What are you smoking?

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Brad Heltemes, MD, DBIM
VP & Medical Director, R&D/Innovation
Munich Re Life US

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A millennium (or two?) of smoking

What impact will the legalization of marijuana and the rising usage of e-cigarettes have on the life insurance industry?

This session discusses the latest medical research and trends in these areas as well as possible mortality implications

Reproduction of a carving from the temple at Palenque, Mexico, depicting a Maya deity using a smoking tube

Ca. 700 AD

Image Open Source: Smoke: a global history of smoking (2004) edited by Sander L. Gilman and Zhou Xun ISBN 1-86189-200-4, p. 10, Public Domain, https://commons.wikimedia.org/w/index.php?curid=2380252

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The Case of the E-Cigarette Conundrum

- Male, 48 years old, commercial contractor. Simplified Issue, face amount $500,000.
- No admitted health history and Rx check “green” – Issued Preferred
- Case was flagged for random holdout; total line exceeded $2,000,000
  - Vitals: 6.0 190, BP 141/90, pulse 82
  - BCP: Chol 302, HDL 74, Ratio 4.08, trigs 200. Otherwise WNL.
  - HOS: Cotinine positive
- Question on application: Have you in the last 12 months used tobacco or any other nicotine products such as cigarettes, cigar, pipe, chewing tobacco, snuff, nicotine gum or nicotine patch? If Yes, provide details: Product type(s), Date Last Used, Frequency of Use.
  - Question on application answered NO.

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E-Cigarette Case (cont.)

When further questioned based on positive cotinine:

Proposed insured states he answered the question correctly and that perhaps his urine was positive because he occasionally vapes - at times they don't contain any nicotine products and just flavors, and at times they will include some nicotine.

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How would you handle this case?

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1. Question was answered correctly and thus obliged to assess as NS

2. Question was answered correctly but there is additional risk, and thus keep NS but amend offer to low substd rate

3. Question was not answered correctly since was using a nicotine product, but risk is minimal, especially since use infrequent and often without nicotine – maintain offer

4. Question was not answered correctly – an APS should be ordered and then assess as Smoker vs NS based on APS info on tobacco use

5. Question was not answered correctly since was cotinine positive and most likely smokes tobacco – policy should be amended as smoker

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It’s just vapor, right?

- Electronic cigarettes – so named because, like tobacco cigarettes, they are primarily nicotine delivery devices
  - Also called ENDS - Electronic Nicotine Delivery Systems
- First developed by Chinese scientists in 2003 with penetration into the US in 2006
- Battery-powered system to heat liquid that produces the inhalable aerosol
- Estimated 466 brands and 7,764 unique flavors
- Regulated since 2016

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Patterns of use

	Use in the U.S. (%) 2017 data
All adults	4.5
Men	5.9
Women	3.7
Ages 18-24	9.2
Middle-schoolers	3.3
High-schoolers	11.7

- Recent data in adults showed increasing use in young adults but decreasing use in older people
- Never tobacco smokers mostly seen in younger age groups – and is increasing
  - Among e-cigarette users aged 45 and up in 2015, only 1.3% had never been cigarette smokers
  - However, this was the case for 40% of 18–24 year olds
- Marketing of products to younger age group with attractive packages and exotic flavors
- The e-cigarette brand Juul has ~80% of the youth market

Tobacco Product Use Among Middle and High School Students - United States, 2011-2017.
Wang TW, et al. MMWR Morb Mortal Wkly Rep. 2018;67(22):629.

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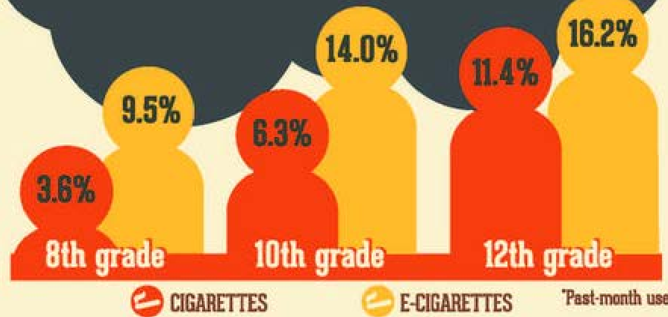
Next generation nicotine – and more?



