Underwriting Marijuana: the Good, the Bad, and the Totally Rad!

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Americans have voted with their wallets and the results are in.

They love marijuana.

Legal sales of marijuana and marijuana products -- like edibles -- reached an estimated $30 billion in 2022, according to a report from MJBizDaily.

That total is more than Americans spent on chocolate and craft beer combined, -- $20 billion and $7.9 billion, respectively -- according to Business Insider.

My Opinion

Our applicants are using Marijuana/Cannabis in record numbers

Marijuana and Cannabis are used interchangeably by me throughout this talk, although for cultural reasons I prefer to call it Marijuana—perhaps we can discuss why over beers later ☺

There is not a lot of good research done, thus far, on all cause mortality and MJ use

There are some distinct associations that are well-researched and substantiated that impact morbidity and mortality

Let's understand the research that is out there and underwrite accordingly.

Agenda

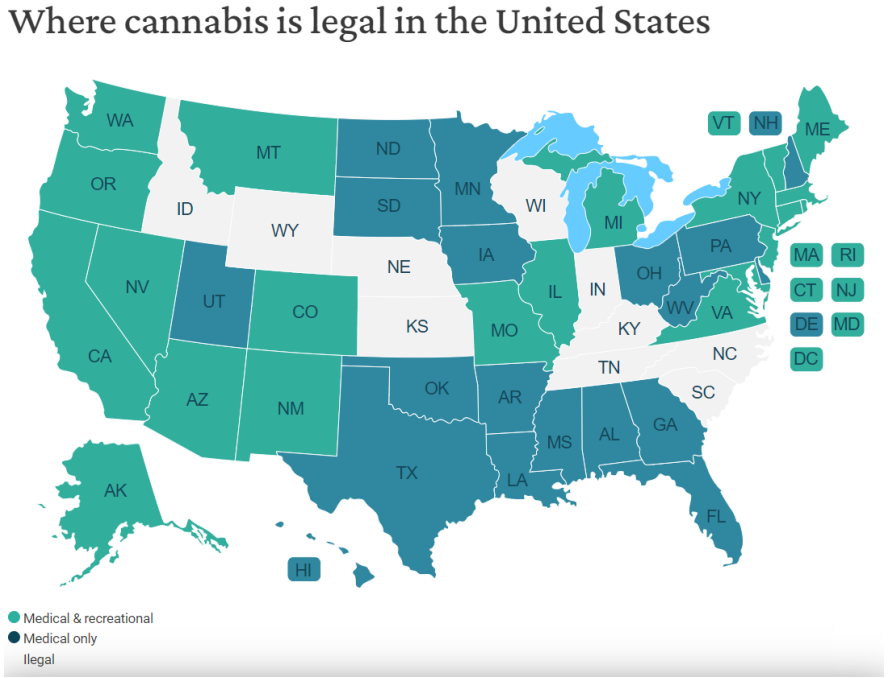
1. Some random facts
2. Good, Bad, Rad
3. Associations that are important to understand to underwrite MJ use
4. Some underwriting tips
5. Some cases for discussion
6. DORITOS

THE OFFICER THEN FOUND THE MAN LYING "ON THE FLOOR IN THE FETAL POSITION" AND "WAS SURROUNDED BY A PLETHORA OF DORITOS, PEPPERIDGE FARM GOLDFISH AND CHIPS AHOY COOKIES," THE REPORT SAID. THE MAN ALSO TOLD POLICE HE COULDN'T FEEL HIS HANDS.

Some random facts…

- Illegal in the US
  - Legal States (Recreational v. Medicinal)
  - Illegal States
  - Decriminalized Cities and States
- Estimated number of users:
  - 2019 CDC: 48.2MM,
  - 2021 NSDUH: 52.5MM
  - Third most used psychoactive substance
- Pew Research poll 11/2022: 88% of US adults=legalize it!
- What's in MJ?
- How's it used?
- What's the dose?

"The Cannigma", 2023



Cannabis sativa and subspecies/varieties—what's in it?

