

Medical Marijuana

Delving into the Weeds

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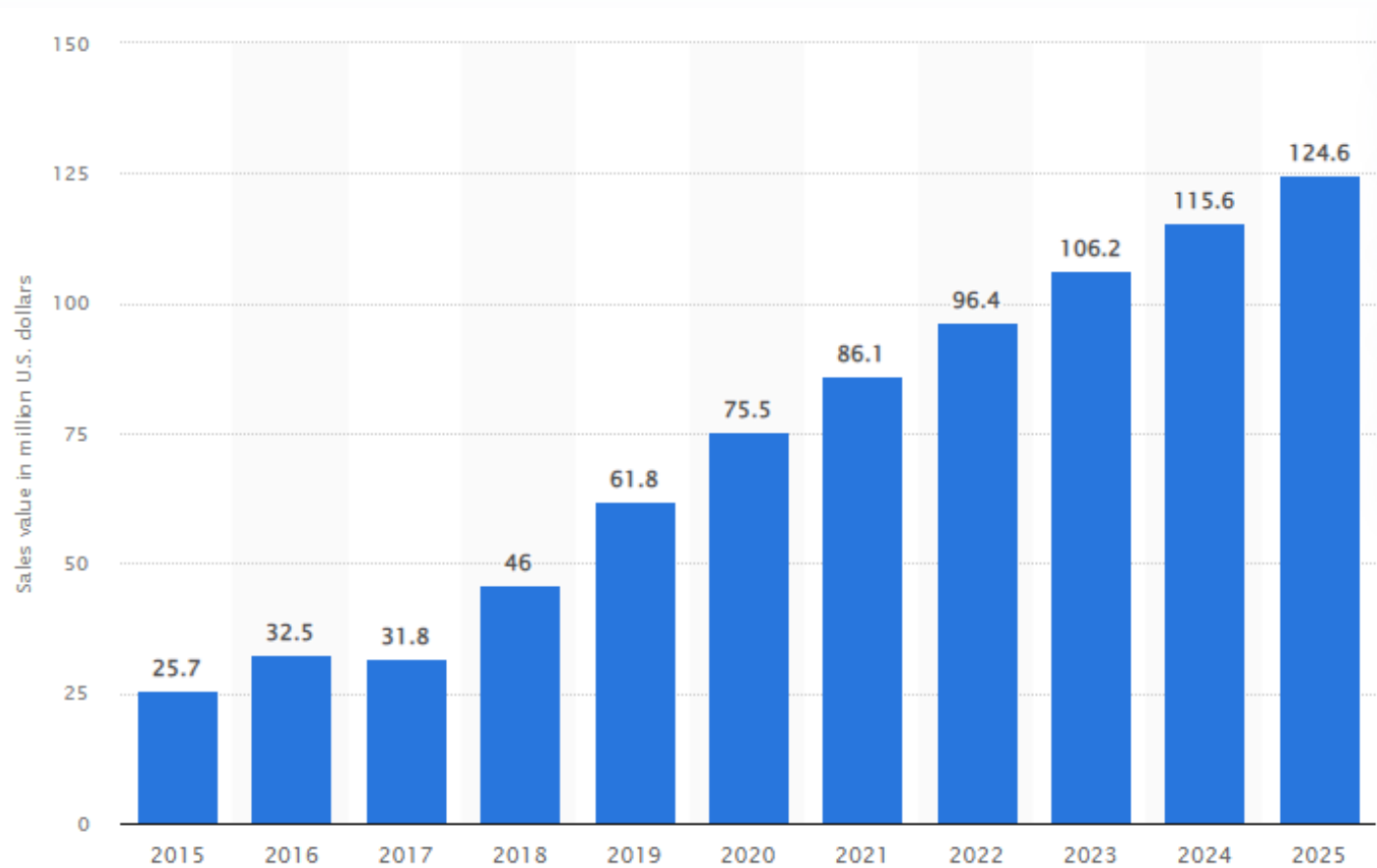


Disclosure

- ✿ Dr. Collins has no financial or non-financial conflicts of interest related to this activity.
- ✿ Non-FDA approved products and indications will be discussed during this presentation.

Forecast of marijuana sales value in Montana's from 2015 to 2025

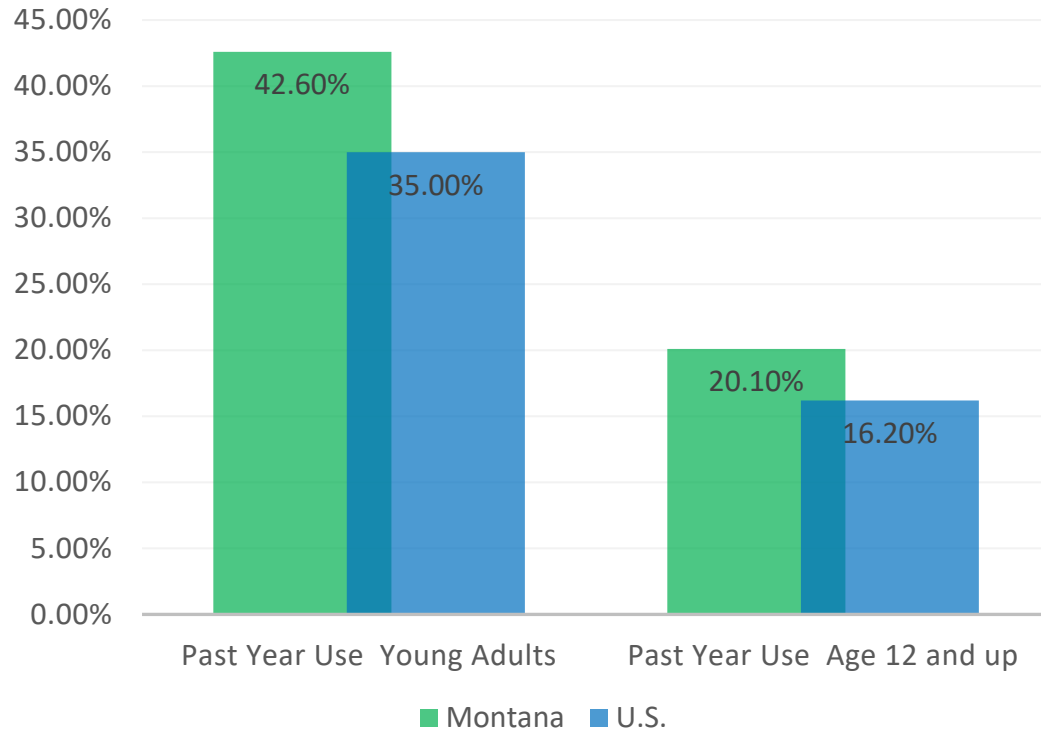
(in million U.S. dollars)