CIGARETTES E-CIGARETTES *Past-month use

TEEN E-CIG USERS ARE MORE LIKELY TO START SMOKING.*2

Start Smoking Within 6 Months

E-CIG USER NON USER

*Includes combustible tobacco products [cigarettes, cigars, and hookahs]

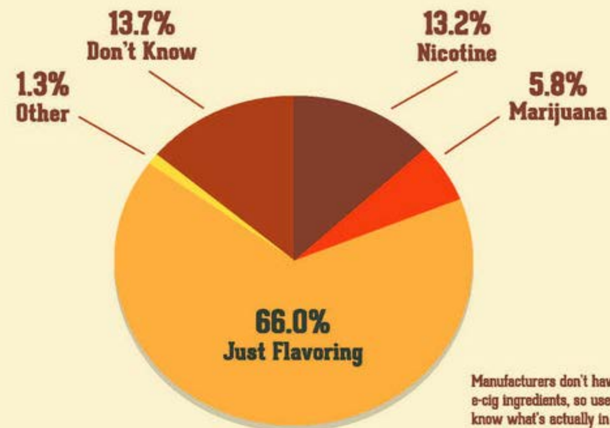
WHAT DO TEENS SAY IS IN THEIR E-CIG?3

13.7% Don't Know

13.2% Nicotine

1.3% Other

5.8% Marijuana



Manufacturers don't have to report e-cig ingredients, so users don't know what's actually in them.

National Institute on Drug Abuse

1. MTF, 2015; 2. Leventhal, 2015; 3. Singh, 2016

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Are some of the trends changing?

E-liquid

Food product

E-liquid

Food product

- Government data shows e-cigarette use up 78% among high schoolers (to 20.8%) from 2017 to 2018.
- Similar use up 50% in middle schoolers since 2017 (to 4.9% in 2018).
- Frequent (~daily) use also increased by nearly 40%.
- Moreover, the declining trend in tobacco use may have stopped.
  - Recent review showed tobacco cigarette use in about 8% of high schoolers – the same as in 2016.

Cullen KA, Ambrose BK, Gentzke AS, et al. Notes from the field: Use of electronic cigarettes and any tobacco product among middle and high school students - United States, 2011-2018. MMWR Morb Mortal Wkly Rep 2018; 67:1276.

(Photo: Federal Dept. of Agriculture)

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Which of the following is NOT an e-cigarette flavor available in the U.S.?

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1. Gummiberry
2. Unicorn Puke
3. Jack Daniels
4. Stoned Smurf
5. Insane Candy Cane

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But better than tobacco?

- Risks with use of combustible tobacco are well known – and substantial
- **Short-term** risks for e-cigarettes appear to be lower than for smoking tobacco
- Some studies have shown that e-cigarettes can lead to successful smoking cessation
  - Recent randomized trial of e-cigs vs other nicotine replacement found 18% using no tobacco at one year compared to 10% with nicotine patch or gum
  - But 80% of them were still using the e-cigs compared to 9% of the others still using a nicotine replacement
- What’s the risk of long term use, and how likely is one to go back to using combustible cigarettes?

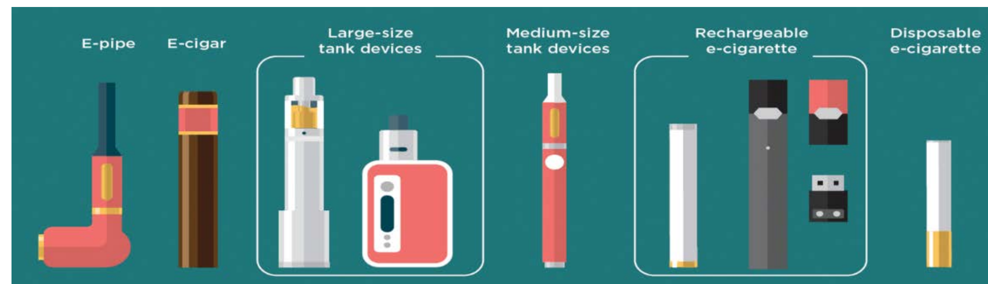

Image source CDC: https://www.drugabuse.gov/publications/drugfacts/electronic-cigarettes-e-cigarettes

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Making headlines

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin — Preliminary Report

StarTribune

2019 LOCAL NEWS PULITZER FINALIST

State sees first vaping death

Halting e-cig use urged after an older person died from a lung injury after using illicit THC.

By JEREMY OLSON
jeremy.olson@startribune.com

65 who died in August after a prolonged hospitalization, the Minnesota Department

The age of the patient is unusual; the majority of people hospitalized in Minnesota for vaping-related lung injuries have been in their teens and early 20s.

"One death from this out-

GROWING RISKS
Federal health officials discourage all vaping until investigations are complete.

Five deaths: The vaping-related deaths were in California, Illinois, Indiana,

Long-term concerns for e-cigarette use

- Lead to nicotine addiction and increase in tobacco use
  - Teen users often move on to tobacco, even when they report using non-nicotine products only
- Evidence of increased MI risk with daily e-cigarette use
- Reports of acute pulmonary failure and of seizures associated with e-cigarette use*
- Manufacturers don't have to report e-cigarette ingredients – and when they do they don't have to be accurate!

