MEDICAL CANNABIS IN PERFORMING ARTIST-CENTRIC CARE

N-of-1 Clinical Trial Approach

John Chong MD BASc MSc DOHS FRCPC FACPM MDPAC(C) ARCT

Medical Director, Musicians' Clinics of Canada, Hamilton, Ontario

Assistant Professor, Department of Family Medicine

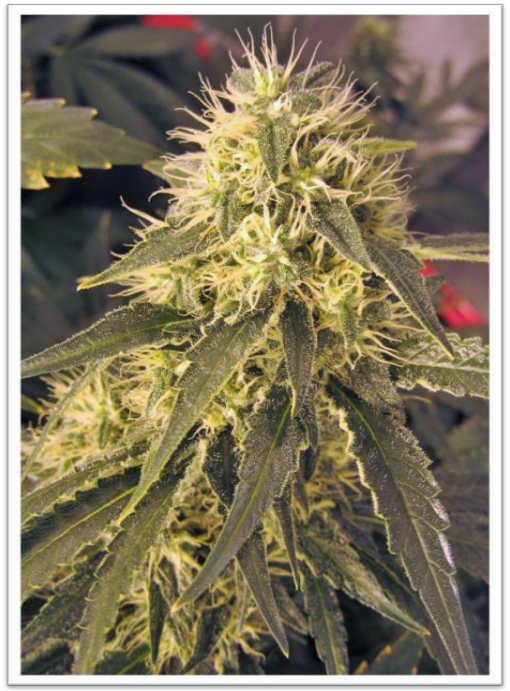
Faculty of Health Sciences, McMaster University, Hamilton, Ontario

Adjunct Professor, Music and Health Research Collaboratory

Faculty of Music, University of Toronto, Toronto, Ontario

Consultant, Glenn Gould School, Royal Conservatory

Consultant, National Youth Orchestra of Canada



OBJECTIVES OF PRESENTATION

- Describe the history and pharmacology of medical cannabis
- Discuss the evidence and controversies regarding the use of medical cannabis
- Facilitate debate about prescribing and dosing medical cannabis preparations
- Discuss an approach to evaluate medical cannabis versus standard treatments

A Brief History of Cannabis

Cultivated for fibres since 4000 BC

Medical use since 2900 BC (China)

Introduced to Western medicine by Dr. William O'Shaughnessy around 1840

1800s and 1900s: common component in patent medicines

Prescribed for Queen Victoria to relieve menstrual cramps

Prohibited in North America in the 1920s-30s, which halted research into medical use

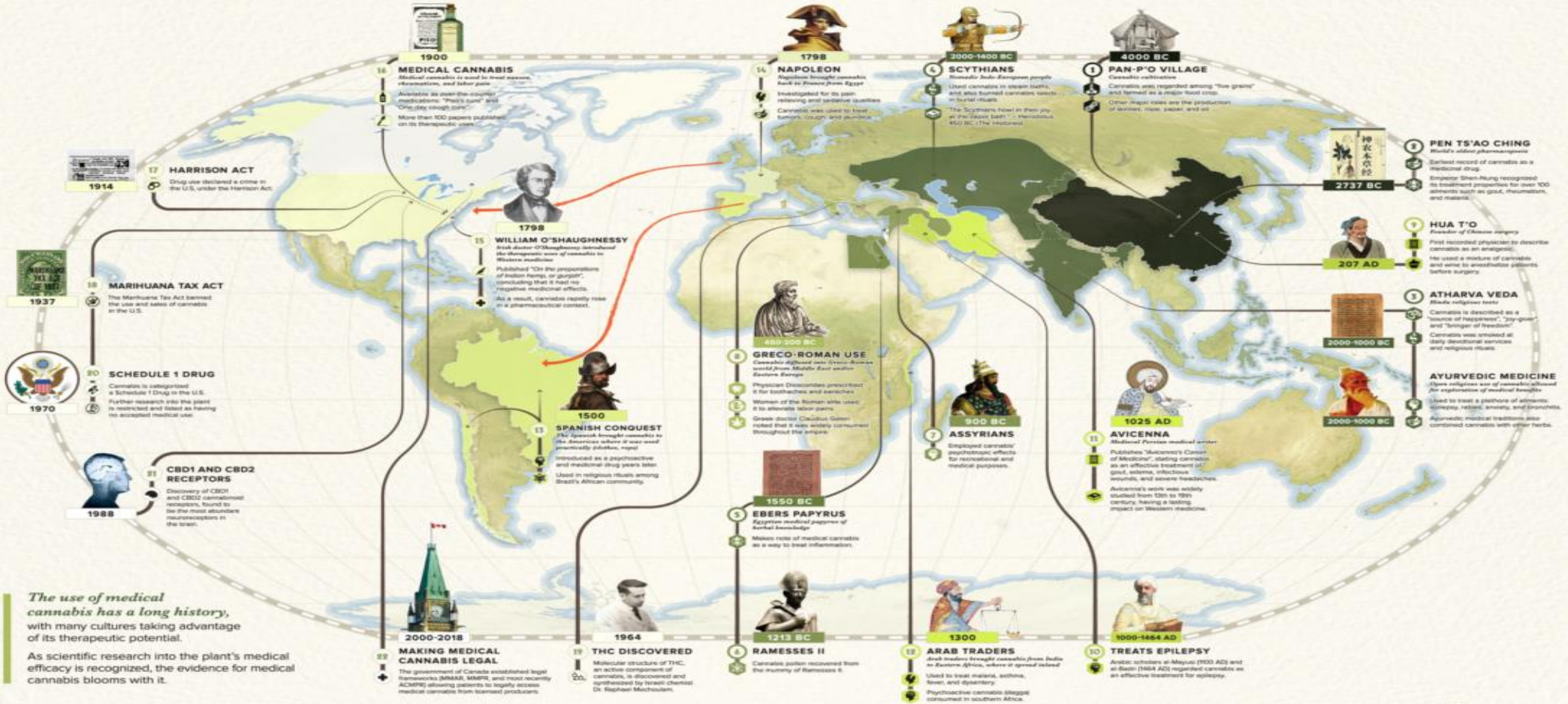
Hill KP, Palastro MD, Johnson B, Ditre JW; Cannabis and Pain: A Clinical Review, Cannabis and Cannabinoid Research. 2017, 2(1): 96-104.

a 6,000 YEAR HISTORY *of*

CANNABIS

THE CANNABIS SPACE IS HIGHLY POLARIZED TODAY.

However, it's less known that the plant has over 6,000 years of documented history – and its therapeutic applications appear to have been realized by most cultures. With medical cannabis making a comeback around the world, it's worth tracing the plant's humble beginnings and how it played a vital role throughout the centuries.



The use of medical cannabis has a long history, with many cultures taking advantage of its therapeutic potential.

As scientific research into the plant's medical efficacy is recognized, the evidence for medical cannabis blooms with it.

Sources
- A Historical Geography of Cannabis. Dr. Barney Warf, Geographical Review 104 (4). © 2014 American Geographical Society of New York.
- History of Medical Cannabis. Andrew Hand (MSc) et al., Journal of Pain Management 9 (4). © 2016 MedReleaf Corp. and Nova Science Publishers, Inc.
- Cannabis: A Complete Guide. Dr. Earnest Small © 2016 CRC Press.

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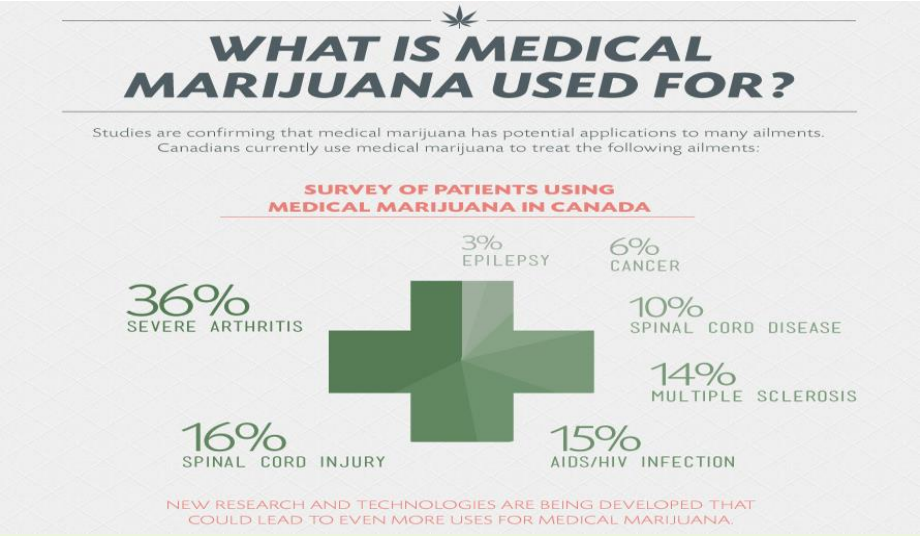
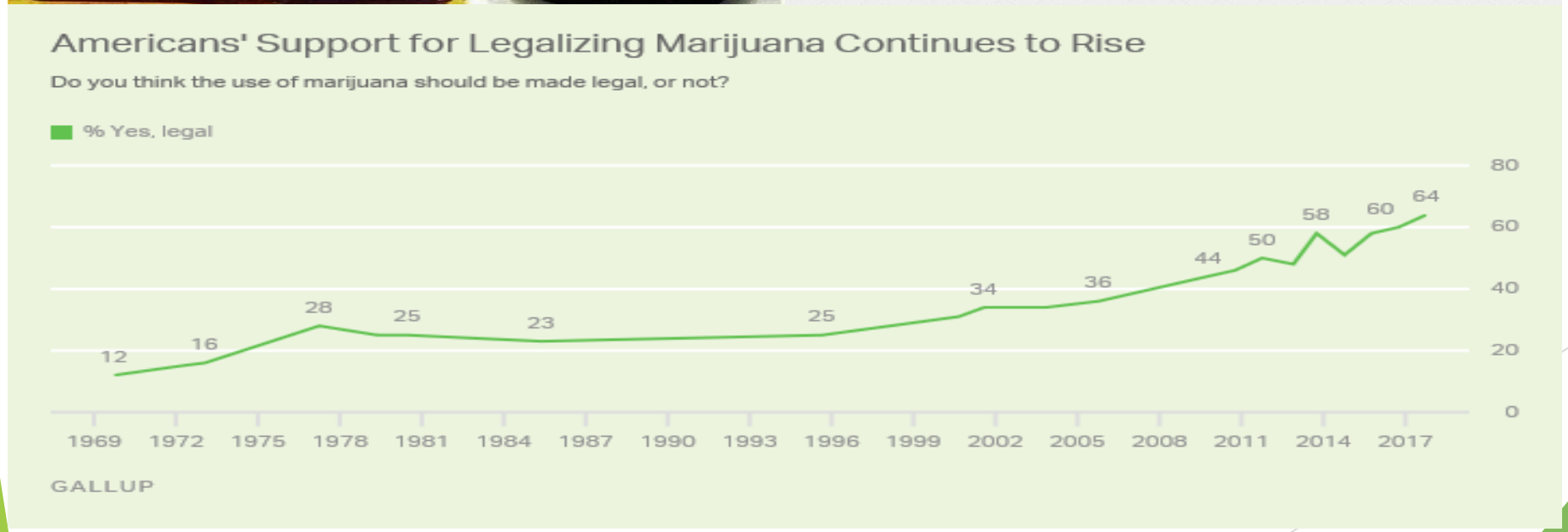
Before and after Reefer Madness (1936) from “planta non grata” to the “wonder cure all” with widespread legalization

From 1850 to 1936, cannabis was used as the primary medicine for more than 100 separate illnesses and/or diseases in the U.S.





Cannabis Production – Trichomes to Capsules

Andre CM, et al. *Front Plant Sci*. 2016;4;7:19.

Cannabinoids

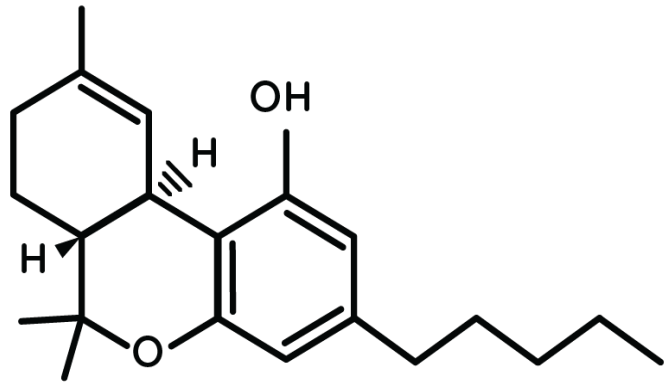
Three categories of molecules that interact with cannabinoid receptors

Endocannabinoids

- Naturally produced in the body
- Part of endocannabinoid system

Phytocannabinoids

- Typical C_{21} structure
- Found in many plants, but highest concentrations in cannabis

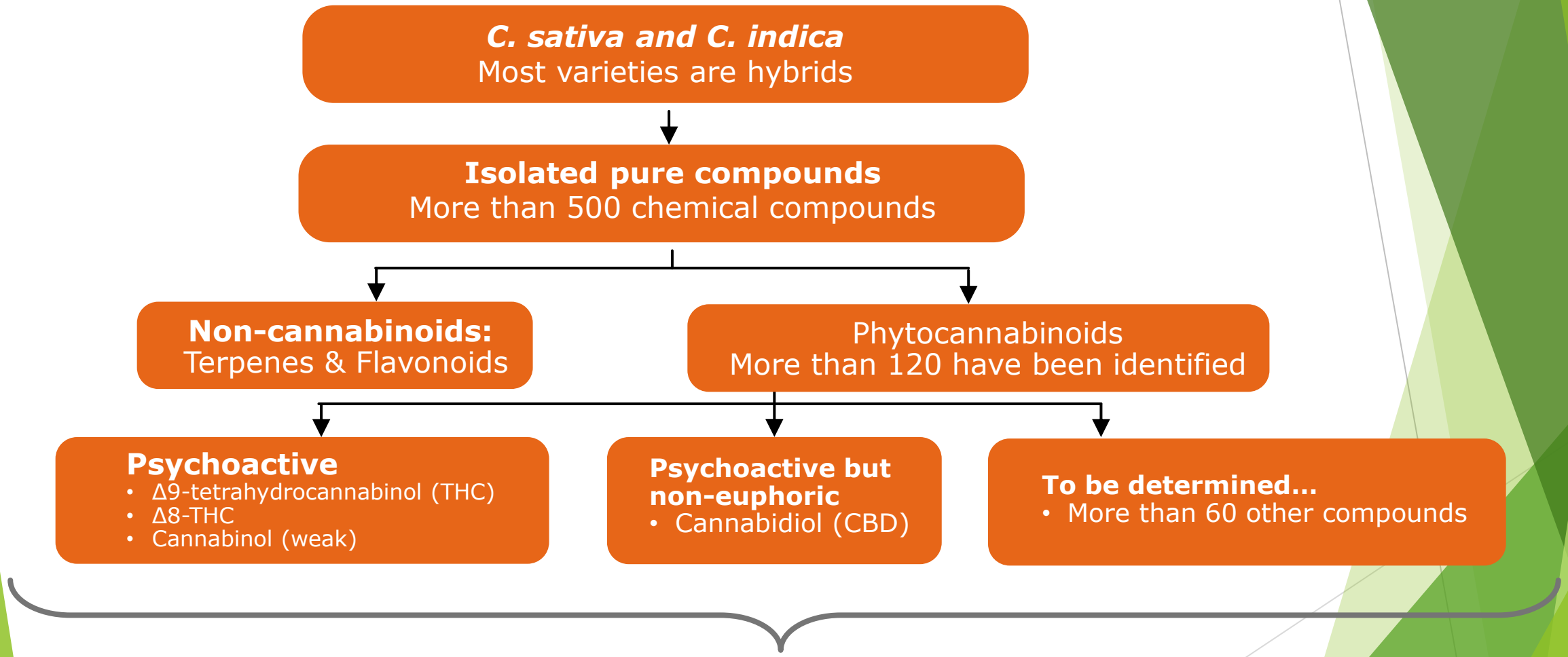


Synthetic cannabinoids

- Pharmaceuticals such as THC analogue known as nabilone

ElSohly M. 2002. Chemical Constituents of Cannabis. In: *Cannabis and Cannabinoids – Pharmacology, Toxicology, and Therapeutic Potential*. The Haworth Press; p. 27-36.