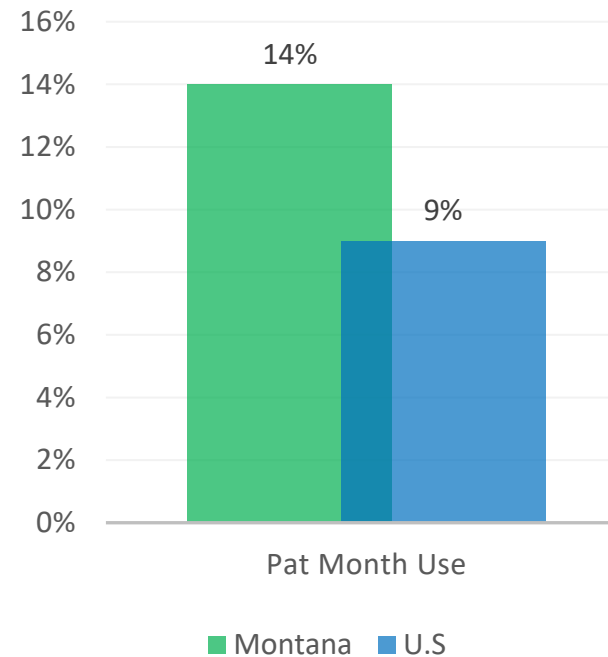
Source: U.S. Census Bureau, University of Montana Institute for Tourism and Recreation Research, MJBizFactbook, MJBizDaily research

Cannabis Use in Montana versus U.S.

Past Year Use (annual averages 2015-2017)



Past Month Use (2017-2018)



Recreational Versus Medical Use

Recreational

- ✻ 21 and older
- ✻ Marijuana flower cannot contain more than 35 percent THC
- ✻ A package of edibles cannot contain more than 100mg of THC
- ✻ Can purchase up to 1 ounce per or the THC equivalent in other forms: 800 milligrams of edibles or eight grams of concentrate.
- ✻ flat 20 percent sales tax. additional local-option 3 percent tax.

Medical

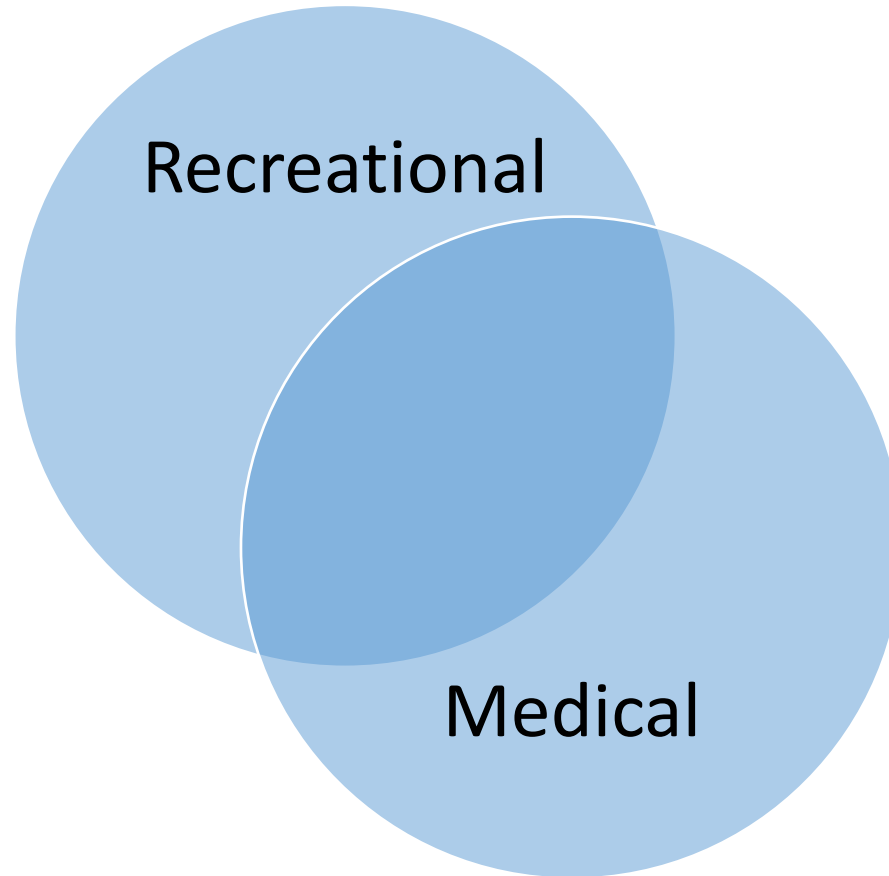
- ✻ 18 and older
- ✻ No limit on marijuana flower concentration
- ✻ No limit on edible quantities
- ✻ 4% tax rate

Recreational Versus Medical Use



Risk vs. Risk

Risk vs.
Benefit



Objectives

- ✦ Describe how different types of marijuana products may impact a patient.
- ✦ Summarize the available evidence using marijuana for therapeutic purposes.
- ✦ List at least three specific safety concerns for the use of marijuana.

