Cannabinoids and Health

Module 7

Lecture 3: Cannabis, Obesity, and Type II Diabetes

Three intersections covered

- Cannabis use may influence obesity and, thus, risk for diabetes
  - It might make it worse
  - Or it might make it better
  - The literature suggests an interesting quandary
- Cannabis might be used to TREAT a major complication of Type 2 Diabetes
  - Diabetic Peripheral Neuropathy
- Potential effects of cannabis use on adherence to diabetes treatment

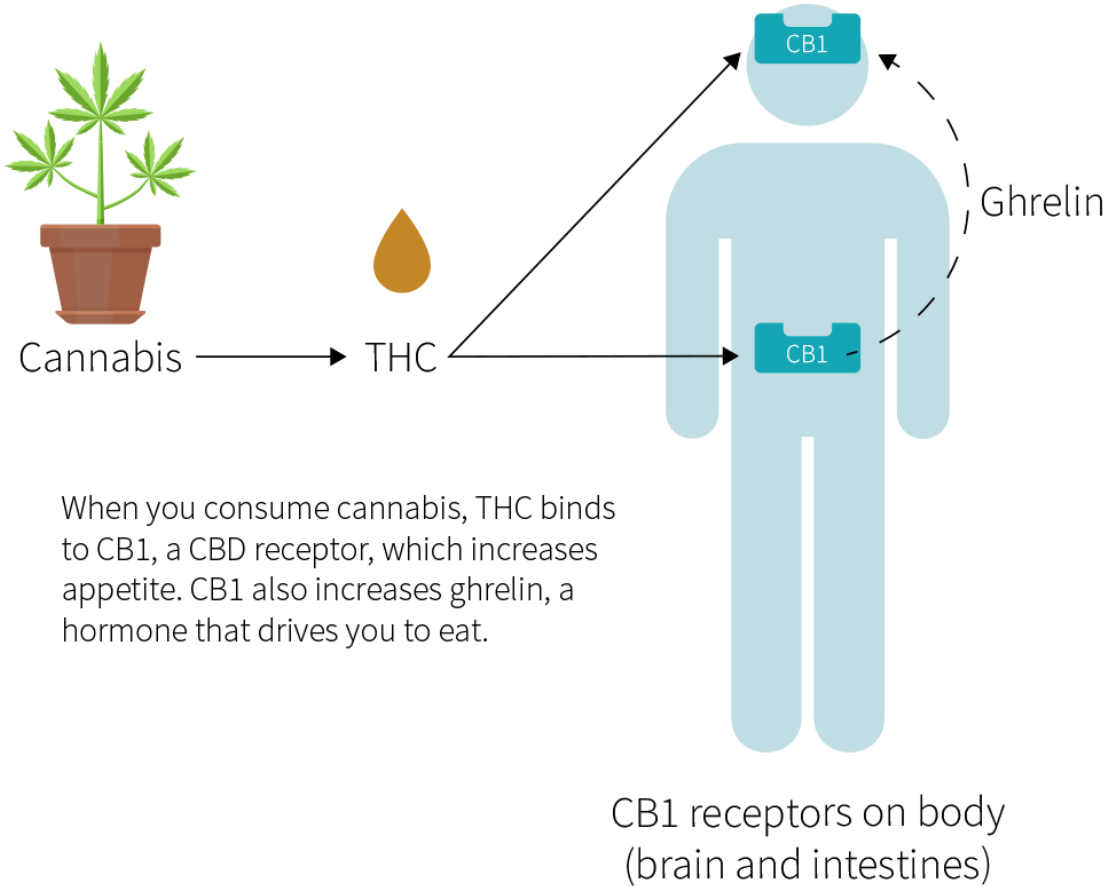
Cannabis and Obesity

- Cannabis has been observed to *increase* appetite far back into history
  - In a *Lancet* publication in 1889, Birch reported that cannabis was valuable in the treatment of opium addiction and that it 'restored the ability to appreciate food.'
- After THC was characterized, a number of studies showed that THC was associated with increased consumption
  - Review by Paton & Pertwee in 1973 characterized experimental studies that showed THC preferentially increased consumption of sweet foods

