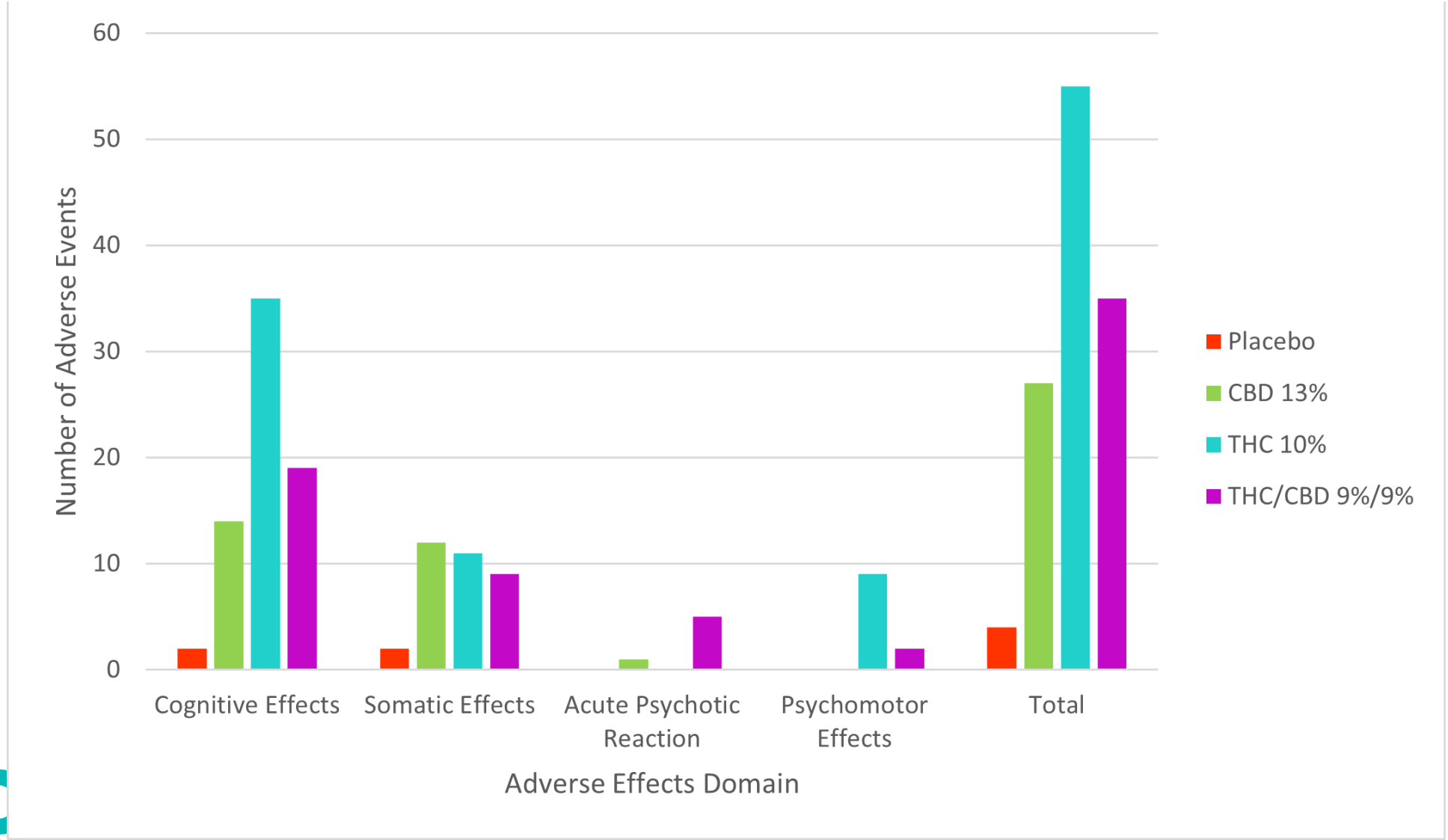

## THC 10%



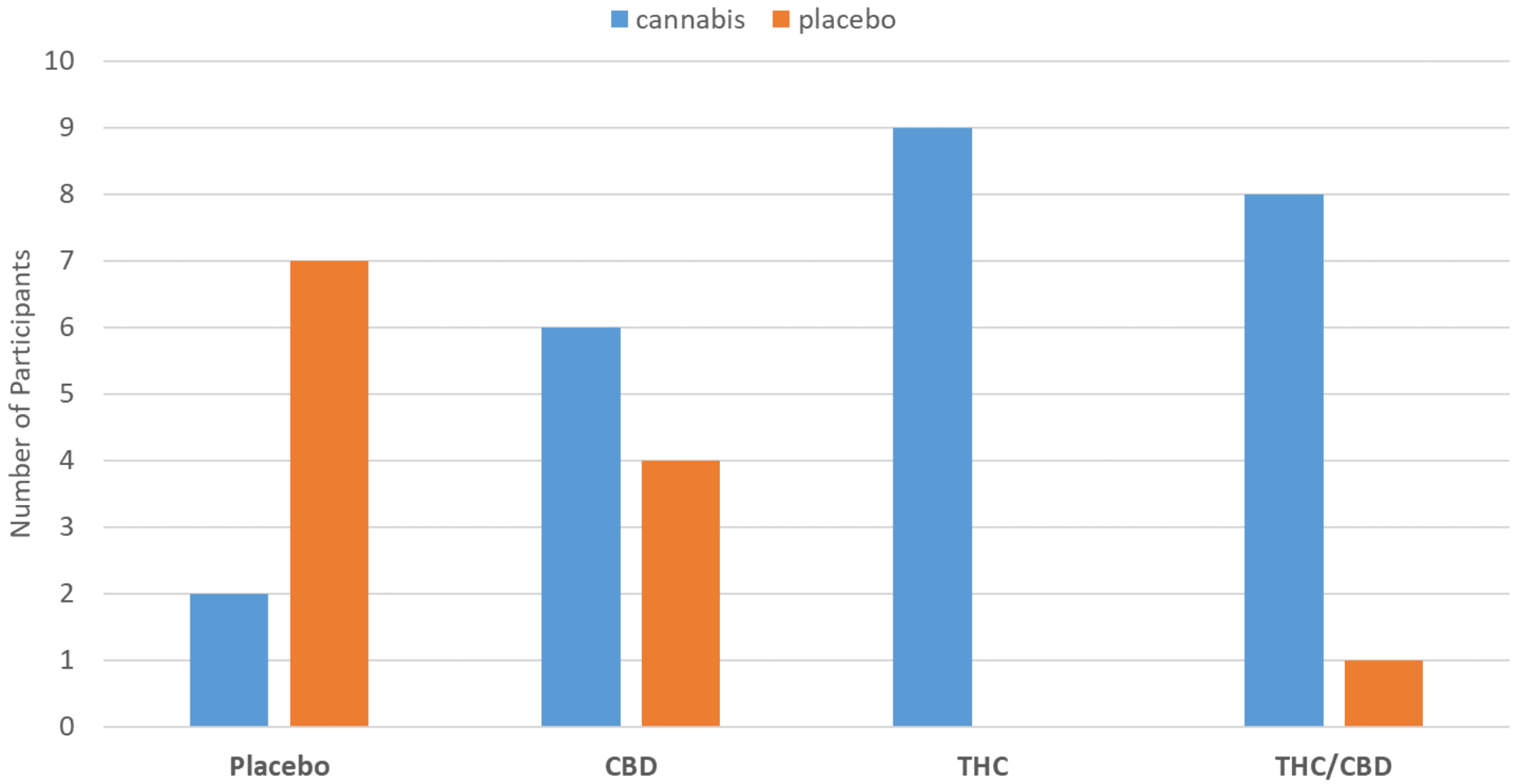

## THC/CBD 9%/9%



# TOLERABILITY



# BLINDING SUCCESS



# LIMITATIONS

- Sample size
- Single dose
- Fixed dose
- Delivery
- Blinding
- Adult population

# NEXT STEP

- Chronic treatment cross-over RCT
- THC-based oil
- Flexible dosing

# In Practice

# AAN GUIDELINES ON CANNABINOIDS

- THC, *adults* – Level C, low confidence
  - Treatment resistant
  - Already using efficiently
- Medical supervision – Level A
- Lowest dose – Level A
- Periodically re-evaluate need – Level A
- Driving – Level A

*Pringsheim et al, 2019*

# POTENTIAL OPTIONS

- Pharmaceutical
  - Nabilone
  - Dronabinol
  - Nabiximols
  - Cannabidiol
- Inhaled cannabis
  - Smoking
  - Vaporizing
  - Vaping
- Oral cannabis
  - Oil
  - Capsules
  - Edibles

# CAUTION

- Harms / functional impact
- Psychosis, mania
- PK/PD interactions – CYP450 2C9, 3A4
- Smoking
- Driving
- Legal

# CONCLUSIONS

- THC – benefit, harms
- CBD – no clear anti-tic effect
- Caution
- Evidence still emerging
- Collaborative relationship
- *Adults*