The influence of medicinal cannabis on glycemic profile, additional laboratory findings, health care resources, and the use of drugs in patient with type II diabetes.

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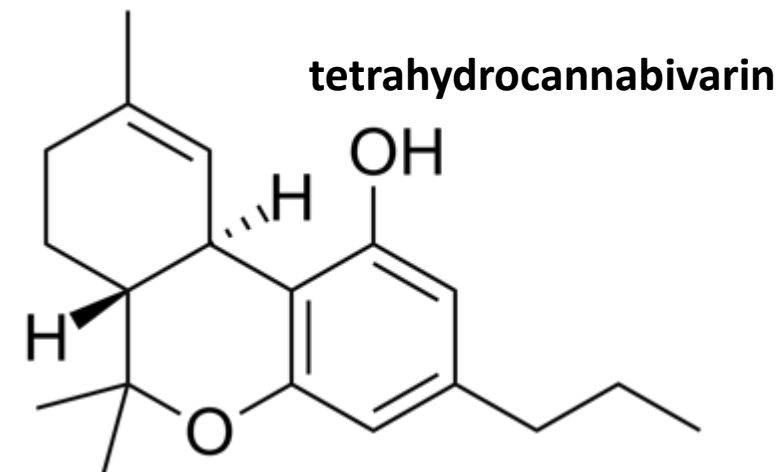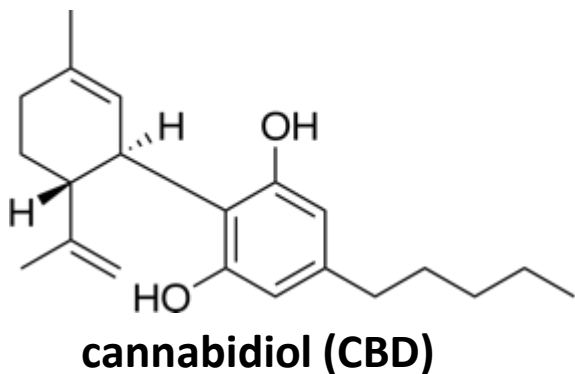
Cannabis and Diabetes

Cannabis and Diabetes

- Cannabis, or marijuana, is a drug derived from the cannabis plant that is used for:
  - recreational use
  - **medicinal purposes**
  - religious or spiritual rites

Cannabis and Diabetes

- Cannabis plants produce a unique family of compounds called cannabinoids.

- Of these, the major psychoactive (brain function-affecting) compound is tetrahydrocannabinol (THC).

- Two other compounds, **tetrahydrocannabivarin (THCV)** and **cannabidiol (CBD)** have been shown to effect (or alter) blood glucose levels and metabolic variables in diabetes studies