An Experiment

- In a study published in 1988, Foltin, Fischman and Byrne put six men in a laboratory for 13 days
- They were given social time and private time, and were also randomly assigned to smoke either two active marijuana cigarettes (2.3% THC) or two placebo marijuana cigarettes each day
- Total daily caloric intake increased by 40% for the THC group
- The increase was due to increased consumption of snack foods, specifically sweets (e.g., candy bars) as opposed to savory items (e.g., potato chips)

Physiology



- Activation of CB1 by THC increases appetite
- Studies show blocking CB1 *decreases* appetite

The paradox…

- Cannabis users have higher average caloric intake levels than nonusers, with differences reported to be as high as 600 additional calories per day
- BUT cannabis use has also been consistently associated with
  - lower body mass index (BMI)
  - lower prevalence of obesity
  - lower rates of type 2 diabetes
  - lower levels of fasting insulin
  - lower insulin resistance, and
  - a 1.5 inch smaller waist circumference
- Data suggest cannabinoids may have a role in insulin sensitivity, diabetes

Two recent, large epidemiological studies suggest effect is reliable

Drug and Alcohol Review (November 2018), 37, 897–902
DOI: 10.1111/dar.12867

BRIEF REPORT

The relationship between cannabis use and diabetes: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III

SAMEER IMTIAZ[1,2] & JÜRGEN REHM[1,2,3,4,5,6]

Epidemiology. 2015 July ; 26(4): 597–600. doi:10.1097/EDE.0000000000000314.

Cannabis Smoking and Diabetes Mellitus: Results from Meta-Analysis with Eight Independent Replication Samples

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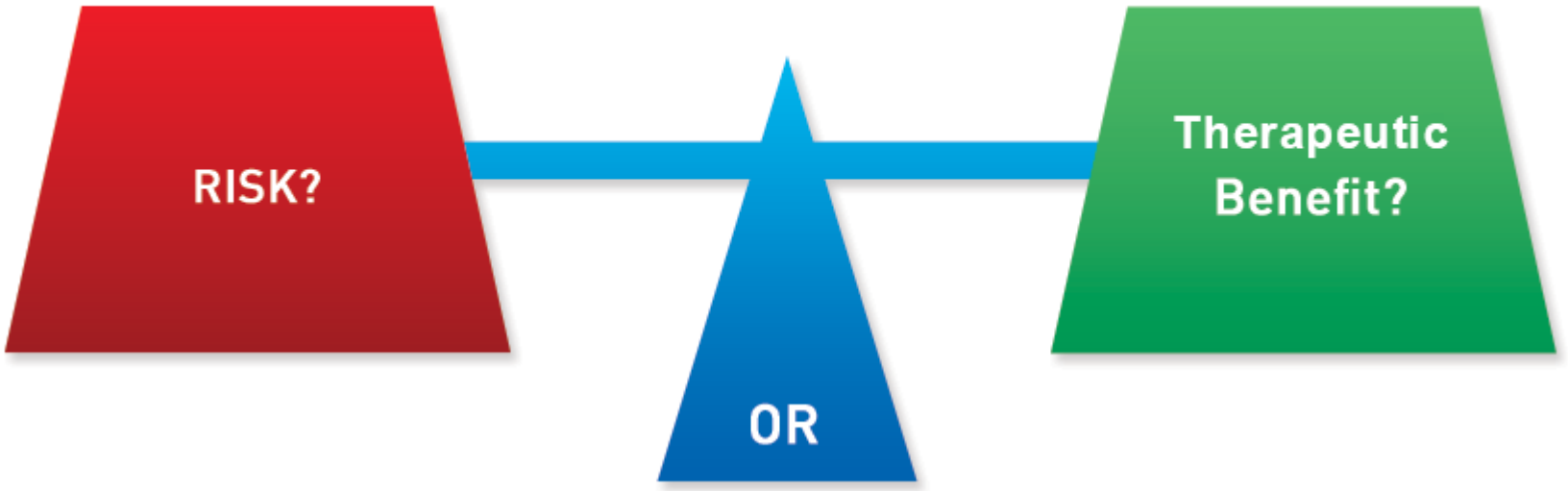
How to explain the paradox?

