

# The endocannabinoid system: What RDs should be aware of when providing services to people who use cannabis

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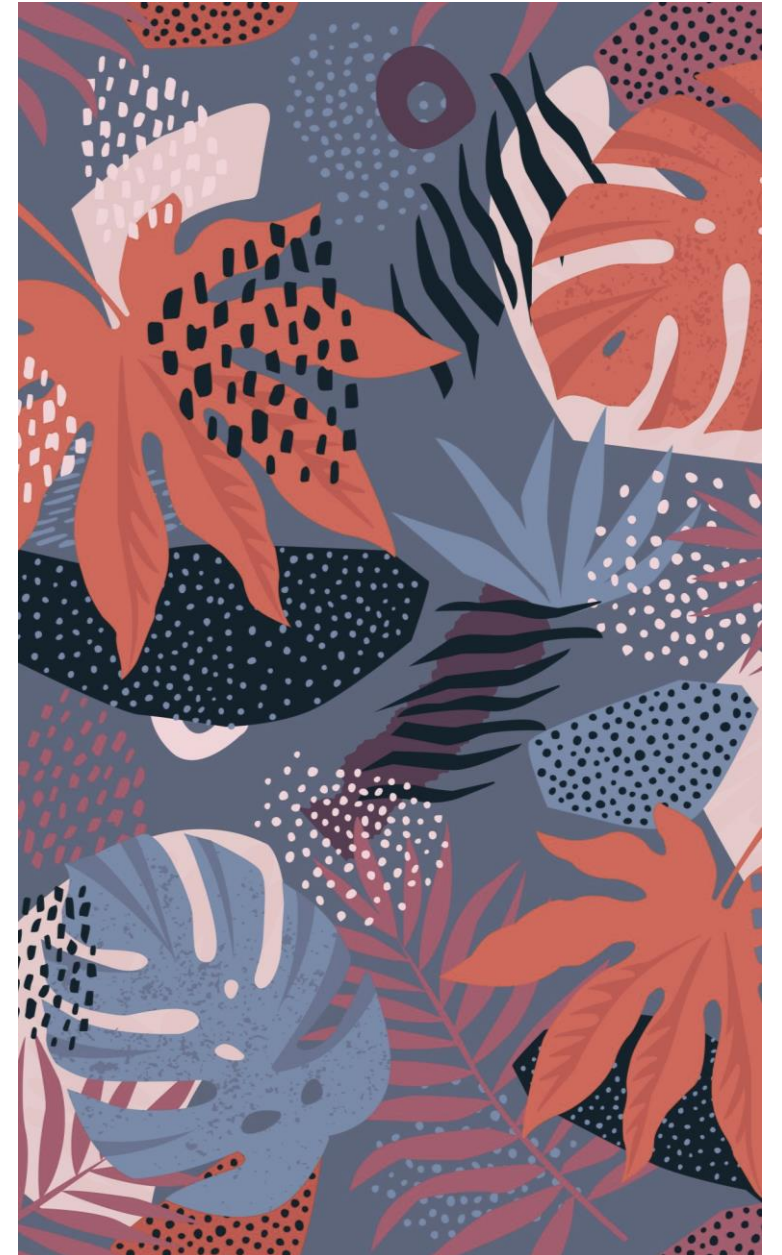
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# Learning Objectives:

## Describe

Describe the components and role of the endocannabinoid system

## Summarize

Summarize the effects of cannabis on the endocannabinoid system within various organ systems

## Review

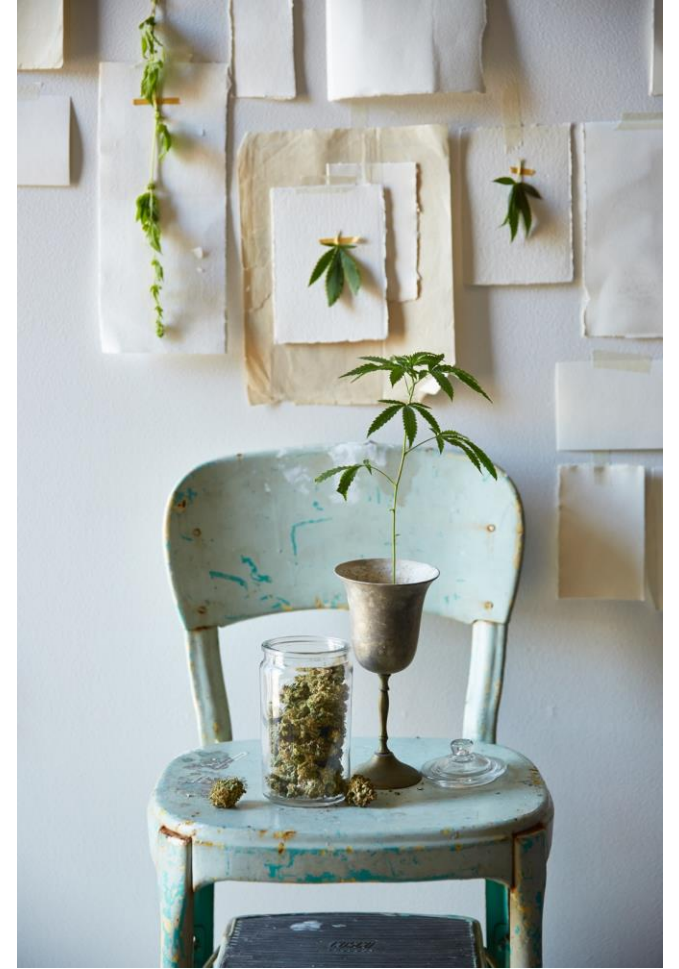
Review practical recommendations for working with patients who use cannabis



# Disclaimer

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The views presented within this talk are my own,  
and do not reflect the views of my employer





# Poll!

Please enter in chat box:

- Area you practice in
- Do you counsel/provide MNT to, or otherwise engage with individuals using cannabis?

