A COMPREHENSIVE ANALYSIS OF MEDICAL MARIJUANA FOR OLDER ADULTS

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OBJECTIVES

- Compare and contrast federal law and state laws regarding the use of marijuana
- Differentiate the components of marijuana and their pharmacologic effects
- Compare and contrast the dosage forms of medical marijuana
- Evaluate the risks and benefits of medical marijuana use in older adults

HISTORY OF MEDICAL MARIJUANA

From www.en.Wikipedia.org

William Brooke O'Shaughnessy
Introduced marijuana to Western medicine in the mid-1800s

HISTORY OF MEDICAL MARIJUANA

- **1851: Marijuana added to US Pharmacopeia**
- **1942: Marijuana removed from US Pharmacopeia**
- **1970: Marijuana classified as Schedule 1 under Controlled Substances Act**
- **1996: California becomes first state to legalize medical marijuana**
- **1998: Alaska, Oregon and Washington legalize medical marijuana**
- **Currently 25 states and the District of Columbia have legalized medical marijuana**

	MEDICAL MARIJUANA LEGALIZED	CANNABIDIOL OIL LEGALIZED	RECREATIONAL MARIJUANA LEGALIZED
ALABAMA		✓	
ALASKA	✓		✓
ARIZONA	✓		
ARKANSAS			
CALIFORNIA	✓		
COLORADO	✓		✓
CONNECTICUT	✓		
DELAWARE	✓		
DISTRICT OF COLUMBIA	✓		✓
FLORIDA		✓	
GEORGIA		✓	
HAWAII	✓		
IDAHO			
ILLINOIS	✓		
INDIANA			
IOWA		✓	
KANSAS			
KENTUCKY		✓	
LOUISIANA	✓		
MAINE	✓		
MARYLAND	✓		
MASSACHUSETTS	✓		
MICHIGAN	✓		
MINNESOTA	✓		
MISSISSIPPI		✓	
MISSOURI		✓	

	MEDICAL MARIJUANA LEGALIZED	CANNABIDIOL OIL LEGALIZED	RECREATIONAL MARIJUANA LEGALIZED
MONTANA	✓		
NEBRASKA			
NEVADA	✓		
NEW HAMPSHIRE	✓		
NEW JERSEY	✓		
NEW MEXICO	✓		
NEW YORK	✓		
NORTH CAROLINA		✓	
NORTH DAKOTA			
OHIO			
OKLAHOMA		✓	
OREGON	✓		✓
PENNSYLVANIA	✓		
RHODE ISLAND	✓		
SOUTH CAROLINA		✓	
SOUTH DAKOTA			
TENNESSEE		✓	
TEXAS			
UTAH		✓	
VERMONT	✓		
VIRGINIA		✓	
WASHINGTON	✓		✓
WEST VIRGINIA			
WISCONSIN		✓	
WYOMING		✓	

MEDICAL MARIJUANA IN WASHINGTON STATE

HEALTHCARE PROVIDERS WHO MAY RECOMMEND MEDICAL MARIJUANA*
Medical doctors (MDs)
Physicians assistants (PAs)
Osteopathic physicians (DOs)
Osteopathic physician assistants (OAs)
Naturopathic physicians (NDs)
Advanced registered nurse practitioners (ARNPs)

**Must be licensed in Washington state*

Healthcare providers must NOT PRESCRIBE marijuana. It is prohibited under federal law to distribute, dispense or possess marijuana.

MEDICAL MARIJUANA IN WASHINGTON STATE

BEFORE PROVIDING A RECOMMENDATION TO A PATIENT A PROVIDER MUST:
Complete a physical exam
Determine that the patient has a qualifying condition
Document qualifying condition in the medical record
Inform the patient of other treatment options
Document other treatment options attempted in the medical record
Advise patients of risks and benefits of medical marijuana
PROVIDER MAY NOT:
Practice solely to authorize medical marijuana
Advertise that they authorize medical marijuana
Hold economic interest in a business that produces, processes or sells MJ

