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

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DISCLOSURE

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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

- α_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

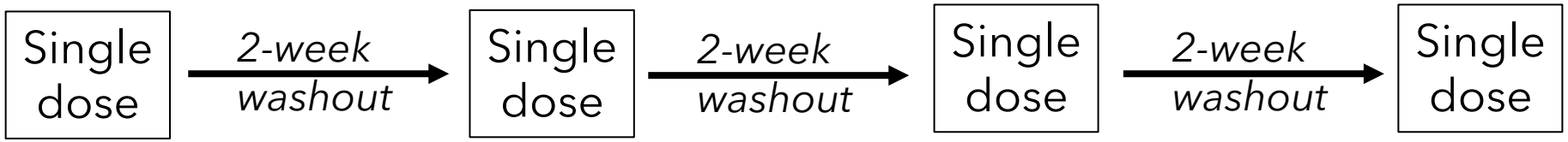
- Primary efficacy endpoint: MRVTRS
- Secondary efficacy endpoints: PUTS, SUDS, CGI-I
- Correlation with cannabinoid plasma levels
- Tolerability

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



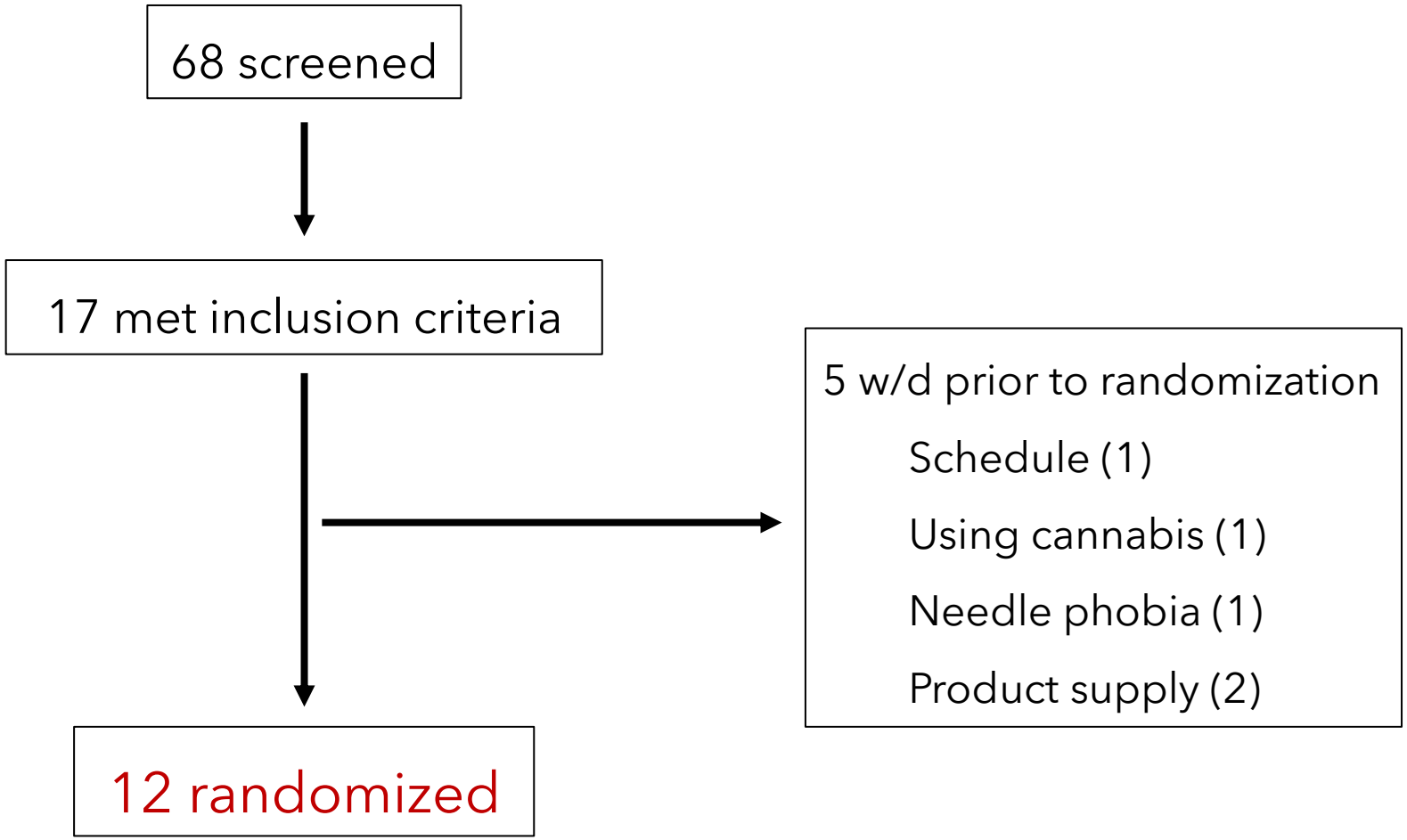
0, 0.5, 1, 2, 3, 5 hours

- 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)

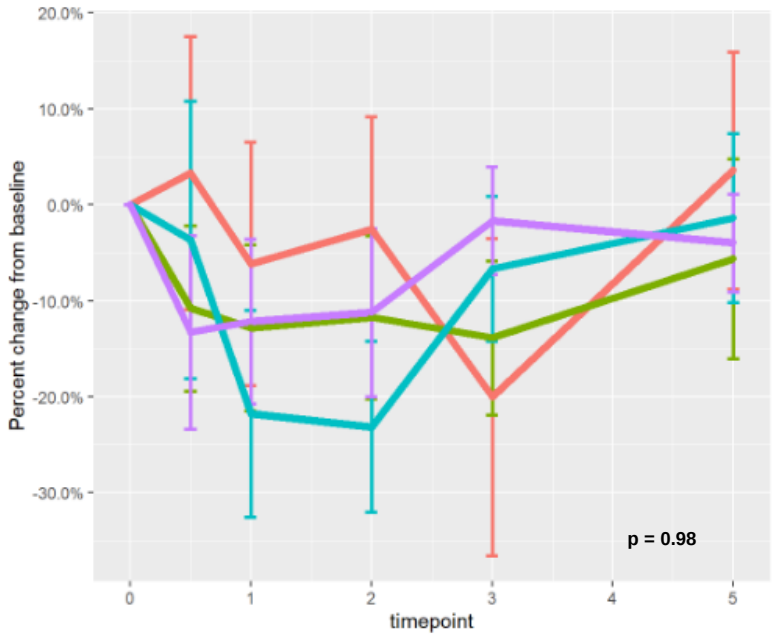
DROPOUTS

3 dropouts

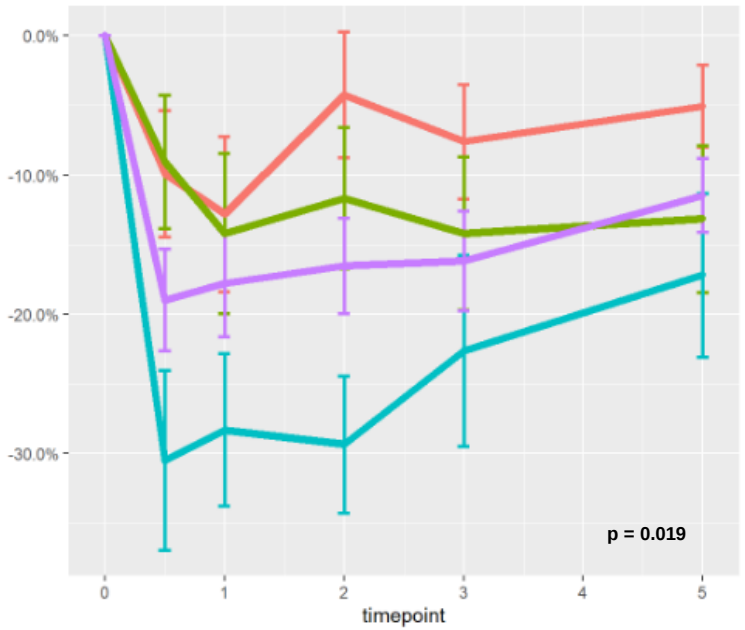
- Adverse event – syncope/seizure (1)
- Unable to draw blood (1)
- Schedule (1)

EFFICACY...