Marijuana Basics



Cannabis

- ✦ Contains over 400 compounds
- ✦ Over 100 cannabinoids
 - Δ^9 -tetrahydrocannabinol - THC
 - Cannabidiol – CBD
- ✦ Over 200 terpenes
- ✦ Sterols
- ✦ Thiols
- ✦ Flavonoids
- ✦ Phenols
- ✦ Fibrous material



Cannabis Plant

Comparing THC and CBD

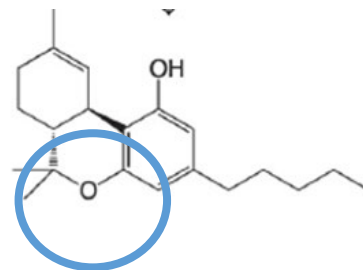
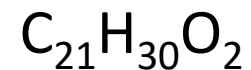
Source

Molecular Formula

Chemical Structure

THC

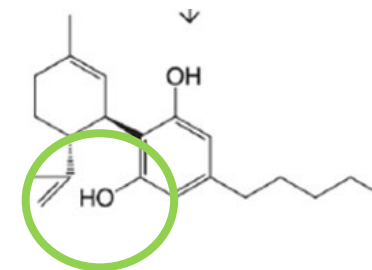
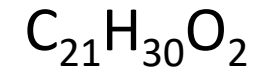
Cannabis sativa



