

# Legal Cannabis

## Higher Potency & Higher Risks

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# Cannabis Sativa—Marijuana



# Legal Cannabis

## Higher Potency & Higher Risks

- **Objectives**

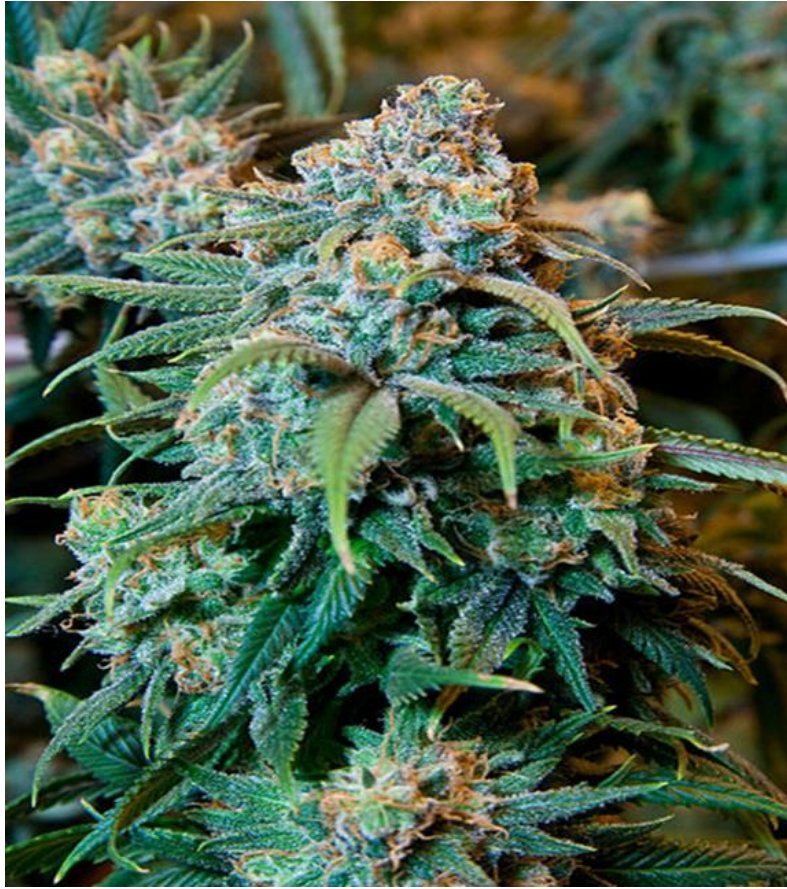
- *Examine data on increased mental and physical health disorders in states with legalized cannabis*
- *Review what's known (and not known) about the cannabis plant and its derivatives*
- *Discuss the dose-response relationship between THC concentration and health consequences*
- *Identify likely issues and scenarios for health care providers given increased availability and strength of cannabis products*

# History of Marijuana

- 1378 – Soudoun Sheikouni, the Emir of the Ottoman Empire outlawed use of hashish and cannabis across his jurisdiction. Sheikouni's prohibition is one of the earliest, if not the earliest, attested cannabis ban in the world, the first “War on Drugs”
- 1798 – Following Napoleon's invasion of Egypt, concerned by his troops' use of hashish and cannabis-based beverages, he banned the drug and the establishments that provided it.
- 1868 – Egypt – 1<sup>st</sup> modern country to outlaw cannabis ingestion
- 1890 – Hashish made illegal in Turkey



# Hashish—Hash, Charas, Norwegian Wood



# History of Marijuana

- Introduced to North America in 1600s by Puritans – Hemp for ropes, sails, clothing; cannabis a common ingredient in medicines, sold openly in pharmacies
- 1937 – Marijuana Tax Act (MTA) – transfer of cannabis illegal throughout US except for medicinal and industrial use, expensive excise tax and detailed logs required
- 1969 – MTA found to be unconstitutional since it violated 5<sup>th</sup> Amendment privilege against self-recrimination

# History of Marijuana

- 1969 - Nixon formally declared a “War on Drugs” that would be directed toward eradication, interdiction, and incarceration
- 1970 – Controlled Substance Act – classified cannabis as having *high abuse potential, no medical use, not safe to use under medical supervision*
- 1986 – Dronabinol placed into Schedule II by DEA
- 2003 – Canada – 1<sup>st</sup> country in world to offer medical marijuana to patients



# Cannabis Sativa—Marijuana





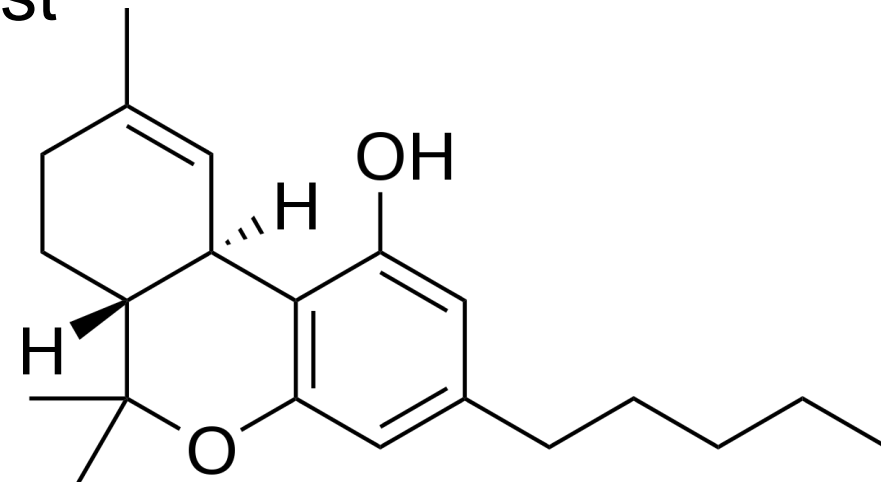
# Sinsemilla

- Spanish term from ***sin*** (without) + ***semilla*** (seed)