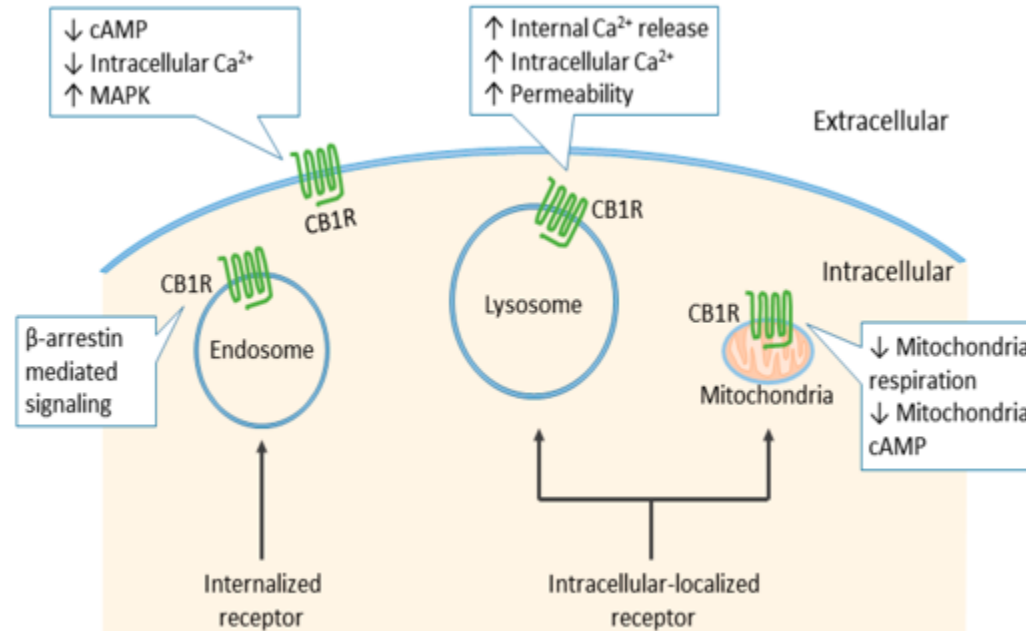**tetrahydrocannabivarin**

cannabidiol (CBD)

Cannabis and Diabetes -Cannabinoid receptors

CB1,CB2 are G-protein coupled **receptors** located throughout the body, are part of the **endocannabinoid system**.
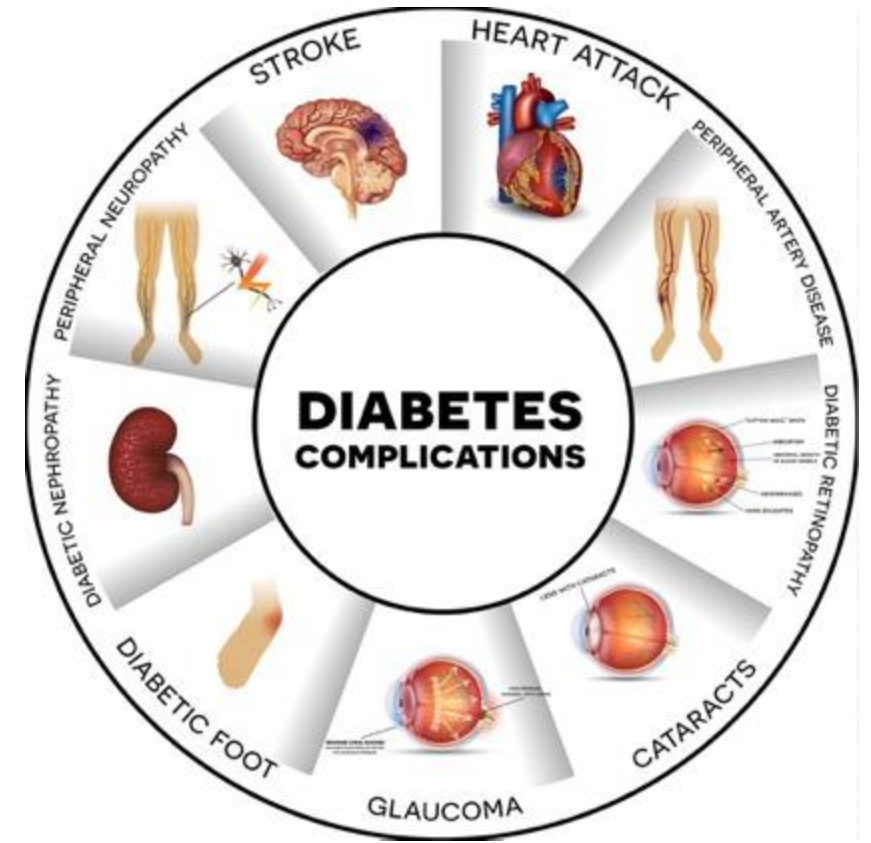involved in a variety of physiological processes

- appetite
- pain-sensation
- Mood
- memory

Type II Diabetes Mellitus

- **Insulin resistance**
- **High sugar levels in the blood**

Possible benefit of cannabis in T2D?

CBD effects on diabetes

- **Stabilization blood sugars(1,2)**
- **Insulin benefits(1,2)**
- **lower prevalence of obesity(3) and diabetes mellitus (4)**

CBD effects on diabetes complications

- **Lowers blood pressure over time (5,6)**
- **Suppresses some of the arterial inflammation(7)**
- **eases the pain of neuropathy(8,9)**
- **Cardio protection(10)**
- **relieves muscle cramps(11)**
- **reduces intra-ocular pressure (12)**

Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III

Figure 1. The prevalence of marijuana users (past and current) among subjects according to fasting glucose levels (in milligrams per decilitre). Per cent and 95% CI are depicted. *p<0.05 compared to glucose level <94 mg/dl.