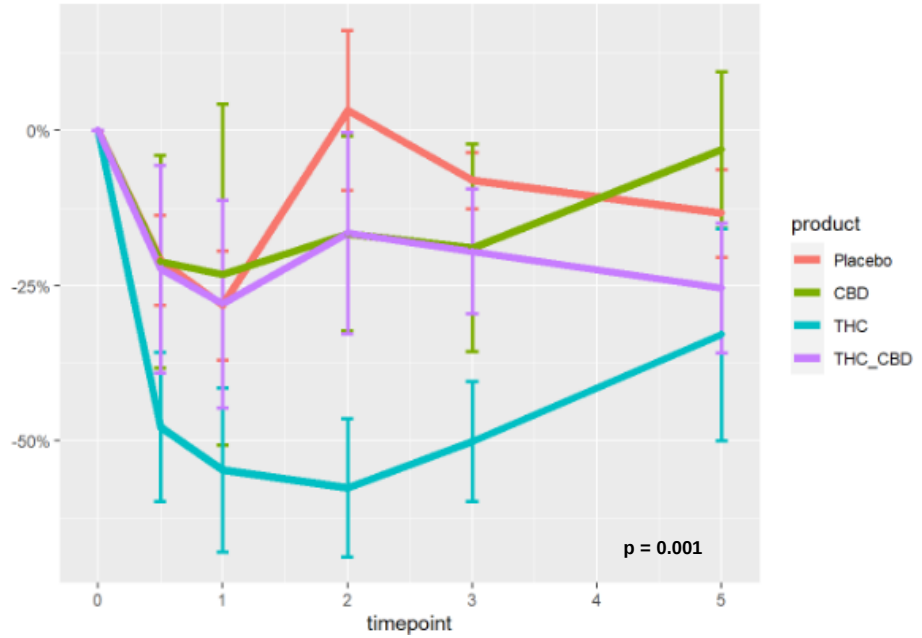
MRVTRS



PUTS

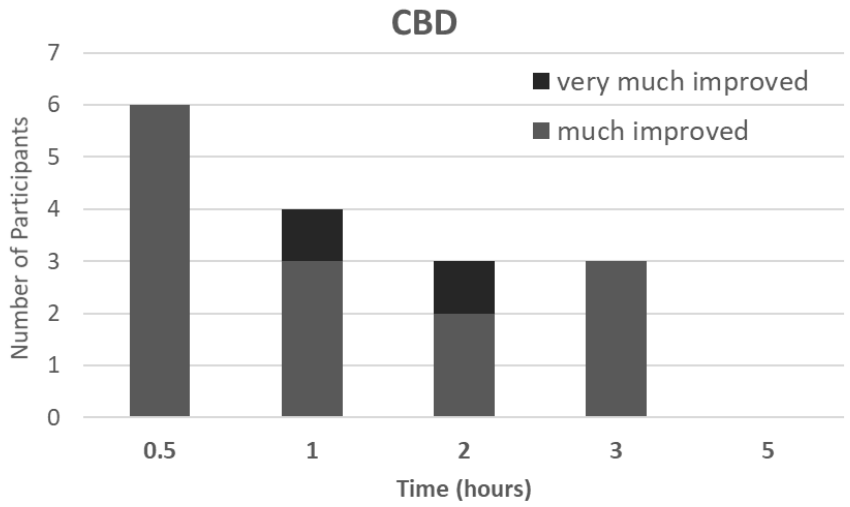


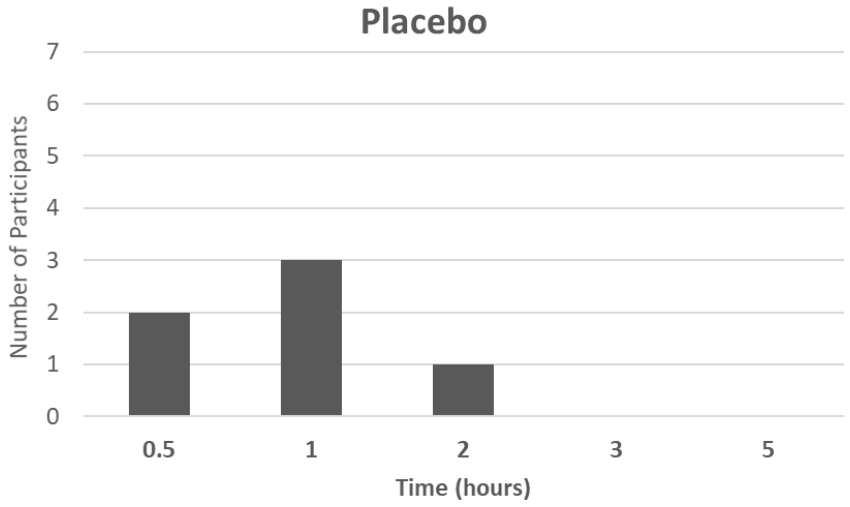