# Cannabis Sativa—Marijuana

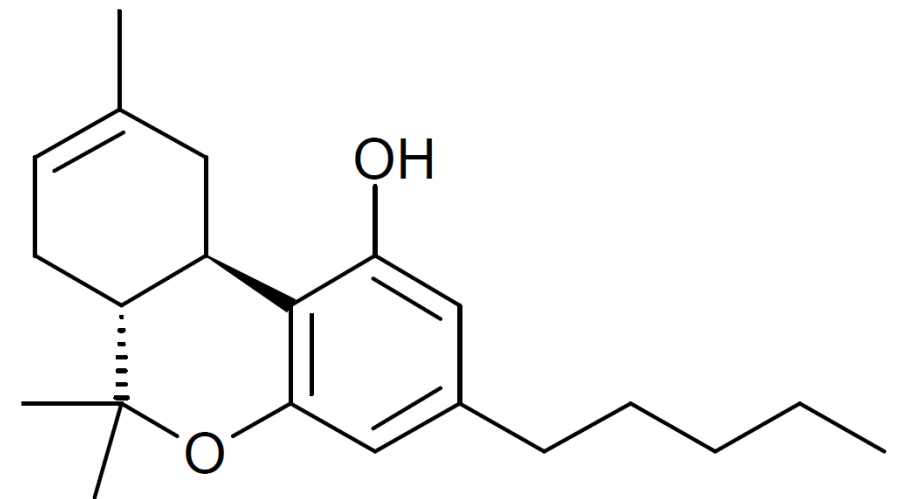
- Complex alkaloid mixture of more than 400 compounds derived from the Cannabis sativa plant
- 84 different compounds described with activity on the cannabinergic system
- Most abundant cannabinoids are
  - Delta-9 tetrahydrocannabinol (most psychoactive)
  - Cannabidiol (CBD)
  - Cannabinol



# Cannabis Indica—Hemp



Delta-8 Tetrahydrocannabinol

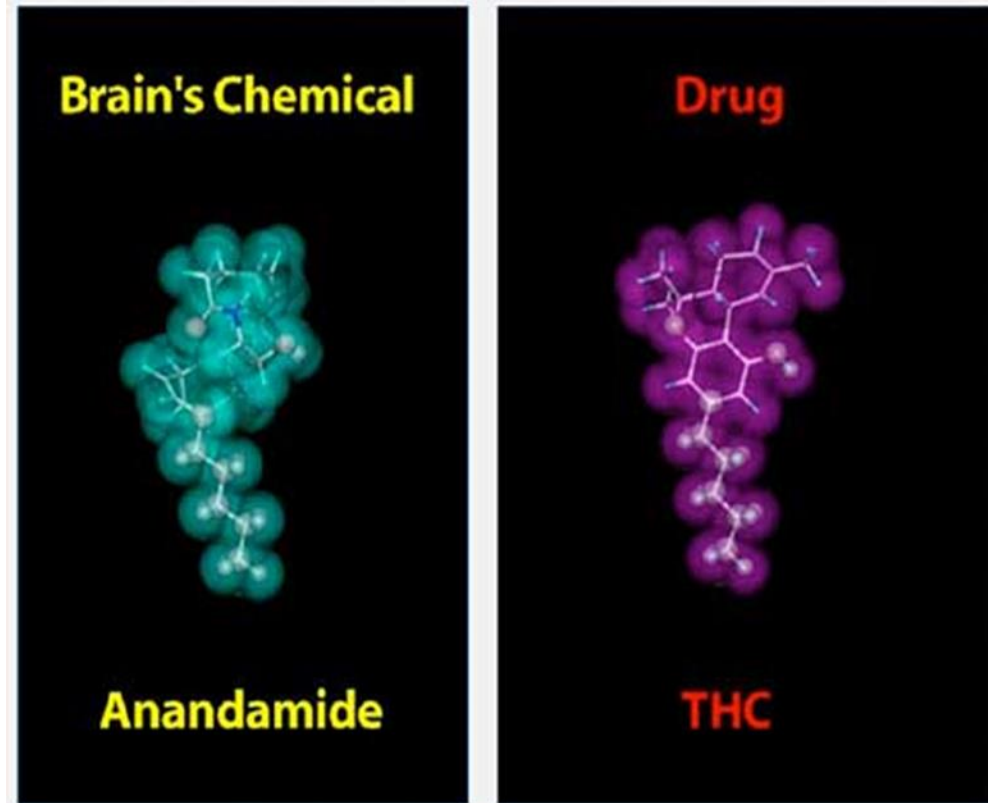




# Cannabinergic System

- Two main cannabinoid receptors
- CB1—present throughout CNS
  - Hippocampus
  - Cortex
  - Olfactory areas
  - Basal ganglia
  - Cerebellum
  - Spinal cord
- CB2 – located peripherally, linked with immune system
  - Spleen
  - macrophages

- THC molecules are ‘imposters’



# Cannabinergic System

- Endocannabinoid system responsible for:
  - Neuronal communication
  - Plasticity
  - Learning
- THC
  - Overwhelms endocannabinoid processing
  - Disrupts information processing
  - Impairs memory