What is in Cannabis?



Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*. 2011;163(7):1344-64.

Cannabis: Two Main Active Compounds

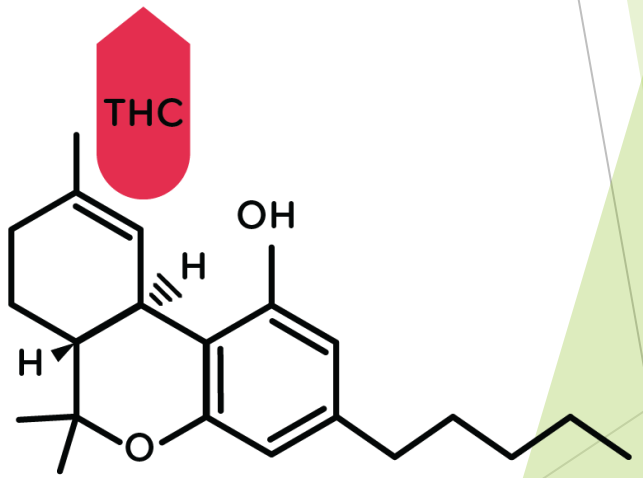
THC

- Responsible for many of the pharmacological effects of cannabis, including its psychoactive effect[1]

Interacts with cannabinoid receptors to induce:[1-3]

- Analgesia
- Antispasmodic activity
- Reduction of chemotherapy-induced nausea and vomiting
- Appetite stimulation
- Decreased intestinal motility

THC
(Delta-9-tetrahydrocannabinol)



Bridgeman MB, Abazia DT; Medicinal Cannabis: History, Pharmacology, and Implications for the Acute Care Setting, Pharmacol Ther. 2017; 42:180-188.

Cannabis: Two Main Active Compounds

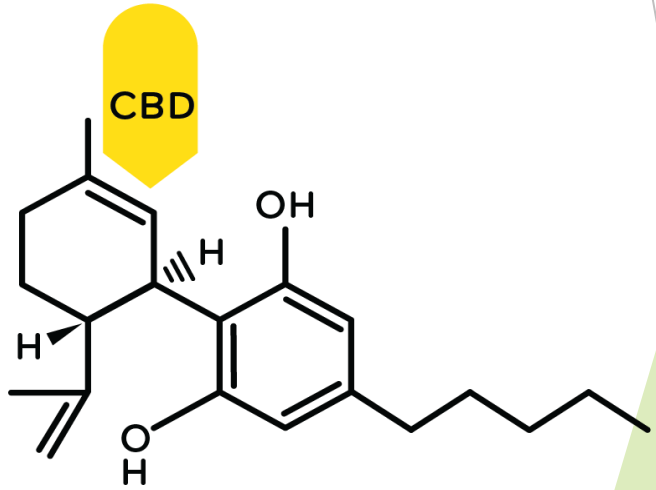
CBD[1]

- Indirect effects on the CB2 receptor
- Affects the activity of a significant number of other targets including ion channels, receptors, and enzymes

Research has indicated CBD has:[1-3]

- Anti-inflammatory
- Analgesic
- Antiemetic
- Antipsychotic
- Anxiolytic
- Anti-seizure effects

CBD (Cannabidiol)



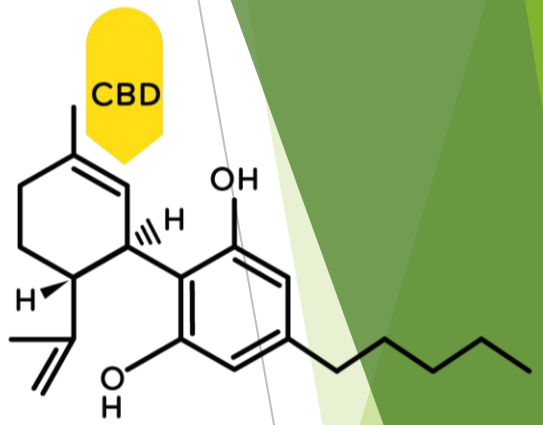
Pisanti S, Malfitano AM, Ciaglia E, Lamberti A, Raneri R, Cuomo G, Abate M, Faggiana G, Proto MC, Fiore D, Laezza C, Bifulco M; Cannabidiol: State of the art and new challenges for therapeutic applications. Pharmacol Ther. 2017 Jul; 175:133-150.

Activation of Cannabinoids

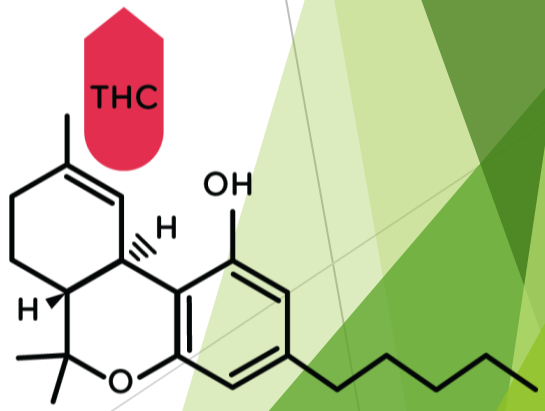
Acidic forms in plant
CBDA
THCA

HEAT

DECARBOXYLATION



Neutral phenols



Russo E. Cannabidiol Claims and Misconceptions. *Trends Pharmacol Sci*. 2017;38(3):198-201.

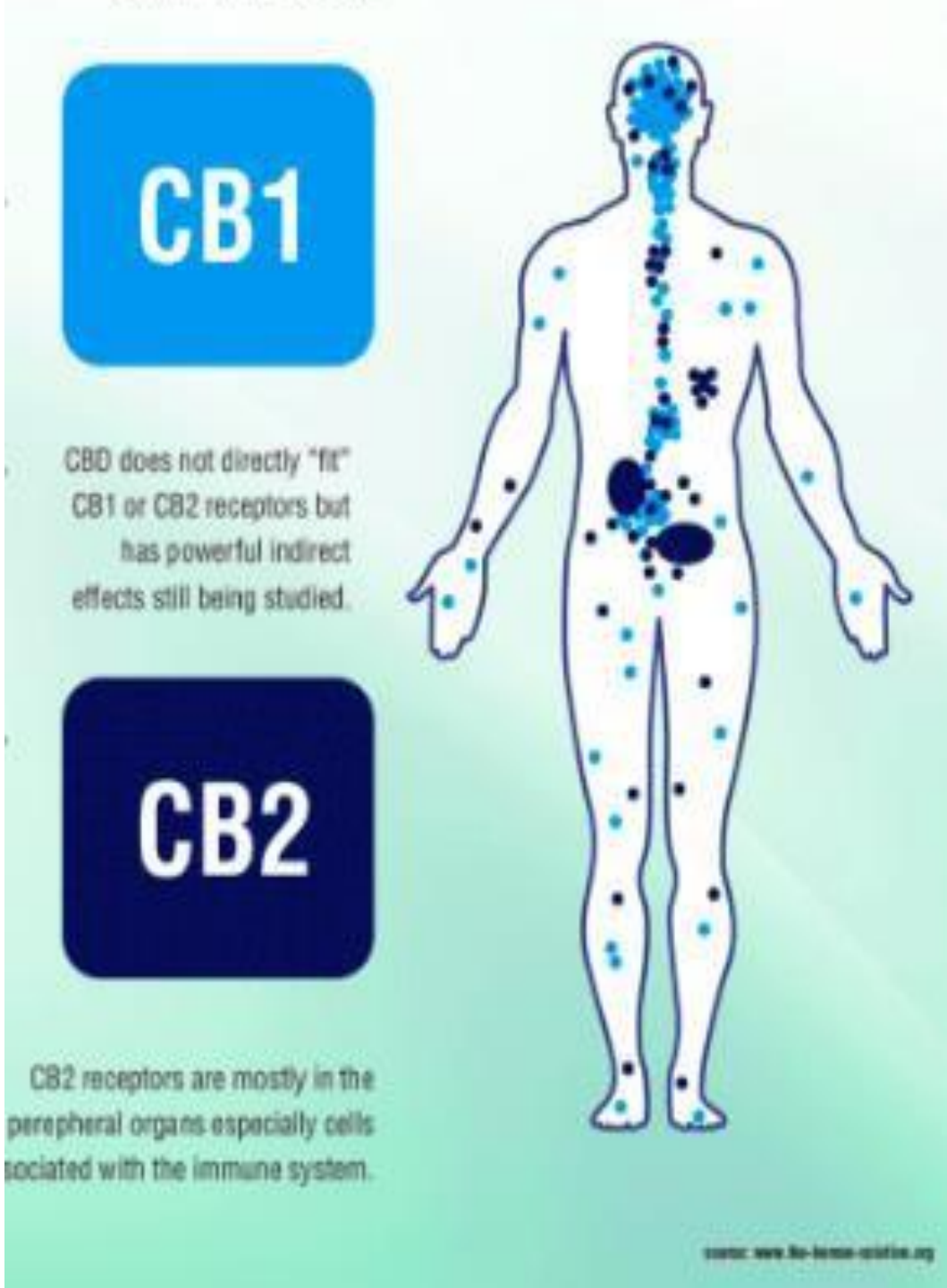
The Endocannabinoid System

- **Functions as homeostatic regulator of pain, stress, inflammation and motility**

- Comprises two main receptors:
  - CB_1 - abundant receptors important in central neurotransmission as well as enteric neurons
  - CB_2 - found on enteric neurons, and expressed by immune and epithelial cells

- Endogenous cannabinoids (Endocannabinoids)
  - N-arachidonoylethanolamine (**anandamide**)
  - 2-arachidonoylglycerol (**2-AG**)

Sharkey KA & JW Wiley. The role of the Endocannabinoid System in the Brain-Gut Axis. Gastroenterology 2016;151:252–266



Low density of CB1 receptors in the pons, brain stem and medulla

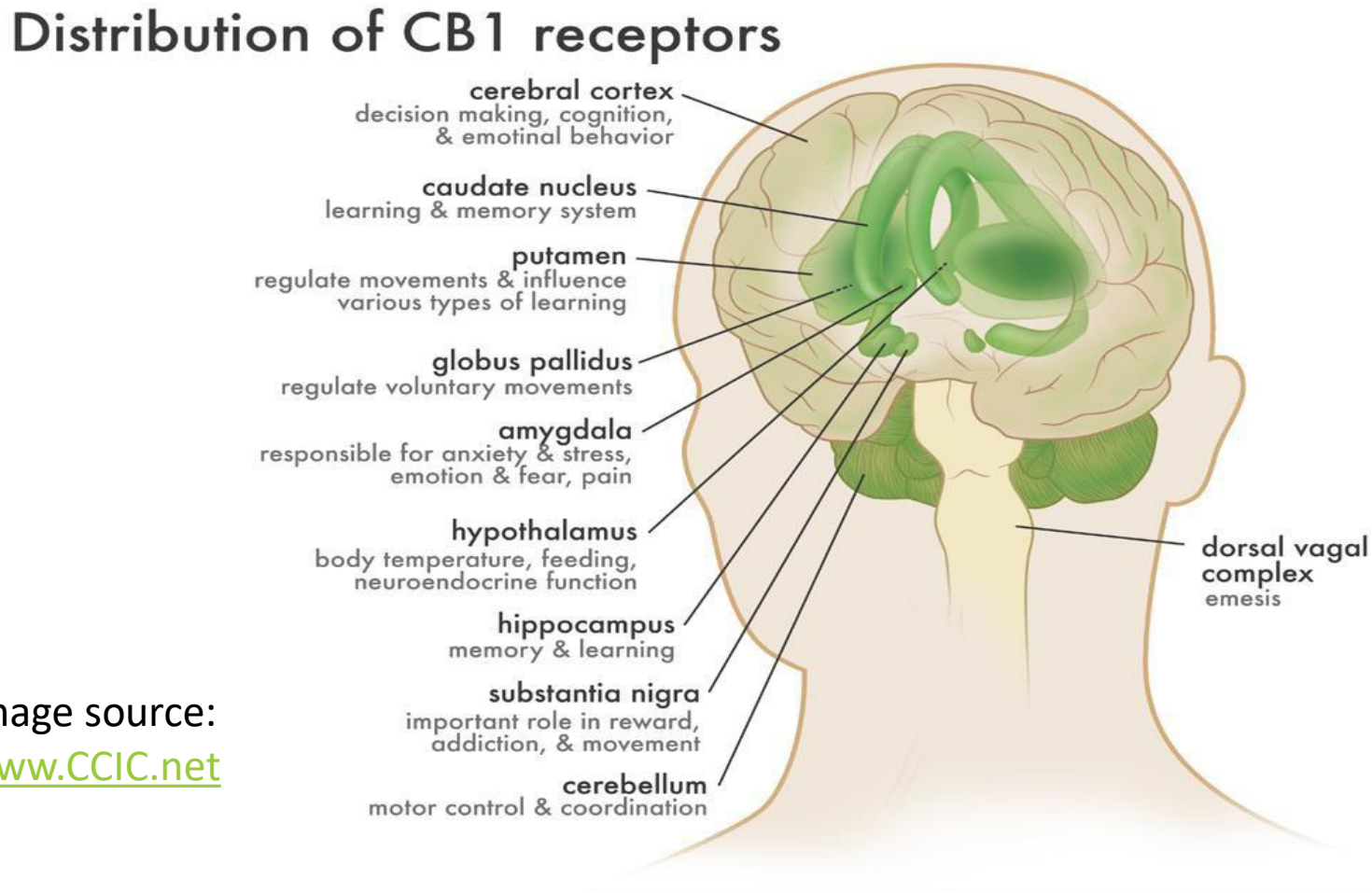
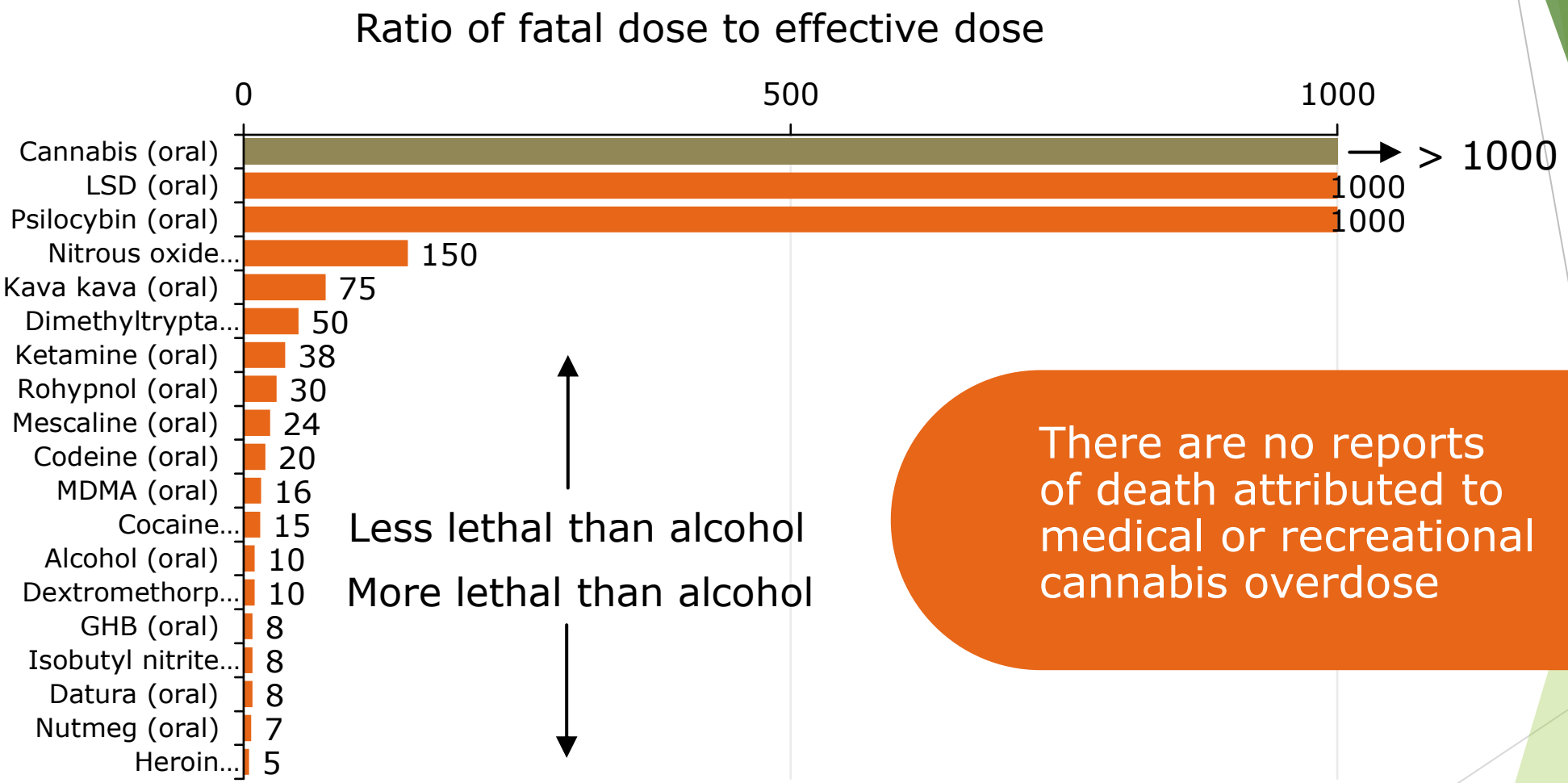