SUDS

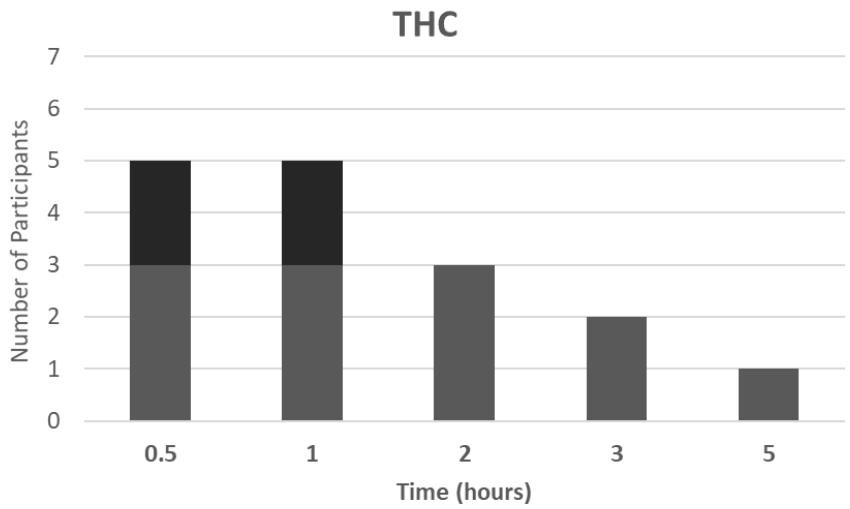


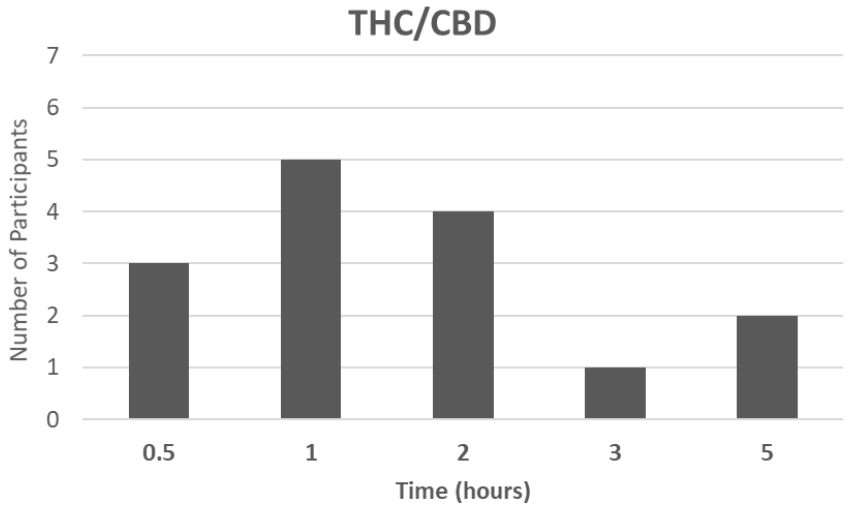
...EFFICACY...

