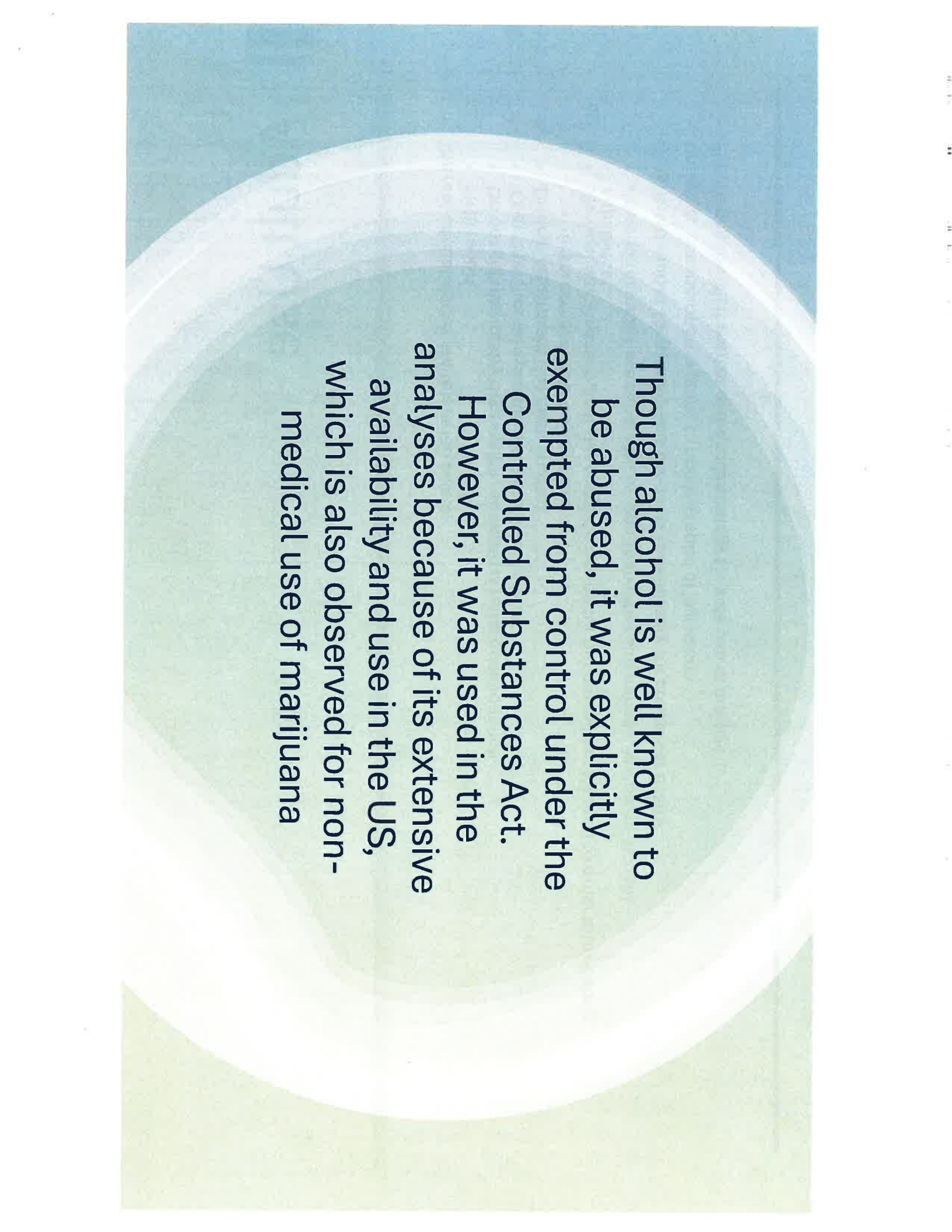




# Adult Use

- The real critical issues are related to safety
  - HHS report
  - Do not get respiratory depression, so death is not a consequence
  - Over time (hours) symptoms spontaneously remit
  - Driving impairment has been studied
    - Enforcement must be legislated
  - Physical and Psychological dependence can occur but are mild compared to other intoxicating substances
  - Adverse reactions are substantially less than other substances, including alcohol
- A regulated market for all cannabis products is necessary for consumer safety
- Underage consumption is going to occur in spite of legislation
- Eliminating the illicit market is the only strategy for safe use at any age





Though alcohol is well known to be abused, it was explicitly exempted from control under the Controlled Substances Act.