HEALTHMED.ORG

- Around 500 chemical compounds, aka cannabinoids, in all parts of the plant
- THC, Delta-9-Tetrahydrocannabinol
  - Single compound that causes a "high"; ^Dopamine (reward center)
- CBD, Cannabidiol
  - ~20% of the active compounds in MJ
- CBN, Cannabinol
  - Third most common cannabinoid found in a cannabis plant, ~1%
  - Activated with Heat and Oxygen to convert to THC->sedation
- CBG, Cannabigerol
  - ~1% and gives rise to the other cannabinoids with application of heat and oxygen
- Around 100 Terpenoids—aroma, flavor, possibly some medicinal benefits

Good

Toxicity (or lack thereof)
There are some possible clinical uses
Expansion of research in US

Bad

Significant Associations
- Morbidity
- Mortality

Regulation

Rad

Medical Marijuana and CBD
No OD's

Good (ish)—2017 CDC Data

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		United States (n = 70,237, 21.7)[1]	
Rank[2]	Referent drug group	Number of deaths	Percent[3]
1	Fentanyl	27,299	38.9
2	Heroin	15,982	22.8
3	Cocaine	14,948	21.3
4	Methamphetamine	9,356	13.3
5	Alprazolam	6,647	9.5
6	Oxycodone	6,053	8.6
7	Morphine	4,874	6.9
8	Methadone	3,286	4.7
9	Hydrocodone	3,072	4.4
10	Diphenhydramine	2,286	3.3
11	Clonazepam	2,055	2.9
12	Diazepam	2,025	2.9
13	Gabapentin	1,848	2.6
14	Amphetamine	1,581	2.3
15	Tramadol	1,333	1.9

Good: Medical marijuana and cannabidiol research expansion act of 12/2/2022

- Rolls back federal restrictions on MJ research
- Speeds up application process (60 days)
- Government must maintain “adequate and uninterrupted supply of marijuana”

- Cannabis researchers have increased dramatically
- 72% of schedule 1 research registrations

Good: clinical uses in the US according to UpToDate®

- Chronic, non-cancer pain: 2018 meta-analysis showed moderate evidence that cannabis reduced pain by 30%, but adverse event rates were high. ?Beneficial decrease in need for opiates?
- PTSD (nabilone 3-5 mg): improvement in nightmares, and some improvement in global outcomes
- Chemotherapy induced nausea: (dronabinol, nabilone); “modest benefits are counterbalanced by an unfavorable side effect profile, especially in older patients”
- Palliative and end-of-life care: studies are limited and may be recommended only as a last ditch effort to improve symptoms—more studies are needed
- Cachexia or wasting: used for decades in AIDS wasting syndrome without good studies to support it but with very favorable case reports.
- RAD ish… Seizure disorders: CBD for Dravet and Lennox-Gastaut syndromes, rare forms of seizure disorder in children; modest efficacy

BAD: Warnings listed in UpToDate®

Importantly, long-term safety of cannabidiol has not been established, and significant concerns exist regarding the potential negative effects of chronic cannabis use on brain development, cognitive function, and school performance [96,97], particularly in children with drug-resistant epilepsy, who may have increased vulnerability to such effects.

The long-term adverse effects of medical cannabis use are not known. One prospective cohort study followed 431 patients with chronic pain for one year and compared patients using medical cannabis with nonusers [96]. There was no difference in serious adverse events between the two groups. However, the medical cannabis group had a higher rate of non-serious respiratory adverse events.

DEA United States Drug Enforcement Administration

Schedule I

Schedule I drugs, substances, or chemicals are defined as drugs with no currently accepted medical use and a high potential for abuse. Some examples of Schedule I drugs are: heroin, lysergic acid diethylamide (LSD), marijuana (cannabis), 3,4-methylenedioxymethamphetamine (ecstasy), methaqualone, and peyote.