CGI-I

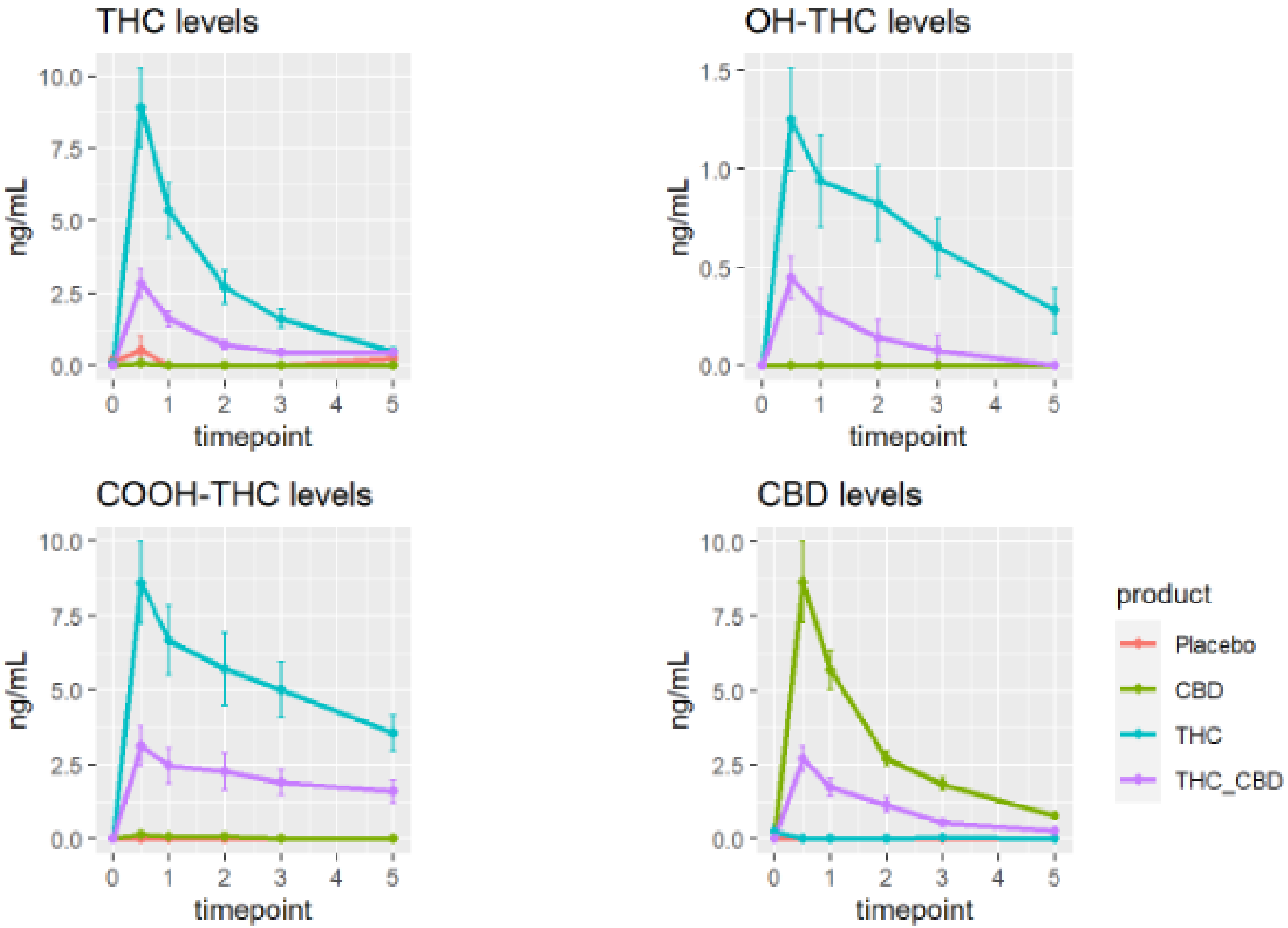








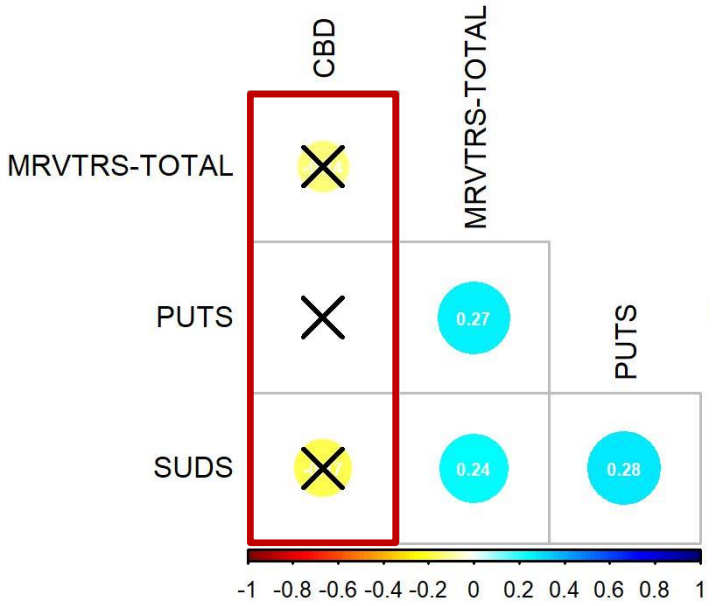
PLASMA LEVELS