However, it was used in the analyses because of its extensive availability and use in the US, which is also observed for non-medical use of marijuana

# Marijuana Sources for Nonmedical and Medical Use

Products containing marijuana or derived from marijuana are generally obtained by the public from four main sources:

- ☐ • State-authorized adult-use (nonmedical) programs
- ☐ • State-authorized medical-use programs
- ☐ • Illicit marketplace – includes unregulated smoke/vape shops, gas stations, convenience stores, marijuana clubs/lounges, person-to-person sales, and illicit cultivation
- ☐ • Home cultivation for personal use (either legal or illegal under state programs)

# Marijuana Economic Impact on Regulated Market from Unregulated Cannabinoid Sources for Nonmedical and Medical Use

- The proliferation of CBD based products, primarily Delta-8 has adversely affected the regulated market.
- Glass shops and “CBD Boutiques” are providing misleading advertising representing they are selling the same product as Medical Marijuana without having to get a card.
- Currently, research on Delta-8 is lacking, as well as other THC products produced from CBD.
- Lack of process supervision, laboratory control, and testing prevents accurate awareness of dosing.



# Problems Without Regulation

Actual quantity of melatonin ranged from 74% to 478% of the declared quantity (1.3-mg to 13.1mg)

As little as 0.1-mg to 0.3-mg of melatonin can increase plasma concentrations into the normal nighttime range.

88% were inaccurately labeled

In products containing CBD, the actual CBD content was 104%-118% of labeled

- Delta 8
- Some manufacturers may use potentially unsafe household chemicals
- From January 1, 2021, Poison Control to February 28, 2022:
  - 2362 exposure cases
  - 41% pediatric
    - 82% unintentional
  - 45% requiring healthcare facility evaluation were pediatric
  - One pediatric fatality



## Underage use: Youth Risk Behavior Surveillance System

20% of students in 9th-12th grade reported using marijuana at least once in the past month during each year evaluated.

past-month alcohol use by high school students (29%) in 2019 was greater than that of marijuana use past month prescription opioid misuse (including codeine, hydrocodone, or oxycodone) (7%) in 2019

# Does the passage of medical and recreation MJ laws lead to an increase in teen MJ use?

- NO
- Youth Risk Behavior Survey 1993-2019
  - There was little evidence that the legalization of medical and recreational marijuana encourages youth marijuana use
  - The overall association between recreational marijuana legalization and marijuana use among adolescents was statistically indistinguishable from zero.
- They are already using drugs and marijuana from the illicit market
- Legalization allows access to safe, unadulterated products the illicit market cannot provide, just as the control of alcohol does not decrease underage use, but simply provides products of known provenance.

Anderson DM, Rees DJ, Sabia JJ, Safford S. Association of Marijuana Legalization With Marijuana Use Among U.S. High School Students, 1993-2019. *JAMA Netw Open*. 2021;4(9):e2124638. doi:10.1001/jamanetworkopen.2021.24638. <https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2793850>

# Psychotic Episode from Marijuana

- Daily use of cannabis and use of high-potency cannabis increase the risk of a psychotic disorder.
  - Self-reported
- Starting use by age 15
- Data not validated by blood, urine, or hair samples
- No direct measure of THC %
- Does not differentiate licit versus illicit market
- No data on CBD content, which may modify Delta-9 effects
- London 45.7 cases/100,000; Amsterdam 37.9/100,000



# Benefit of Controlled Adult Use Market

Provide for safety  
of products  
available in the  
market

Undermine the  
illicit market with  
products of known  
provenance

# Driving and Cannabis

## CONCLUSIONS AND RELEVANCE

Smoking cannabis *ad libitum* by regular users resulted in simulated driving decrements.

However, when experienced users control their own intake, driving impairment cannot be inferred based on THC content of the cigarette, behavioral tolerance, or THC blood concentrations.

Participants' increasing willingness to drive at 1 hour 30 minutes may indicate a false sense of driving safety. Worse driving performance is evident for several hours post smoking in many users but appears to resolve by 4 hours 30 minutes in most individuals.

Further research is needed on the impact of individual biologic differences, cannabis use history, and administration methods on driving performance.

*JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2021.4037

## CONCLUSIONS AND RELEVANCE

- In a crossover clinical trial that assessed driving performance during on-road driving tests, the SDLP (standard deviation of lateral position/lane weaving) following vaporized THC-dominant and THC/CBD-equivalent cannabis compared with placebo was significantly greater at 40 to 100 minutes but not 240 to 300 minutes after vaporization;
- there were no significant differences between CBD-dominant cannabis and placebo.
- however, the effect size for CBD-dominant cannabis may not have excluded clinically important impairment, and the doses tested may not represent common usage.

*JAMA*. 2020;324(21):2177-2186. doi:10.1001/jama.2020.21218



# National Survey on Drug Use and Health (NSDUH)

The prevalence of past-year use of alcohol was 5-6 times greater than nonmedical use of marijuana

Nonmedical marijuana use an average of less than 5 days/month while another 30% reported nonmedical marijuana use for an average of more than 20 days/month benzodiazepines (4%), hydrocodone, oxycodone, tramadol (2% each), cocaine or crack (less than 2%), and illicit fentanyl, heroin, and ketamine (less than 1% each).