Contains **cyclic** ring

CBD

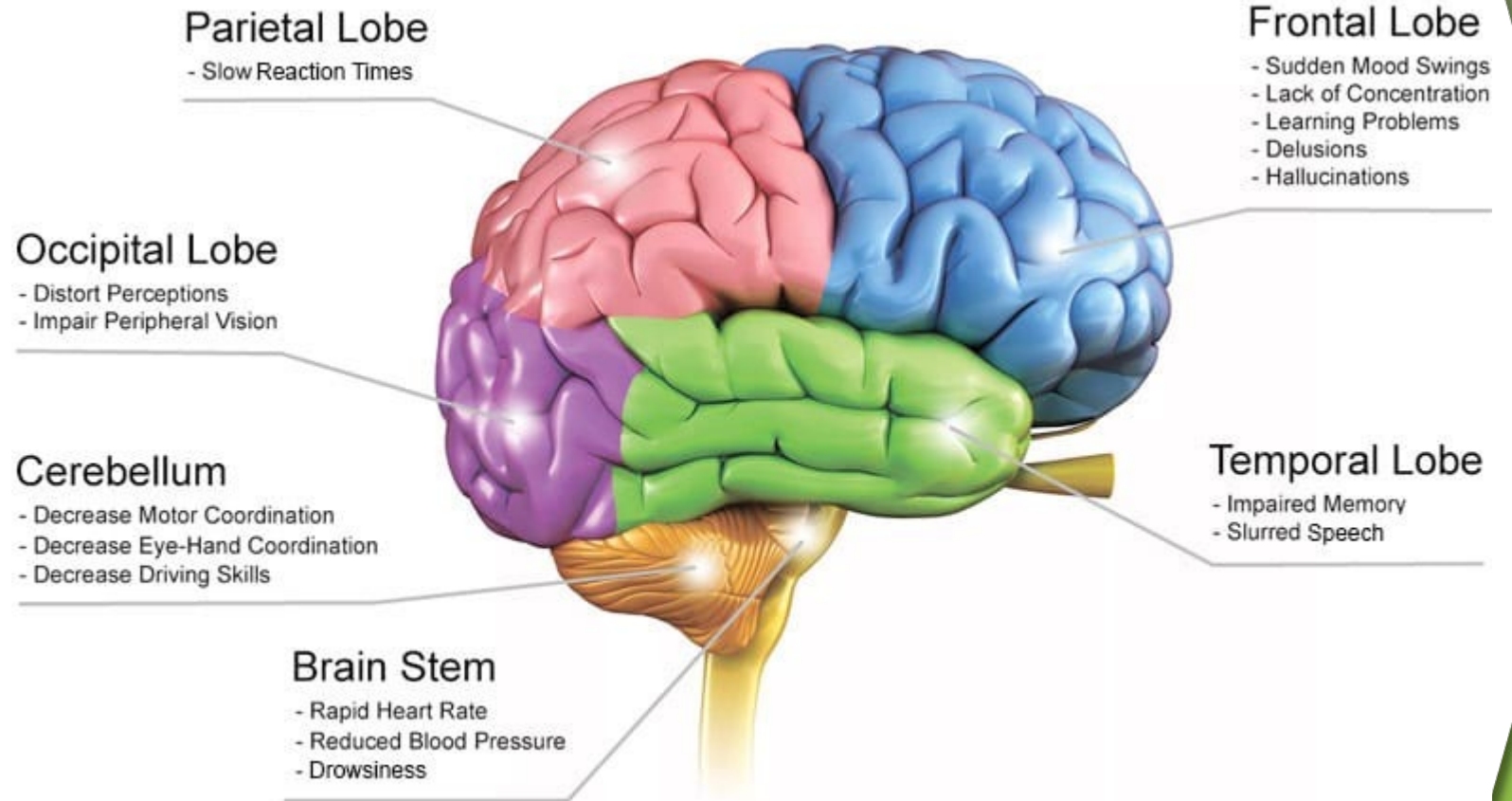
Cannabis sativa



Contains **hydroxyl** group

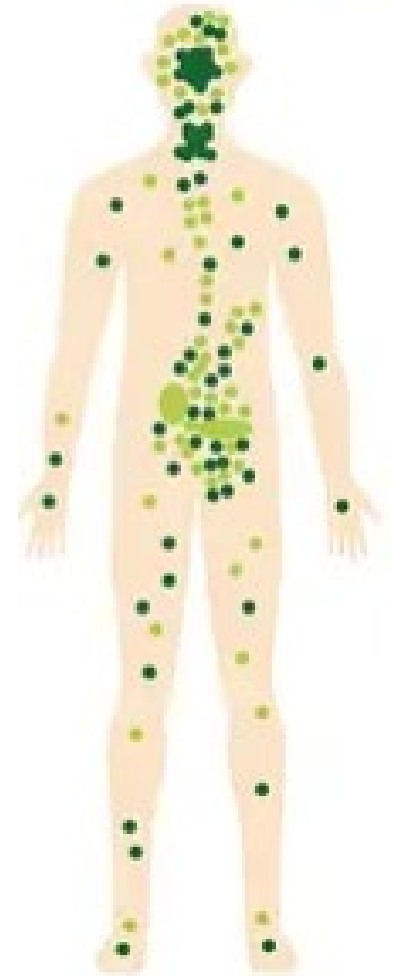
THC Activity

- ✦ Primarily at CB1 receptors in the brain
- ✦ Abundant in parts of brain that regulate movement, coordination, learning and memory, higher cognitive functions such as judgement and pleasure



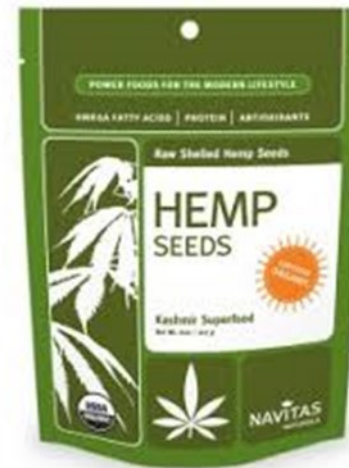
CBD Activity

Receptor	Action	Possible Effect
CB1	Direct antagonist and negative modulator antagonist	Attenuation of impaired learning, memory, and psychosis effects inducted by THC
CB2	Antagonist and inverse agonist	Anti-inflammatory effects
GPR55	Antagonist	Possible vasodilation, anti-inflammatory effects
5HT-1A	Agonist	May have antidepressant and anxiolytic effects
TRPV-1	Agonist	May have a role in pain responses and regulation of body temperatures
Adenosine A2A	Enhanced adenosine concentrations	Pain and anti-inflammatory effects
FAAH enzyme	Inhibition	Decreased breakdown of anandamide and intracellular transport of THC



Hemp

- ✦ Legal limit of 0.3% THC
- ✦ Likely to increase in the future to 1%



Marijuana Effects Dependent on Formulation

- ✦ THC versus CBD
- ✦ Concentration of Cannabinoid
- ✦ Plant Strain



SATIVA



INDICA



RUDERALIS

Marijuana Formulations



Current FDA Approved Cannabis Products

✦ THC

- ✦ Dronabinol (Marinol®)

 - ✦ Capsules (Schedule III)

 - ✦ Oral solution (Schedule II)

- ✦ Nabilone (Cesamet®)

 - ✦ Capsules (Schedule II)

✦ CBD

- ✦ Cannabidiol (Epidiolex®)


 - ✦ Oral solution (Schedule V)