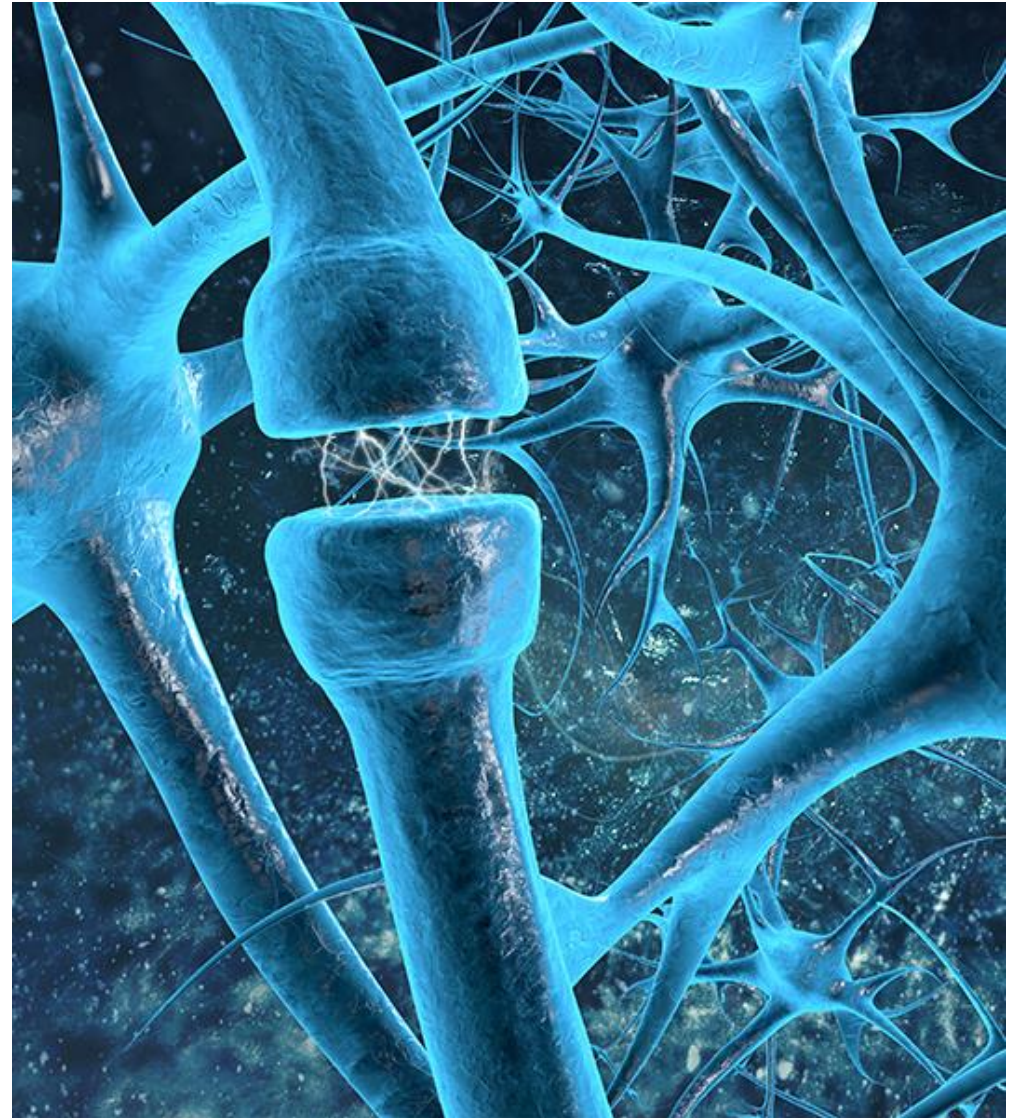


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# The Endocannabinoid System (ECS)

## **Neuromodulatory system:**

1. Cannabinoid Receptors (CB1, CB2)
2. Endocannabinoids (ligands, or signaling molecules)
3. Metabolic Enzymes (regulate the synthesis and degradation of the endocannabinoids)



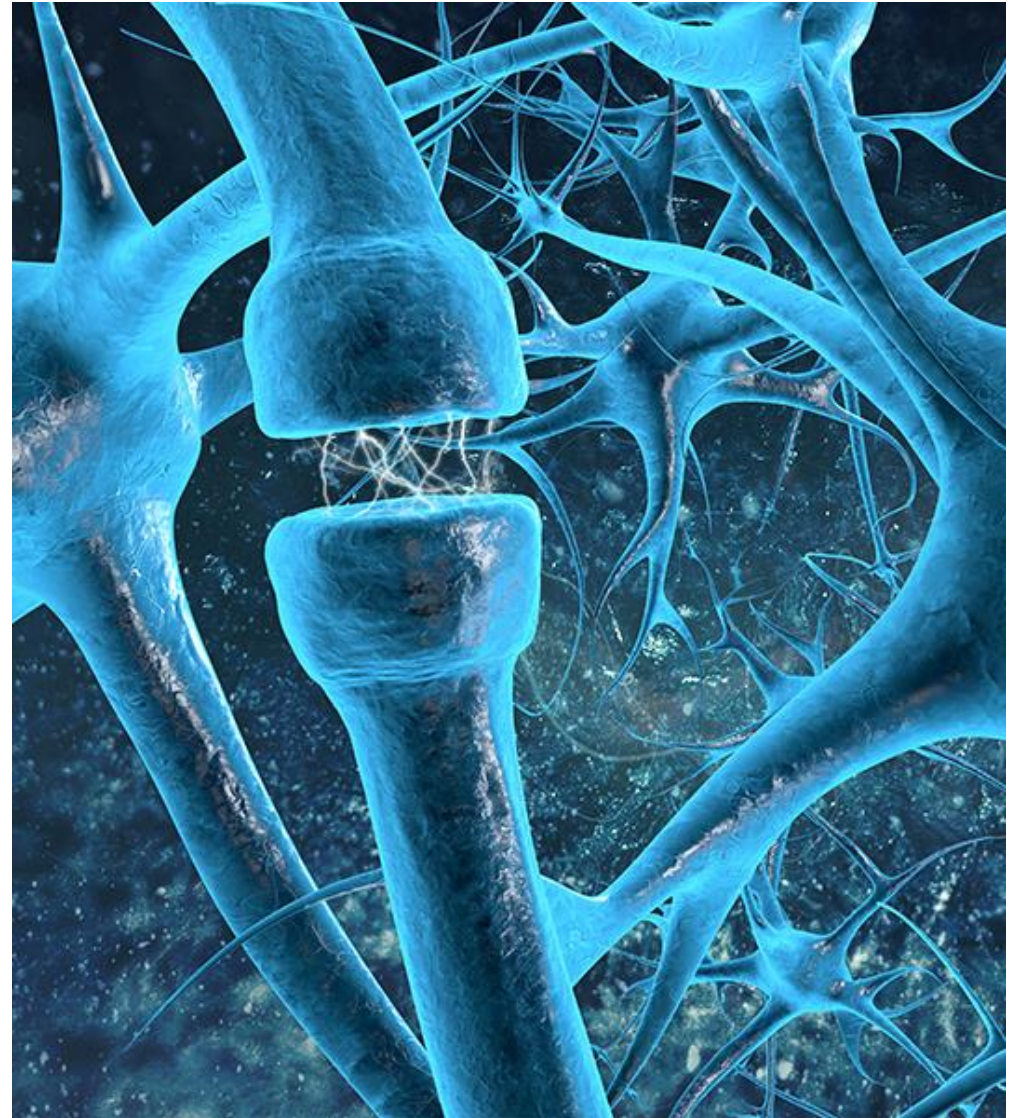


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# The Endocannabinoid System (ECS)

## Receptors:

1. Cannabinoid Receptor 1 (CB1)
  - i. Brain
  - ii. Nervous system
  - iii. Gastrointestinal system
  - iv. Cardiovascular system
  - v. Uterus
  - vi. Ovary
2. Cannabinoid Receptor 2 (CB2)
  - i. Immune and hematopoietic cell lines
  - ii. Spleen
  - iii. Tonsils
  - iv. Uterus
3. Additional Receptors with CB activity
  - i. Vanilloid Receptors (TRPV1, TRPV2...)
  - ii. G-Protein Coupled Receptors (GPCR)



# The Endocannabinoid System: Cannabinoids

Type	Name	Comments
Endogenous (bioactive lipids)	N-arachidonylethanolamind (Anandamide)	Runners high? “bliss”
	2-arachidonoylglycerol (2-AG)	
Exogenous (Phytocannabinoids)	$\Delta^9$ - Tetrahydrocannabinol (THC)	Primarily in <i>Cannabis Sativa</i>
	Cannabidiol (CBD)	Primarily in <i>Cannabis Indica</i>
	Cannabigerol (CBG)	First purified cannabinoid
Exogenous (Synthetic & Purified)	Dronabinol	FDA approved
	Nabilone	FDA approved
	Nabiximols	Canada, Europe
	Rimonabant	Europe- withdrawn
	Epidiolex®	FDA approved

Schrot & Hubbard Annals of Medicine, 48; 128-141 (2016)  
 Lu & Anderson Can J. Physiol Pharmacol 95:311-327 (2017)  
 Gerich et al, Am J of Gastroenterology 110; 208 (2015)  
 Fuss et al Proc Natl Acad Sci ;112(42):13105-8 (2015).  
 Martin et al Clin Pharmacokinet;57(5):539-545.(2018)