# Synthetic Cannabinoids

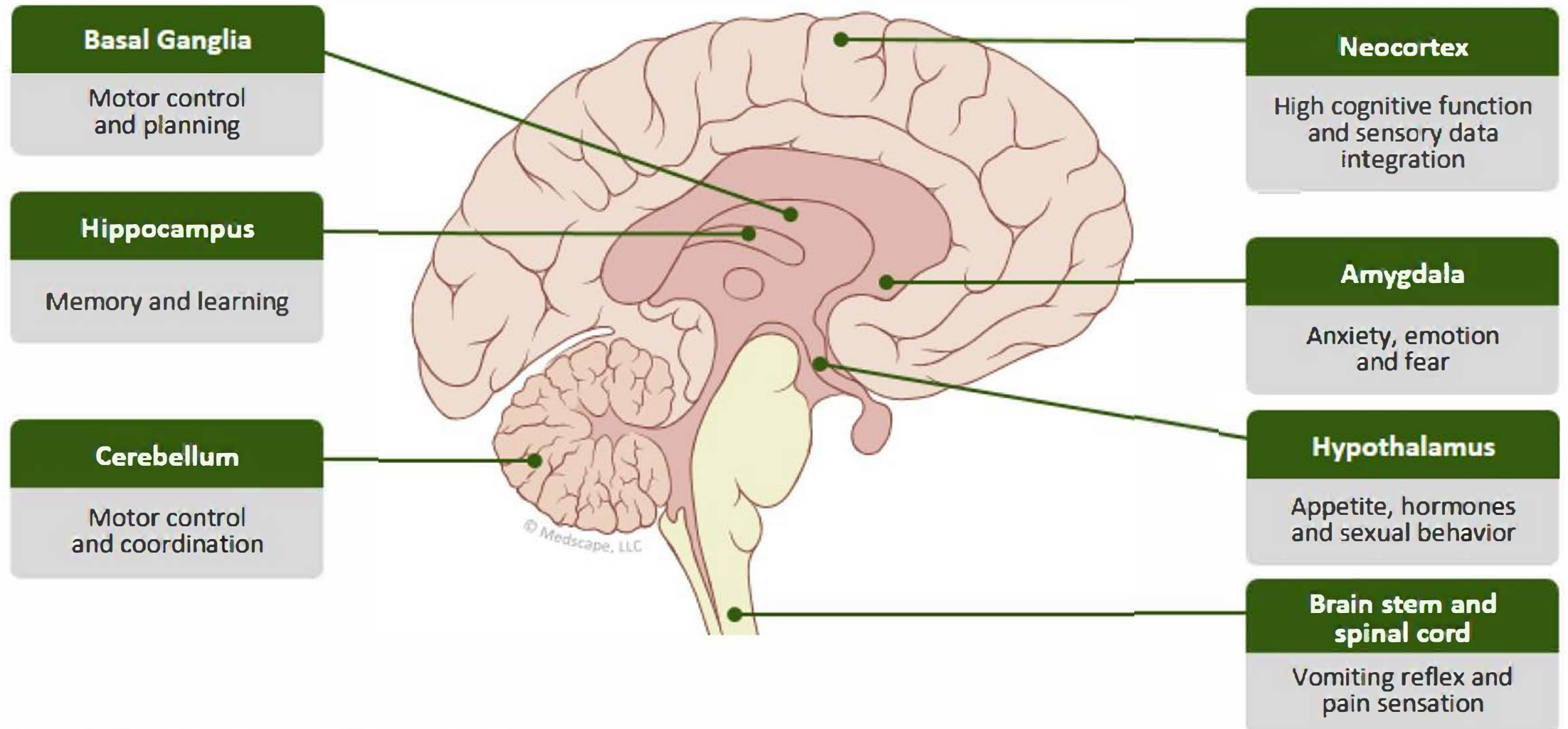
- Synthetic cannabinoids are FULL agonists at CB1 receptor
  - Stronger than Sinsemilla cannabis
- (THC and natural cannabinoids are partial agonists)
- Synthetic cannabinoids not detectable on routine UDS
- Familiar street names:
  - K2
  - Spice
  - Kush
  - Blaze
  - RedX Dawn
  - Black Magic

# Synthetic Cannabinoids

- Psychosis with synthetics:
  - Catatonic posturing
  - Bizarre behavior
  - Grandiosity
  - Persecutory ideation
  - Disinhibition
  - Aggression
- Tachycardia, palpitations, chest pain
- May overwhelm stabilizing effect of anti-psychotics, even with parenteral administration