BAD: Increased incidence of Schizophrenia, especially amongst young males with CUD (Cannabis Use Disorder)

- Hjorthoj, C et al. Association between Cannabis Use Disorder and Schizophrenia Stronger in Young Males than in Females. Psychological Medicine; 04May2023.
- Danish Health Registry
- 6.9MM individuals: 45K cases of schizophrenia between 1972 and 2021
- Hazard ratios for those with CUD subsequently being diagnosed with Schizophrenia

	No CUD	Males with CUD adjusted hazard ratio (95% CI)	Females with CUD adjusted hazard ratio (95% CI)	*P* value for the sex difference
Overall	1 (ref.)	2.42 (2.33–2.52)	2.02 (1.89–2.17)	$p < 0.001$
By age group	No CUD	Males with CUD adjusted incident rate ratio (95% CI)	Females with CUD adjusted incident rate ratio (95% CI)	
16–20 years	1 (ref.)	3.84 (3.43–4.29)	1.81 (1.53–2.15)	$p < 0.001$
21–25 years	1 (ref.)	2.58 (2.38–2.79)	1.91 (1.27–1.64)	$p = 0.02$
26–30 years	1 (ref.)	2.33 (2.12–2.57)	2.08 (1.72–2.52)	$p = 0.70$
31–40 years	1 (ref.)	2.13 (1.94–2.34)	2.31 (1.92–2.78)	$p = 0.91$
41+ years	1 (ref.)	2.18 (1.87–2.54)	2.98 (2.32–3.84)	$p = 0.16$

BAD: CUD—3:10 users, especially at younger ages
DSM 5 Diagnostic Criteria

A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:
1) Cannabis is often taken in larger amounts or over a longer period than was intended.
2) There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
3) A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
4) Craving, or a strong desire or urge to use cannabis.
5) Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.
6) Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
7) Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
8) Recurrent cannabis use in situations in which it is physically hazardous.
9) Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.
10) Tolerance, as defined by either of the following:
a) A need for markedly increased amounts of cannabis to achieve intoxication or desired effect.
b) Markedly diminished effect with continued use of the same amount of cannabis.
11) Withdrawal, as manifested by either of the following:
a) The characteristic withdrawal syndrome for cannabis.
b) Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

Specify current severity:
Mild: Presence of 2 to 3 symptoms.
Moderate: Presence of 4 to 5 symptoms.
Severe: Presence of 6 or more symptoms.

BAD: EVALI

E-cigarette or Vaping Associated Lung Injury

- Dx code U07.0
- Identified in Sep ‘19
- Peak by Mar ‘20
- “Clinical manifestations of EVALI in adolescents before and during the COVID-19 pandemic”, Abdallah, MD et al in Pediatric Pulmonology 2022 Dec 28
- 41 adolescents, 40 used THC, all had EVALI
- Rx: Steroids, Oxygen and supportive care

Likely etiology

- Vitamin E acetate added to THC for vaping to allow the THC to travel from the lungs to the brain more quickly
- Findings: respiratory symptoms, CT with ground glass opacities, usually bilateral
- “Oil spill in the lungs”

RAD: Clinical Practice Guidelines for Cannabis and Cannabinoid-Based Medicines in the Management of Chronic Pain and Co-Occurring Conditions

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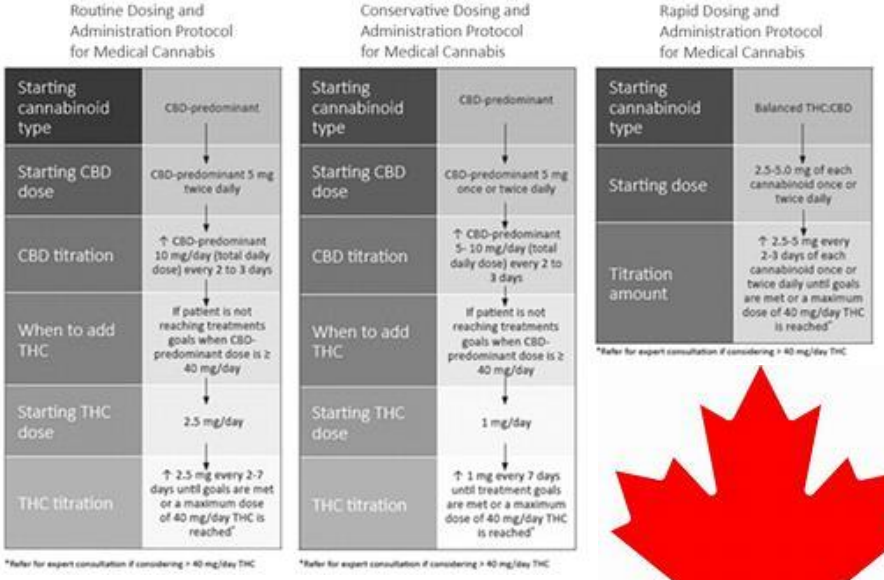
Alan D. Bell et al.