MEDICAL MARIJUANA IN WASHINGTON STATE

QUALIFYING CONDITONS	
Cancer	Intractable pain*
HIV	Glaucoma, acute or chronic*
Multiple sclerosis	Crohn's disease with debilitating symptoms*
Epilepsy or other seizure disorder	Hepatitis C with debilitating nausea/intractable pain*
Spasticity disorders	Chronic renal failure requiring hemodialysis
Post traumatic stress disorder *(starting 7/24/15)*	Traumatic brain injury *(starting 7/24/15)*
Diseases, including anorexia, which result in NV, wasting, appetite loss, cramping, seizures, muscle spasms or spasticity*	

unrelieved by standard medical treatments and medications

MEDICAL MARIJUANA IN WASHINGTON STATE

DOCUMENTATION OF AUTHORIZATION MUST:
Be on tamper-resistant paper and be signed/dated
Beginning 7/24/15, all new authorizations must be on form developed by DOH
DOCUMENTATION OF AUTHORIZATION MUST INCLUDE:
Patient's name, address, DOB
Health care provider's name, address, phone number, license number
The date of issuance and expiration

NEW CHANGES TO MEDICAL MARIJUANA IN WASHINGTON

	Outgoing Rules	Cannabis Patient Protection Act (2015)
Registry*	Not required	Voluntary; patient recognition card will be provided
Possession Amounts*	24 oz usable; 15 plants	8 oz usable; 6 plants (provider may authorize up to 16 oz and15 plants)
		If DO NOT join voluntary registry: limited to 6 oz usable and 4 plants
Collective Gardens*	Up to 10 patients/designated providers may grow collectively	Collectives NOT allowed; phased out by July 2016
		Cooperatives allowed: 4 patients/60 plants
Retail Locations*	Not regulated	Licensed stores w/medical endorsement
		Registry patients exempt from sales tax
Authorization** Expiration	None	≥18yo: 12 months
		<18yo: 6 months
		Authorizations must be renewed in person
New additions**	N/A	Notify DOH if write >30 authorizations/month
		Med records subject to inspection by disciplining body

*Change beginning 7/1/16
**Change beginning 7/24/15

MEDICAL MARIJUANA IN WASHINGTON STATE: *DEPARTMENT OF HEALTH PRACTICE GUIDELINES*

- ***Advice about the potential risks of the medical use of marijuana to include:***
  - The variability of quality and concentration of medical marijuana
  - Adverse events, including falls or factures
  - Use of marijuana during pregnancy or breast feeding
  - The need to safeguard all marijuana and marijuana infused products from children and pets or domestic animals.

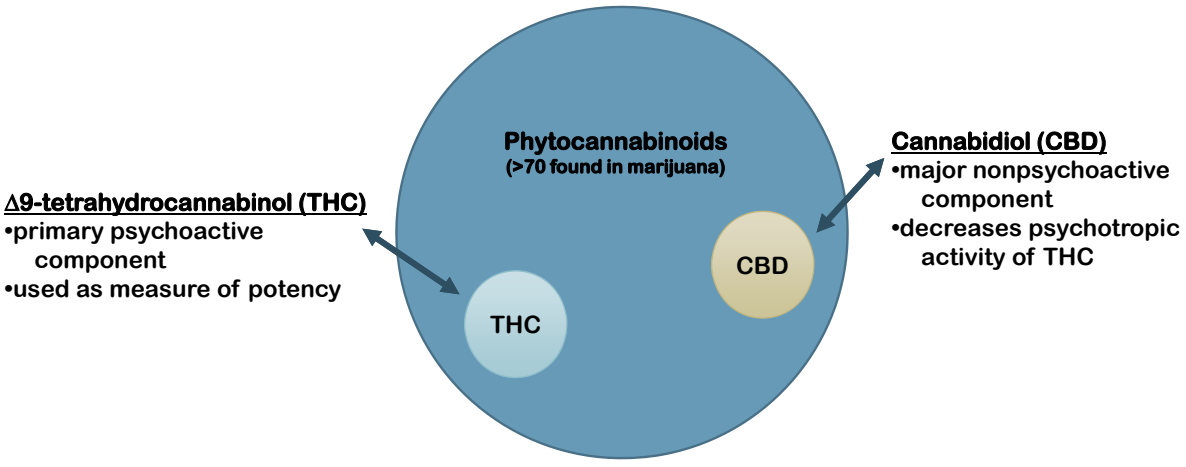
http://www.doh.wa.gov/Portals/1/Documents/2300/2014/PracticeGuidelinesFinal.pdf