# High CB1 Cannabinoid Receptor Density



# Times Have Changed: 2007

## Medical Marijuana in the USA

Eleven Years of Marijuana Reform & Compassion

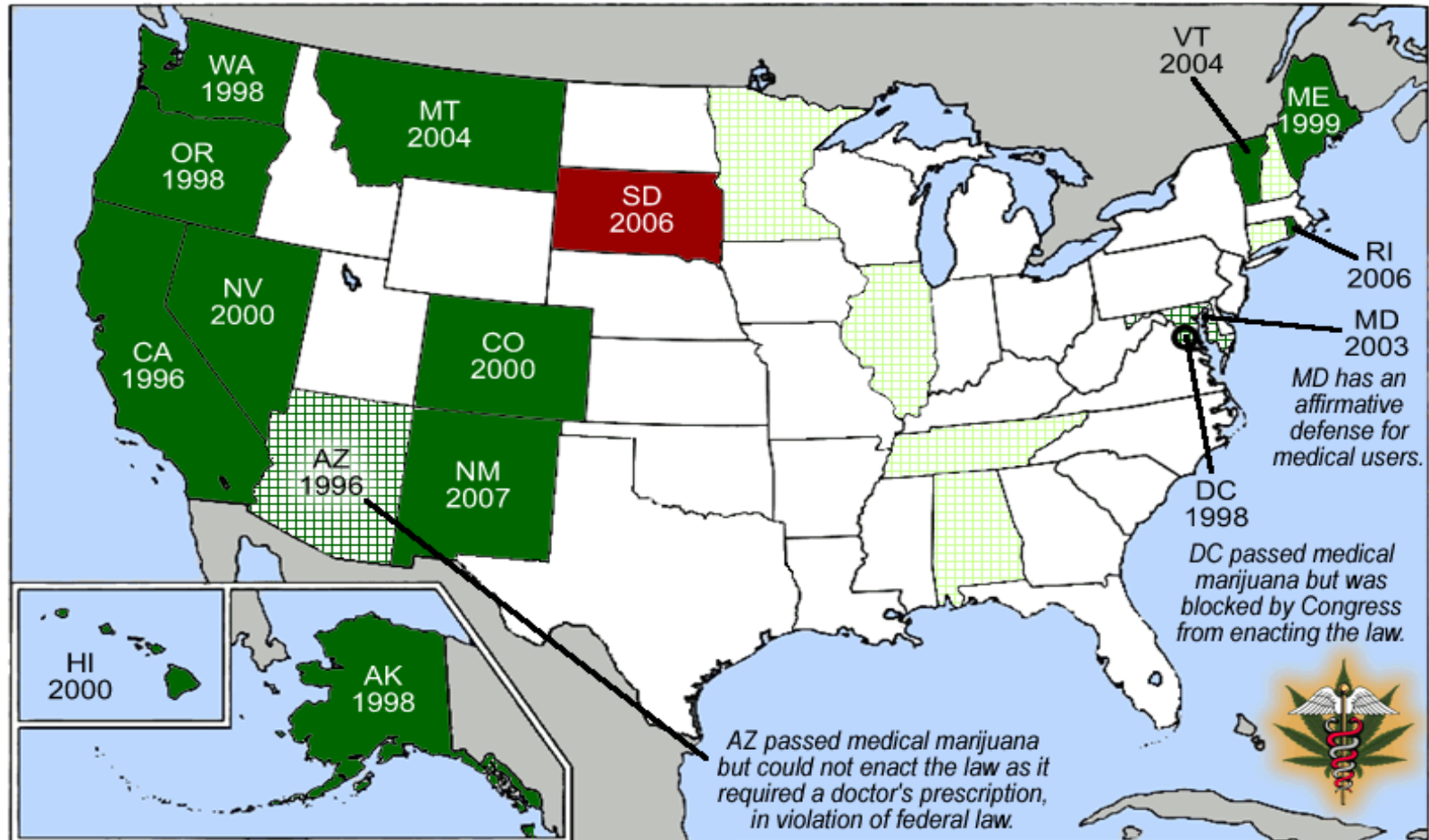
©2007 Oregon NORML [www.ornorml.org](http://www.ornorml.org)

Medical Marijuana is Accepted

Considering Medical Marijuana

Medical Marijuana is Rejected

Special Circumstances



# FOR Easing Cannabis Regulations:

## 2019 Forbes Survey

- Cannabis has medicinal benefits
- Law enforcement could focus more on other crimes
- Individual freedom and choice
- Potential tax revenue
- Regulation would make it safer
- Don't believe marijuana is harmful

# **AGAINST** Easing Cannabis Regulations:

## 2019 Forbes Survey

- Increased car accidents due to impaired driving
- Marijuana is a gateway to harder drugs
- More people would use marijuana
- Legalization wouldn't benefit society or people
- Believe that marijuana is harmful
- Believe that drug use is immoral



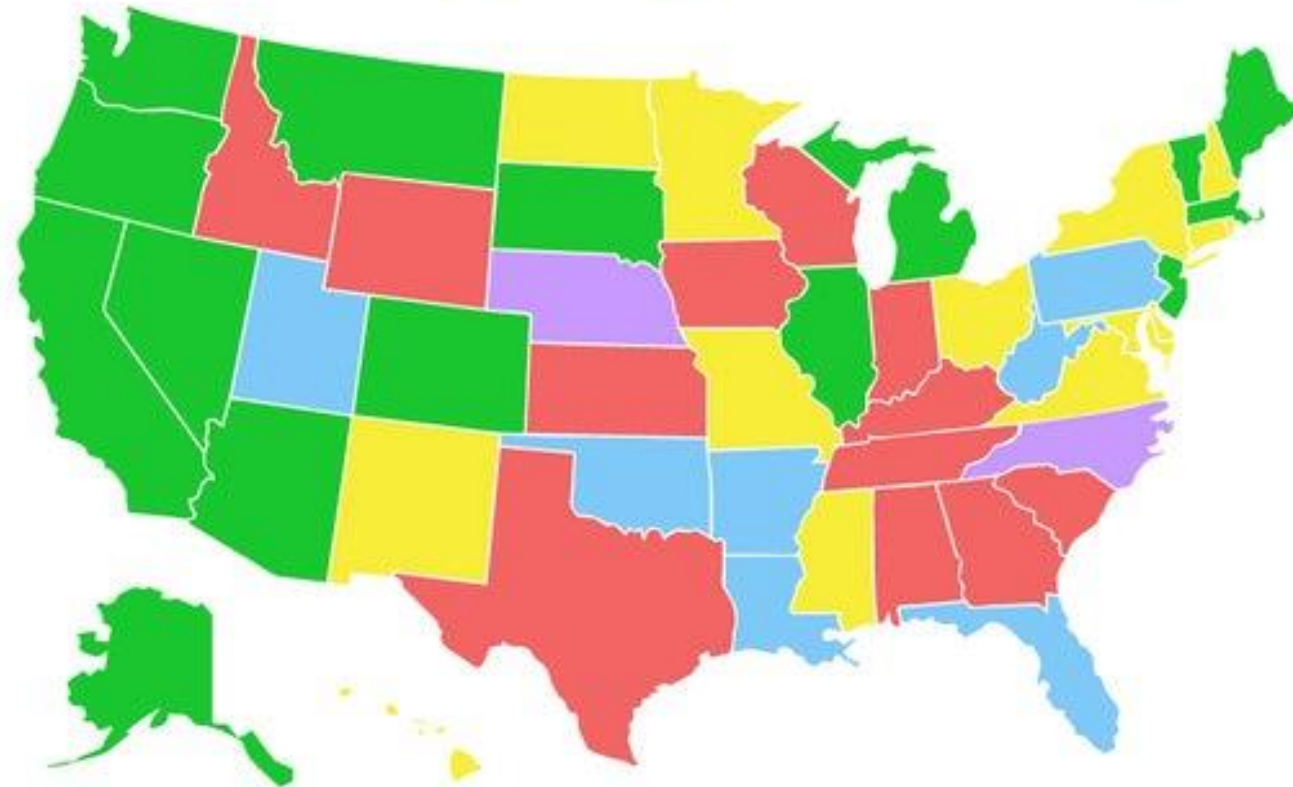
# Times are changing...