- Cannabis and Cannabinoid Research, 27 March 2023; Alan D. Bell et al.
- 47 pain management articles, >11,000 patients
- 20 global experts from a variety of specialties in 9 countries
- Placed a high value on: improving chronic pain, functionality, and addressing frequent co-occurring conditions like insomnia, anxiety, depression, mobility, and inflammation
- “We recommend the use of CBD as monotherapy, replacement, or adjunct treatment, in people living with chronic pain, for the management of chronic pain including central and/or peripheral neuropathic pain to improve outcomes.” Strong recommendation based on Moderate-Quality Evidence
- Also Strongly recommended: People living with HIV and chronic pain, MS and chronic pain, Arthritis pain, Fibromyalgia, Sleep problems, Sleep deprivation, Appetite loss, Anxiety, Unsatisfactory analgesia from opiates, and to decrease opioid doses associated with treatment of chronic pain

Bhasker et al.



RAD: Cure for CUD?

- AEF0117, a drug that blocks CB1 receptor and is a synthetic mimic of pregnenolone
- Phase 2a just completed
- 19%/38% reduction in subjective effect of THC for the 0.06 mg and 1.0 mg dose, respectively
- Associated with decreased MJ use
- No adverse events, no withdrawal symptoms
- Recruitment for 2b underway in 11 addiction centers across the US—watch for results in 2024
- Haney, M., Vallée, M., Fabre, S. *et al.* Signaling-specific inhibition of the CB_1 receptor for cannabis use disorder: phase 1 and phase 2a randomized trials. *Nat Med* **29**, 1487–1499 (2023). https://doi.org/10.1038/s41591-023-02381-w

Marijuana CAN kill you!
And here's how....

- You light up in the middle of a hairspray testing facility and burst into hell fire.
- 150 pounds of marijuana is dropped from a Cessna falling at the speed of sound onto your naked, sun bathing body, thereby crushing you to death.

- You go sliding into your house at the speed of a cheetah and accidently slip on a bag of weed, falling on your head and breaking it to bits.

Ways you CAN'T die: smoking it, eating it, dabbing it, tincturing it, vaoporizing it.

RxLeaf.com

Approach to Underwriting those who use MJ

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01

First, think about the overall facts of the case…

02

Then, think about the favorable and unfavorable factors that might be associated with excess morbidity and mortality in MJ users…

03

Then, think about the amount of MJ used and how that might impact the associated risks…

What we don’t know…

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- No studies on all-cause mortality with respect to use of Cannabis/MJ/CBD
- Even though we know there are associations with mortal conditions, some of them strongly associated, there are no good mortality studies on which to rely
- We don’t know what the average or “appropriate” dose is
- We don’t know the “dose” in almost all recreational products
- We can’t predict, based on different metabolic rates and storage capacity (i.e. body fat percentage), how individuals will react to a specific “dose” via a specific route and when that will be gone from the system
- We don’t know when we will know, but as long as MJ continues to be a Schedule 1 drug, studies will be hard to come by.

What we do know…

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- Cannabis, itself, is not lethal at any known dose via any known route
- Third most used psychoactive substance worldwide, after EtOH and Tobacco (52.5MM in US--NSDUH)
- MJ associated mortality decreases with age, to a point
- There are associations with mortal conditions and Cannabis
  - MVA's
  - Other Accidents, Suicides, Drug Overdoses
- There are associations with excess morbidity and use of Cannabis
  - CUD (younger ages, males, smokers), CAD
  - Acute intoxication
  - Schizophrenia
  - Exacerbation of major psychiatric conditions (Bipolar and GAD)
  - Chronic bronchitis
- There are complications from Cannabis use at young ages with respect to brain development
- There are no strong associations with lung cancer or significant chronic lung disease, even when smoked (yet?)