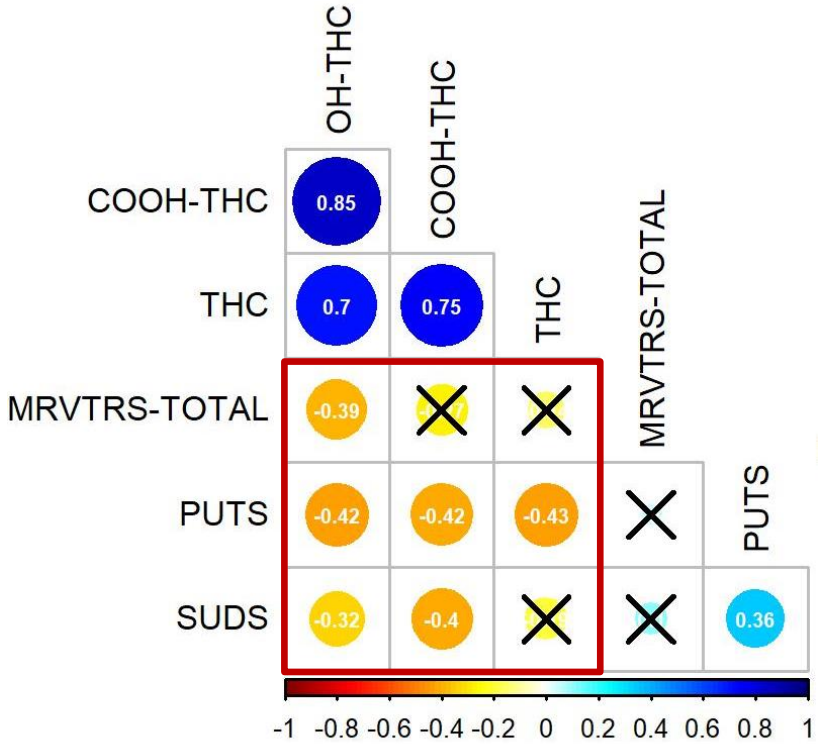
...EFFICACY

Correlations with cannabinoid plasma levels across all time points