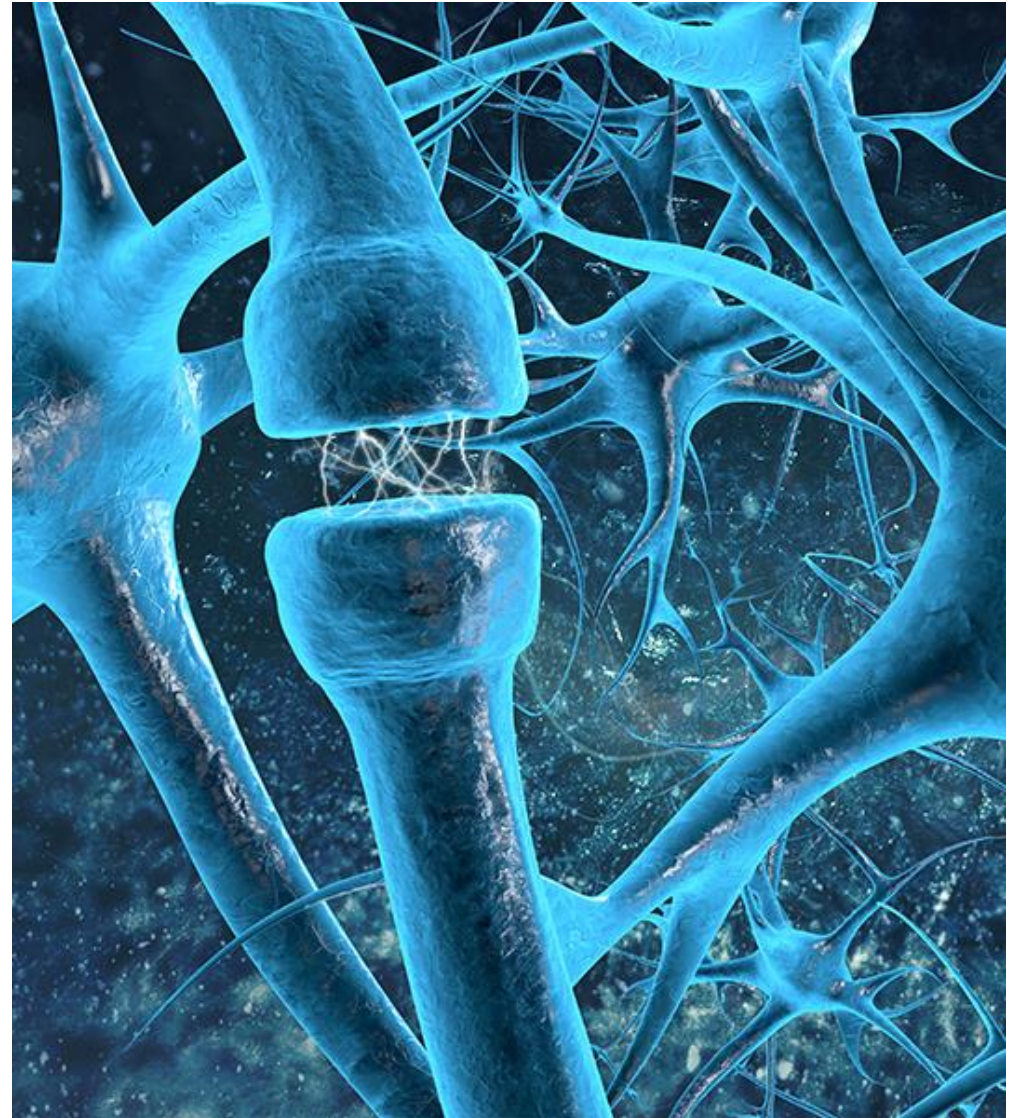


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# The Endocannabinoid System (ECS)

## Metabolic Enzymes (degradation):

1. Fatty acid amide hydrolase (FAAH) – primarily metabolizes anandamide and 2-AG
2. Monoacylglycerol lipase (MAGL)- primarily for 2-AG



# The Endocannabinoid System (ECS)

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## CB1:

- Regulate appetite and energy expenditure
- Analgesic effect for pain
- GI motility
- Mood
- Sleep

## CB2:

- Regulate inflammation
- Prevention of GI inflammation



# The Endocannabinoid System (ECS): Cardiovascular System

## CB1 Activation:

- Activation of sympathetic nervous system
- Decreased heart rate
- Decreased blood pressure\*
- Decreased myocardial contractility
- Increased coronary dilation

## CB2 Activation:

- Potential Anti-Atherogenic Effects\*(?)





# The Endocannabinoid System (ECS): Cardiovascular System

## Polymorphism in FAAH (C385A): ↓ FAAH activity

- Increased risk of myocardial infarction
- Predisposition to hypotension
- FAAH polymorphism was associated with increased risk of MA among those with chronic heart failure

## Polymorphism of CB1 gene CNR1

- Higher cholesterol levels with a SNP (genotype AA) of CNR1



# The Endocannabinoid System (ECS): Gastrointestinal System

## CB1 Activation:

- Increase appetite; food intake
- Decrease emesis (due to impact on motility)
- Reduce gastric acid secretion
- Reduce gastric emptying

## CB2 Activation:

- Present in smaller concentrations compared to CB1
- Less of a role in the gut, however, potentially reduce GI inflammation

# What is cannabis?

A close-up photograph of a cannabis flower, showing the intricate structure of the buds and the fine, golden trichomes that cover them. The lighting is warm and focused on the flower, with a blurred background of other parts of the plant.

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**SLANG TERMS: WEED, POT MARIJUANA,  
REEFER, MARY JANE**

A photograph of a cannabis plant with several large, green, serrated leaves. The plant is in the foreground, and the background is a soft, out-of-focus green, suggesting a growing environment.



# Cannabis has had a complicated history...

Date	Event
2700 BC	Chinese Emperor Shen Nung reported healing properties of cannabis (evidence of cannabis found on/in mummies)
1213 BC	Cannabis used by Egyptians for glaucoma and inflammation
1611-1762	Jamestown Settlers bring cannabis to North America
1850	Cannabis added to U.S. Pharmacopeia
1915-1927	States begin passing cannabis prohibition laws
1937	“Marihuana Tax Act” promoted by Harry Anslinger caused decreased in prescriptions
1942	Cannabis removed from the U.S. Pharmacopeia
1970	Controlled Substances Act classifies cannabis as having “no accepted medical use”
1990	Scientists discover cannabinoid receptors

# Pharmacologic Effects of Cannabis (Broadly)

- >400 compounds;
  - Delta-9-THC
  - CBD
- Used for centuries for
  - Stress
  - Pain
  - Nausea/vomiting
  - Epilepsy
- Rigorous studies on interactions with nutrients are lacking



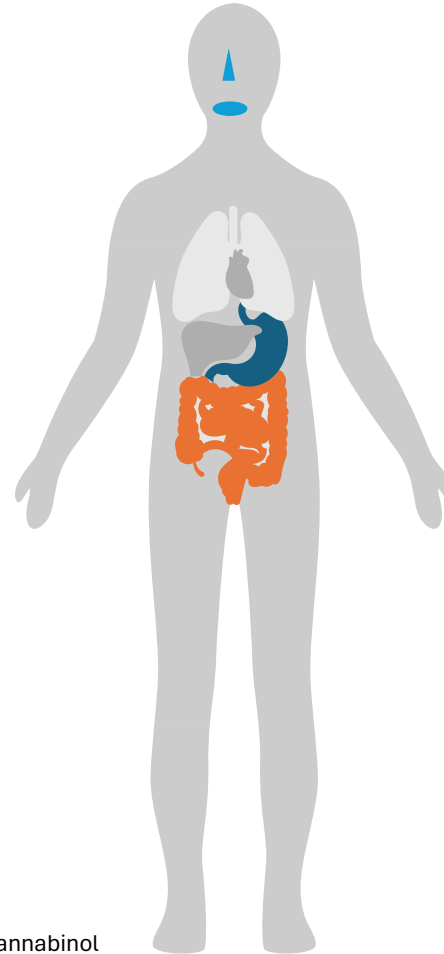
# Cannabis and effects on ECS- GI

## How does cannabis impact the gastrointestinal tract?

The endocannabinoid system receptors (CB1 & CB2) are found in many organ systems throughout the body<sup>1</sup>:

- Gastrointestinal system
- Cardiovascular system
- Nervous system

Components like delta-9-tetrahydrocannabinol (THC) within cannabis interact with these receptors<sup>1</sup>



1

### Appetite

THC increases food intake<sup>2,3</sup>

2

### Taste and smell

THC may alter taste and smell<sup>6,7</sup>

3

### Gastric acid secretion

THC may decrease gastric acid secretion<sup>5</sup>

4

### Gastrointestinal motility

THC slows gastrointestinal motility<sup>4</sup>  
Decreased gastric emptying  
Decreased LES Tone  
Decreased colon motility

CB1: Cannabinoid Receptor 1, CB2: Cannabinoid Receptor 2, THC: delta-9-tetrahydrocannabinol  
LES: Lower Esophageal Sphincter

<sup>1</sup> McPartland et al PLoSOne 2014 <sup>2</sup>Foltin et al *Appetite* 1988 <sup>3</sup> Mattes et al. *Pharmacol Biochem Behav.* 1994 <sup>4</sup> Izzo and Sharkey *Pharmacol. Ther.* 2010 <sup>5</sup>Pazos et al. *J. Histochem. Cytochem.* 2008 <sup>6</sup>Walter et al *Br. J. Clin. Pharmacol.* 2014 <sup>7</sup>Tarragon and Moreno *Chem. Senses* 2019





# Cannabis and effects on ECS- Appetite

How much food?	What kind of food?	Does it matter?
<p><u>Population studies:</u> 2835 vs 2271 calories<sup>1</sup> 3365 vs 2746 calories<sup>2</sup></p> <p><u>Experimental studies:</u> ↑ calories by 40%<sup>3</sup> 3726 vs 2545 calories<sup>4</sup></p>	<p><u>Population studies:</u> ↑ salted snacks, chips, popcorn, pretzels and ↓ Fruit<sup>1</sup> ↓ Diet quality<sup>5</sup></p> <p><u>Experimental studies:</u> ↑ “Sweet solids e.g. candy bars” and between meal snacks<sup>3</sup></p>	<p><u>Population studies:</u> ↓ Serum antioxidants<sup>1</sup> No difference in BMI<sup>2</sup> ↓ BMI<sup>6</sup></p> <p>Does this difference in food intake persist?</p>

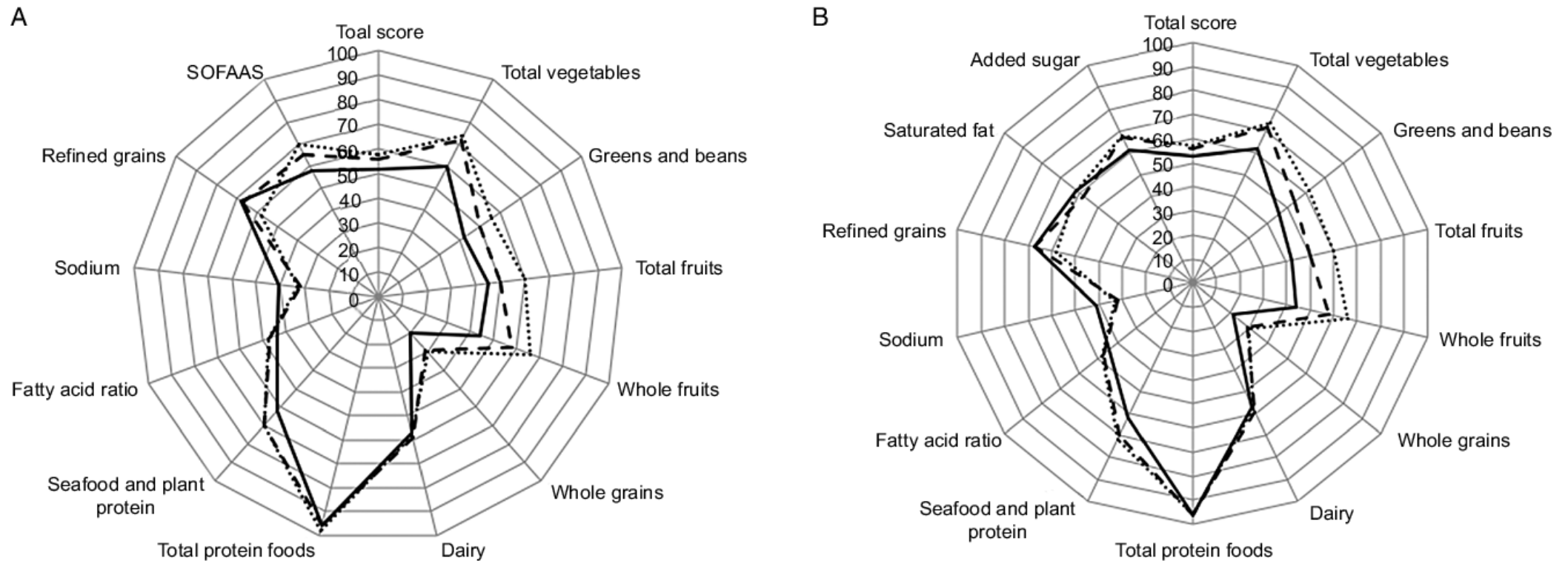
<sup>1</sup>Smit and Crespo *Pub Health Nutr* 2001 <sup>2</sup>Rodondi et al *Am J Cardiol* 2006 <sup>3</sup>Foltin et al *Appetite* 1988 <sup>4</sup>Mattes et al 1994 *Pharmacol Biochem Behav*

<sup>5</sup>Gelfand and Tangney *Pub Health Nutr* 2020 <sup>6</sup>Ngueta et al *Obesity* 2015

# Cannabis and effects on ECS- Appetite



Dietary Quality Differs Among Cannabis Use Groups: Data from the National Health and Nutrition Examination Survey 2005-2016 (Gelfand & Tangney 2020 *Public Health Nutrition*)