Marijuana Testing


Marijuana Detection Times

Blood & Saliva   A few hours

Urine 

One time use  Up to 13 days

Regular use  Up to 45 days

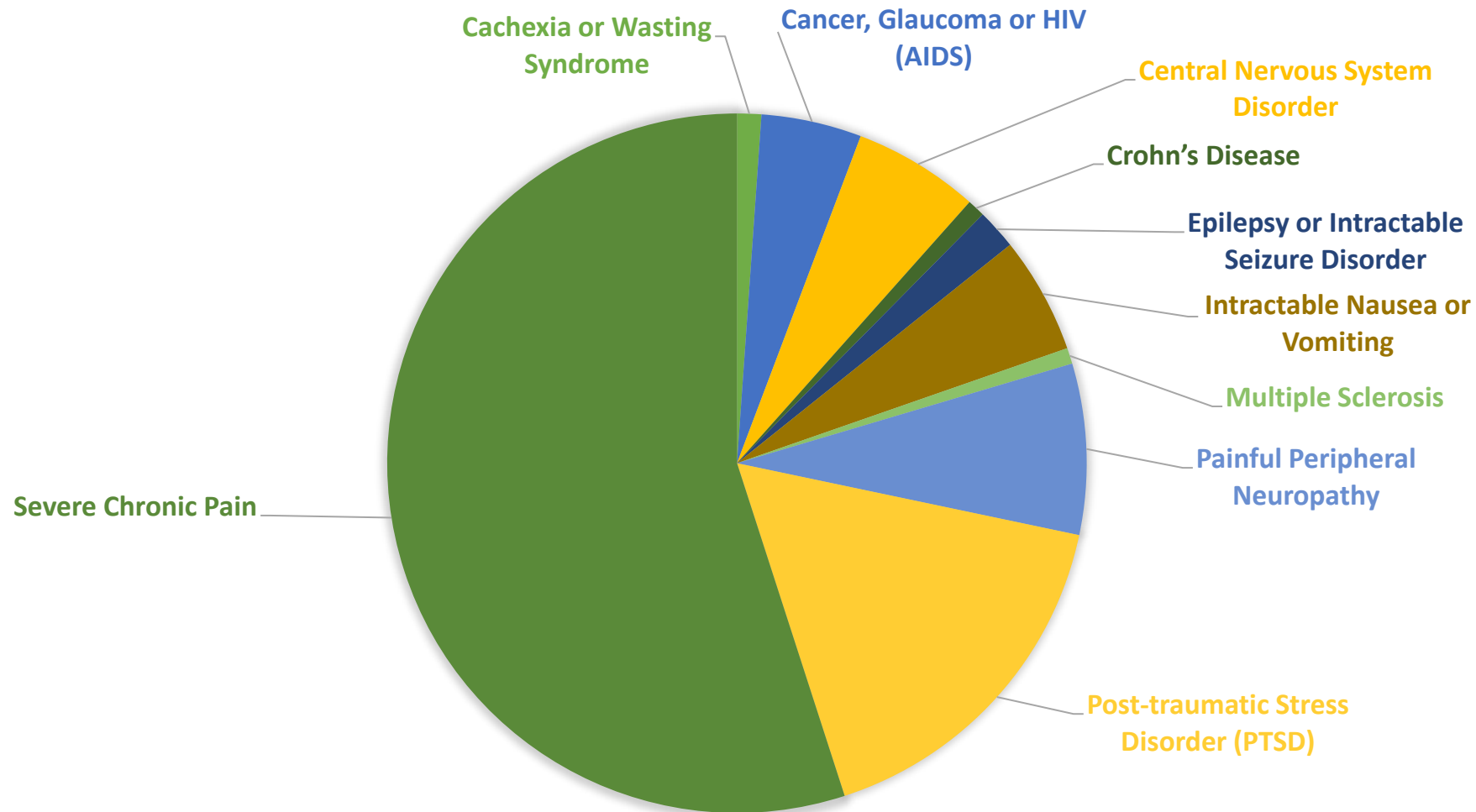
Heavy use  Up to 90 days

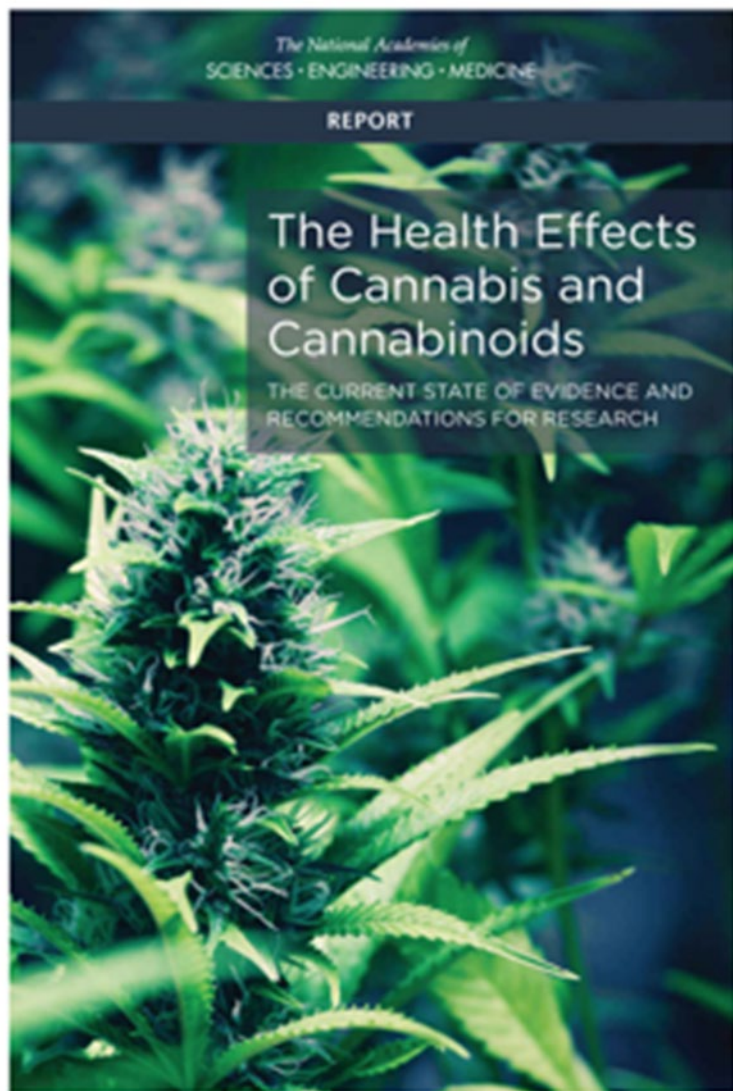
Hair   Up to 90 days

Marijuana Efficacy



Enrollment by Medical Condition





Committee on the Health Effects of Marijuana:
An Evidence Review and Research Agenda

Board on Population Health and Public Health Practice

Health and Medicine Division

A Report of

The National Academies of
SCIENCES • ENGINEERING • MEDICINE

THE NATIONAL ACADEMIES PRESS

Washington, DC

www.nap.edu

National Academies: Health Effects of Cannabis

- ✦ **No or insufficient evidence** to support or refute that cannabinoids are effective for...
 - ✦ cancer-associated anorexia cachexia syndrome and anorexia nervosa
 - ✦ cancers, including glioma
 - ✦ irritable bowel syndrome
 - ✦ **epilepsy**
 - ✦ spasticity in patients with paralysis due to spinal cord injury
 - ✦ chorea and certain neuropsychiatric symptoms - Huntington's disease
 - ✦ symptoms associated with amyotrophic lateral sclerosis (ALS)
 - ✦ Parkinson's disease or levodopa-induced dyskinesia
 - ✦ dystonia
 - ✦ treatment for mental health outcomes in individuals with schizophrenia or schizophreniform psychosis
 - ✦ achieving abstinence in the use of addictive substances

National Academies: Health Effects of Cannabis

CONCLUSION 4-1

There is substantial evidence that cannabis is an effective treatment for chronic pain in adults.

Cannabinoids for Medical Use

Chronic Pain

🌿 Results

🌿 Reduction in pain of at least 30%

🌿 **37% versus 31% placebo** (OR 1.41 95% CI, 0.99-2.00)

🌿 Reduction in pain on 10 point numerical scale

🌿 **-0.46** (95% CI, -0.80—0.11)

🌿 Limitations

🌿 Small, short, difficult to blind studies

🌿 Conclusion

🌿 Cannabis may provide pain relief in the short term

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Medical Cannabis Effects on Opioid Use

✦ Retrospective study of 77 medical cannabis patients (intractable pain)

✦ 45% female; avg 54 years

Primary Outcome: amount of opioid use

✦ Milligram morphine equivalents

	Baseline (mg)	6 months (mg)	P-value
Morphine equivalents, median (IQR); n=74	105 (43.75 to 155.63)	65.9 (28.13 to 150)	P = 0.001
Morphine equivalents, average \pm SD; n=74	140.64 \pm 184.64	103.1 \pm 115.31	P = 0.009

✦ Patients using cannabis for intractable pain may have experienced a significant reduction in opioid use.