DEFINITIONS

Endocannabinoids	Phytocannabinoid Botanicals: MEDICAL MARIJUANA (Cannabis)	Cannabis-Derived Pharmaceuticals
Produced in human tissues	Illegal/illicit	Prescription Drugs
Endogenous cannabinoids	Cannabinoids found in *Cannabis sativa* or *Cannabis indica*	Synthetic version of one specific phytocannabinoid: •Dronabinol (Marinol®) •Nabilone (Cesamet®)
		Cannabis-derived liquid extract: •Nabiximols (Sativex®)*

**Not currently available in the US: undergoing Phase III trials for cancer pain*

DEFINITIONS



PHARMACOLOGIC ACTIONS OF MARIJUANA

- **CNS**
  - **Euphoria, dysphoria, anxiety**
  - **Heightened sensory perception**
  - **Generalized CNS depression**
  - **Mental clouding, memory impairment**
  - **Incoordination**
  - **Tolerance**
  - **Dependence**
  - **Analgesia**
  - **Antiemetic, hyperemetic**
  - **Increased appetite**
- **Cardiovascular**
  - **Tachycardia**
  - **Supine hypertension**
  - **Postural hypotension**
  - **Increased risk of MI within 1hr smoking**
- **Other**
  - **Decreased intraocular pressure**
  - **May have antispasmodic effects**
  - **May have anti-inflammatory effects**
  - **May have neuroprotective effects**
  - **Complex immunomodulatory effects**

Health Canada: Information for Health Care Professionals—Cannabis and the cannabinoids (2013).

CANNABIS-DERIVED PHARMACEUTICALS: DRONABINOL (MARINOL®, *C-III*)

- Synthetic THC
- Available as capsules: 2.5mg, 5mg, 10mg
- <u>INDICATIONS:</u>
  - Chemotherapy-induced NV
  - HIV-associated anorexia with weight loss
- <u>ADVANTAGES:</u>
  - FDA approved; pharmaceutical grade product
- <u>DISADVANTAGES:</u>
  - Doesn't work rapidly
  - Amount of drug that reaches the bloodstream varies from person to person
  - Difficult to titrate to effect

CANNABIS-DERIVED PHARMACEUTICALS: NABILONE (CESAMET®, *C-II*)

- Synthetic cannabinoid similar to THC
- Available as capsules: 1mg
- INDICATIONS:
  - Chemotherapy-induced NV
  - HIV-associated anorexia with weight loss
- ADVANTAGES:
  - FDA approved; pharmaceutical grade product
- DISADVANTAGES:
  - Doesn't work rapidly
  - Amount of drug that reaches the bloodstream varies from person to person
  - Difficult to titrate to effect

CANNABIS-DERIVED PHARMACEUTICALS: NABIXIMOLS (SATIVEX®, *PHASE III TRIALS IN US*)

- Approved in 27 countries
- Cannabis-derived extract of THC and cannabidiol ("liquid cannabis")
- Available as oral mucosal spray: 2.7mg THC-2.5mg CBD/spray
- INDICATIONS (in Canada):
  - Relief of spasticity in patients with multiple sclerosis who have not responded to other therapies
  - Relief of neuropathic pain in patients with multiple sclerosis
  - Adjunct in patients with advanced cancer who experience moderate to severe pain during highest tolerated dose of strong opioid therapy
- ADVANTAGES:
  - Pharmaceutical grade product
  - Contains both THC and CBD
  - Less variability in absorption than dronabinol and nabilone

Contraindications (in Canada) include:
-significant hepatic/renal impairment
-serious CVD
-h/o schizophrenia/psychotic disorder

MARIJUANA DOSAGE FORMS

CANNABIS	HASH	HASH OIL
Flowering tops/leaves/stalks of mature female plant	Dried cannabis resin	Oil based extract of hash
THC content: -historically 0.5-5% -WA recreational pot: 16% (average)	THC content: -2-20% or higher	THC content: -15-50% or higher

MARIJUANA DOSAGE FORMS

INHALATION	ORAL (aka "Edibles")	TRANSDERMAL
Smoking	Capsules	Ointment
Vaporizers	Cooking oils (olive, coconut, etc)	Balm
	Butter	Patch
	Soda	
	Mints	
	Candy	
	Baked goods	
	Crackers	