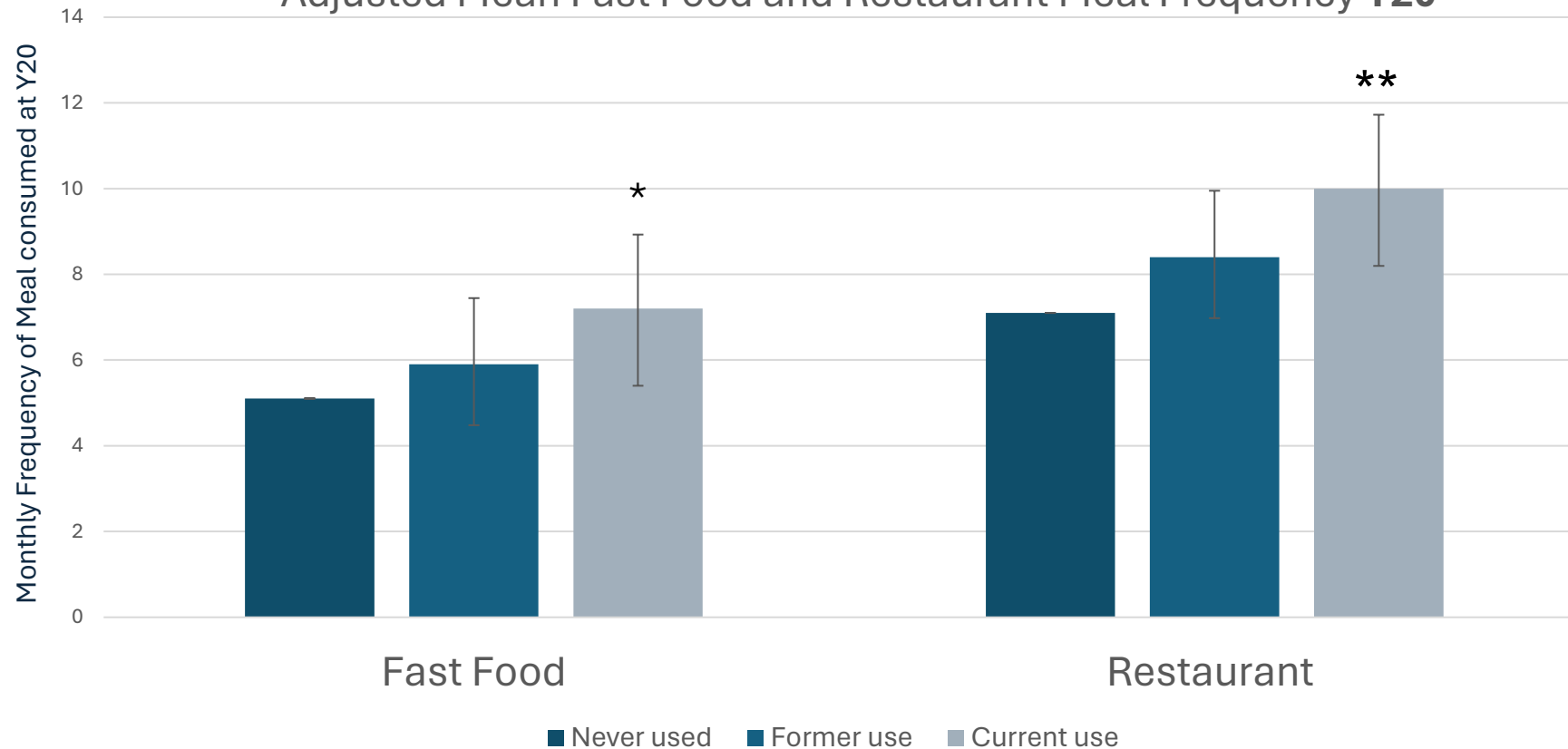


**Fig. 2** Total score and individual component scores of cannabis use groups for Healthy Eating Index (HEI)-2010 (A) and HEI-2015 (B). Subcomponent scores shown are percentages of total possible points (scores were divided by total possible points to get a percentage); the total score remains out of 100. **Dotted lines represent never users, long dashed lines represent previous users, and solid black line represents current cannabis users** (Total N=17,855; Never use n=8216; Former Use n=7127; Current use n=2510)



# Monthly Fast Food and Restaurant Frequency (*unpublished data*)

Adjusted Mean Fast Food and Restaurant Meal Frequency Y20



Adjusted for sex, center, race, age, marital status, education, body mass index, physical activity, cigarette smoking, alcohol use

\*p=0.049 ( $\beta$  2.1 95% CI: 0.4, 3.8 for current vs never use)

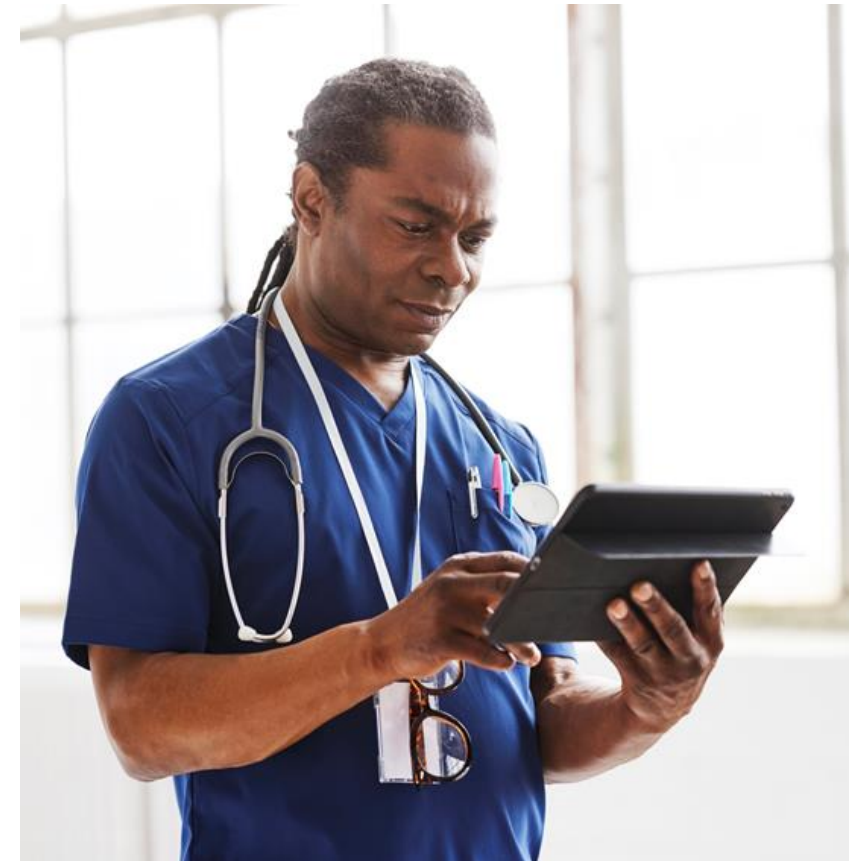
\*\*p<0.01 ( $\beta$  2.8 95% CI: 1.1, 4.6 for current vs never use)



# Cannabis and effects on ECS- GI

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- Hyperemesis syndrome
  - Chronic cannabis use (daily)
  - Episodic vomiting (cyclic)
  - Relief by cessation of cannabis
  - Pathologic bathing behavior
    - Long hot showers or baths
  - Symptoms usually present  $\geq 6$  mos
  - \*\*\* Controversy in the literature, very heterogenous cases, hard to diagnose







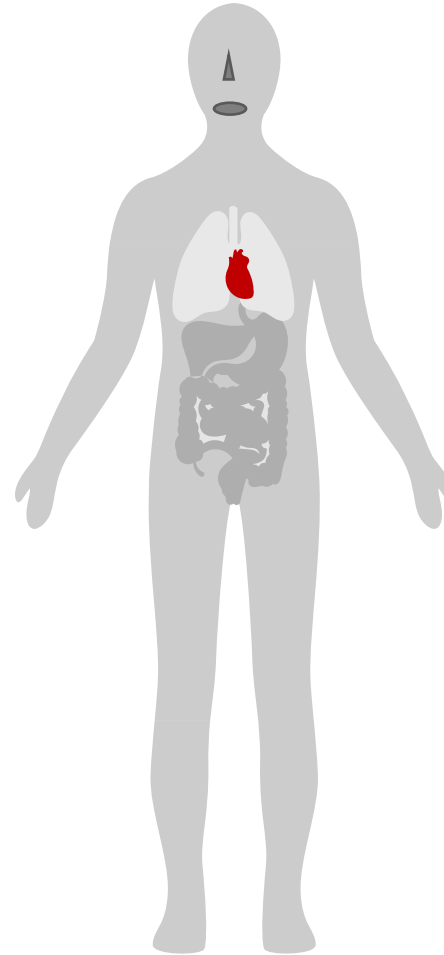
# Cannabis and effects on ECS- CV

## How does cannabis impact the cardiovascular system?

The endocannabinoid system receptors (CB1 & CB2) are found in many organ systems and tissue throughout the body<sup>1</sup>:

- Gastrointestinal system
- Cardiovascular system
- Nervous system

Components like delta-9-tetrahydrocannabinol (THC) within cannabis interact with these receptors<sup>1</sup>



1

### Cannabis use Activates Sympathetic Nervous System

Increases heart rate  
Increases supine blood pressure  
Increases platelet activation  
\*\*CBD alone may have different effects