National Academies: Health Effects of Cannabis

CONCLUSION 4-7

4-7(a) There is **substantial evidence** that oral cannabinoids are an effective treatment for improving patient-reported **multiple sclerosis spasticity** symptoms, but limited evidence for an effect on clinician-measured spasticity.

Cannabis for Spasticity Due to MS

- ✦ Systematic review of cloned THC/CBD product used outside the U.S.

✦ Results

- ✦ Improved Ashworth scale compared to placebo

- ✦ -12% (95% CI -.24 - 0.01)

- ✦ Improved spasticity using a numerical scale

- ✦ 0.76 (95% CI -1.38 - -0.14)

✦ Conclusion

- ✦ Cannabis may provide a modest subjective improvement in spasticity due to MS.

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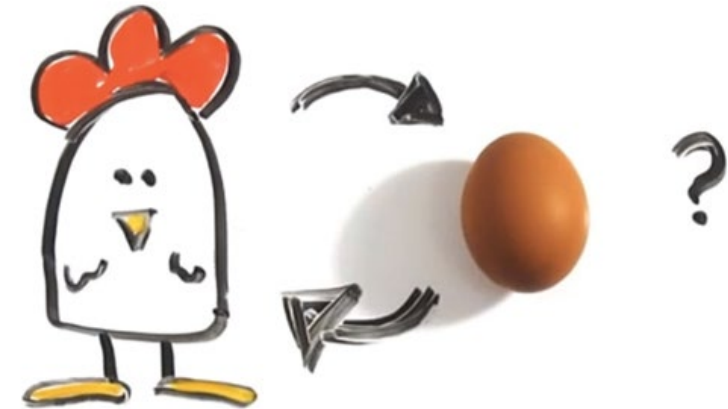
Sleep Abnormalities with Cannabis: A Comprehensive Review

- ✦ There is an initial improvement in **subjective** sleep complaints.
- ✦ **Objective** measurements have shown both positive and negative effects.
- ✦ Tolerance to beneficial effects occurs in chronic users.
- ✦ Prominent negative effects on sleep occur during withdrawal.



Cannabinoids and Post-traumatic Stress Disorder (PTSD)

- ✦ High prevalence of cannabis use among PTSD patients.
- ✦ Higher levels of PTSD symptoms with increased marijuana use.
- ✦ Small studies suggest possible benefit



Study	n	cannabinoid	Outcome
Jetly (2015)	10	THC - nabilone	"significant relief"
Roitman (2014)	10	THC - nabilone	"improvement in global symptom severity, frequency of nightmares and hyperarousal symptoms"
Fraser (2009)	34	THC - nabilone	"lessening in nightmare severity"

Safety Concerns



Cannabis Adverse Effects

Short term

dizziness
euphoria
anxiety
↓ psychomotor function
cognitive impairment
memory impairment
sedation
hallucinations
↑ heart rate,
wt gain

cardiac arrhythmias/MI
↓ pulmonary function
vision disturbances
↓ blood sugars
MS relapse
↑ risk of bleed
vomiting
urinary tract infections
withdrawal

Long term

addiction
dependence
withdrawal
depression
memory impairment
cognition decline
↓ pulmonary function
Cannabis Hyperemesis Syndrome

worsening symptoms of
schizophrenia
MS relapse
relationship problems
lower life satisfaction
less academic success
less career success

Adverse Effects of Medical Cannabinoids: a Systematic Review

- ✦ Review of cannabis studies for adverse drug reactions (ADRs)
 - ✦ 23 randomized controlled trials
 - ✦ 4779 adverse events reviewed
- ✦ Majority of ADRs were non-serious (96.6%)
- ✦ Rate of the non-serious events was higher with medical use versus controls (RR 1.86 95% CI 1.57-2.21)

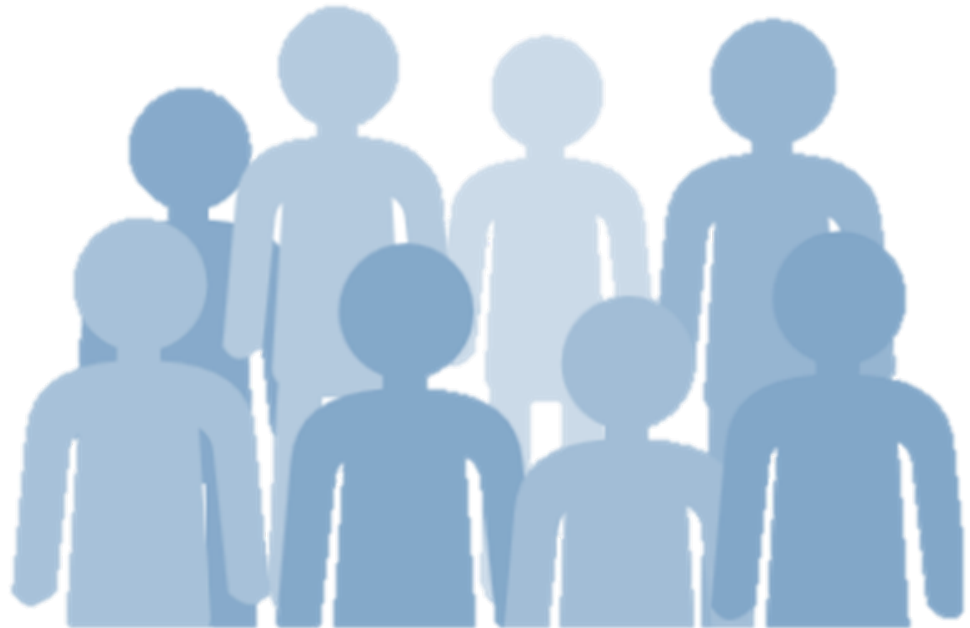
Patient Safety

- ✦ Focus on patient specific factors

- ✦ Drug interactions

- ✦ Comorbid conditions

- ✦ High risk populations



Patient Safety - Drug Interactions

- ✦ Many significant interactions including with high risk medications
- ✦ Majority of interactions are additive Central Nervous System Depression
 - ✦ Systemic >>> Topical
 - ✦ Dose dependent
 - ✦ Frequency dependent
 - ✦ Duration dependent



Patient Safety - Comorbid Conditions

Respiratory Disease

- ✦ Association between **long-term cannabis smoking** and worse respiratory symptoms more frequent chronic bronchitis episodes.
- ✦ Association between **cessation** of cannabis smoking and improvements in respiratory symptoms.