Image source:
www.CCIC.net

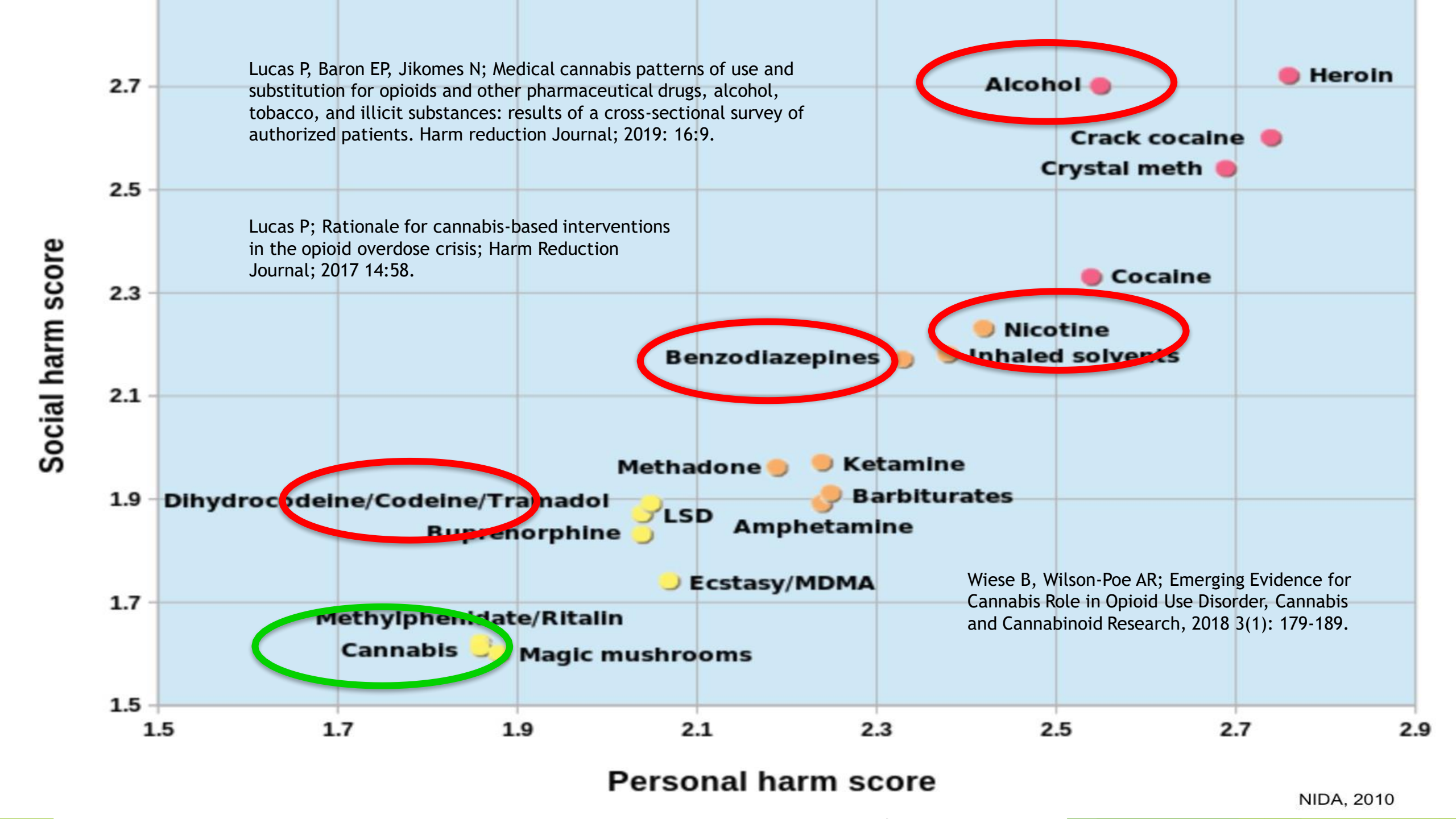
Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. aem. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html. Published October 12, 2018.

Toxicity



There are no reports of death attributed to medical or recreational cannabis overdose

Gable R. The Toxicity of Recreational Drugs. *American Scientist*. 2006; 94(3):206-8.


Lucas P, Baron EP, Jikomes N; Medical cannabis patterns of use and substitution for opioids and other pharmaceutical drugs, alcohol, tobacco, and illicit substances: results of a cross-sectional survey of authorized patients. Harm reduction Journal; 2019: 16:9.
Lucas P; Rationale for cannabis-based interventions in the opioid overdose crisis; Harm Reduction Journal; 2017 14:58.
Wiese B, Wilson-Poe AR; Emerging Evidence for Cannabis Role in Opioid Use Disorder, Cannabis and Cannabinoid Research, 2018 3(1): 179-189.
Alcohol
Heroin
Crack cocaine
Crystal meth
Cocaine
Nicotine
Inhaled solvents
Benzodiazepines
Methadone
Ketamine
Barbiturates
Amphetamine
LSD
Dihydrocodeine/Codeine/Tramadol
Buprenorphine
Ecstasy/MDMA
Methylphenidate/Ritalin
Cannabis
Magic mushrooms
Social harm score
Personal harm score
2.7
2.5
2.3
2.1
1.9
1.7
1.5
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1.9
2.1
2.3
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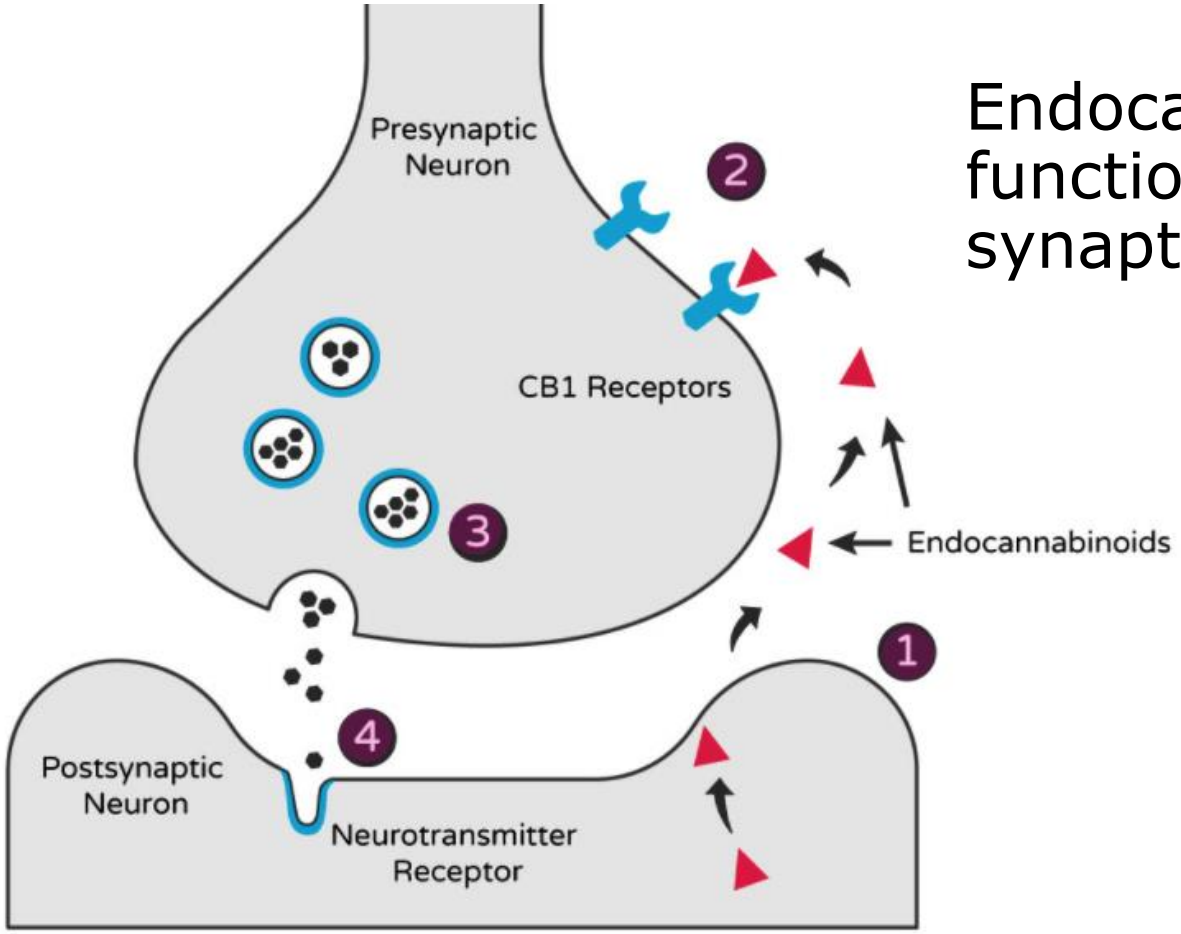
NIDA, 2010