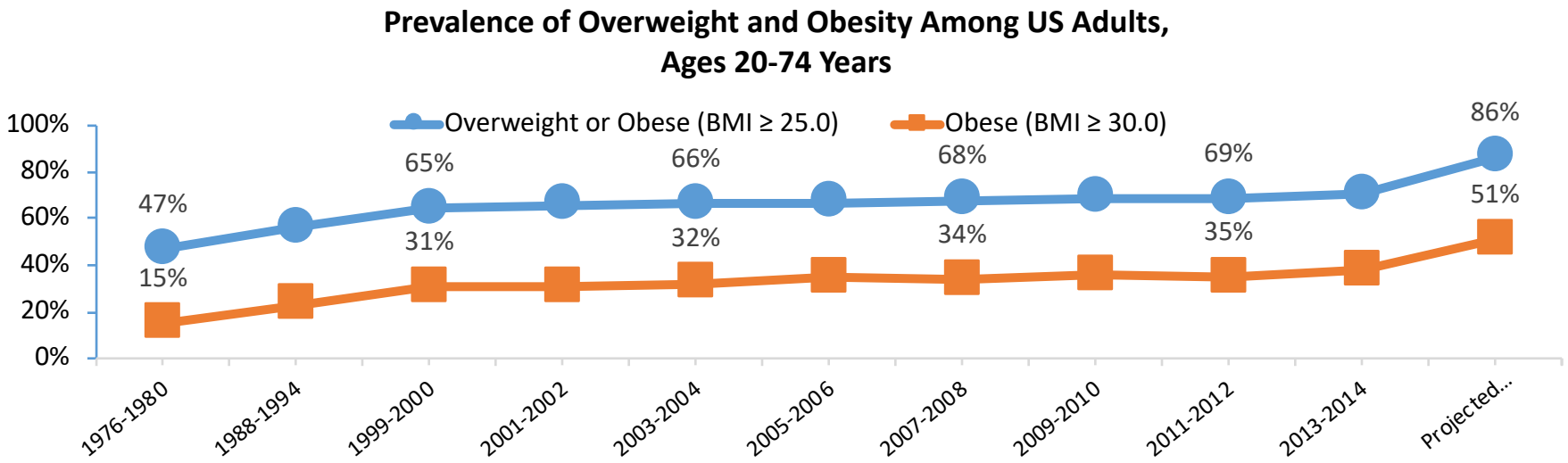
- Most research focused on THC, which increases energy intake by binding to CB1 receptors.
- Cannabidiol (CBD) appears to antagonize both CB1 and CB2 receptors, and research suggests THC and CBD may also have differential effects on metabolic processes
- Whereas THC acutely increases caloric intake, administration of CBD in rodents results in reduced feeding behavior
- When a cannabis extract containing CBD was administered to obese rats, it resulted in weight reduction
- CBD reduces risk of diabetes in diabetic mice

Inflammation may be the link

- Both THC and CBD exert inhibitory effects on inflammatory cytokines, but their activities seem to involve distinct intracellular pathways
- Studying THC and CBD amounts and ratios in cannabis is critical to understanding their physiological effects
- It is well known that pro-inflammatory shifts are strongly associated with the development of insulin resistance, so cannabis's (particularly CBD's) anti-inflammatory effects may be key players in understanding lower insulin resistance and lower risk for type 2 diabetes in cannabis users.