Peak Blood [THC] Reached
INHALED: within 10 minutes
ORAL: up to 4 hours

MARIJUANA DOSAGE FORMS

- From Department of Colorado Public Health & Environment Report
  - Typical marijuana cigarette (joint) in Colorado contains:
    - About 0.5gm of marijuana with THC content of 12-23%
    - Between 60-115mg of THC
- Typically a "dose" of recreational marijuana is considered to be 10mg THC
- Marijuana from pre-1960s contained more equal proportions of THC and CBD
- Marijuana currently available has been bred to contain higher concentrations of THC

Monitoring Health Concerns Related to Marijuana in Colorado: 2014
https://www.colorado.gov/pacific/cdphe/retail-marijuana-public-health-advisory-committee

MARIJUANA DOSAGE FORMS: *ACCURACY OF PRODUCT LABELING FOR EDIBLES*

	Accurately Labeled	Underlabeled	Overlabeled
Overall (3 cities)			
Products tested, N=75	13 (17%)	17 (23%)	45 (60%)
THC (mg) label range	15-200	20-1000	2-325
THC (mg) actual range	15-183	34-1236	<1-267
Seattle, WA			
Products tested, N=23	1 (4%)	4 (17%)	18 (78%)
THC (mg) label range	180	34-180	20-250
THC (mg) actual range	164	46-206	<1-136

JAMA. 2015;313(24):2491-2493.

THERAPEUTIC USES OF MEDICAL MARIJUANA: *QUALIFYING CONDITIONS IN WASHINGTON STATE*

- Intractable pain
- Muscle spasms

→ **Most common uses of medical marijuana**

- Cancer
- HIV
- Glaucoma, acute or chronic
- Multiple sclerosis
- Crohn's disease with debilitating symptoms
- Epilepsy or other seizure disorder
- Hepatitis C with debilitating nausea/intractable pain
- Chronic renal failure
- Posttraumatic stress disorder
- Traumatic brain injury
- Diseases, including anorexia, which result in NV, wasting, appetite loss, cramping, seizures, muscle spasms or spasticity

THIS LIST IS NOT EVIDENCED BASE

THERAPEUTIC USES OF MEDICAL MARIJUANA: *WHAT IS THE EVIDENCE IN THE GENERAL POPULATION?*

- Systematic Review and Meta-analysis by Whiting PF, et al (*JAMA*, June 2015)
  - Included 79 trials (6462 patients)
  - *Moderate-quality evidence that marijuana associated with improvement in chronic pain and spasticity*
    - 31 studies for chronic neuropathic or cancer pain: only one used smoked THC
    - 21 studies for spasticity due to MS or paraplegia: none included smoked THC
  - *Low-quality evidence that marijuana associated with improvement in NV due to chemotherapy, weight gain in HIV, sleep disorders, Tourette syndrome*
- Clinical Review by Hill KP (*JAMA*, June 2015)
  - Included 28 trials (for indications other than NV and appetite stimulation)
  - *Evidence suggesting marijuana may be efficacious* for chronic pain, neuropathic pain and spasticity due to MS
    - 3 studies included smoked marijuana

THERAPEUTIC USES OF MEDICAL MARIJUANA: *WHAT IS THE EVIDENCE FOR PAIN IN THE GENERAL POPULATION?*

- Systematic review of randomized trials for chronic non-cancer pain by Deshpande et al (2015)
  - Included 6 trials (n=226) with max duration of 5 days
    - Formulations were smoked or vaporized
    - Total daily THC dose ranged from 1.875mg to 34mg
  - ADRs: HA, sedation, dysphoria, poor concentration, dizziness, impaired memory
  - *Conclusion: evidence to support use of low-dose marijuana in refractory neuropathic pain of moderate severity with concomitant analgesics*
- Meta-analysis of inhaled cannabis for chronic neuropathic pain by Andreae, et al (2015)
  - Included 5 randomized placebo-controlled double blind trials (n=178) with max duration of 2 weeks
    - Formulations were inhaled via cigarettes, vaporizer or pipe
  - ADRs: anxiety, disorientation, HA, dizziness, psychosis, memory impairment, increased heart rate
  - *Conclusion: inhaled cannabis results in short-term reduction in neuropathic pain for 1 in every 5 to 6 patients treated*