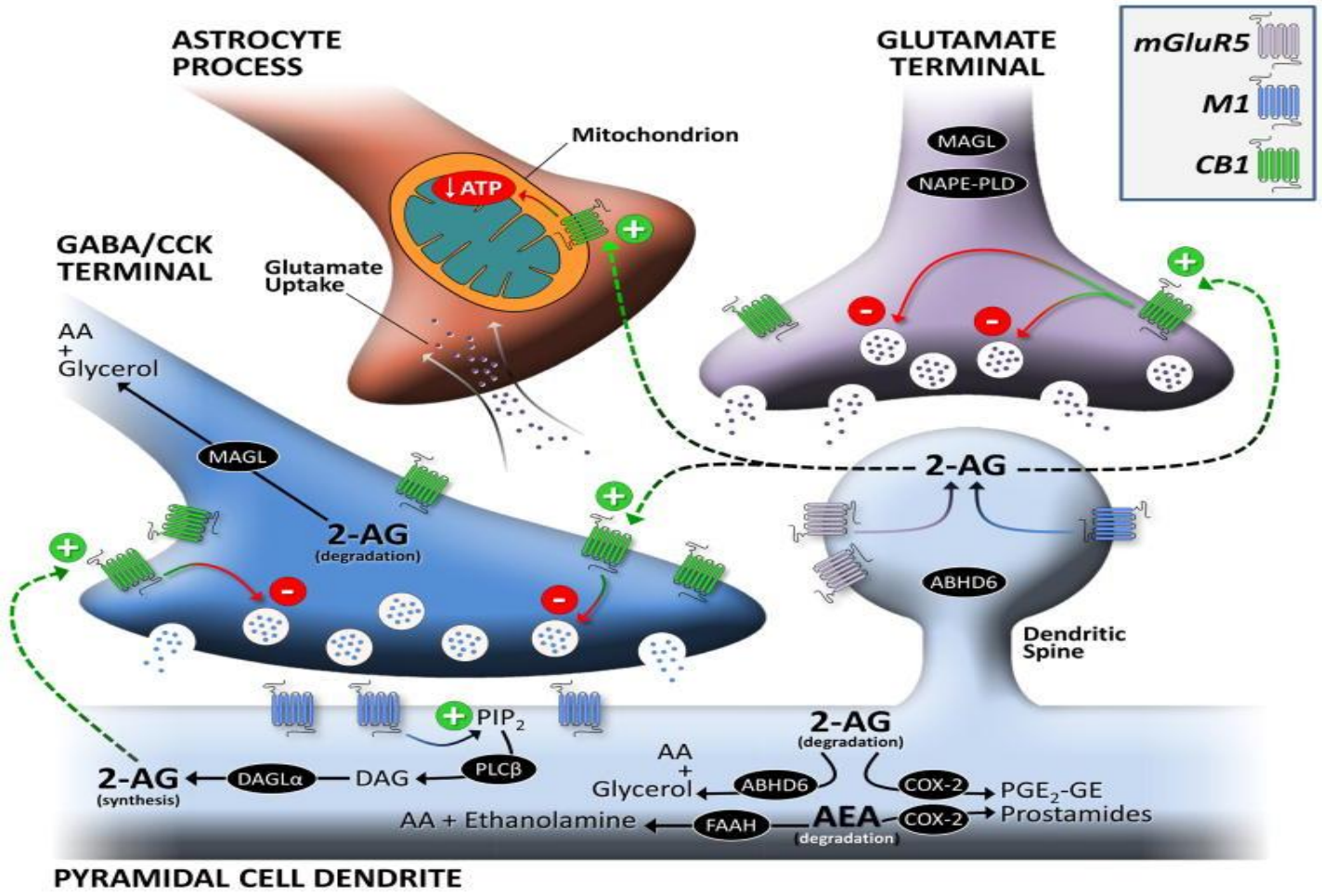
Endocannabinoids in the Nervous System



Endocannabinoids function as retrograde synaptic messengers

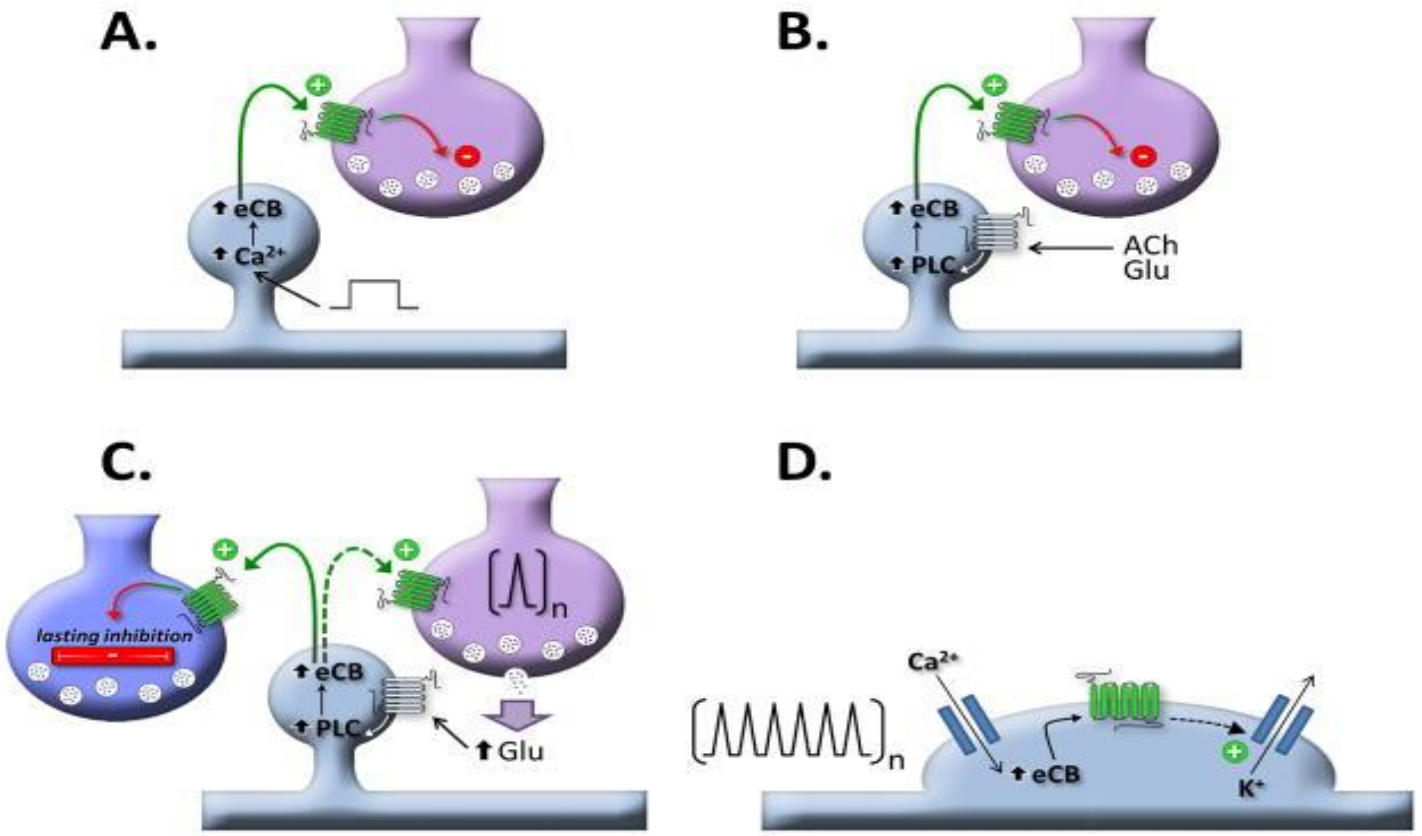
Castillo PE, et al. Endocannabinoid signaling and synaptic function.*Neuron*. 2012; 76(1):70-81.

Endocannabinoid system at the synapse



Lu, Hui-Chen, Mackie, Ken: An introduction to the endogenous cannabinoid system. Biol Psychiatry. 2016; 79(7): 516-525.

Endocannabinoid plasticity regulation



Lu, Hui-Chen, Mackie, Ken: An introduction to the endogenous cannabinoid system. Biol Psychiatry. 2016; 79(7): 516-525.

Summary of Evidence for Cannabis and Cannabinoid Efficacy

Substantial Evidence

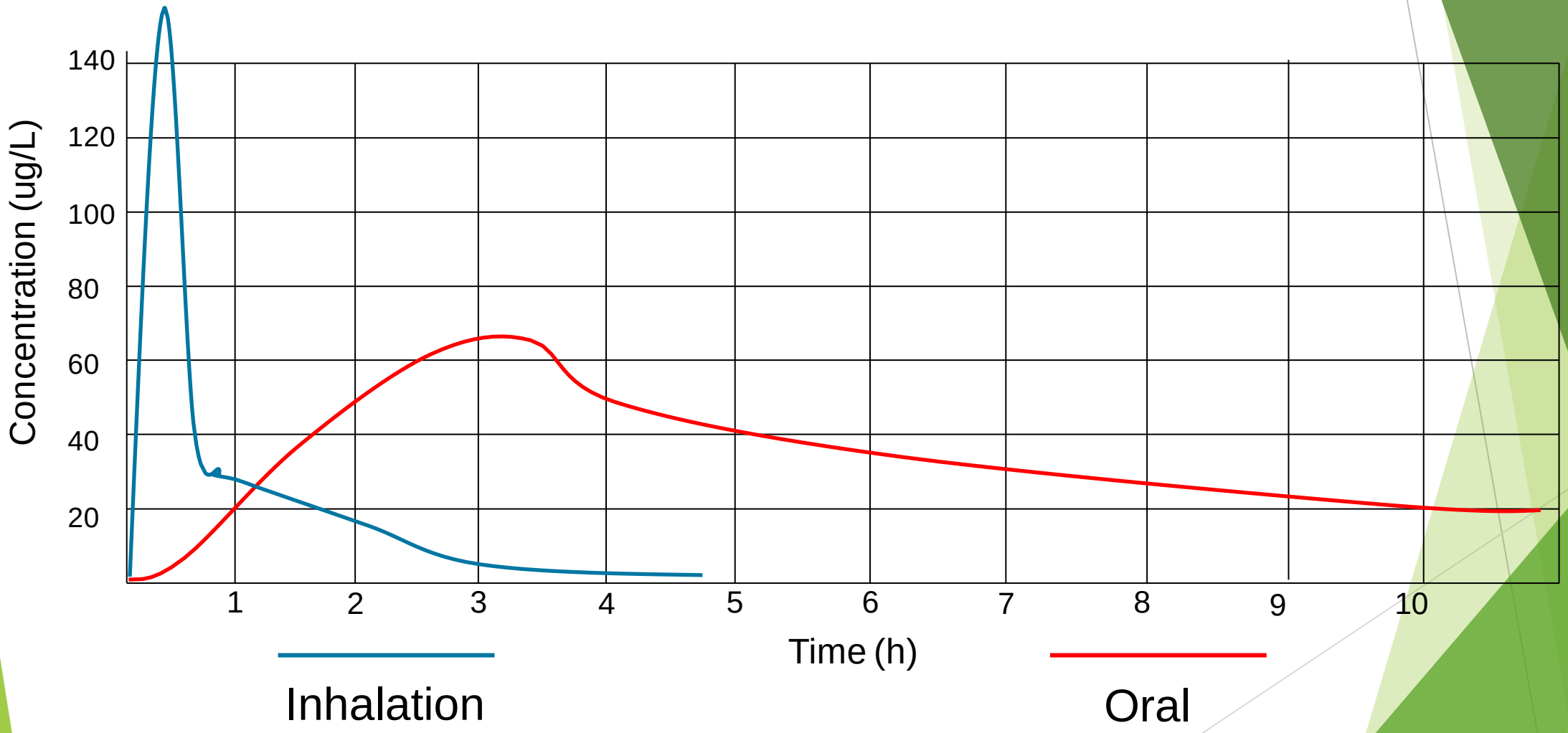
- Treatment of chronic pain and neuropathic pain in adults
- Chemotherapy-induced nausea and vomiting
- For improving patient-reported MS spasticity

Limited Evidence

- Anxiety disorders (PTSD, SAD, GAD)
- Drug-resistant seizures/epilepsy/anticonvulsant (pediatric)
- Improving short-term sleep outcomes individuals with OSA, fibromyalgia, chronic pain and multiple sclerosis
- Cancers, including glioma
- Cancer-associated anorexia and anorexia nervosa
- Symptoms of IBS
- Spasticity in patients with paralysis due to spinal cord injury
- Symptoms associated with ALS
- Motor disorders (Huntington's disease, Parkinson's disease, Tourette syndrome)
- Achieving abstinence in the use of addictive substances
- Mental health outcomes in individuals with schizophrenia

National Academies of Sciences. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*. 2017.

Pharmacokinetics: *Inhalation vs. Ingestion*



Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clin Pharmacokinet. 2003;42(2):327-360

THC Pharmacokinetics

- **Metabolism**
  - Oral Bioavailability ≈ 6-7% (extensive first pass metabolism)vs. Inhaled Bioavailablity 10%-35%
  - Metabolized by the Cytochrome P450 system (CYPP450 2C9/2C18/19), with over 100 metabolites
  - Propensity for drug interactions, yet clinically important interactions not well defined due to limited research

  Elimination
  - Half life ranges from 25-36 hours for THC, other metabolites can be 5-7 days
  - After a single or multiple use, detectable in urine for 3-12 days; metabolites up to 25 days

Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. aem. https://www.canada.ca/en/health-canada/services/drugs- medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html. Published October 12, 2018.

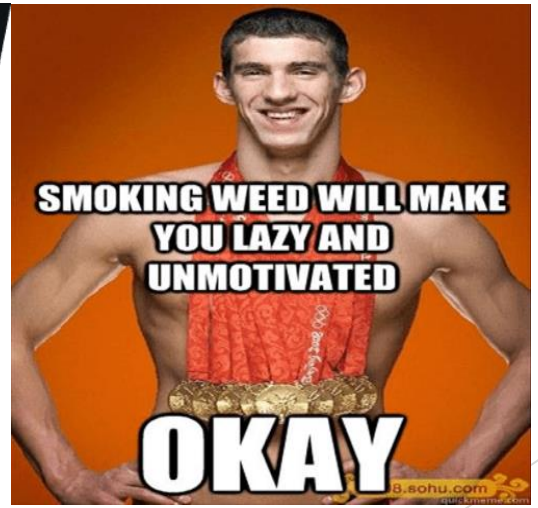
Cannabis: Adverse Events (AEs)

Most common AEs

- Drowsiness/fatigue
- Dizziness
- Dry mouth
- Cough, phlegm, bronchitis (smoking only)
- Anxiety
- Nausea
- Cognitive effects

Majority of AEs are associated with THC

- They are dose-dependent
  - 'Start Low, Go Slow' to mitigate effects
- Combine CBD with THC to further reduce THC-related AEs



MacCallum C, Russo EB; Practical considerations in medical cannabis administration and dosing; European Journal of Internal Medicine; (2018) 49:12-19.

Why Is There Not More Clinical Trial Evidence?

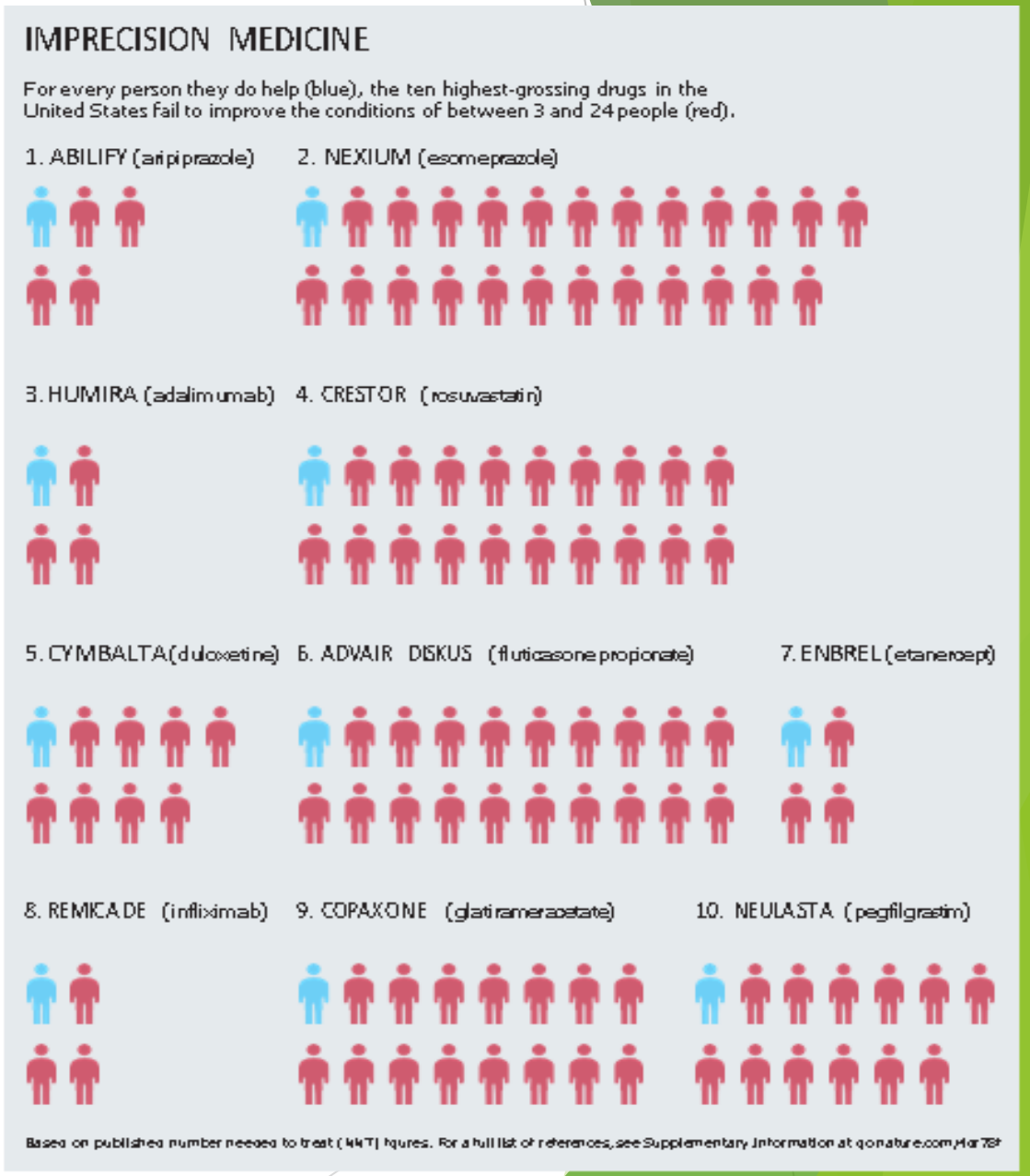
- Study of the endocannabinoid system is still in its infancy
- Until recently, there has been no legal access to medical cannabis
- Difficulties with standardization of product and dose
- Lack of development and supply of a true placebo
- Ethical issues with regards to standard of care and running blind studies
- Numerous population-based studies have been conducted on recreational users, but not medical users

Allen GM et al. Simplified guideline for prescribing medical cannabis in primary care. Can Fam Physician. 2018 Feb; 64(2):111-120.