- **Vox.com**
- Election Day was a major rejection of the war on drugs
  - *In every state where marijuana legalization or another drug policy reform was on the ballot, it won.*
- By [German Lopez](#)
  - [@germanlopez](#)
  - [german.lopez@vox.com](mailto:german.lopez@vox.com)
  - Nov 4, 2020, 9:30am EST

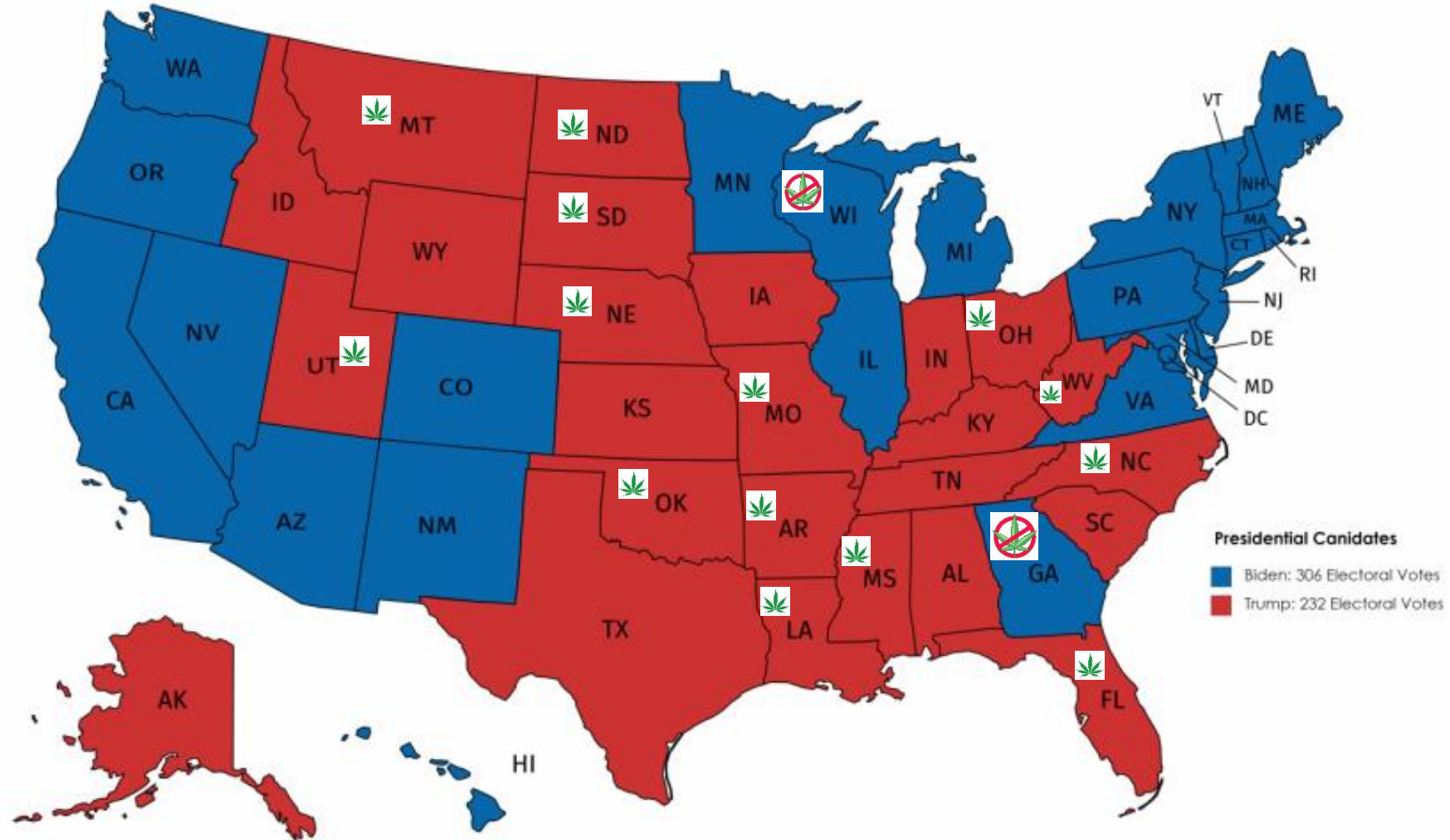
# Times Have Changed—2021

## Marijuana laws in the US

Fully illegal   Decriminalized   Medical   Medical and decriminalized   Legalized



# And It's Not Red Vs. Blue



# From popular media:

- *A handful of other states across the country that have already legalized and decriminalized the drug for recreational and medical use, suggesting that voters have changed their minds about **whether marijuana is a gateway drug and whether people deserve to go to jail for possessing it.***
- *Fatherly.com 2/23/2021*



# Marijuana Legalization

## Recreational and “Medicinal” use

- Adults 21 and older
- May legally possess and use
- May legally purchase (eventually)
- Home - growing allowed (for some states)
- Penalties for illicit production, distribution and importation will remain
- State agencies will regulate
  - Production
  - Distribution
  - Sales
  - Taxation
- Local jurisdictions may be able to ban marijuana retailers within their borders

