Marijuana in a Medical Context

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Medical Excuse Marijuana

As with any medication that possesses significant side effects, it is imperative to understand that there are important medical, legal, and social consequences to the use of marijuana for medicinal applications. All medicines must be approved by the FDA

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Fundamental Problems with Marijuana as Medicine

- **The FDA has not approved as a medicine**
- Marijuana is mostly smoked, but impure
- Unpredictable doses
- Significant Side Effects relative to indications
- Useful elements largely available commercially

Scientific Status of Medical Excuse Marijuana

- Legislative processes bypass the FDA and jeopardize the public
- <u>Specific Cannabinoids</u> might be useful and worth studying
- Smoking impure preparations problematic/Doses unpredictable
- Oral THC (Marinol) Epidiolex readily available
- Sativex and are on the horizon

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Marijuana

- Impurity-over 500 substances, over 80 cannabinoids
- Resembles tobacco in constituents.
- High THC concentrations 2-30%
- 1/2 life 5-7 days

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Proposed Medicinal Uses of Marijuana

Nausea of Chemotherapy

Glaucoma

- Appetite Stimulation
- Multiple Sclerosis & Neuro diseases
- Pain
- Misc- Cramps, Sleep, Depression
- "Any Chronic Condition" wording

Review of Reviews for Medicinal Applications

- 1975 citations, 72 systematic reviews
- pain management multiple sclerosis (MS), injury, and cancer.
- Small benefit for pain,
- Adverse effects were reported in most reviews comparing cannabis with placebo (49/59, 83%) and in 20/24 (83%) of the reviews comparing cannabis to active drugs.
 Pratt et al. Systematic Reviews (2019) 8:320

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For Appetite 37.7%

2011;43:128-135



Pain

- Screening 1975 citations, 72 systematic reviews
- Adverse effects were reported in most reviews comparing cannabis with placebo (49/59, 83%) and in 20/24 (83%)
- Small number of results showed a benefit for reducing pain, considering pain in general.
 - Pratt et al. Systematic Reviews (2019) 8:320 https://doi.org/10.1186/s13643-019-1243-x

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Pain

- Healthy volunteers doses 0,2,4,8% THC
- Decrease of pain medium doses
- Increase of pain higher doses
- Specific substance responsible? Anesthesiology. 2007;107:785-96

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What is an effective dose?

- Evaluation of neuropathic pain
- Diabetic, post herpetic, idiopathic, lumbosacral, brachial plexopathy
- Pain reduction similar to level of reduction with other standard medications.
- Massive doses appear unnecessary

Wilsey et al Journal of pain 2013;136-148

Marijuana for Neuropathic pain

38 subjects / # who had 30% reduction

Placebo	Medium 3.53	Low 1.29
27%	57%	61%

- Significant dose-related effects on memory and learning
- Both groups reported feeling high, stoned, impaired, medium greater than low dose.
- Massive doses appear unnecessary















Concentration

- Decision-making
- Inhibition
- Impulsivity
- Working memory
- Verbal fluency
- Concept formation and planning

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Structural Change on MRI

- 48 marijuana users
- Abnormal Gray Matter volume
- Abnormal Orbitofrontal Cortex
- Part of the reward network of the brain
- Cumulative deleterious effect on OFC

Filbey et al Proceedings of the National Academy of Sciences, 2014;111:16913-16918

J Addict Med 2011;5:1-8

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Structural Damage to Brain

- **5**9 users 33 controls
- Ave age 33, Ave use 15 yrs, started 16.7 yo
- Ave joints /mo=147
- Ave life joints 25922
- Demonstrated axonal connectivity impairment in hippocampus, splenium of corpus callosum, commissural fibers Bain 2012;135:2245-22

Neuropsychological Decline

- 1037 individuals
- Pot use at 18,21,26,32,38 y/o
- Neuropsych testing at 13 before pot and 38
- Broad Neuropsychological decline across all domains even controlling for education
- 10% (101-91) IQ difference between never and persistent user.
- 6-point IQ decline age 13-38 w/ persistent use Proc Natl Acad Sci U S A. 2012 Aug 27