Rajavashisth TB, Shareef M, Nadisto C, Pan D, Sinha SK, Ortega J, Friedman TC. Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III. BMJ open. 2012 Jan 1;2(1):e000494.

Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III

Figure 3. OR and 95% CI of having diabetes mellitus (DM) among past and current marijuana users relative to non-marijuana users.

Rajavashisth TB, Shaheen M, Norris KC, Pan D, Sinha SK, Ortega J, Friedman TC. Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III. BMJ open. 2012 Jan 1;2(1):e000494.
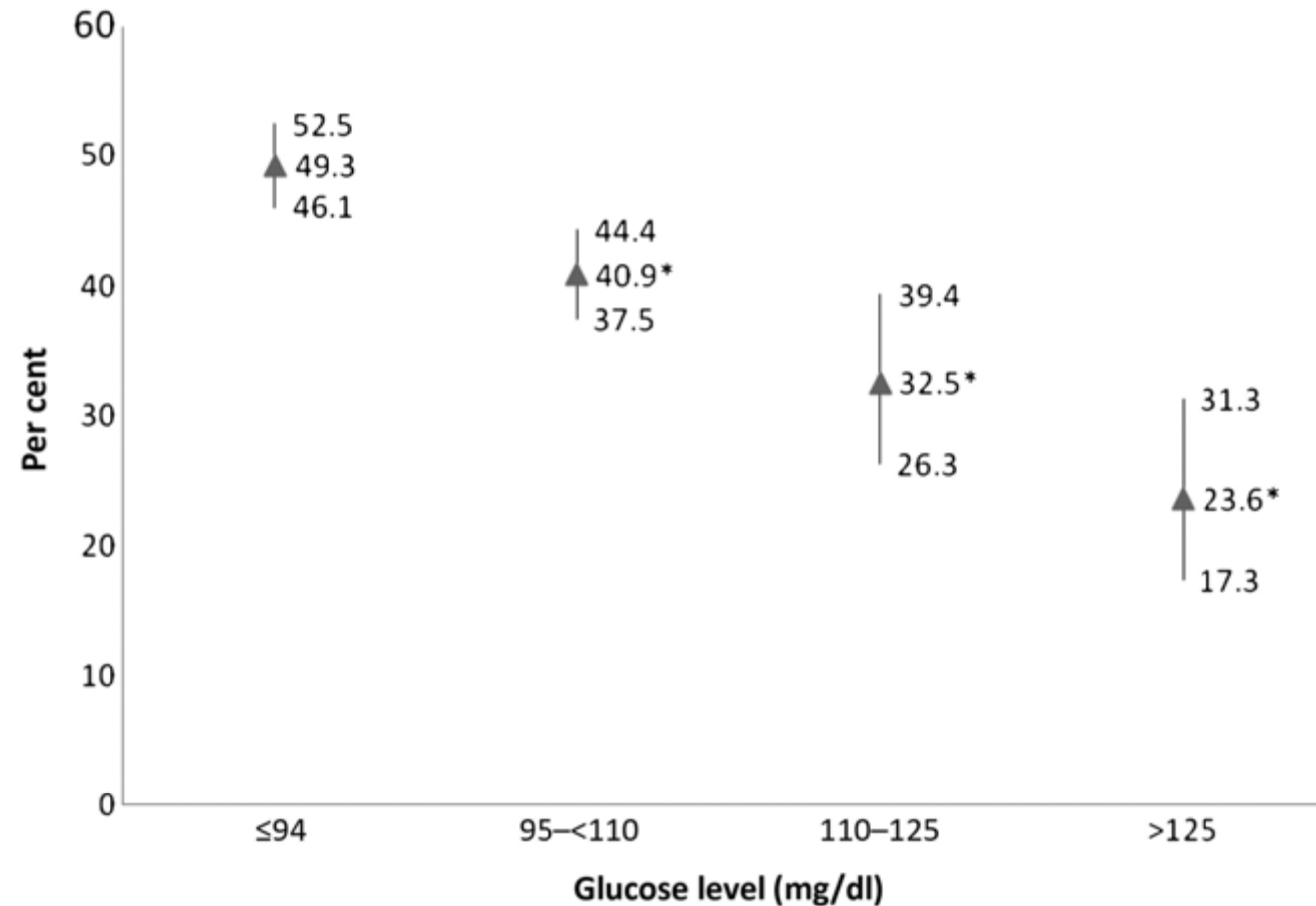
Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III