Those uninsurable folks from my perspective…

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- Age <18
- Known history in the recent past of drug or EtOH abuse
- Schizophrenia
- Recent history of suicidal ideation or attempt
- Evidence of cognitive impairment
- CUD diagnosed in the recent past
- Progressively increasing use of MJ
- Current Major Depression that is moderate to severe
- A combination of unfavorable factors that might be expected to increase the risk associated with use of a psychoactive substance

Favorable and Unfavorable Factors

- Favorable
  - Job and Home Stability
  - Started using after 18 y/o or so…
  - Infrequent use (ideally less than daily)
  - No concomitant use of cigarettes or other substances
- Unfavorable
  - Heavy use of other substances (EtOH, illicit drugs, ?tobacco in smokers and vapers of MJ)
  - Underlying moderate to severe depression, especially at younger ages
  - Underlying major psychiatric disease (e.g. Bipolar, Psychosis)
  - Known CUD
  - DUI, MVA, Reckless driving or other evidence of risky behavior
  - ED visits associated with MJ use

Pricing the risk for morbidity and mortality

- Risks seem to be higher at the younger ages
  - How young is too young?
  - 25 y/o
- Risks seem to be higher with more frequent use
  - How much is too much?
  - There is really is no maximum amount but beware of those using MJ multiple times daily.
  - What should be the cut-off?
    - Infrequent: up to four times monthly
    - Regularly: up to 20 times monthly
    - Heavy: >20 times monthly
- How do you price risk when no good studies exist?
- Is there a difference between recreational and medical MJ use?

Case 1

27 y/o NBA player in NY; applying for $20MM

- Application shows no medical problems
- Sports physical
  - 6’2”, 210 lbs, asymptomatic
  - Echo: LVIDd 6cm, LA 4cm, valves and wall thickness normal
  - Exam normal
  - EKG sinus bradycardia with rate of 40, otherwise normal
  - PMH: nil
  - Medications: none
  - Extensive labs: normal
- Admits to MJ use up to 6 times a week to “help him sleep”

Case 2

49 y/o Real Estate Broker in NC; applying for IDI, $20K/month to 65 y/o

- 6’1”, 267 lbs.
- OSA (AHI 54.7, Oxygen sat to 83%)
- Chronic L shoulder pain affecting golf game
- Otherwise, healthy
- Insurance labs: mild dyslipidemia, otherwise normal
- PCP records: severe L shoulder pain that Ortho says will require replacement
  - Rx: MJ edibles 1-2 times per week; no other medications
  - Compliant with CPAP based on recent download from machine

Case 3

21 y/o male student; parents applying for $1MM VUL

- Application: student, parents own and are beneficiaries; agent letter—savings vehicle for PI
- Medical questions: all “no” but admits to medical MJ use for anxiety
- Drug Questionnaire: MJ only drug used; two to three times daily for anxiety; never hospitalized or required treatment for overuse/abuse
- Medical Records: “Healthy young man”; senior in college—pre-med; moderate to severe social anxiety; trials of antidepressants and anxiolytics->non-compliance due to side effects; good results with THC/CBD gummies two to three times daily; tobacco never user, no EtOH, no drugs of abuse; no other medical problems.

All hail WILLIE! Questions?

Additional References

- Azofeifa A, Rexach-Guzmán BD, Hagemeyer AN, Rudd RA, Sauber-Schatz EK. Driving Under the Influence of Marijuana and Illicit Drugs Among Persons Aged ≥16 Years — United States, 2018. MMWR Morb Mortal Wkly Rep 2019;68:1153–1157
- UpToDate sections: Gorelick, D; “Cannabis use disorder in adults”, and “Cannabis use: Epidemiology, pharmacology, comorbidities, and adverse effects”; UpToDate©, updated 10/7/22
- NASEM conclusions on "The Health Effects of Cannabis and Cannabinoids: the Current State of Evidence and Recommendations for Research"; January 2017
- ACC Abstract presentation: Association of Cannabis Use Disorder with risk of Coronary Artery Disease, A Mendelian Randomization Study March 5, 2023
- Fischer, Benedikt et al. Crude estimates of cannabis-attributable mortality and morbidity in Canada--implications for public health focuse interventions. Journal of Public Health. Vol 38, No. 1, pp183-188. January 28,2015
- Pinho, P., Rigatti, S., Jaegerman, A., Stout, R. Marijuana Use; Real mortality impact or all just smoke and mirrors. On The Risk, Vol. 36, No. 4, pp. 60-64; 2020