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Poor Life Outcomes with Pot

- Never used cannabis vs daily before age 17 Increased odds of :
 - later cannabis dependence (17.95, 9.44–34.12),
 - use of other illicit drugs $(7 \cdot 80, 4 \cdot 46 13 \cdot 63)$,
 - suicide attempt (6.83, 2.04–22.90).
- Reductions in:
 - high- school completion
 - degree attainment

ancet Psychiatry 2014; 1: 286–93

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From the horse's mouth

"I used to smoke this stuff regulerly I quit because I needed to pass a test to get a job. The reason I am writing is because I never had any of thougs side effects you talk about don't get me wrong its not for every body. But you don't need to say untrue things about it coordination imparment that's bs it allows you to focus better on single things its perfect for kids like I was that cant concetrate on ting well you don't have to reply to this email I am just bored and looking at stuff on the net and emailing people and going on and on cause I cant sleep well you have a nice day.



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Marijuana and Fatal Crashes California 2008

- Five years following medical excuse marijuana dispensaries 1240 fatal crashes compared to 631 for the five years prior
- 8.3% of fatal single vehicle crashes
- 5.5% fatal passenger crashes
- Use rate estimated at 16-20%
- Rivals alcohol as top cause of fatalities

Crancer and Crancer Involvement of marijuana in California Fatal Vehicle Cracher

Psychiatric and Behavioral Disorders

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Psych and Behavioral Risk

 Cannabis use disorder is a common comorbidity and risk marker for self-harm, all-cause mortality, and death by unintentional overdose and homicide among youths with mood disorders.
 These findings should be considered as states contemplate legalizing medical and recreational marijuana, both of which are associated with increased CUD.

JAMA Pediatr. doi:10.1001/jamapediatrics.2020.5494

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Psychosis Related to %THC

- Presence of psychosis related to percentage of THC
- Threshold appears about 10% THC concentration
- Daily use increased risk

Lancet Psychiatry 2019; 6: 427–36 Published Online March 19, 2019

Persistence of Psychosis

- Risk of psychosis -no prior psychosis who used pot, 1.9 times greater that non-users in ave 3.5 years.
- Continued pot use risk of future psychosis was 31% vs 20% in those who did not continue use out to approx 8.5 years.
 BMJ 2011;342: d738

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PTSD and Marijuana Use

- 2000 participants in VA treatment programs
- Non-users had significantly less symptoms
- Prior users who quit had less symptoms
- Users had higher levels of violence,
- New users had higher levels of violence and also turned more to other drugs
- Commented: "Most people assume things based on their own experience... People assume that there aren't a lot of risks....there really are"

Yale University December 2014 Presented to the AAAP

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Impulsivity and Hostility

- Impulsivity increased with use on same day and day prior
- Hostility self-rated increased interpersonal hostility
- Hostility perceived in others increased Drug AlcoholDepend. (2015), http://dx.doi.org/10.1016/j.drugaledep.2014.12.029

Depression

- Depressive responses measured
- Lower doses= Serotonin agonist
- Higher doses= Serotonin suppressant
- Effect was the Medial Prefrontal Cortex J Neuroscience 2007;27:11700-11711

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Marijuana and Bipolar Illness

- 166 first-episode bipolar I disorder patients.
- Cannabis and alcohol associated with the first episode of mania

Bipolar Disorder 2008;10:738-741

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Sexual Assault/ Victimization

- Alcohol and Marijuana predict violence. Kraanen Journal of Substance Abuse Treatment 46 (2014) 532–539
- Marijuana-associated partner aggression Moore Clinical Psych Review 28 (2008) 247-274
- College Drug Use and Partner Violence Nabors Journal of Interpersonal Violence 25(6) 1043–1063
- Dating Aggression by Adolescents Reyes Journal of Adolescence 37 (2014) 281–289