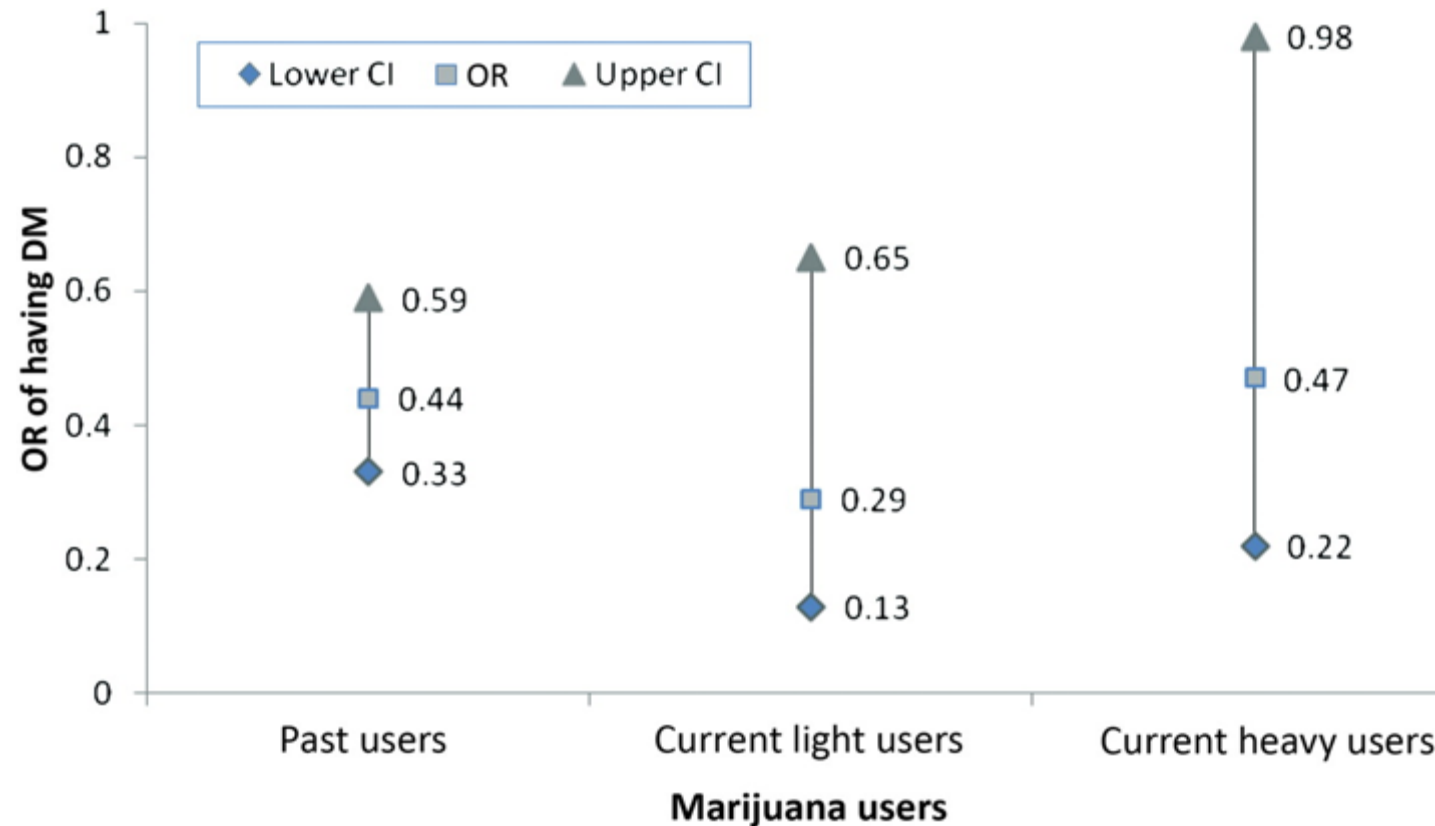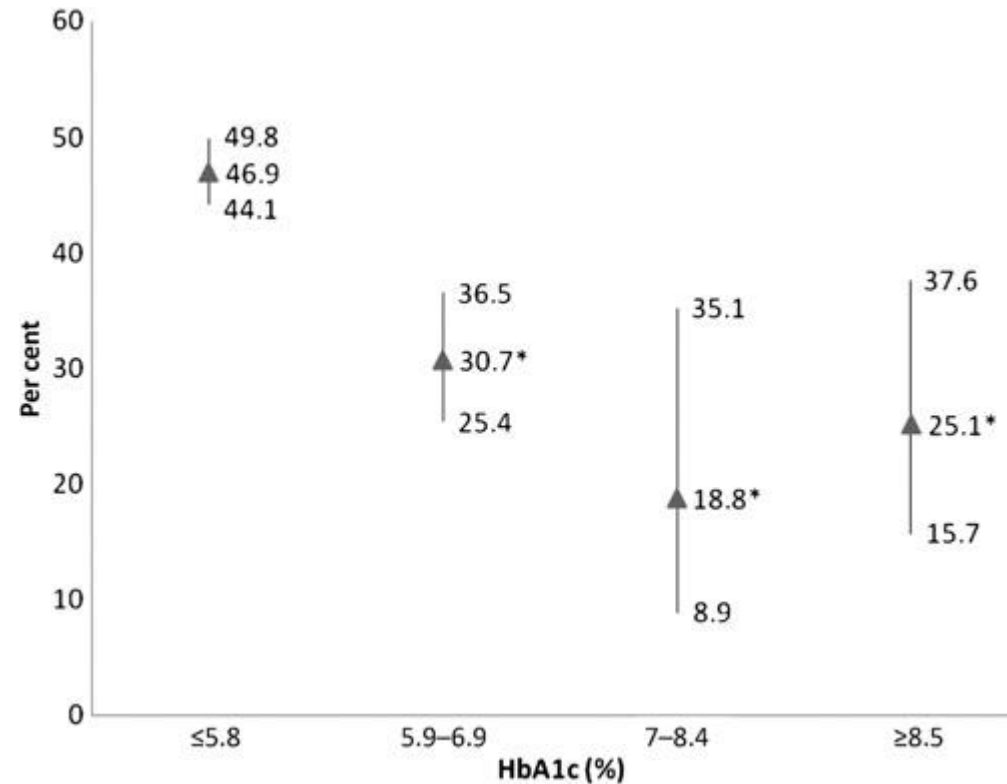

Figure 2. The prevalence of marijuana users (past and current) among subjects according to plasma hemoglobin A1c (HbA1c) levels. Per cent and 95% CI are depicted. *p<0.05 compared to ≤5.8%.

Rajavashisth TB, Shaheen M, Norris KC, Pan D, Sinha SK, Ortega J, Friedman TC. Decreased prevalence of diabetes in marijuana users: cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III. BMJ open. 2012 Jan 1;2(1):e000494.

Beneficial effect of cannabis use on glucose, insulin and insulin resistance in the US general adult population.

Table 2 Mean Values (Standard Errors) of Fasting Insulin and Glucose According to Average Marijuana Use Among Participants from the National Health and Nutrition Examination Survey, 2005 to 2010

	No. of Persons	Frequency of Cannabis Use			P Value
		Never	Past Use	Current Use	