Do n-of-1 trials have a role in clinical science and practice?

N-of-1 trials that focus exclusively on the objective, empirically determined optimal intervention for a single patient are compatible with the ultimate end point of clinical practice: the care of individual patients.

Meta-analyses of the outcomes of multiple n-of-1 trials could be compared with standard treatment regimens and help put into context the utility and practicality of n-of-1 trials.



Nicholas J. Schork. Time for one-person trials. Nature 2015; 520: 609-611.

Guyatt G, Sackett D, Taylor DW, Chong J, Roberts R, Pugsley S; Determining Optimal Therapy - randomized trials in individual patients. New England Journal of Medicine. 1986; 314(14): 889-92.

Canada Health Act 1984

Organization Of Canadian Symphony Musicians

1986

Musicians' Clinics of Canada

2023

Universality Accessibility Portability

Chong J. Using Biofeedback and Awareness to Enhance Treatment of the Musician. In Performing Arts Medicine 1st Edition. Ed. Elson L. 2018 Elsevier ISBN: 9780323662123

ALLOSTATIC OVERLOAD

AROUSAL TO STRESSORS

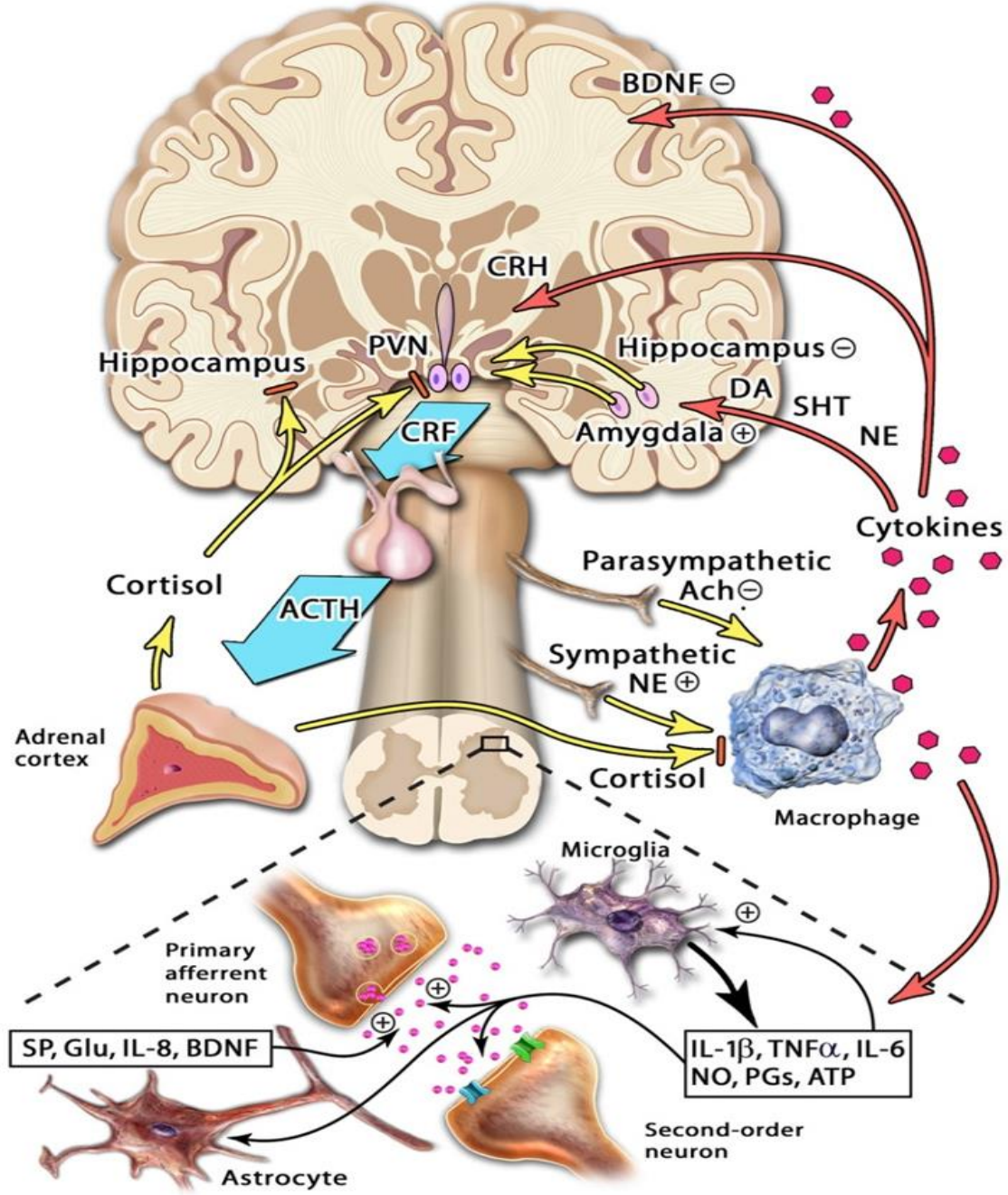
RAPID RESPONSE

FEED FORWARD SYSTEM

LACKING BOUNDARIES

STUCK "ON"

NO "OFF"



PSYCHO
NEURO
ENDOCRINE
IMMUNE
EPIGENETIC
EFFECTS

ONE YEAR STRESS = 6 YEARS CELLULAR AGING
Blackburn (2009)

HEART
STROKE
DIABETES
CANCER
ARTHRITIS
MULTIPLE SCLEROSIS
DEMENTIA

Approximately 250 medical cannabis n-of-1 trials are in progress at the Musicians' Clinics of Canada

- Common medical problems:
  - Chronic pain
  - Anxiety/Stress
  - Insomnia
- Prevalence of chronic pain and sleep issues increases with aging
- Comorbidities increase with age and chronic stress/adverse lifestyle

Webb, Charles W, and Sandra M Webb. "Therapeutic Benefits of Cannabis: A Patient Survey." *Hawai'i Journal of Medicine & Public Health* 73, no. 4 (April 2014): 109–11. Bonn-Miller, Marcel O., Matthew Tyler Boden, Meggan M. Bucossi, and Kimberly A. Babson. "Self-Reported Cannabis Use Characteristics, Patterns and Helpfulness among Medical Cannabis Users." *The American Journal of Drug and Alcohol Abuse* 40, no. 1 (January 2014): 23–30. https://doi.org/10.3109/00952990.2013.821477.

Every patient is an N-of-1 trial requiring assessment of risk, good patient education, setting expectations and ongoing careful follow up.

- **Design issues in n-of-1 clinical trials**
  - Randomization of treatment order, carryover effects, washout periods and blinding are key design elements that need to be considered in n-of-1 trials.
- **The analysis of n-of-1 clinical trials**
  - Methods that account for serial correlation in comparing the response to two or more treatments, such as certain time-series analyses, are necessary.
  - More research into how to identify and accommodate carryover effects in n-of-1 trials is clearly needed.

Demeyin WA, Frost J, Ukoumunne OC, Briscoe S, Britten N; N of 1 trials and the optimal individualisation of drug treatments: a systematic review protocol. Systematic Reviews 2017, 6:90-97.

N-of-1 studies

PRO:	CON:
Can be done in any patient	Not generalizable to other patients
Results take into account all patient variables	
Crossover design allows for control period	May require multiple treatment periods to find an ideal solution
Inexpensive	

G Guyatt, D Sackett, J Adachi, R Roberts, J Chong, D Rosenbloom, J Keller. (1988). A clinician's guide for conducting randomized trials in individual patients. Canadian Medical Association Journal. 139(6): 497-503.

Lillie EO, Patey B, Diamant J, Issell B, Topol EJ, Schork NJ. The n-of-1 clinical trial: the ultimate strategy for individualizing medicine? Per Med. 2011; 8(2): 161–173.

Future directions and collaboration

- **Combining and evaluating multiple n-of-1 trials**
  - Randomized controlled trials cast a wide net initially by studying many patients in a unified manner, then winnow things down to what might work best in an individual patient over time and through additional studies of the subjects in the large trial.
  - The n-of-1 approach essentially starts out small and focused, and then works its way towards insights that would immediately benefit a much larger group of patients by combining n-of-1 trial outcomes in a meta-analysis.

Mirza RD, Punja S, Vohra S, Guyatt G. The history and development of N of 1 trials. Journal of the Royal Society of Medicine 2017; 110:330-340.

Impact of Medical Cannabis on Recovery from Playing - Related Musculoskeletal Disorders in Musicians: An Observational Cohort Study

Dr Kat Cottrell MBBS BSc DipABRSM, Dr John Chong MD BASc MSc DOHS FRCPC FACPM CGPP ARCT

McMaster University

Musicians' Clinics of Canada

Background

- Playing-related musculoskeletal disorders (PRMD) are 'pain, weakness, numbness, tingling or other symptom that interferes with the ability to play the instrument at the level you are accustomed to' [1]
- PRMD can affect musicians' ability to work, their mental health and sense of self [2]
- Musicians have an 84% lifetime prevalence of PRMD [3]
- Many types of analgesia are inappropriate for this population [4, 5, 6, 7]
- Cannabidiol (CBD) has been shown to have anti-inflammatory, neuroprotective properties, improve sleep and physical functioning, and reduce perception of pain [8,9]
- Medical cannabis has been shown to be safer than other analgesia in terms of serious adverse events [10]

STUDY AIM: To explore the impact and safety of medical cannabis for PRMD

Methods

Musicians' Clinics of Canada Routine PRMD Care

Treatment includes biofeedback, psychotherapy and lifestyle interventions. PRMD patients are offered medical cannabis as part of their treatment plan. Questionnaires are completed by patients before each visit:

- The Musculoskeletal Pain Intensity and Interference Questionnaire for Musicians (MPIIQM) [11]
  - MPIIQM40 for pain intensity
  - MPIIQM50 for pain interference
- The Depression, Anxiety and Stress Scale (DASS-21) [12]
- Questionnaire on medical cannabis dosing, positive and negative effects

Retrospective Observational Cohort Study

- McMaster HiREB approval: May 2021
- Consent obtained from patients who attended the clinic between Jan 2019 and Jan 2020, >18 years old with PRMD

Data Collection

- The 204 eligible study participants were split into 3 groups:
  - 'Non-cannabis users' who declined medical cannabis (42)
  - 'New medical cannabis users' with baseline questionnaire data (61)
  - 'Long-term medical cannabis users' without baseline questionnaire data prior to starting medical cannabis (101)
- Questionnaire data from participants' first visit in the study period, and a subsequent visit six-months later were collected

Data Analysis

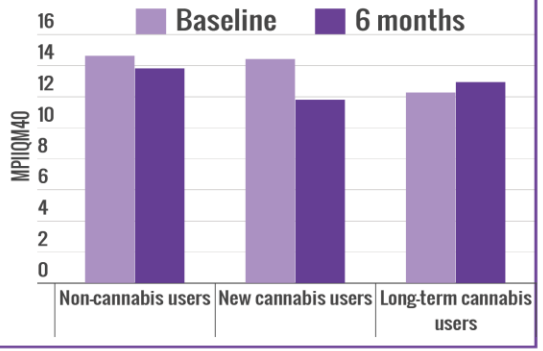
- Baseline and six-month data were compared within each group using paired t-tests
- Between group differences were assessed using ANOVA

Results

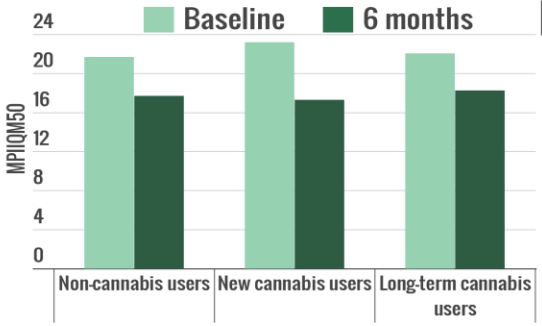
Pain Intensity (MPIIQM40)

New cannabis users had a **significant reduction in pain intensity** (p=.002) at six-months.

A **significant difference** in **pain intensity** was shown for new vs long-term cannabis users (p=.023) at six-months.



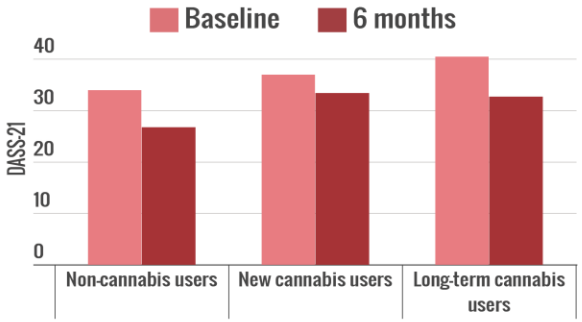
Pain Interference (MPIIQM50)



Non-users (p=.035), **new users** (p=.002) and **long-term cannabis users** (p=.009) all had **significant reductions in pain interference** at six-months.

Mental Health (DASS-21)

Non-cannabis users (p=.003) and **long-term cannabis users** (p=.001) had **improvements in DASS-21** scores at six-months.



Medical Cannabis

Daily Medical Cannabis dose at six-months:

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Discussion

Impact of Medical Cannabis on PRMD

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- CBD/THC dosing were within guideline recommendations [8]
- No patients experienced any serious adverse events, in keeping with previous studies [10]

Limitations

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  - For example cost of medical cannabis, comorbidities and disease chronicity

Further Questions

- Future qualitative studies are planned to explore the subjective positive and negative effects of medical cannabis in musicians
- Further studies are required to explore the long-term impacts of medical cannabis for PRMD, ideally as a randomized controlled trial

References

1. Zaza C, Charles C, Muszynski A. The meaning of playing-related musculoskeletal disorders to classical musicians. Social Science & Medicine. 1998;47(12):2013-23.
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Contact us at: admin@musiciansclinics.com

MEDICAL CANNABIS IN PERFORMING ARTIST-CENTRIC CARE

Approach to Safe Prescribing

John Chong MD BASc MSc DOHS FRCPC FACPM MDPAC(C) ARCT

Medical Director, Musicians' Clinics of Canada, Hamilton, Ontario

Assistant Professor, Department of Family Medicine

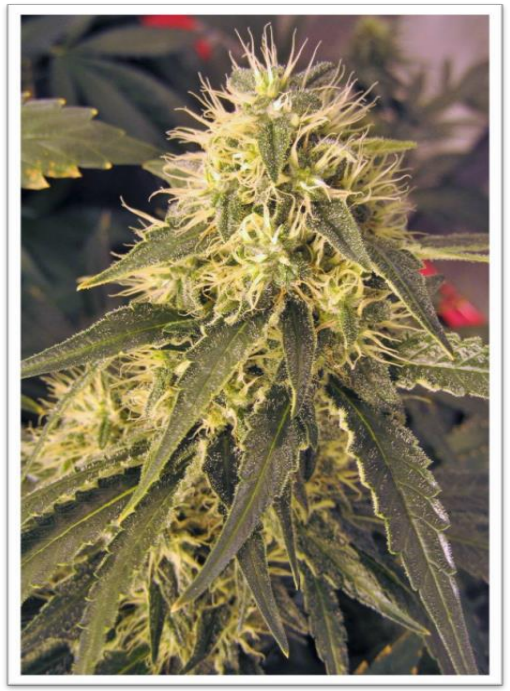
Faculty of Health Sciences, McMaster University, Hamilton, Ontario