Patient Safety - Comorbid conditions

Cardiovascular Disease

- ✦ THC is a cardiac stimulant
 - ✦ Acute exposure
 - ✦ Increased blood pressure, postural hypotension
 - ✦ Increased heart rate
 - ✦ May lead to increased risk of stroke and myocardial infarction
- ✦ Risk may be greater depending on
 - ✦ Route
 - ✦ Dose
 - ✦ Duration
 - ✦ Cardiac history
 - ✦ Contributing medications

Patient Safety - Comorbid conditions

Mental Health Conditions

- ✦ Acute psychotic symptoms during intoxication

- ✦ Decreased memory

 - ✦ Worse with increasing years of regular use

- ✦ Impaired cognition

 - ✦ With regular use impairment lasts
to 2 days after last use

up

Patient Safety - Comorbid conditions

Mental Health Conditions

- ✦ Regular marijuana use is associated with increased risk of anxiety and depression
 - ✦ Weekly or more frequent cannabis use in teenagers predicted an approximately twofold increase in risk for later depression and anxiety (OR1.9, CI1.1 to 3.3) after adjustment for potential baseline confounders
- ✦ Dependence may occur with increased risk with more frequent use
 - ✦ Dependence - average 9% lifetime dependence
 - ✦ Heavy users - 50%

Patient Safety - Comorbid conditions

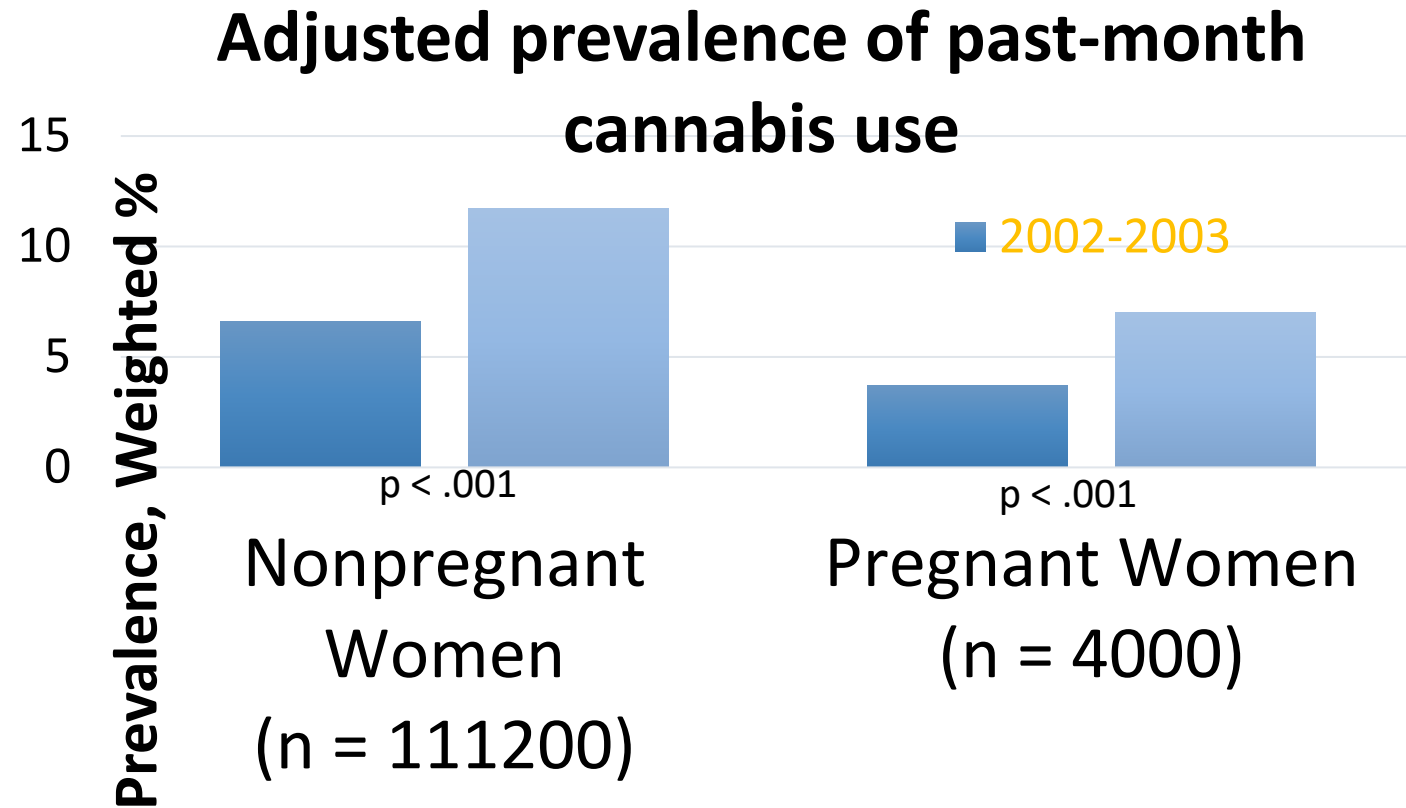
Mental Health Conditions

- ✦ Meta-analysis of the association between the level of cannabis use and risk of psychosis. (Marconi 2016)
 - ✦ 18 studies
 - ✦ 66,816 individuals
- ✦ Higher levels of cannabis use were associated with increased risk for psychosis in all the included studies.
- ✦ Risk of schizophrenia and other psychosis-related outcomes among the heaviest cannabis users compared to the nonusers OR of 3.90 (95% CI 2.84 to 5.34)