Marijuana Dependence

- Most patients claimed serious problems with cannabis, and 78.6% met criteria for cannabis dependence.
- Two thirds reported withdrawal. Cannabis is a reinforcer. produces both dependence and withdrawal and reinforces cannabis use.
- Regular cannabis use rapid as tobacco progression, and more rapid than alcohol CrowleyDrug and Alcohol Dependence 1998;50:27-37













Newborn Effects

- Birthweight
- Length
- Head Circumference
- Abnormal Development
- Neurological Irritability

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Fetal Effects: 14 y/o

- 524 subjects
- Confounding variables controlled
- Greatest effect first Trimester >1joint /day
- Fetal exposure= 14 y/o Wechsler composite
- Poor Intelligence age 6
- Attention and Depression age 10

Neurotoxicology and Teratology Goldschmidt and Day 34 (2012) 161–167

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Use During Pregnancy

- 70% of Colorado dispensaries recommended use of marijuana for nausea in first trimester
- Few recommended discussion with healthcare providers.

Obst/Gyn 2018:131;1031-1037





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Marijuana and Crime Nationally

- Chance of being arrested = 1 in every 11,000 – 12,000 joints smoked
- Less than 1% serving time for simple possession of marijuana

RAND, 2010. Altered State? Assessing How Marijuana Legalization in California Coul Multiple Sources including Bureau of Justice Statistics & Caulkins and Sevigny (2005) U.S. Sentencing Commission, 2011.

• Median amount of marijuana = 115 pounds





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Adult Marijuana Use Colorado

- 485,000 Colorado adult regular marijuana users (at least once/mo) = 9% population
- Heavy users (daily) = 21.8% of user population and 66.9% of demand
- Colorado near daily users 35.29% higher than national average
- Alcohol consumption unchanged in Colorado since 2005





Colorado Dispensaries

- 493 medical/212 recreational dispensaries
- 149 medical/63 recreational marijuana infused product factories
- 729 medical/279 recreational cultivation operations
- 0 medical/8 recreational testing facilities
- One marijuana store in Denver for every 3,780 residents
- "Denver has more marijuana dispensaries than liquor stores or licensed pharmacies."

Colorado Department of Revenue, Marijuana Enforcement Division; July 24, 2014 Dr. Christian Thurstone, M.D., attending physician, Denver Health Medical Center

Marijuana and Fatal Crashes			
Colorado Since Dispensaries			
F	atal crashes THO	C Ave Percent THC	
2006	21	2.9	
2007	23	2.9	
2008	31	4.4	
2009	37	5.7	
2010	42	7	
2011	52	8.9	
		2010Colo Dept of Transportation	



Traffic D	Traffic Deaths Related to Marijuana When a DRIVER Tested Positive for Marijuana (Colorado)				
Crash Year	Total Statewide Fatalities	Percentage Total Fatalities			
2006	535	6.2%			
2007	554	5.8%			
2008	548	6.6%			
2009	465	8.8%			
2010	450	10.2%			
2011	447	13.0%			
2012	472	13.8%			
2013	481	11.4%			
2014	488	15.4%			
2015	547	17.9%			
2016	608	20.6%			
2017	648	21.3%			
2018	632	18.2%			
2019	596	21.3%			



Marijuana and Crime

All reported Denver crime

al Incident Based Reporting System

(compare Jan-June 2013 to Jan-June 2014)

- Person Crime ↑ 18.1%
- All Offenses ↑ 114.9%

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Colorado Taxation

- 2015 Taxes 1.3% of all state taxes
- \$2.6 million added to \$5.4 Billion ed costs
- State marijuana taxation director says very little financial benefit to the state after cost of administration taken out.











Questions to be addressed

- Is Medical Marijuana More Dangerous Than Legal Drugs?
- Should Marijuana Be a Medical Option?
- Is Marijuana a "Gateway" or "Steppingstone" Drug?