THERAPEUTIC USES OF MEDICAL MARIJUANA: *WHAT IS THE EVIDENCE FOR MULTIPLE SCLEROSIS IN THE GENERAL POPULATION?*

- Systematic Review by American Academy of Neurology (Koppel, et al; 2014)
  - Spasticity in MS
    - Oral cannabis extract (THC/CBD or CBD) effective
    - THC and nabiximols probably effective
  - MS central pain or painful spasms:
    - Oral cannabis extract (THC/CBD or CBD) effective
    - THC and nabiximols probably effective
  - MS bladder frequency:
    - nabiximols probably effective

THERAPEUTIC USES OF MEDICAL MARIJUANA: *WHAT IS THE EVIDENCE FOR EPILEPSY IN THE GENERAL POPULATION?*

- Cochrane Review: Cannabinoids for Epilepsy (Gloss and Vickrey; 2014)
  - "No reliable conclusions can be drawn at present regarding the efficacy of cannabinoids as a treatment for epilepsy. The dose of 200 to 300 mg daily of cannabidiol was safely administered to small numbers of patients generally for short periods of time, and so the safety of long term cannabidiol treatment cannot be reliably assessed."
- Systematic Review by American Academy of Neurology (Koppel, et al; 2014)
  - "Data are insufficient to support or refute the efficacy of cannabinoids for reducing seizure frequency."
- First prospective study of cannabidiol in treatment-resistant epilepsy by Devinsky et al (2016)
  - Open-label trial of patients (1-30yo) with severe, intractable, child-onset, treatment-resistant epilepsy (n=214)
  - Cannabidiol (Epidiolex) 2-5mg/kg/day divided BID; max dose 50mg/kg/day
  - 36.5% median reduction in monthly motor seizures
  - ADRs: somnolence, decrease appetite, diarrhea, fatigue, convulsion

THERAPEUTIC USES OF MEDICAL MARIJUANA IN OLDER ADULTS

- Are elderly patients using medical marijuana (MMJ)?
  - Use increasing but prevalence unknown
  - In a survey from 31 countries, 6.5% of MMJ users aged 61-76
  - In the Netherlands, >5500 patients prescribed MMJ between 2003-2010
    - 31% of those using MMJ aged 61-80
    - 6% of those using MMJ aged >80
- Is there evidence to support the use of MMJ in the elderly?

J Psychoactive Drugs. 2013;45:199–210.
Eur J Clin Pharmacol. 2013;69:1575–1580.

Efficacy and Safety of Medical Cannabinoids in Older Subjects: Systematic Review (*van den Elsen, et al)*

Author/Design	Indication/*Efficacy*	Subjects/ Mean Age	Dose	Adverse Effects (cannabinoid vs. control)
Ungerleider et al (1982) RCT (crossover) Control: prochlorperazine	Chemotherapy induced NV *Both drugs equally effective*	n=214 47 (18-82)	Oral THC 7.5-12.5mg 5 times daily	Sedation (78 vs. 56, p<0.01) Physiological[a] (62 vs. 24, p<0.01) Psychological[b] (59 vs. 10, p<0.01)
Carroll et al (2004) RCT (crossover) Control: placebo	PD: levodopa-induced dyskinesia *No improvement*	n=19 67 (51-78)	Oral THC:CBD 0.034-0.25mg THC/kg daily	Drowsy/lethargic (9 vs. 6) Detached (4 vs. 0) Dry mouth (4 vs. 1)
Pickering et al (2011) RCT (crossover) Control: placebo	COPD: CO_2 induced breathlessness *No improvement*	n=5 67 (66-68)	Sublingual THC 2.7mg-CBD 2.5mg QID	Cardiac arrhythmia (2 vs. 0) Mild intoxication (1 vs. 0) Drowsiness (1 vs. 0)

[a]Physiological: includes dizziness, HA, dry mouth, tachycardia, chills, or increased pain
[b]Psychological: includes mental clouding, space/time distortion, short-term memory loss or dissociative reaction
Ageing Research Reviews. 2014;14:56-64.