Insulin (μU/mL)*	4606	10.1 (0.2)	8.8 (0.2)	7.5 (0.3)	<.0001
Glucose (mg/dL)	4657	103.5 (0.7)	100.6 (0.7)	99.7 (1.1)	.007
HOMA-IR*	4606	2.5 (0.05)	2.2 (0.06)	1.8 (0.07)	<.0001
HbA1c (%)	3076	5.5 (0.03)	5.4 (0.03)	5.4 (0.05)	.03
Triglycerides* (mg/dL)	4627	108.5 (2.0)	111.1 (2.0)	110.8 (2.9)	.37
HDL-C (mg/dL)	4635	53.4 (0.4)	53.9 (0.6)	53.9 (0.7)	.78
BMI (kg/m^2)	4633	29.1 (0.2)	28.5 (0.2)	27.2 (0.3)	<.0001
Waist circumference (cm)	4602	97.4 (0.5)	97.6 (0.5)	93.6 (0.8)	.0002
SBP (mm Hg)	4347	117.4 (0.6)	117.0 (0.4)	118.8 (0.7)	.08
DBP (mm Hg)	4330	70.4 (0.4)	70.5 (0.4)	69.3 (0.6)	.17

BMI = body mass index; DBP = diastolic blood pressure; HbA1c = hemoglobin A1c; HDL-C = high-density lipoprotein cholesterol; HOMA-IR = homeostasis model assessment of insulin resistance; SBP = systolic blood pressure.
   *Means for insulin, HOMA-IR, and triglycerides are geometric.