# Marijuana Decriminalization

## Not the Same as Legalization

- Reflects changing social and moral views about cannabis
- Does not allow for sale of cannabis
- Removes criminal penalties for possession or use
  - No criminal prosecution
  - No incarceration
- Implementation of fines and civil penalties
- Often coincides with contingencies:
  - Referral for clinical assessment
  - Educational activities
  - Requirement for treatment of addiction
- Penalties for illicit production, distribution and importation will remain (similar to legalization)

# FDA- Approved Cannabinoids Are Already Available in U.S.




- **Dronabinol (Marinol®) = (Synthetic  $\Delta$ 9-THC);**
  - **Schedule III, approved for CINV, wasting syndrome in AIDS**
- **Nabilone (Cesamet®) = (Synthetic cannabinoid)**
  - Schedule II, approved for CINV
- **Nabiximols (Sativex®) = (1:1 CBD/THC)**
  - oral mucosal spray, not approved in U.S., used in Canada and Europe. Currently in Phase III trials in US for MS, cancer pain, CINV

# Marijuana and Addiction

- Approximately 8-10% of regular marijuana users develop dependence.
- 17% develop dependence if use begins as teenager
- **25-50% of daily smokers develop dependence/addiction**
- Compared with
  - 15% - alcohol
  - 26% - opiates
  - 32% - nicotine



# High THC / Low CBD and Psychosis

- Frequency of use: Cannabis Use  Psychosis
  - Daily – high psychosis association, especially w/ high potency THC
  - Non-daily – variable psychosis association, not related to potency
  - < Weekly – no psychosis association, regardless of potency
- Genetic risk of psychosis: Cannabis Use  Psychosis
- Bidirectional relationship most likely: Cannabis Use  Psychosis
- Next priorities:
  - Determine who is at risk from daily potent use
  - Address identified at risk with
    - Educational strategies
    - Mitigation efforts

# Cannabis Use Disorder

## *DSM-5 Criteria*

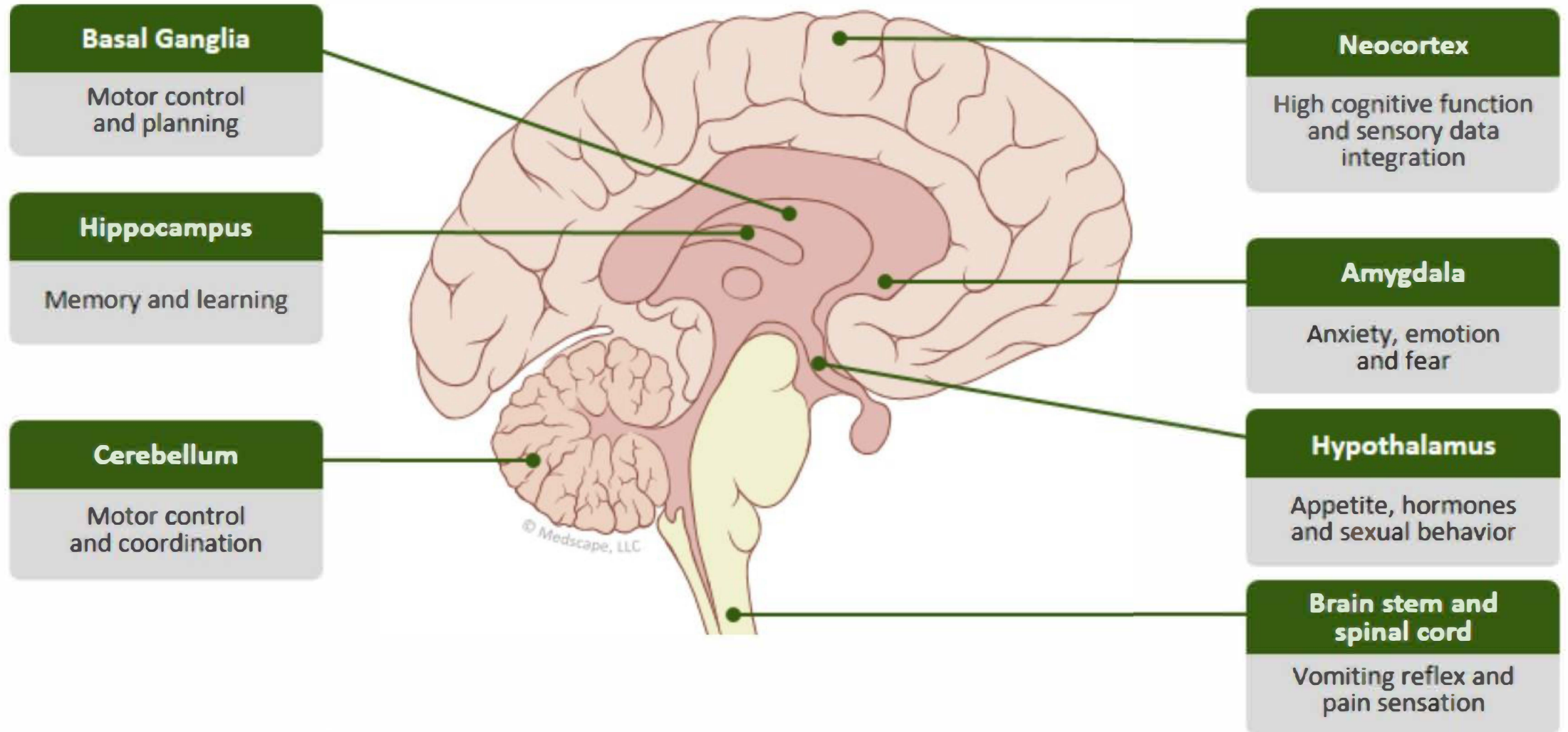
### **DSM-5 Criteria for CUD**

**A. Problematic pattern of cannabis use leading to clinically significant impairment or distress**

**B.  $\geq 2$  of the following occurring over a 12-month period**

1. Cannabis often taken in larger amounts or over a longer period of time than was intended
2. Persistent desire or unsuccessful effort to cut down or control cannabis use
3. Great deal of time spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects
4. Recurrent use resulting in failure to fulfill major role obligations at work, school, or home
5. Continued use despite persistent or recurrent social or interpersonal problems caused or exacerbated by its effects
6. Important social, occupational, or recreational activities given up or reduced because of cannabis use
7. Recurrent cannabis use in situations in which it is physically hazardous (eg, driving or operating machinery)
8. Continued use despite persistent or recurring physical or psychological problem caused or exacerbated by its effects
9. Tolerance
10. Withdrawal
11. Craving or strong desire to use