2

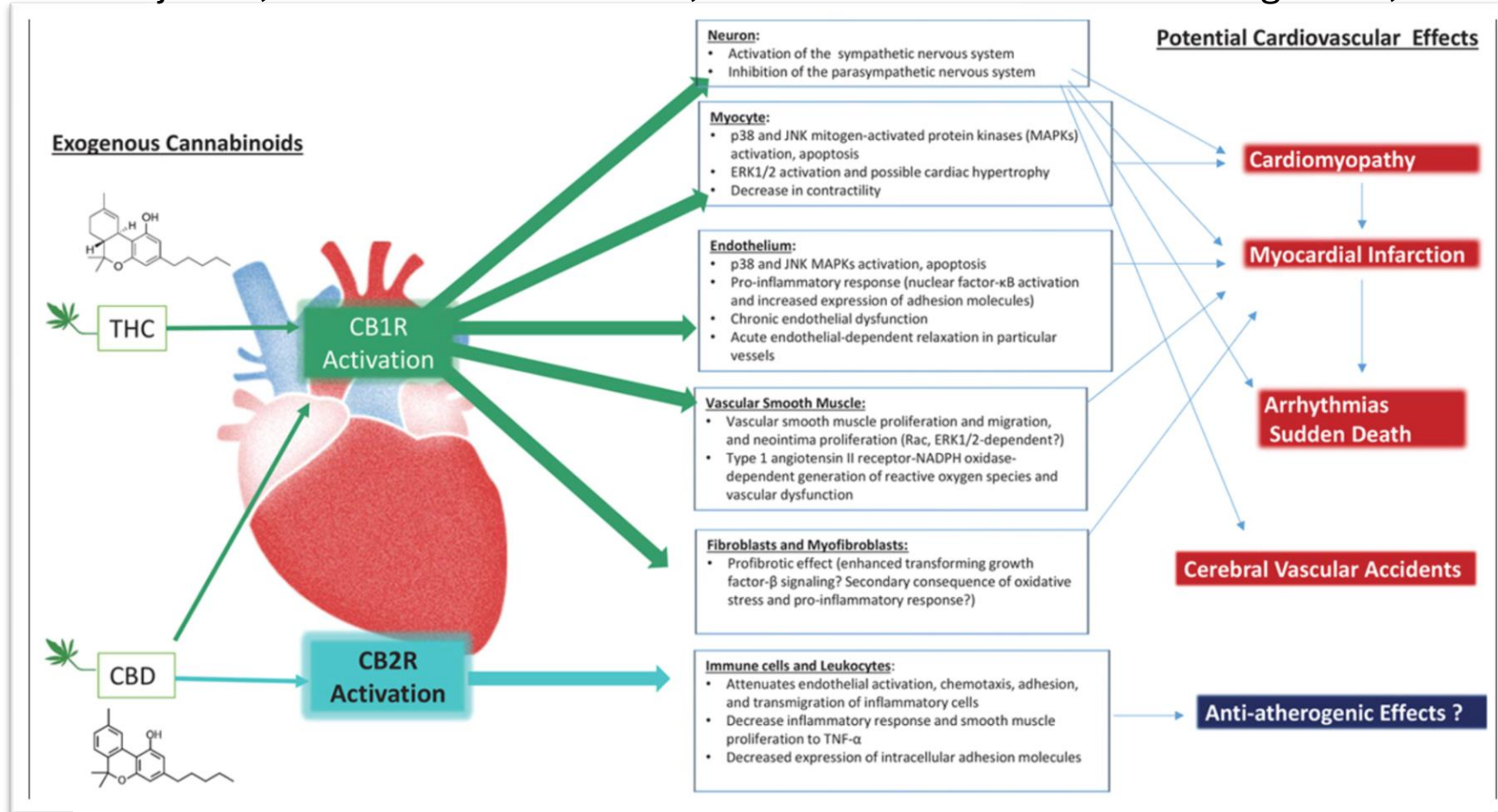
### Cerebrovascular Events

Weekly use associated with increased risk of stroke/transient ischemic attack

3

### Myocardial Infarction

Data are mixed, short term, many are observational  
Increased arrhythmia's



**Figure 5. Effects of exogenous cannabinoids on the cardiovascular system.** CB<sub>1</sub>R indicates cannabinoid receptor subtype 1; CB<sub>2</sub>R, cannabinoid receptor subtype 2; CBD, cannabinoid; ERK, extracellular signal-regulated kinases; JNK, c-Jun N-terminal kinase; MAPK, mitogen-activated protein kinases; THC, Δ-9-tetrahydrocannabinol; TNFα, tumor necrosis factor-α; and ?, questionable. Data derived from DeFilippis et al,<sup>20</sup> Pacher et al,<sup>21</sup> and Rezkalla and Kloner.<sup>22</sup>



# Cannabis and effects on ECS-CV

**Hypertension**

No association with cannabis use and BP<sup>1</sup>

Sustained cannabis use not associated with HTN<sup>2</sup>

CBD may be associated with ↓ BP<sup>3</sup>

**Atherosclerotic Cardiovascular Disease Risk Score**

UK BioBank: positive association between estimated 10 year ASCVD and heavy lifetime use in males only<sup>4</sup>

NHANES: No association between cannabis use and ASCVD<sup>5</sup>

Cannabis was associated elevated ASCVD score<sup>6</sup>

**Metabolic/Dyslipidemia**

NHANES: Lower levels of fasting insulin, HOMA—IR, smaller waist circumference<sup>7</sup>

No association between self-reported cannabis use and cardiometabolic profiles (dyslipidemia, diabetes, obesity)<sup>5</sup>

<sup>1</sup>Corroon et al Am J HTN 36;651-659 (2023)  
<sup>2</sup>Sha et al J Clin Hypertens. 25;47-52 (2023)  
<sup>3</sup> Kumric et al Biomedicine & pharmacotherapy (2023)  
<sup>4</sup> Valle Eur J Internal Med 111;69-76 (2023)  
<sup>5</sup>Alhassan et al Circulation (2023)  
<sup>6</sup>Skipina et al Am J Cardiol 165;46-50 (2022)  
<sup>7</sup>penner et al Am J Med 1236; 583-9 (2013)



# New Study found increased risk of arrhythmias:



European Society  
of Cardiology

European Heart Journal (2024) 45, 475–484  
<https://doi.org/10.1093/eurheartj/ehad834>

**CLINICAL RESEARCH**

*Epidemiology, prevention, and health care policies*

## **Cannabis for chronic pain: cardiovascular safety in a nationwide Danish study**

**Anders Holt** <sup>1,2\*</sup>, **Nina Nouhravesh** <sup>1</sup>, **Jarl E. Strange** <sup>1,3</sup>,  
**Sebastian Kinnberg Nielsen**<sup>1</sup>, **Anne-Marie Schjerning** <sup>4,5</sup>, **Peter Vibe Rasmussen**<sup>1</sup>,  
**Christian Torp-Pedersen** <sup>6,7</sup>, **Gunnar H. Gislason** <sup>1,5,7,8,9</sup>, **Morten Schou** <sup>1,8</sup>,  
**Patricia McGettigan** <sup>10</sup>, and **Morten Lamberts** <sup>1,8</sup>

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Received 4 June 2023; revised 20 November 2023; accepted 1 December 2023; online publish-ahead-of-print 11 January 2024

Authors found increased risk of  
\*Did not adjust for cigarette  
smoking (limitation of using this  
type of data, information on  
smoking was not available)



# The impact of cannabis on health outcomes is still emerging, and challenging because

Confounding variables:



- Often have to use observational data
- Lack of high-quality evidence
- Placebo controlling is difficult due to psycho-affective impact
- Very important to critically evaluate the literature

# Recommendations for the RD- Assessment

For individuals using cannabis, additional assessment questions include:

- Medical or recreational use?
  - If medical, what reasons are they consuming it for?
  - Prescribed by MD, or self-prescribed?
- How often, and when do they consume?
  - During the day when it could impact food intake?
  - Night time only use?