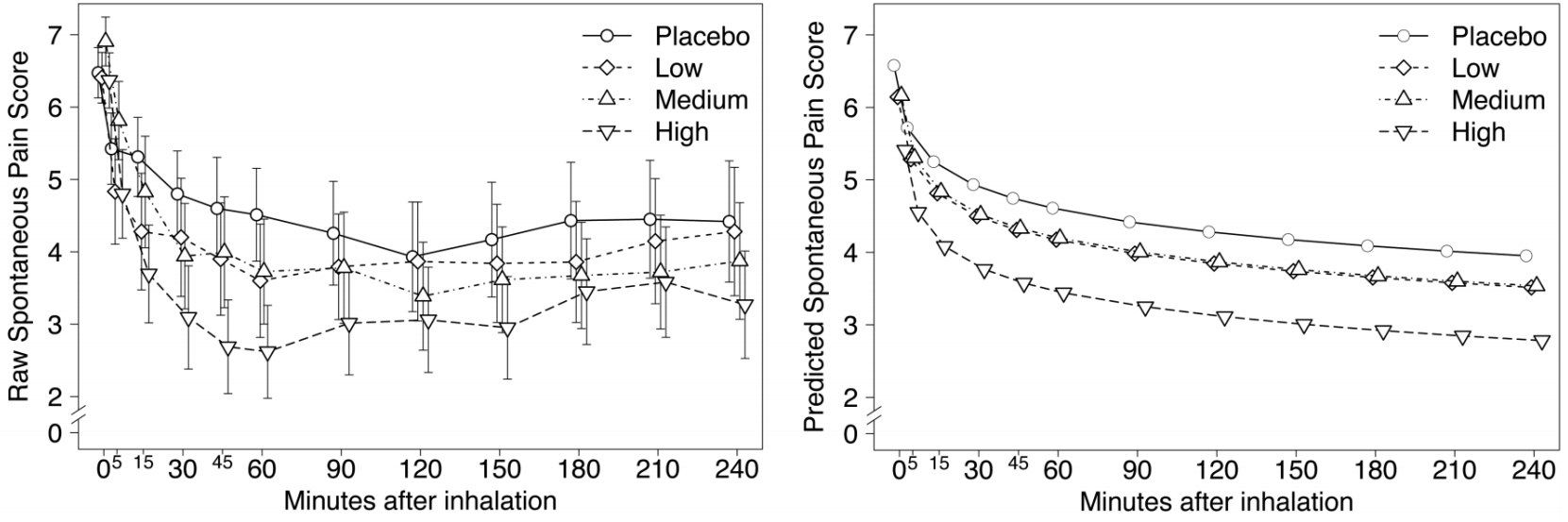
An important question to answer





The case of peripheral neuropathy

- Whether cannabis is helpful or harmful to obesity and diabetes, it is already being used to treat a very common complication of type 2 diabetes: peripheral neuropathy
- Study by Wallace et al. (2015) tested difference between placebo, low (1% THC), medium (4% THC), or high (7% THC) doses of cannabis in 16 patients with treatment-refractory pain



The case of peripheral neuropathy

- Not all studies show a positive effect
- Selvarajah et al. (2010) compared Sativex to placebo in a double-blind trial
- Both groups showed improvement in pain, but there were no differences between groups
- Three points worth noting
  - Depression was a major confound, as more depressed patients experienced better outcomes regardless of condition
  - Patients continued using whatever neuropathy medication they were already taking
  - Placebo effects were quite strong, suggesting something about diabetic neuropathic pain

Cannabis versus other treatments

- As Wallace et al study showed, cannabis was effective even for patients whose pain was NOT responsive to other common treatments
  - Most common side effects were “euphoria” and “somnolence”
- Recall other treatments for neuropathic pain (anti-seizure medications, anti-depressants)
  - Side effects of those medications included sweating, nausea, sleepiness, dizziness, decreased appetite and constipation
- Selvarajah et al study shows that much more research is needed

Cannabis and Adherence

- Remember that adherence is a big problem for people with type 2 diabetes

- Only about 50% of adults with Type 2 Diabetes:
  - achieve recommended targets for blood glucose levels
  - achieve recommended blood pressure targets
  - achieve recommended levels of cholesterol

- When thinking about people with chronic conditions (like diabetes) using cannabis, the question of whether cannabis will affect adherence is important

Cannabis and Adherence

- Influence of cannabis on adherence seems to depend on the medical or psychiatric condition being treated
  - No effect of cannabis use on HIV mediation adherence, but cannabis *dependence* related to lower adherence
  - Cannabis had adverse effects on anti-psychotic medication adherence

- To date, there do not seem to be studies testing disease management or treatment adherence in people with type 2 diabetes who use cannabis compared to those who do not

Conclusions – Part 1

- Cannabis seems to cause an acute increase in appetite, particularly for sweet snacks
- Paradoxically, cannabis use is related to lower BMI, better insulin function, and lower rates of type 2 diabetes
- Mechanisms are not well understood but could be related to the anti-inflammatory properties of THC, CBD or the combination

Conclusions – Part 2

- Cannabis is being used to treat peripheral neuropathic pain in people with diabetes
  - Evidence is mixed on its effectiveness, but more studies need to be done
  - Side effect profile seems favorable when compared to anti-seizure and anti-depressant medications
- Unclear whether cannabis affects disease management and medication adherence for people with diabetes
  - It seems to negatively impact adherence in other conditions, however, so is important to study