Adjunct Professor, Music and Health Research Collaboratory

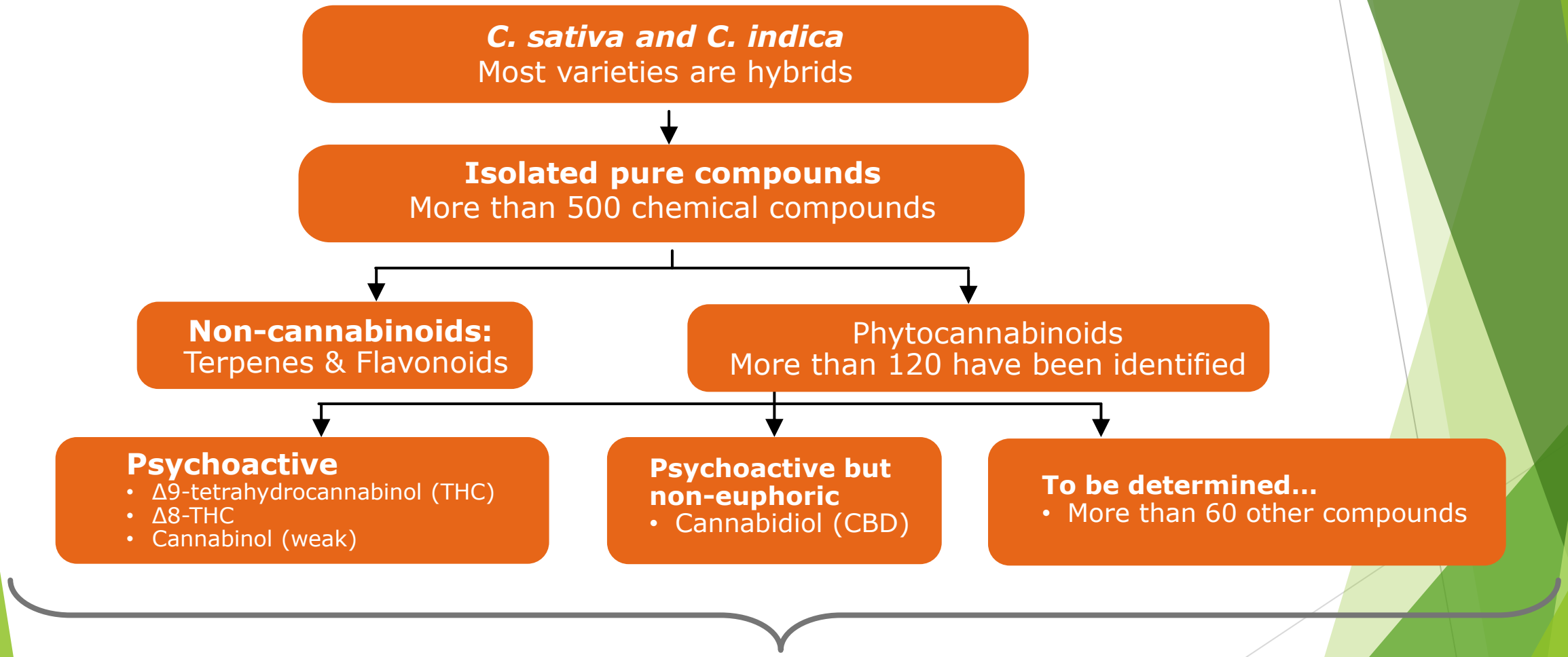
Faculty of Music, University of Toronto, Toronto, Ontario

Consultant, Glenn Gould School, Royal Conservatory

Consultant, National Youth Orchestra of Canada



What is in Cannabis?



Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br J Pharmacol*. 2011;163(7):1344-64.

Cannabis: Two Main Active Compounds

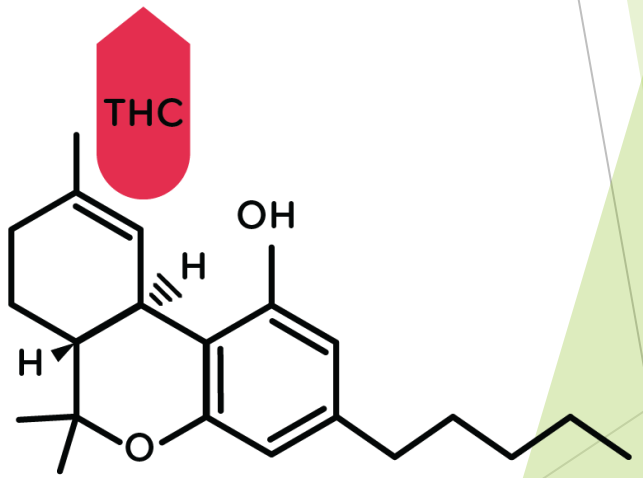
THC

- Responsible for many of the pharmacological effects of cannabis, including its psychoactive effect[1]

Interacts with cannabinoid receptors to induce:[1-3]

- Analgesia
- Antispasmodic activity
- Reduction of chemotherapy-induced nausea and vomiting
- Appetite stimulation
- Decreased intestinal motility

THC
(Delta-9-tetrahydrocannabinol)



Bridgeman MB, Abazia DT; Medicinal Cannabis: History, Pharmacology, and Implications for the Acute Care Setting, Pharmacol Ther. 2017; 42:180-188.

Cannabis: Two Main Active Compounds

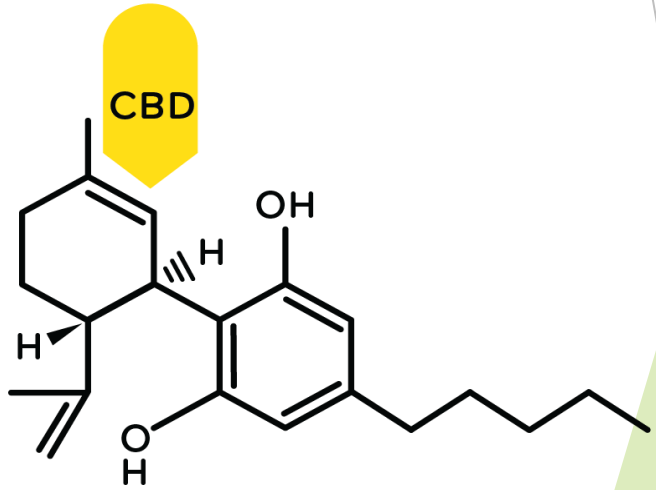
CBD[1]

- Indirect effects on the CB2 receptor
- Affects the activity of a significant number of other targets including ion channels, receptors, and enzymes

Research has indicated CBD has:[1-3]

- Anti-inflammatory
- Analgesic
- Antiemetic
- Antipsychotic
- Anxiolytic
- Anti-seizure effects

CBD (Cannabidiol)



Pisanti S, Malfitano AM, Ciaglia E, Lamberti A, Raneri R, Cuomo G, Abate M, Faggiana G, Proto MC, Fiore D, Laezza C, Bifulco M; Cannabidiol: State of the art and new challenges for therapeutic applications. Pharmacol Ther. 2017 Jul; 175:133-150.

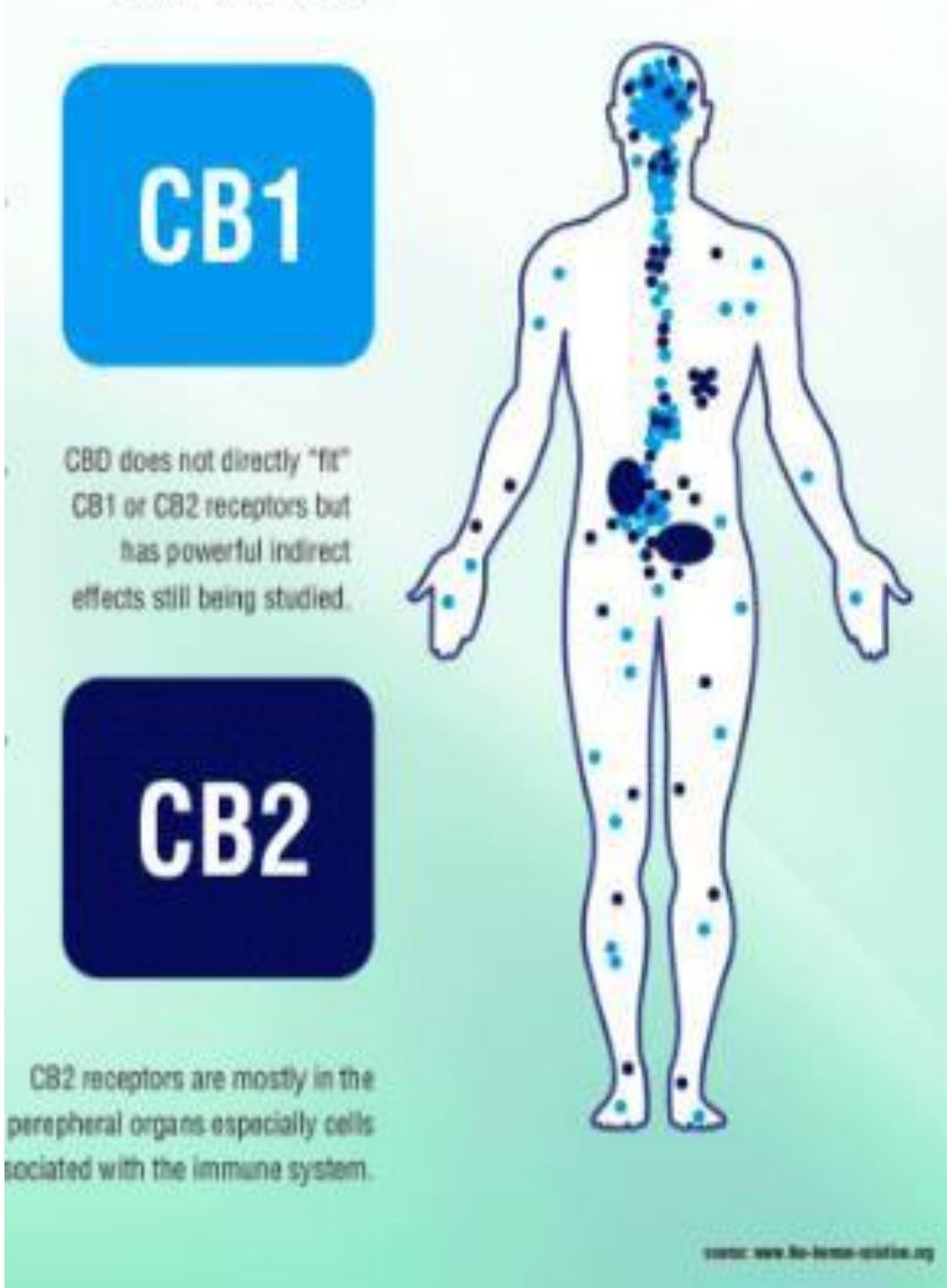
The Endocannabinoid System

- **Functions as homeostatic regulator of pain, stress, inflammation and motility**

- Comprises two main receptors:
  - CB_1 - abundant receptors important in central neurotransmission as well as enteric neurons
  - CB_2 - found on enteric neurons, and expressed by immune and epithelial cells

- Endogenous cannabinoids (Endocannabinoids)
  - N-arachidonoylethanolamine (**anandamide**)
  - 2-arachidonoylglycerol (**2-AG**)

Sharkey KA & JW Wiley. The role of the Endocannabinoid System in the Brain-Gut Axis. Gastroenterology 2016;151:252–266



Low density of CB1 receptors in the pons, brain stem and medulla

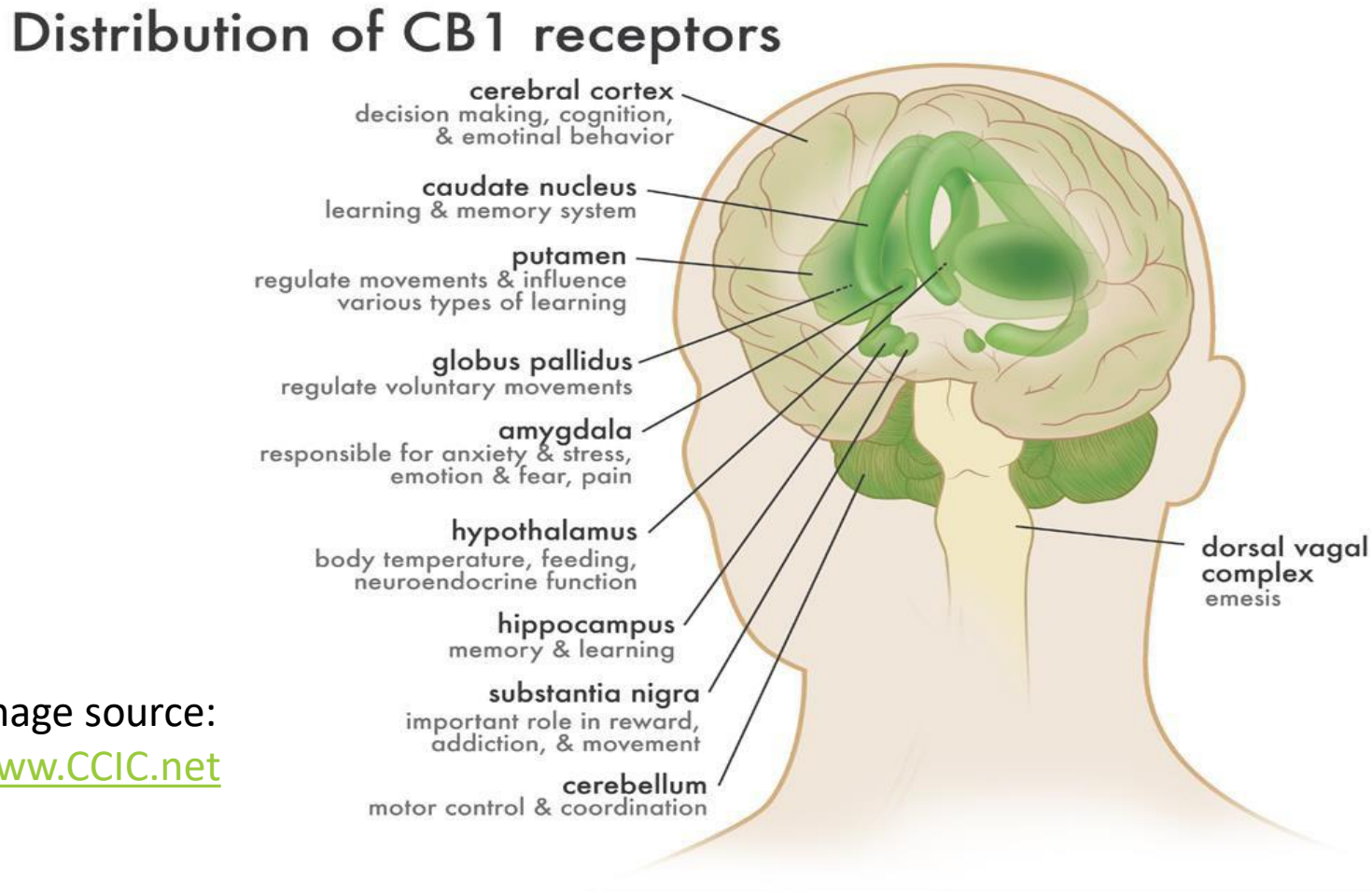
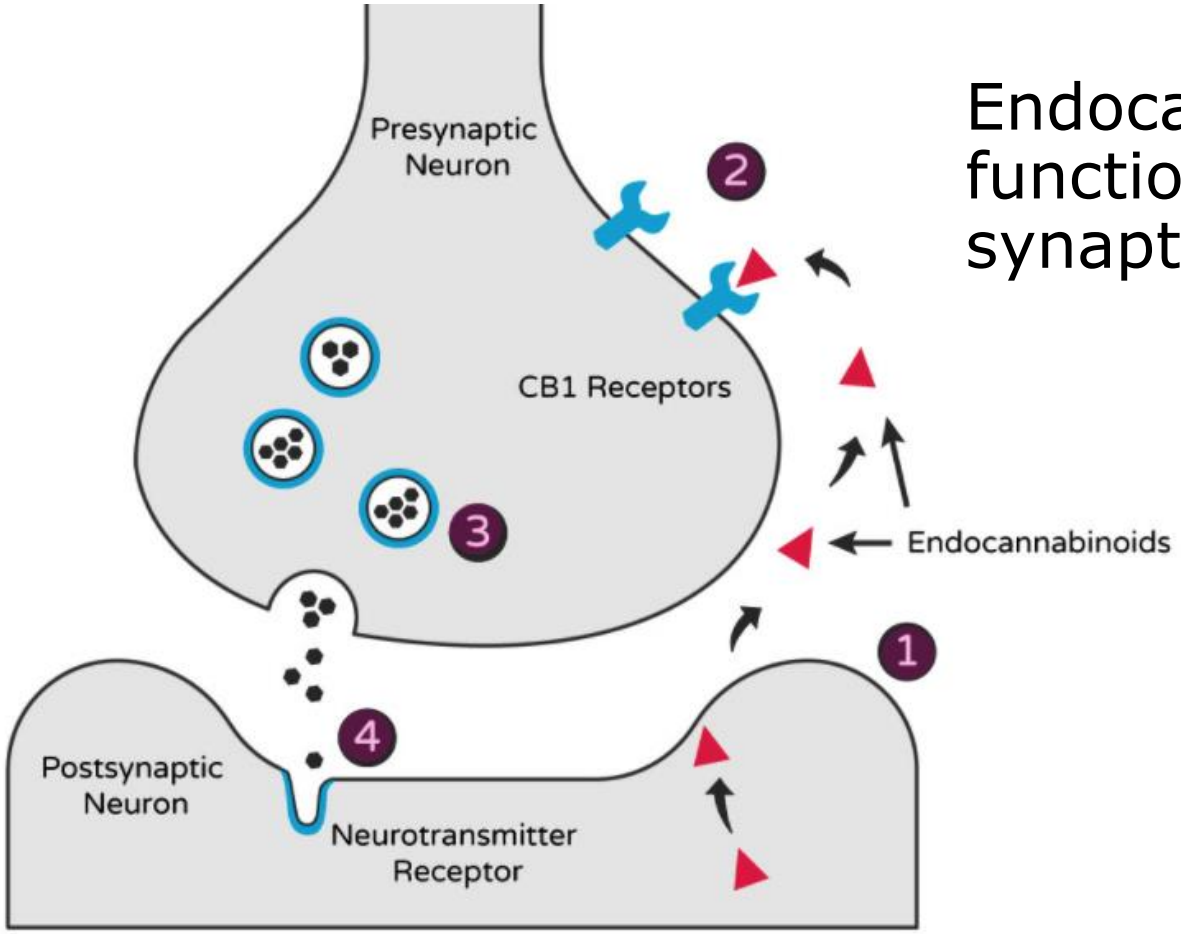