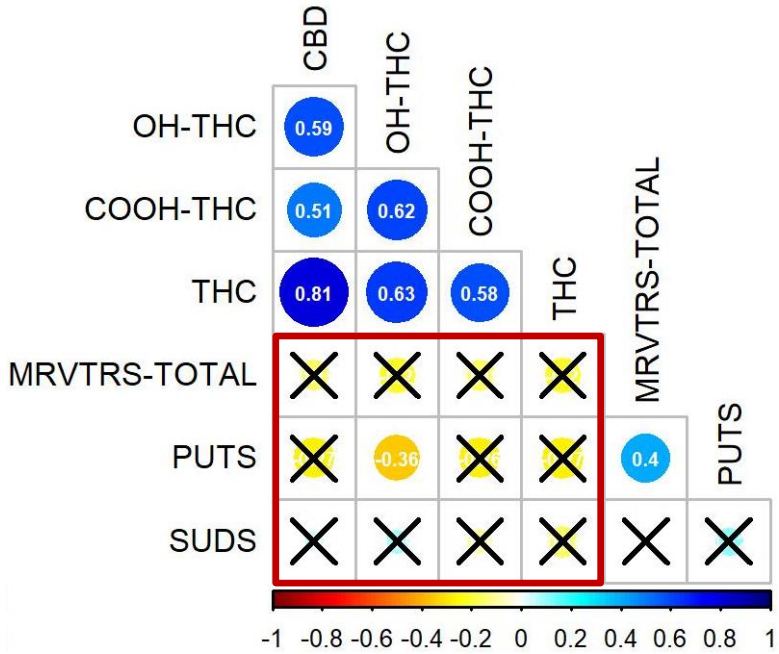
CBD 13%



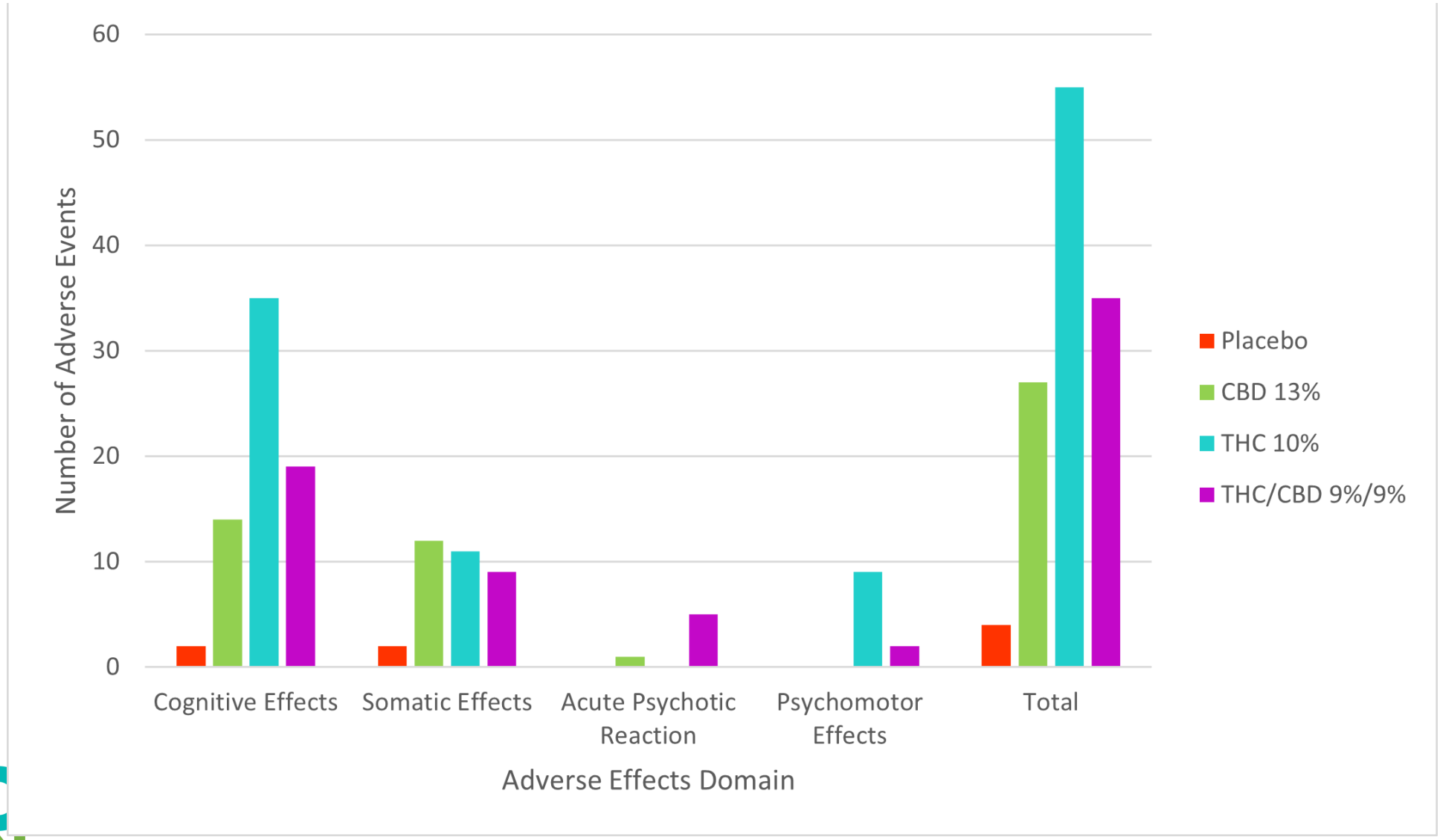
THC 10%