Penner EA, Buettner H, Mittleman MA. The impact of marijuana use on glucose, insulin, and insulin resistance among US adults. The American journal of medicine. 2013 Jul 1;126(7):583-9.

Possible no-benefit of cannabis in T2D

1. The relation between diabetes and cannabis is not conclusive yet

Possibly no-benefit of cannabis in T2D?

1. The relation between diabetes and cannabis is not conclusive yet
2. There is still limited data regarding the relationship between cannabinoid and metabolic processes

Possible no-benefit of cannabis in T2D

1. The relation between diabetes and cannabis is not conclusive yet

2. Their is still limited data regarding the relationship between cannabinoid and metabolic processes

3. Other studies showed that among young type 1 diabetes patients a deterioration in glycemic profile with the use of cannabis as a "street drug"(13)

Possible no-benefit of cannabis in T2D

chronic cannabis smokers had relative visceral adiposity and adipose tissue insulin resistance but no effect was found on-

- hepatic steatosis,

- glucose insulin insensitivity,

- impaired pancreatic b-cell function,

- glucose intolerance,

- or dyslipidemia

compared with age-, sex-, ethnicity-,

and BMI-matched control individuals.

Muniyappa R, Sable S, Ouwerkerk R, Mari A, Gharib AM, Walter M, Courville A, Hall G, Chen KY, Volkow ND, Kunos G. Metabolic effects of chronic cannabis smoking. Diabetes care. 2013 Mar 21:DC_122303.

Cannabis and diabetic neuropathy

Cannabis and diabetic neuropathy

- Many diabetic patients suffer from chronic peripheral neuropathic pain
- The neuropathic pain causes major difficulty in patients' daily functions
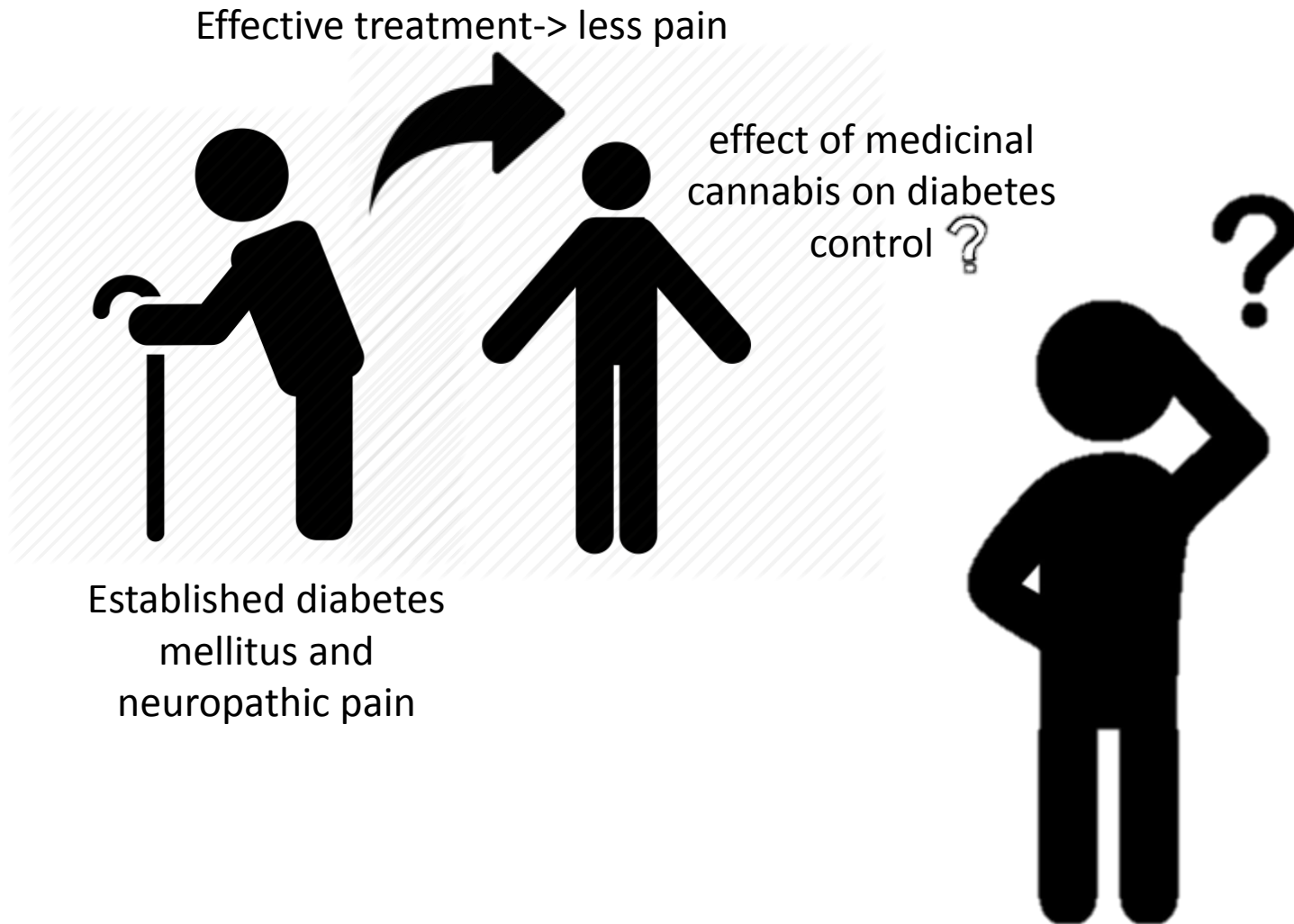
The use of cannabis in diabetic neuropathy