Image source:
www.CCIC.net

Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. aem. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html. Published October 12, 2018.

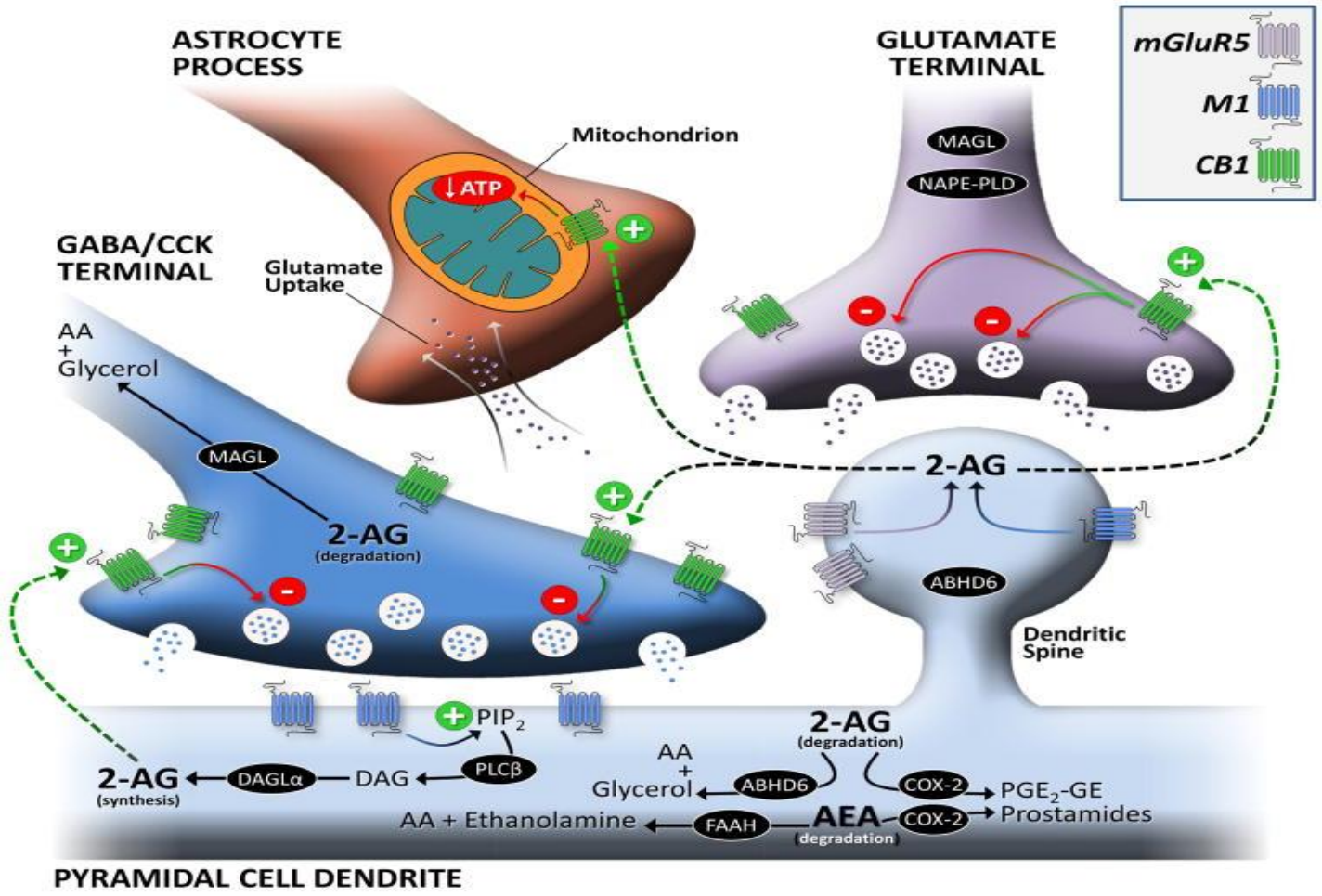
Endocannabinoids in the Nervous System



Endocannabinoids function as retrograde synaptic messengers

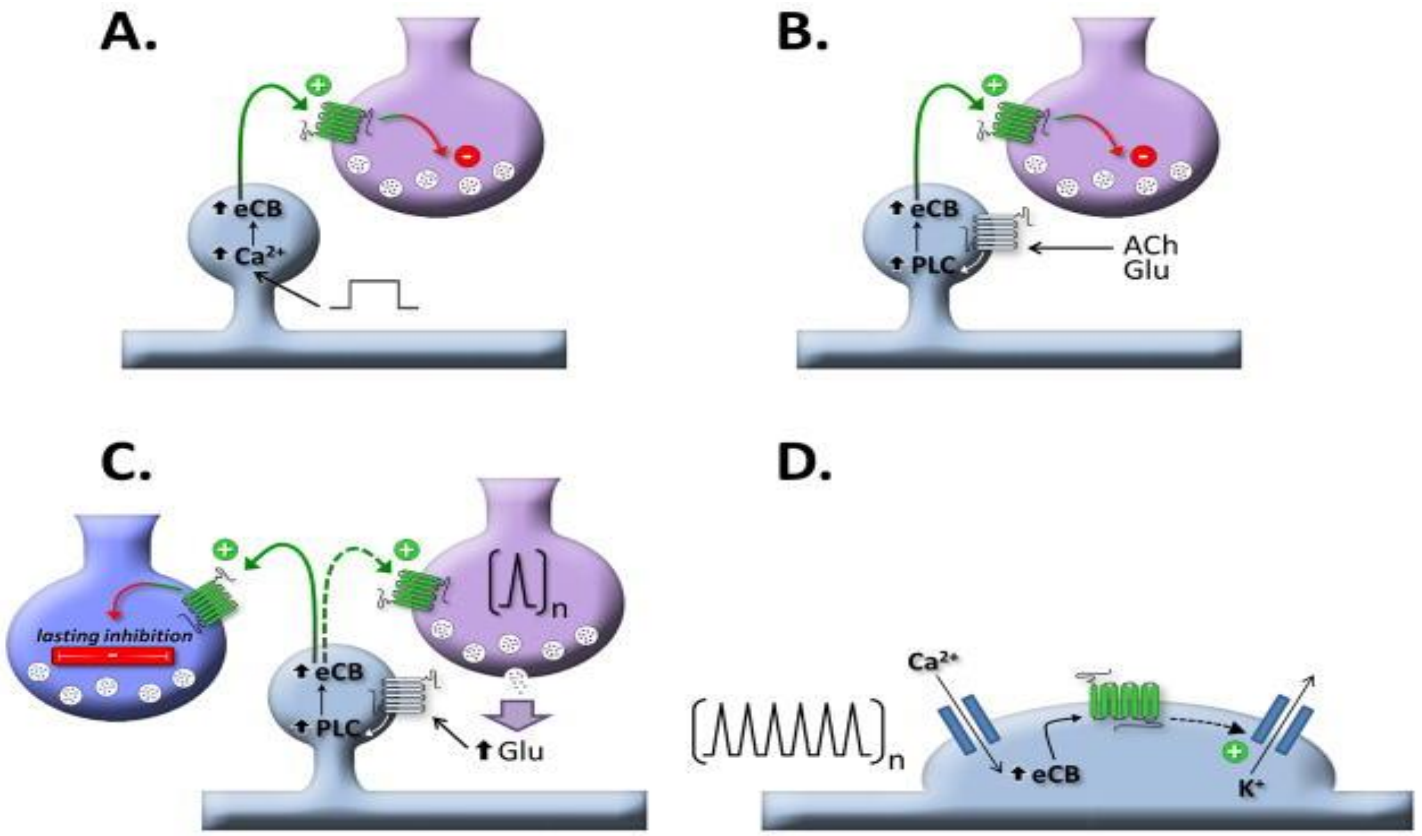
Castillo PE, et al. Endocannabinoid signaling and synaptic function.*Neuron*. 2012; 76(1):70-81.

Endocannabinoid system at the synapse



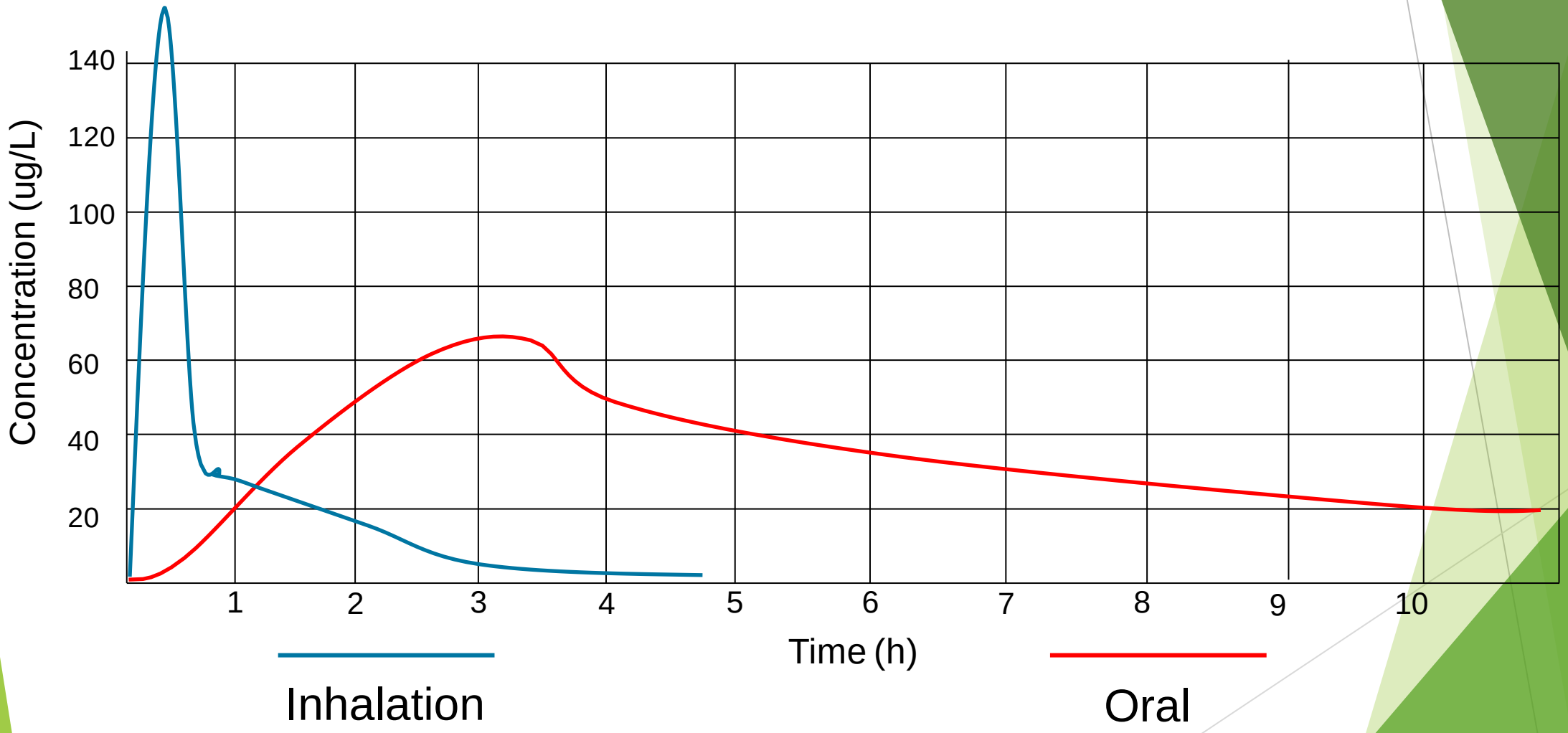
Lu, Hui-Chen, Mackie, Ken: An introduction to the endogenous cannabinoid system. Biol Psychiatry. 2016; 79(7): 516-525.

Endocannabinoid plasticity regulation



Lu, Hui-Chen, Mackie, Ken: An introduction to the endogenous cannabinoid system. Biol Psychiatry. 2016; 79(7): 516-525.