Patient Safety - High Risk Populations

Pregnancy

🌿 Marijuana use among pregnant woman doubled between 2002 and 2017



Patient Safety - High Risk Populations

Pregnancy



- ✦ Of 400 Colorado dispensaries contacted:
- ✦ 69% recommended marijuana for the treatment of morning sickness
- ✦ Only 31.8% recommended a discussion with a health care provider without prompting

Patient Safety - High Risk Populations

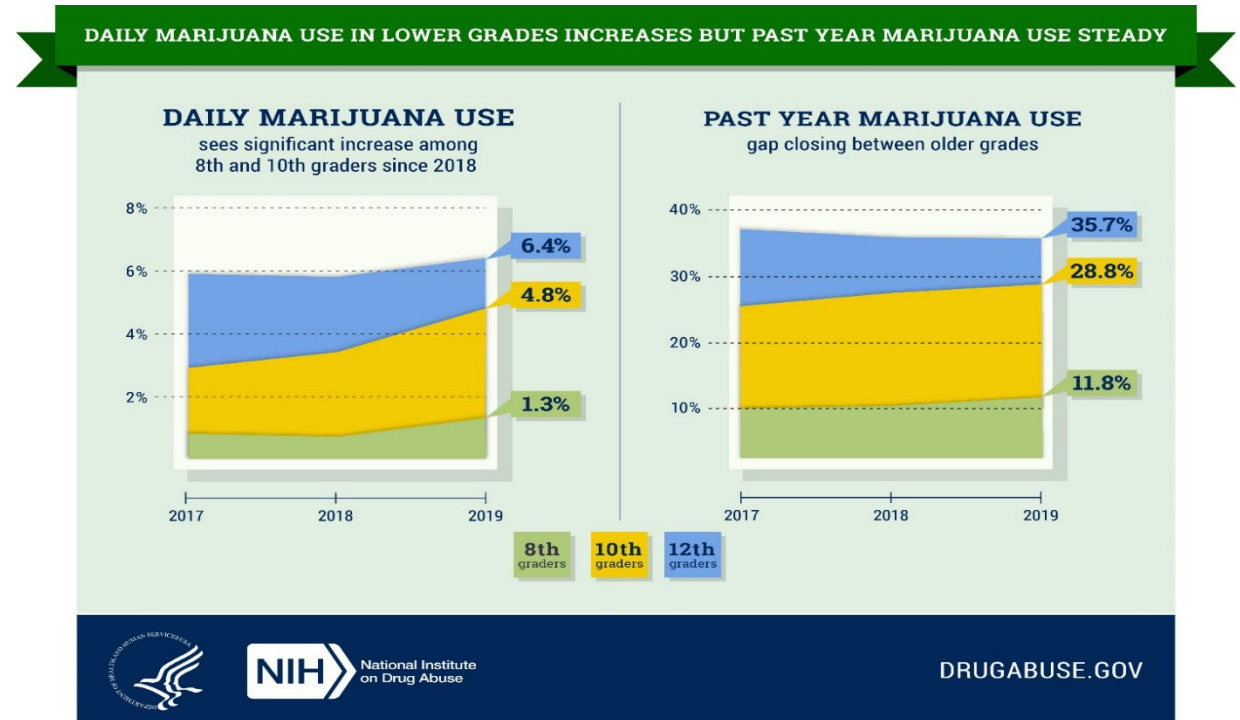
Pregnancy

- ✦ No known safe amount of marijuana during pregnancy
- ✦ Marijuana crosses the placenta and enters the fetal brain
- ✦ May disrupt the endocannabinoid system
- ✦ Associated with increased risk of lower birth weights
- ✦ Possible pregnancy complications for mother and increased admission to neonatal ICU

Patient Safety - High Risk Populations

Adolescence

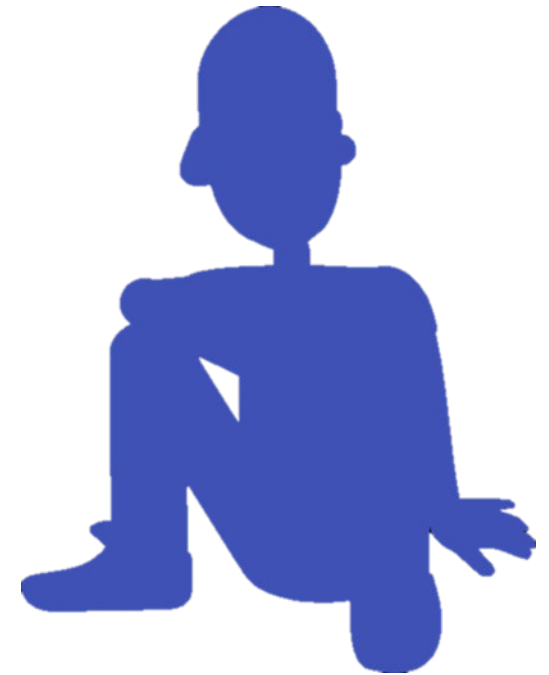
- ✦ **38%** of high school students report having used marijuana in their life
- ✦ **71%** of high school seniors do not view regular marijuana smoking as being very harmful



Patient Safety - High Risk Populations

Adolescence

- ✦ Perceptions regarding the harm of marijuana may contribute to risky behaviors
- ✦ A developing brain may be more vulnerable to marijuana effects
- ✦ Higher doses, frequencies, and durations pose greater risk



Other safety considerations

✦ Labeling

- ✦ May be absent or inaccurate

✦ Driving

- ✦ Abstain from driving for at least 6 hours after smoking or 8 hours after oral consumption

✦ Storage

- ✦ Keep in a locked box, away from children and pets



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