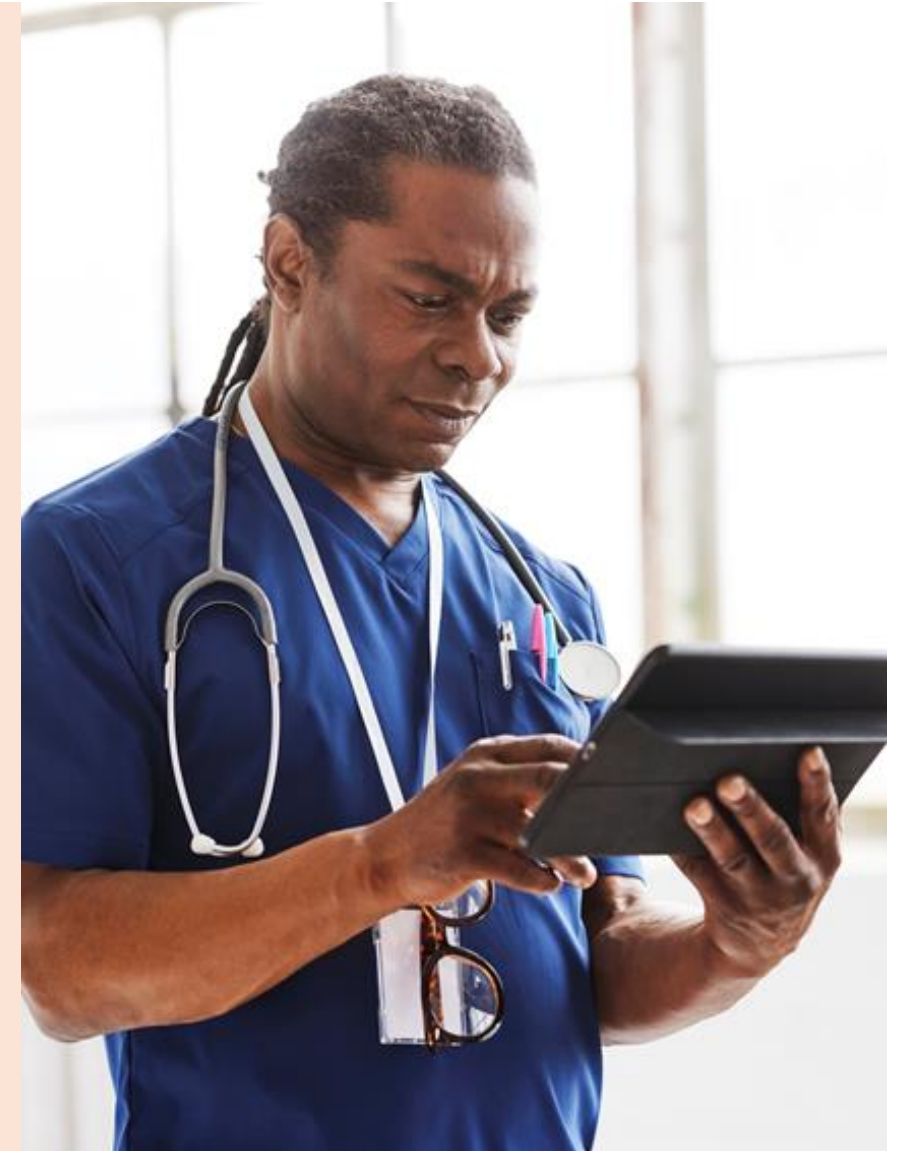
# Recommendations for the RD- Assessment

- Mode of intake?
  - Edible?
  - Smoking?
  - Tincture?
  - Transdermal patch?
  - Suppository? (more likely for medical use if severe N/V)
- If obtaining cannabis at a dispensary, dose and type of cannabinoid consumed (CBD, THC, Delta-8?)



## Recommendations for the RD

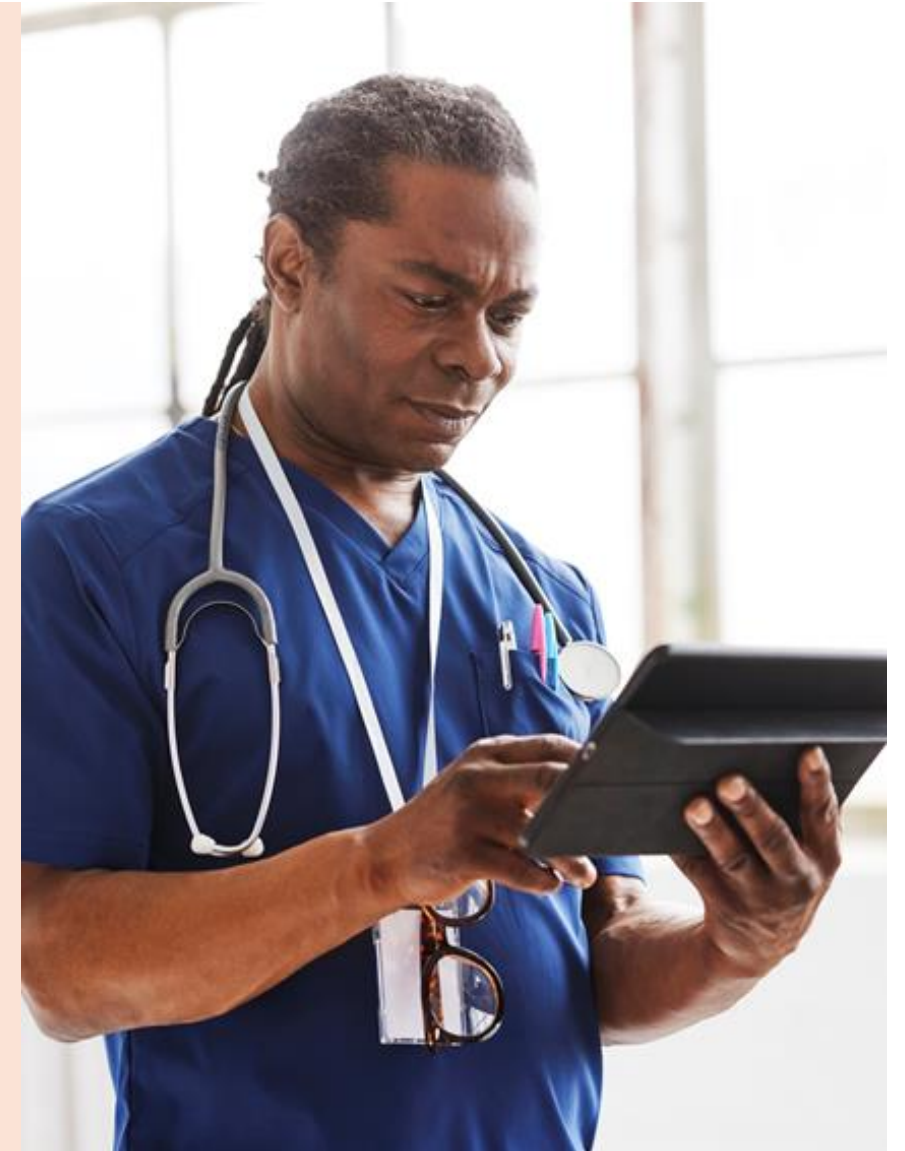
- Does their healthcare team know?
- Oral care routine? (dry mouth can have negative effects on oral) health
- Diet assessment and timing- when are they using cannabis in relation to when they are eating meals and snacks
- Focus on the gut ;)
  - We already do this, but keep in mind the impact of cannabis on GI motility
- If the individual has a cardiac condition/any history of cardiac diagnoses, consult with care team (with the individuals permission)- remember that CBD alone may contribute to lowered BP