Pharmacokinetics: *Inhalation vs. Ingestion*



Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. Clin Pharmacokinet. 2003;42(2):327-360

THC Pharmacokinetics

- **Metabolism**
  - Oral Bioavailability ≈ 6-7% (extensive first pass metabolism)vs. Inhaled Bioavailablity 10%-35%
  - Metabolized by the Cytochrome P450 system (CYPP450 2C9/2C18/19), with over 100 metabolites
  - Propensity for drug interactions, yet clinically important interactions not well defined due to limited research

  Elimination
  - Half life ranges from 25-36 hours for THC, other metabolites can be 5-7 days
  - After a single or multiple use, detectable in urine for 3-12 days; metabolites up to 25 days

Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. aem. https://www.canada.ca/en/health-canada/services/drugs- medication/cannabis/information-medical-practitioners/information-health-care-professionals-cannabis-cannabinoids.html. Published October 12, 2018.

ALLOSTATIC OVERLOAD

AROUSAL TO STRESSORS

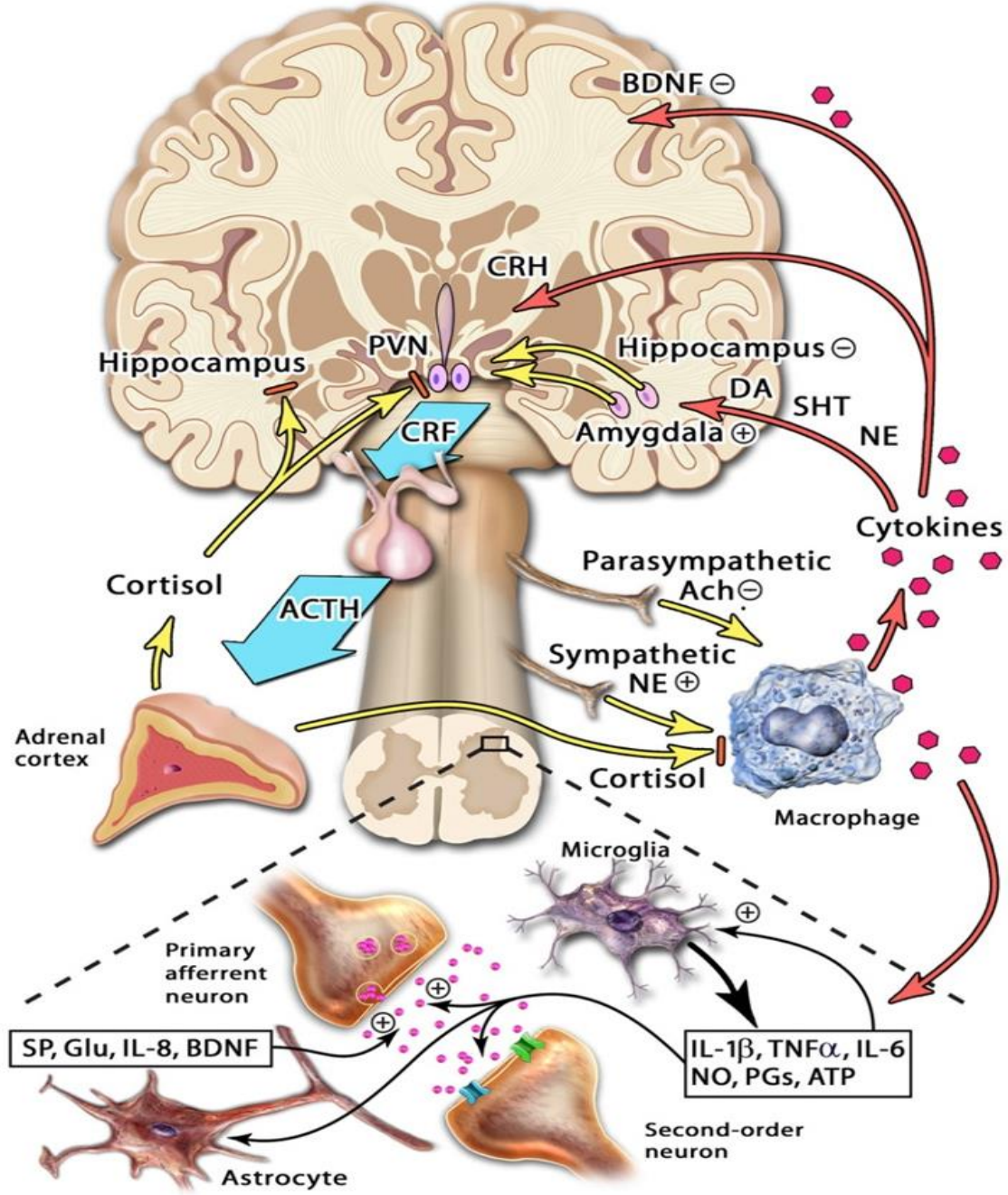
RAPID RESPONSE

FEED FORWARD SYSTEM

LACKING BOUNDARIES

STUCK "ON"

NO "OFF"



PSYCHO
NEURO
ENDOCRINE
IMMUNE
EPIGENETIC
EFFECTS

ONE YEAR STRESS = 6 YEARS CELLULAR AGING
Blackburn (2009)

HEART
STROKE
DIABETES
CANCER
ARTHRITIS
MULTIPLE SCLEROSIS
DEMENTIA

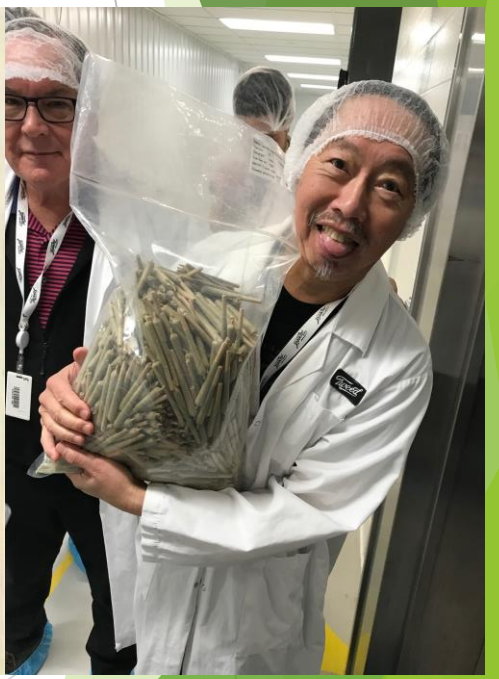
Prescribing Considerations

- Cannabis-based medical extracts taken orally can be considered long-acting medications
- Patients can use supplemental doses of more rapidly-acting inhaled (vaporized) cannabis to maintain symptomatic control for acute changes in symptoms
- Therefore, the cannabis oil and soft gel quantity must be considered alongside the recommended inhaled dried cannabis quantity as part of the patient's total daily authorized dried cannabis quantity
- Because the effects of oral and inhaled administration are different, the equivalency factor should not be used to establish an oral dose

MacCallum C, Russo EB; Practical considerations in medical cannabis administration and dosing; European Journal of Internal Medicine; (2018) 49:12-19.

Principles of Safe Prescribing

- Use oils and capsules whenever possible to provide accurate and reproducible dosing
- Start low and go slow
- See how far you can get with CBD
- Add THC to maximum tolerated CBD to:
  - Maximize target symptom relief
  - Minimize off target effects
    - Euphoria
    - Sedation
    - Nausea
- Most patients do NOT want to get high



MacCallum C, Russo EB; Practical considerations in medical cannabis administration and dosing; European Journal of Internal Medicine; (2018) 49:12-19.

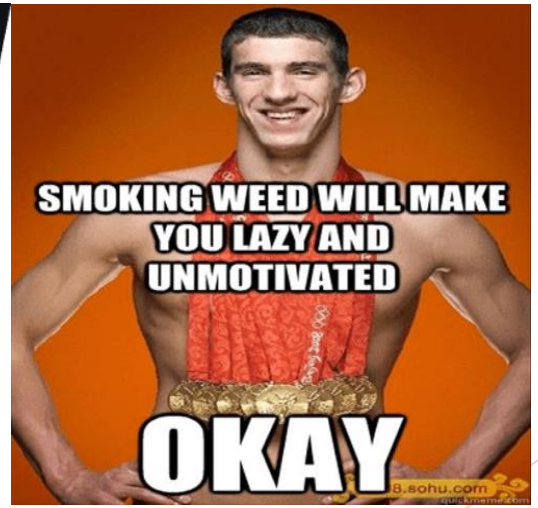
Cannabis: Adverse Events (AEs)

Most common AEs

- Drowsiness/fatigue
- Dizziness
- Dry mouth
- Cough, phlegm, bronchitis (smoking only)
- Anxiety
- Nausea
- Cognitive effects

Majority of AEs are associated with THC

- They are dose-dependent
  - 'Start Low, Go Slow' to mitigate effects
- Combine CBD with THC to further reduce THC-related AEs



MacCallum C, Russo EB; Practical considerations in medical cannabis administration and dosing; European Journal of Internal Medicine; (2018) 49:12-19.

Step 1.
Start with CBD

- Advise the patient to purchase cannabis oil containing CBD only (no THC) in highest concentration available

Practical Tip:
Take the patient to a Licensed Producer website and demonstrate how to select the appropriate product

Step 2.
Titrate CBD

- Start with 5 mg CBD at bedtime
- Increase by 5 mg every 2 days up to 40 mg if tolerated
- Dose may be limited by:
  - Nausea
  - Cost

Practical Tips:

- 5 mg of 20% CBD oil is 0.25 ml
- Titration to 40 mg should take 16 days
- 40 mg of CBD will cost ~ $4.50

Step 3.
Follow up Assessments

- See the patient in follow up at 3–4 weeks and then every 12 weeks
- Do objective assessments of response e.g. MPIIQM, DASS-21, PSQI

Practical Tip:

- Encourage the patient to keep a daily diary of:
  - Effect on target symptom
  - Tolerability

Step 4.
Add THC if Needed

- If target symptom relief has not been adequately treated, add THC
- Use the highest THC concentration product available

Practical Tip:
Take the patient to a Licensed Producer website and demonstrate how to select the appropriate product

Step 5.
Titrate THC - **SLOWLY**

- Start with ~ 2.5 mg THC add to max tolerated CBD at bedtime
- Increase by 2.5 mg every 3rd or 4th day up to 10 mg
- Dose will be limited by euphoria which will typically start at ~ 10 mg

Practical Tips:

- 2.5 mg of 25% THC oil is 0.1 ml
- Titration to 10 mg should take 16 days
- 10 mg of THC will cost ~ $1.00

Step 6.
Determine if BID or TID dosing needed

- If daytime dosing is needed, eliminate or reduce THC to a level that does not cause euphoria
- Maintain full dose of CBD for daytime use

Practical Tip:
Patients must not operate motor vehicles or engage in hazardous activities if euphoric

Step 7.
The Art of Medicine

- Work with the patient to adjust the CBD and THC to optimize:
  - Target symptom relief
  - Avoidance of euphoria and other side effects
  - Cost

Practical Tips:

- Use diaries, open frank discussion
- Most patients do NOT want to get high
- Watch for Cannabis Use Disorder
- Speak with family members

Impact of Medical Cannabis on Recovery from Playing - Related Musculoskeletal Disorders in Musicians: An Observational Cohort Study

Dr Kat Cottrell MBBS BSc DipABRSM, Dr John Chong MD BASc MSc DOHS FRCPC FACPM CGPP ARCT

McMaster University

Musicians' Clinics of Canada

Background

- Playing-related musculoskeletal disorders (PRMD) are 'pain, weakness, numbness, tingling or other symptom that interferes with the ability to play the instrument at the level you are accustomed to' [1]
- PRMD can affect musicians' ability to work, their mental health and sense of self [2]
- Musicians have an 84% lifetime prevalence of PRMD [3]
- Many types of analgesia are inappropriate for this population [4, 5, 6, 7]
- Cannabidiol (CBD) has been shown to have anti-inflammatory, neuroprotective properties, improve sleep and physical functioning, and reduce perception of pain [8,9]
- Medical cannabis has been shown to be safer than other analgesia in terms of serious adverse events [10]

STUDY AIM: To explore the impact and safety of medical cannabis for PRMD

Methods

Musicians' Clinics of Canada Routine PRMD Care

Treatment includes biofeedback, psychotherapy and lifestyle interventions. PRMD patients are offered medical cannabis as part of their treatment plan. Questionnaires are completed by patients before each visit:

- The Musculoskeletal Pain Intensity and Interference Questionnaire for Musicians (MPIIQM) [11]
  - MPIIQM40 for pain intensity
  - MPIIQM50 for pain interference
- The Depression, Anxiety and Stress Scale (DASS-21) [12]
- Questionnaire on medical cannabis dosing, positive and negative effects

Retrospective Observational Cohort Study

- McMaster HiREB approval: May 2021
- Consent obtained from patients who attended the clinic between Jan 2019 and Jan 2020, >18 years old with PRMD

Data Collection

- The 204 eligible study participants were split into 3 groups:
  - 'Non-cannabis users' who declined medical cannabis (42)
  - 'New medical cannabis users' with baseline questionnaire data (61)
  - 'Long-term medical cannabis users' without baseline questionnaire data prior to starting medical cannabis (101)
- Questionnaire data from participants' first visit in the study period, and a subsequent visit six-months later were collected

Data Analysis

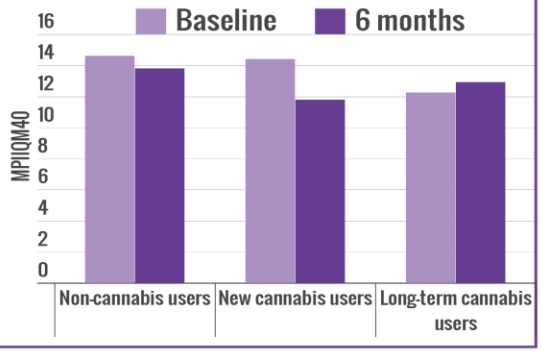
- Baseline and six-month data were compared within each group using paired t-tests
- Between group differences were assessed using ANOVA

Results

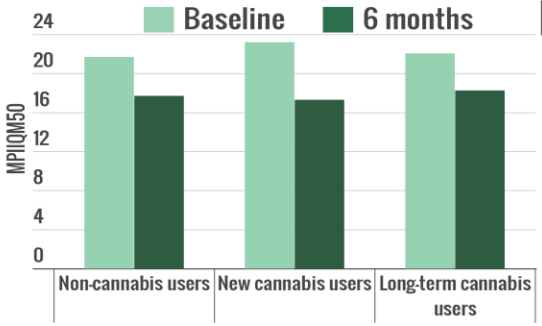
Pain Intensity (MPIIQM40)

New cannabis users had a **significant reduction in pain intensity** (p=.002) at six-months.

A **significant difference** in **pain intensity** was shown for new vs long-term cannabis users (p=.023) at six-months.



Pain Interference (MPIIQM50)



Non-users (p=.035), **new users** (p=.002) and **long-term cannabis users** (p=.009) all had **significant reductions in pain interference** at six-months.

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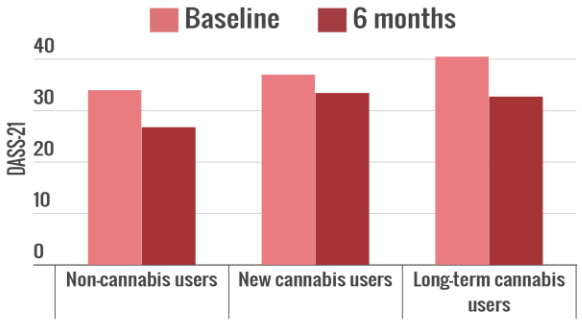

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THANKS FOR YOUR ATTENTION

QUESTIONS?