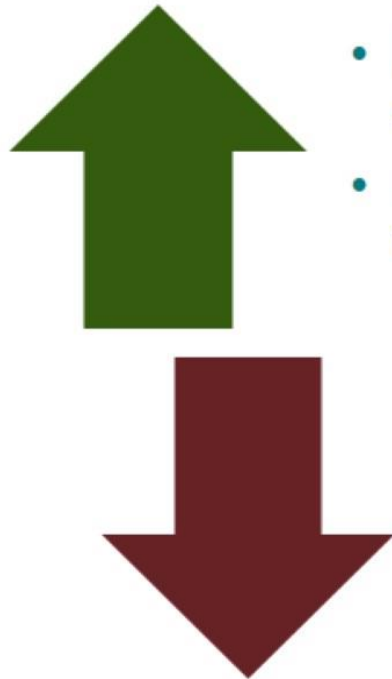
# High CB1 Cannabinoid Receptor Density



# Health and Safety—Cannabis and Driving

## Cannabis Effects on Driving *Occasional Users in a Driving Simulator*

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- Increased variability in speed
- Increased variability in vehicle gap maintenance
- Increased Standard Deviation of Lateral Placement, a measure of weaving
- Reduced speed relative to speed limit

Duration of impairment after consumption (smoking): 4 to 6 hours

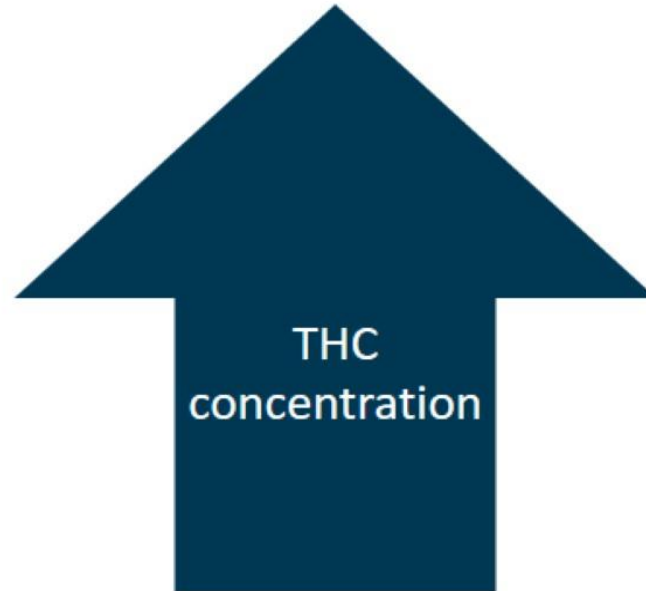
Hartman RL, et al. *Clin Chem*. 2013;59:478-492; Hartman RL, et al. *Drug Alcohol Depend*. 2015;154:25-37; Hartman RL, et al. *J Appl Toxicol*. 2016;36:1418-1429.



# Health and Safety—Cannabis and Driving

## Cannabis Effects on Driving *Iowa/NIDA Driving Simulator Study*

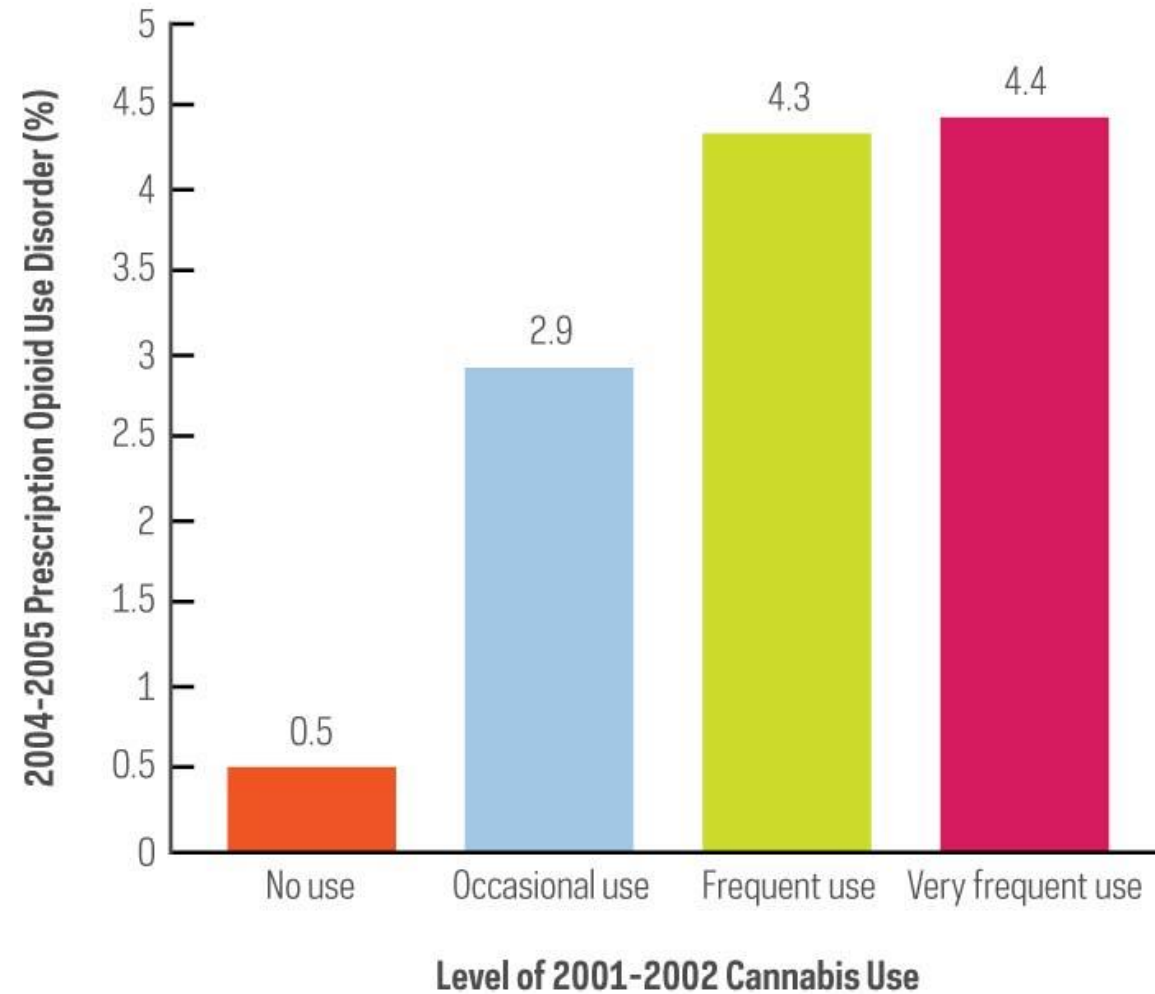
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- Greater movement within a lane
- Reduced speed
- Greater lane deviations requiring steering correction
  - Weaving within the lane