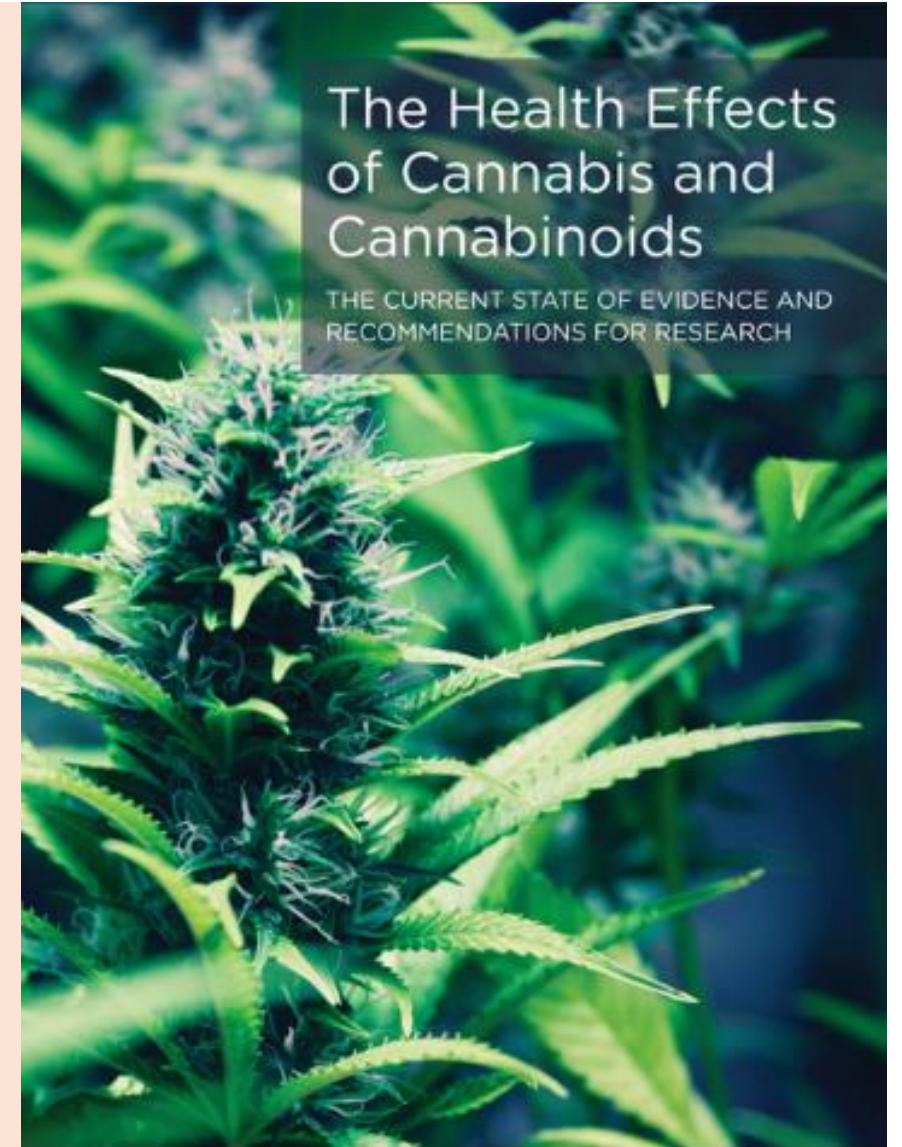
## Recommendations for the RD

- Focus on goal of your MNT, remembering that cannabis can:
  - slow digestion
  - decrease gastric acid production
  - increase energy intake, and alter food choices towards a poorer diet quality
  - potential to decrease blood pressure if taking only CBD
  - Potential to alter other aspects of the CV system and recommend patient monitor how they feel (dizziness, heart palpitations, etc)



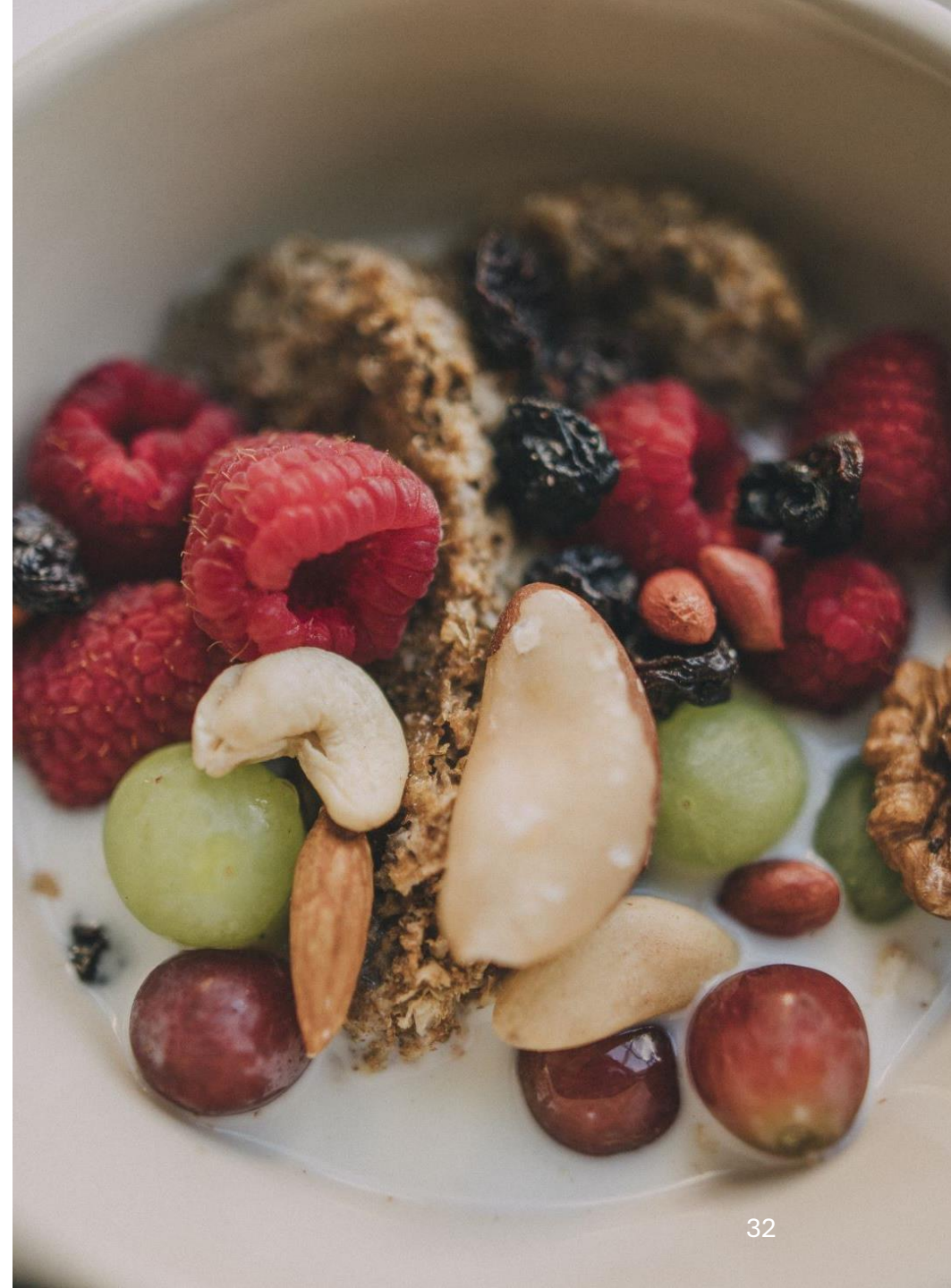
## Recommendations for the RD: Additional Resources

- National Academies of Sciences Engineering and Medicine Report- 2017
- On the older side now but, comprehensive



# Summary & Wrap Up

- The endocannabinoid system is complex, and plays a role in regulating many, many, bodily processes
- Cannabis use can impact diet by increasing energy intake, altering food choices, may tend towards a diet of poorer quality and increased foods from restaurants/fast food establishments
- Cannabis can have implications on gut and cardiovascular health, but the extent of which is still being discovered
- Important to critically review the literature
- Work together with your healthcare team





Thank you!

Questions?

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