Cannabinoids in Late-Onset Alzheimer's Disease (*Ahmed, et al)*

Author/Design	Indication/*Efficacy*	Subjects/ Mean Age	Dose	Adverse Effects
Volicer et al (1997) RCT (crossover) Control: placebo 12 weeks	AD: food refusal & disturbed behavior *Decreased severity of disturbed behavior*	n=12 72.7 ± 4.9	Dronabinol 2.5mg BID	Grand mal seizure (1 vs. 0), Anxiety (11 vs. 12), Tiredness (9 vs. 5), Somnolence (8 vs. 4), Euphoria (7 vs. 5)
Walther (2006) Open-label 2 weeks	AD: nocturnal motor activity *Reduce nocturnal motor activity/agitation*	n=6 81.5 ± 6.1	Dronabinol 2.5mg daily	None
Walther et al (2011) RCT (crossover) Control: placebo 4 weeks	AD: agitation and circadian disturbances *Reduce nighttime activity, strengthened circadian rhythms*	n=2 75, 81	Dronabinol 2.5mg daily	None
Woodward (2014) Retrospective chart review	AD: behavioral and appetite disturbances *Decrease in all domains Pittsburgh Agitation Scale; improvement sleep duration and percentage meals consumed*	n=40 dementia patients (13 w/AD) Age not reported	Dronabinol, mean dose 7.03mg/day	Sedation (9), delirium (4), UTI (3), confusion (2)

Clin Pharmacol Ther. 2015;97(6): :597-606.

Cannabinoids for Neuropsychiatric Symptoms of Dementia

Author/Design	Primary outcome/ *Efficacy*	Subjects/ Mean Age	Dose	Adverse Effects
van den Elsen et al (Dec 2015) RCT (crossover) Control: placebo 12 weeks	Change in NPI score *THC did not reduce NPI compared to placebo*	n=22 76.4	Oral THC 0.75mg BID 1.5mg BID	Dizziness, somnolence
Van den Elsen et al (June 2015) RCT Control: placebo 3 weeks	Change in NPI score *No difference between treatment groups*	n=50 78.4	Oral THC 1.5mg TID	Adverse effects similar between THC and placebo groups
Shelef (2015) Open-label 4 weeks	Change in CGI and NPI scores *CGI: 6.5 to 5.7; p<0.01* *NPI: 44.4 to 12.8; p<0.01*	n=10 73.2	Medical cannabis oil (1.65% THC) 2.5mg BID 5mg BID 7.5mg BID	Only 3 reported: dysphagia, fall/pelvic fracture, increased confusion

Am J Geriatr Psychiatry. 2015; 23:1214-1224.
Neurology. 2015;84:2338–2346.
J Alzheimer's Disease. 2016;51:15-19.

THERAPEUTIC USES OF MEDICAL MARIJUANA IN OLDER ADULTS

- Glaucoma
  - The American Academy of Ophthalmology and the American Glaucoma Society do not recommend marijuana for glaucoma
- Parkinson's Disease
  - An American Academy of Neurology review in 2014 reported that oral cannabis extract probably ineffective for levodopa-induced dyskinesias (moderate evidence)
- Alzheimer's Disease
  - Further research is needed

http://www.aao.org/complimentary-therapy-assessment/marijuana-in-treatment-of-glaucoma-cta--may-2003
http://www.americanglaucomasociety.net/patients/position_statements/marijuana_glaucoma
https://www.aan.com/Guidelines/Home/GetGuidelineContent/651

ACUTE ADVERSE EFFECTS OF MARIJUANA

TOXIC REACTIONS ***(as seen in overdose/accidental ingestion by children)***	
Anxiety	NV
Hallucinations	Dry mouth
Panic episodes	Dizziness
Dyspnea	Somnolence
Chest pain	Respiratory depression
Tachycardia	Coma

ACUTE ADVERSE EFFECTS OF MARIJUANA: *ACCIDENTAL INGESTION BY CHILDREN*

EDIBLE

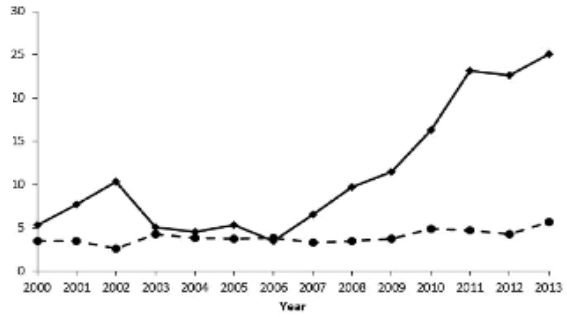
From www.legalmarijuanadispensary.com

NON-EDIBLE

From www.drugstore.com

ANNUAL RATE OF MARIJUANA EXPOSURE AMONG CHILDREN YOUNGER THAN 6 YEARS (NATIONAL POISON DATA SYSTEM 2000-2013)

Rate per million children



States where MJ legalized prior to 2000

States where MJ not legal

Clin Pediatrics. 2016;55(5):428-436.