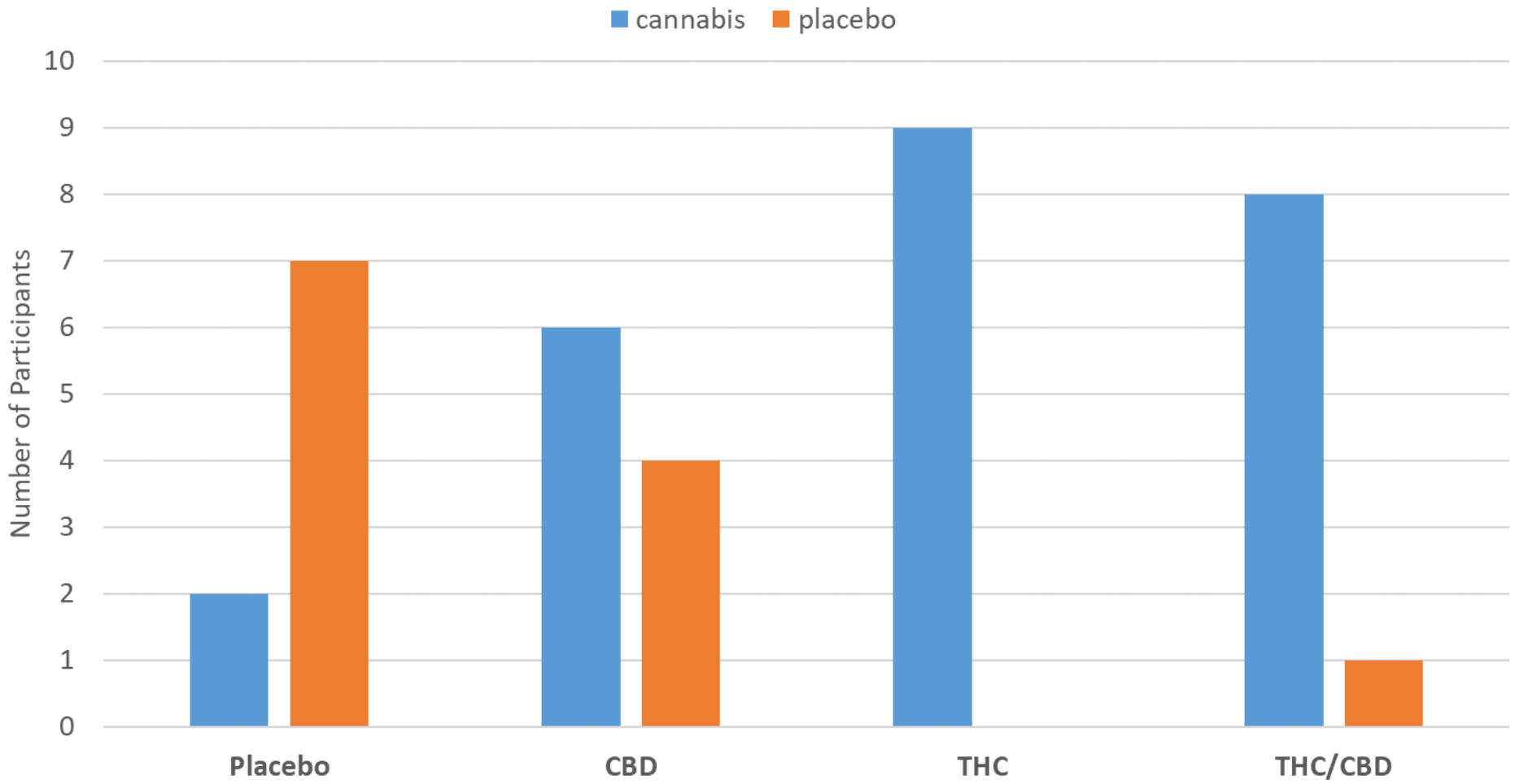
THC/CBD 9%/9%



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*