Hartman RL, et al. *Drug Alcohol Depend.* 2015;154:25-37.

# Cannabis and Rx Opioid Use Disorder



# Cannabis and Opioid Use Disorder

- Majority of individuals who misuse **Rx pain meds and/or heroin** initiate drug use early teens
  - Alcohol
  - Marijuana
- Biologically primes brain for enhanced response to other drugs later in life
- Journal of Addiction Medicine (2018)
  - Nationally representative data
  - **Medical marijuana users have twice the risk for prescription opioid misuse compared to non-users of medical marijuana**

# Cannabis and Opioid Overdose Mortality

- M. A. Bachhuber, B. Saloner, C. O. Cunningham, C. L. Barry, Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. JAMA Intern. Med. 174, 1668–1673 (2014).
- Association between medical cannabis laws and opioid overdose mortality has reversed over time. Chelsea L. Shover, Corey S. Davis, Sanford Gordon, Keith Humphreys Proceedings of the National Academy of Sciences Jun 2019, 116 (26) 12624-12626; DOI: 10.1073/pnas.1903434116
- [https://www.pnas.org/content/116/26/12624?blm\\_aid=29695](https://www.pnas.org/content/116/26/12624?blm_aid=29695)

# What Is the Evidence for Cannabis as a Medication?

- Nausea and vomiting in cancer chemotherapy (CINV)
  - 2010 Cochran review- “probably effective” in children but with high incidence of side effects; inadequate evidence for effectiveness in adults
  - European meta-analysis of synthetic cannabinoids showed superior anti-emetic effects but higher side effects
  - Additional concern- cannabis induced hyperemesis
- Glaucoma- probably not effective in reasonable doses
- Wasting syndrome in AIDS- inadequate evidence, studies flawed
- Muscle spasms, spasticity- variable results with MS, small studies
- Insomnia- small study showed improvement in sleep patterns in fibromyalgia patients
- Pain- reviews show some benefits but studies are hard to compare



# What Are Risks, Adverse Effects

- Side effects
- Addiction
- Impaired motor skills
- Cognitive impairment
- Motivational impairment
- Risks associated with method of consumption
- Special risks for adolescents
  - Impact on brain development
  - Psychotic syndromes
- Cyclic vomiting syndrome
- Accidental ingestion by children or household pets

# Liability Concerns for Providers

- Duty of care: Does recommending marijuana constitute a traditional provider-patient relationship?
- Breach of duty: Does recommending marijuana, despite lack of high-quality evidence for its efficacy constitute a breach of duty?
- Causation: Was patient harmed by exposure to recommended marijuana?
- No documented malpractice cases. Yet.
- Be wary of recommending/certifying marijuana for mental health or medical issues for which high-quality evidence does not exist.

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**Mental health-related emergency department visits associated with cannabis in Colorado.** Academic Emergency Medicine, Vol 25 (5), May 2018

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**The Arguments for and Against Marijuana Legalization in The U.S.** <https://www.forbes.com/sites/niallmccarthy/2019/06/14/the-arguments-for-and-against-marijuana-legalization-in-the-u-s-infographic/?sh=7a8c148c678b>

**Medical marijuana users are more likely to use prescription drugs medically and nonmedically.** Journal of Addiction Medicine, 2018 12(4), 295-299

**Talking to Your Patients About Cannabis and Driving Safety (Medscape CME 0.5 credits)**

[https://www.medscape.org/viewarticle/938043\\_slide](https://www.medscape.org/viewarticle/938043_slide)

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# Q&A Thank you.

[www.HazeldenBettyFord.org](http://www.HazeldenBettyFord.org)



## **Cigna Behavioral Health Awareness**

If you are a Cigna customer and have questions about Substance Use treatment or about your benefits and how to use them, please contact:

Stephanie Gissal - 800.274.7603 x398516

Alex Turner - 800.274.7603 x513597

Wanda Russell – 800.274.7603 x342063