- Neuropathy is the most common complication of diabetes
- In studies of controlled cannabis extract (eCBD) it was found to attenuate diabetic neuropathic pain.
- Animal studies suggest eCBD effect might be mediated by:
  - relieving mechanical allodynia
  - restoring the physiological thermal pain perception
  - reducing **glutathione (GSH)** content in the liver suggesting that eCBD provides protection against oxidative damage

de Lima ME, Colpo AZ, Rosa H, Salgueiro AC, da Silva MP, Noronha DS, Santamaría A, Folmer V. Ilex paraguariensis extracts reduce blood glucose, peripheral neuropathy and oxidative damage in male mice exposed to streptozotocin. Journal of Functional Foods. 2018 May 31;44:9-16.

Cannabis, diabetes and diabetic neuropathy

- Diabetes control depends both on life style changes and medication
- We ask would cannabis in pain control affect the daily function and demonstrate better control over objective diabetes parameters?

Cannabis, diabetes and diabetic neuropathy

Effective treatment-> less pain

effect of medicinal cannabis on diabetes control

Established diabetes mellitus and neuropathic pain

Maybe increased activity?
Allow better lipid profile?

Aim of the study

- To collect and analyze **objective data** among a **big population** of type II diabetes patients in relation to diabetes control, such as-
  - **HbA1C**
  - **blood glucose level**
  - **cholesterol**
  - **triglyceride**
  - **renal function**
  - **ER visits**
  - **clinic visits**
  - **medication use (pain control and diabetes control)**

before and within a year after the beginning of medicinal cannabis use

Research model

- retrospective cross- sectional research focusing on

  T2D population
- ages 40-80 with chronic pain non cancer pain
- and are using prescribed

  medicinal cannabis.
- N=785, from Sheba Medical Center

Research questions

main-

- Does prescribed use of cannabis cause changes in objective diabetic measurements?

secondary-

- If so, does it affect diabetes directly by altering glucose levels and insulin resistance?

- Does it more affect diabetes indirectly by affecting lipid profile, renal function, drugs, ER or clinic visits and more diabetic related complications?

Summery

- Further studies are needed to show a direct and indirect effect of cannabis on DM.

- Prescribed medicinal cannabis for neuropathic pain in T2D is now becoming more prevalent

- Our aim is to collect and analyze data on patients with established T2D using medicinal cannabis

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Thank you for listening!

Questions?