# WHAT, IF ANY, RISK THERE IS TO THE PUBLIC HEALTH

The risks to public health posed by marijuana are low compared to other drugs of abuse (e.g., heroin, cocaine, benzodiazepines), based on an evaluation of various epidemiological databases for ED visits, hospitalizations, unintentional exposures, and most importantly overdose deaths.

For overdose deaths, marijuana is always in the lowest rankings among comparator drugs

although abuse of marijuana produces clear evidence of a risk to public health, that risk is relatively lower than that posed by most other comparator drugs





# Psychic or Physiological Dependence

experimental data and clinical reports demonstrate that chronic, but not acute, use of marijuana can produce both psychic and physical dependence in humans

symptoms associated with both kinds of dependence are relatively mild for most individuals, although the severity may be greater with increased exposure to marijuana

# Considerations for Scheduling of Marijuana

Actual of relative potential for abuse

Scientific evidence of its pharmacological effect

State of current scientific knowledge regarding the drug

History and current pattern of abuse

Scope, duration, and significance of abuse

Risk to the public health

Psychic or physiological dependence liability

Immediate precursor or a substance already controlled



# THE SCOPE, DURATION, AND SIGNIFICANCE OF ABUSE

Medical outcomes from abuse of selected drugs is that for all measures that were evaluated from 2015 to 2020, the rank order of the comparators in terms of greatest adverse consequence typically places alcohol, heroin, and/or cocaine in the first or immediately subsequent positions, with marijuana in a lower place in the ranking



How does marijuana work?

Delta-9 THC is an agonist  
(stimulates) CB1 receptors,  
to produce its effects.





# Conclusions

Marijuana has a potential for abuse less than the drugs or other substances in Schedules I and II.

Marijuana has a currently accepted medical use in treatment in the United States

Abuse of marijuana may lead to moderate or low physical dependence or high psychological dependence

## HUMAN ENDOCANNABINOID SYSTEM

### CB1

CB1 Receptors Target

- x Motor Activity
- x Thinking
- x Motor Co-ordination
- x Appetite
- x Short Term Memory
- x Pain Perception
- x Immune Cells

### CB2

CB2 Receptors Are  
Much Broader Than  
CB1 And Influence  
Most Of The Body

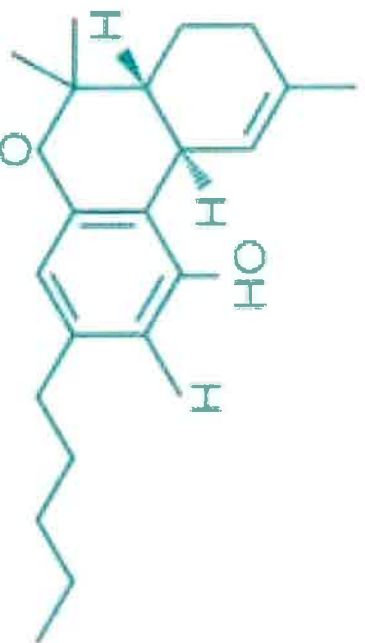
- x Gut
- x Kidneys
- x Pancreas
- x Adipose Tissue
- x Skeletal Muscle
- x Bone health
- x Eyes
- x Tumours
- x Reproductive System
- x Immune System
- x Respiratory Tract
- x Skin health
- x CNS
- x Cardiovascular System
- x Liver

AMSTERDAM  
GENETICS

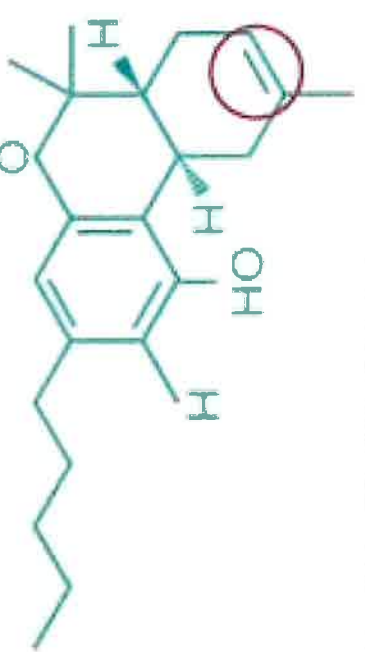
## Receptors

- Cb1: Less prevalent
- THC only binds to Cb1
- Cb2: More prevalent
- Accepts broader range of cannabinoids
- Discovering others

## Delta 9 THC



## Delta 8 THC



# Delta 8

Delta 9 has a double bond at the ninth carbon atom and Delta 8 at the eighth

Seven indications were selected for evaluation under Part 2 of the CAMU test based on conclusions from Part 1 of the CAMU test as well as the FDA's analysis of the landscape of medical use of marijuana. The indications evaluated are anorexia related to a medical condition, anxiety, epilepsy, inflammatory bowel disease, nausea and vomiting (e.g., chemotherapy-induced), pain, and post-traumatic stress disorder

The available data do provide some level of support for the way marijuana is being used in clinical practice