ACUTE ADVERSE EFFECTS OF MARIJUANA

CNS EFFECT:	CARDIAC EFFECTS	DOSE RELATED IMPAIRMENT OF:
Anxiety	↑ heart rate	Reaction time
Panic reactions	Fluctuation in blood pressure	Information processing
Psychotic symptoms		Perceptual-motor coordination
		Motor performance
		Attention
		Tracking behavior

- **IMPAIRED ABILITY TO DRIVE**
- **INCREASED RISK CRASHES**

ACUTE ADVERSE EFFECTS OF MARIJUANA: *RISK OF DRIVING IMPAIRMENT*

Colorado Department of Public Health & Environment Report:
Findings from Systematic Literature Review
NOT GENERALIZABLE TO ELDERLY

SUBSTANTIAL EVIDENCE	MODERATE EVIDENCE
Increased risk of driving impairment at blood [THC] 2-5ng/mL	Ingesting ≥ 15mg THC may lead to blood [THC] >5ng/mL
Smoking >10mg THC leads to blood [THC] near or >5ng/mL within 10 minutes	Inhaling vaporized THC leads to blood [THC] similar to smoking same dose
Smoking/ingesting >10mg THC leads to driving impairment	Higher blood [THC] in impaired drivers now than in the past
Waiting at least *6 hours after smoking* or *8 hours after ingesting* <18mg THC resolves/nearly resolves driving impairment	Waiting at least 6 hours after smoking <35mg THC resolves/nearly resolves impairment

Monitoring Health Concerns Related to Marijuana in Colorado: 2014
https://www.colorado.gov/pacific/cdphe/retail-marijuana-public-health-advisory-committee

CHRONIC ADVERSE EFFECTS OF MARIJUANA

DEPENDENCE	RESPIRATORY (if smoked)	CNS
Risk: 1 in 10 of long-term users	Chronic bronchitis	Memory/cognitive impairment
Risk: 1 in 6 of adolescent users	↓ pulmonary function	Psychotic symptoms/disorders
Risk: 1 in 2-3 of daily users	Pulmonary infections	**OTHER**
	Precancerous lesions	Cannabinoid hyperemesis syndrome

Potential contaminants in cannabis
- *Aspergillus* fungus, bacteria
- Aluminum, cadmium
- Pesticides
- Glass beads/sand

POTENTIAL DRUG-DRUG INTERACTIONS
(FROM PUBLISHED CLINICAL EVIDENCE)

Increased CNS depressant effect	Increased THC effect	Increased concomitant drug effect	Decreased concomitant drug effect
Alcohol Phenytoin CNS depressants: *Opioids* *Benzodiazepines* *Sedative hypnotics* *Barbiturates* *Antihistamines* *Muscle relaxants*	Disulfiram Ketoconazole	Clozapine Hydrocortisone Phenytoin Warfarin Clobazam*	Clozapine Indinavir Phenytoin Theophylline

THC metabolized by CYP3A4 and CYP2C9
CBD metabolized by CYP3A4 and CYP2C19

From: Monitoring Health Concerns Related to Marijuana in Colorado: 2014
https://www.colorado.gov/pacific/cdphe/retail-marijuana-public-health-advisory-committee
**Epilepsia.* 2015;56(8):1246-51.

CHALLENGES

- Marijuana use is deemed illegal by the federal government
- Medical marijuana production/manufacturing is not well regulated
- Doses of cannabinoids in marijuana products varies widely and may not be consistent
- Most marijuana research is in people who smoked for recreational use
- Most research regarding medical use of marijuana has been with cannabis-derived pharmaceuticals

CLINICAL APPLICATION

- Document use of medical marijuana in the medical record
- Counsel on variability of quality and concentration of medical marijuana
- Counsel patients on delayed time to effect after ingestion of oral marijuana
- Counsel patients on adverse effects; caution falls/fractures
- Counsel on potential drug interactions particularly CNS depressants/EtOH
- Advise patients not to drive after using medical marijuana
- Warn of risk of accidental ingestion in children/pets and to keep medical marijuana away from children/pets

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