So just what is being inhaled?

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What exactly is being inhaled?

Basic ingredients are **propylene glycol** and **vegetable glycerin**

- Safe (GRAS) in usual liquid form but have potential for toxicity when inhaled
  - Hyperosmolality
  - Lactic acidosis
  - CNS depression

Heating coil can release **toxic metals** such as lead, chromium and manganese into the aerosol

Formaldehyde is a by-product of vapor – known to be carcinogenic

- Deposited deeper into the lungs than with tobacco smoking
- However, e-cigarette levels of formaldehyde and acrolein are found at much lower concentrations than seen with smoking

Biopsies from chronic vapors show marked **changes to the lining of the bronchioles**

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But what about nicotine?

- Nicotine concentrations are usually listed in a range from 0 to 36 mg/mL
  - How much nicotine is inhaled varies substantially by delivery method
- Actual amounts vary widely by brand, and even within the same label
- Many products misrepresent the true concentration
  - 91% of samples labeled as 0 mg/mL of nicotine were found to contain nicotine
- Significant effects of early nicotine exposure on the developing prefrontal cortex
  - Adversely affects concentration and memory
  - Increases susceptibility to nicotine and, possibly, other drug addiction
- Nicotine may contribute to CV and cancer risk but the data are not convincing

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Impact to underwriting

- Mortality and morbidity data on long-term consequences of use is lacking
- Use will generally lead to positive levels of cotinine
- How can we distinguish e-cig use from tobacco smoking?
  - Can we count on the app answers?
  - Carbon monoxide not useful in insurance setting
  - Thiocyanate – present in smoke and not in vapor, but somewhat limited accuracy
  - Potential to use epigenetic testing?

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Assessment? Less risk? Have you considered…

…specialized rates for the vaper?

Reviti Life, Giggle Insurance

…what your app questions ask?

…if your applicants know (or reveal) what is in their e-cigarette?

…how likely an e-cigarette only user is to begin (or resume) tobacco use? Does age matter?

…if anti-selection will increase once word is out of an e-cigarette class?

Image courtesy of Giggleinsurance.com

Some conclusions

- There is **strong** evidence that e-cigarettes are addictive
- E-cigarette use **increases** the likelihood of smoking tobacco – and marijuana
- E-cigarettes *may* aid in smoking cessation with a possible **reduction** in health risk but *to what degree is not clear*
- The lungs are not designed to handle anything other than air very well – exposure to e-cigarette aerosols could **increase** the risk of lung disease, cardiovascular disease, cancer, and adverse reproductive outcomes, though *to what extent remains uncertain*

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Up in Smoke…..and Vapor!

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What else might you be smoking?

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The Case of the Cannabis Card

- 37 year old male, Rancher from CO; face amount $2,000,000
- MIB; nil sign IAI hits in 2016
- Application and exam questions are similar - Has the Proposed Insured(s) ever used marijuana, narcotic or hallucinogenic drugs other than as prescribed by a licensed physician or received treatment for a drug habit?
  - Answered No
- Medical hx:
  - 2017 Torn rotator cuff - Rx cortisone injection 7/17 and arthroscopic repair 11/17. No complications. Uses CBD tincture, has medical cannabis card.
- Script check: Eligible – no hits
- BCP/HOS: WNL
- Based on APS, ad hoc testing done for Cannabinoids - Results + (17ng/mL)

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Cannabis case (cont.)

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Drug Q sent:
In the past 10 years, has the Proposed Insured named above used:

- Barbiturates, sedatives or tranquilizers habitually? □ Yes □ No
- LSD, marijuana or any amphetamine? X Yes □ No
- Heroin, morphine or other narcotic drug? □ Yes □ No

List below the drug, dosage, frequency, reason taken and length of time:

Drug:	Dosage/Frequency:	Why Taken:	How long:
Marijuana CBD	Depends / one joint, a few bowls, or vaping Daily / 100 mg	Helps to relax Helps with joint pains	4 years

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How would you assess this situation?

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1. NS, and no debits, since likely prescribed use of CBD only and otherwise healthy
2. NS, hold to STD – due to regular CBD and presumed occasional legal cannabis use
3. NS, plus mild-mod substd for cannabis use given the high positive THC
4. Standard Smoker – due to smoking marijuana
5. Smoker, and additional debits for daily cannabis use – smokes marijuana, plus chronic pain issue

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Let's weed out some of the issues . . .

2727 BCE: Traditional Chinese herbal medicine (tea)

1840: Cannabis sativa brought to Europe via India and became popular in many medications through the 19th century.

1906: Pure Food and Drug Act

1937: Marihuana Tax Act

1970: Controlled Substances Act – Schedule I

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Marijuana Laws by State

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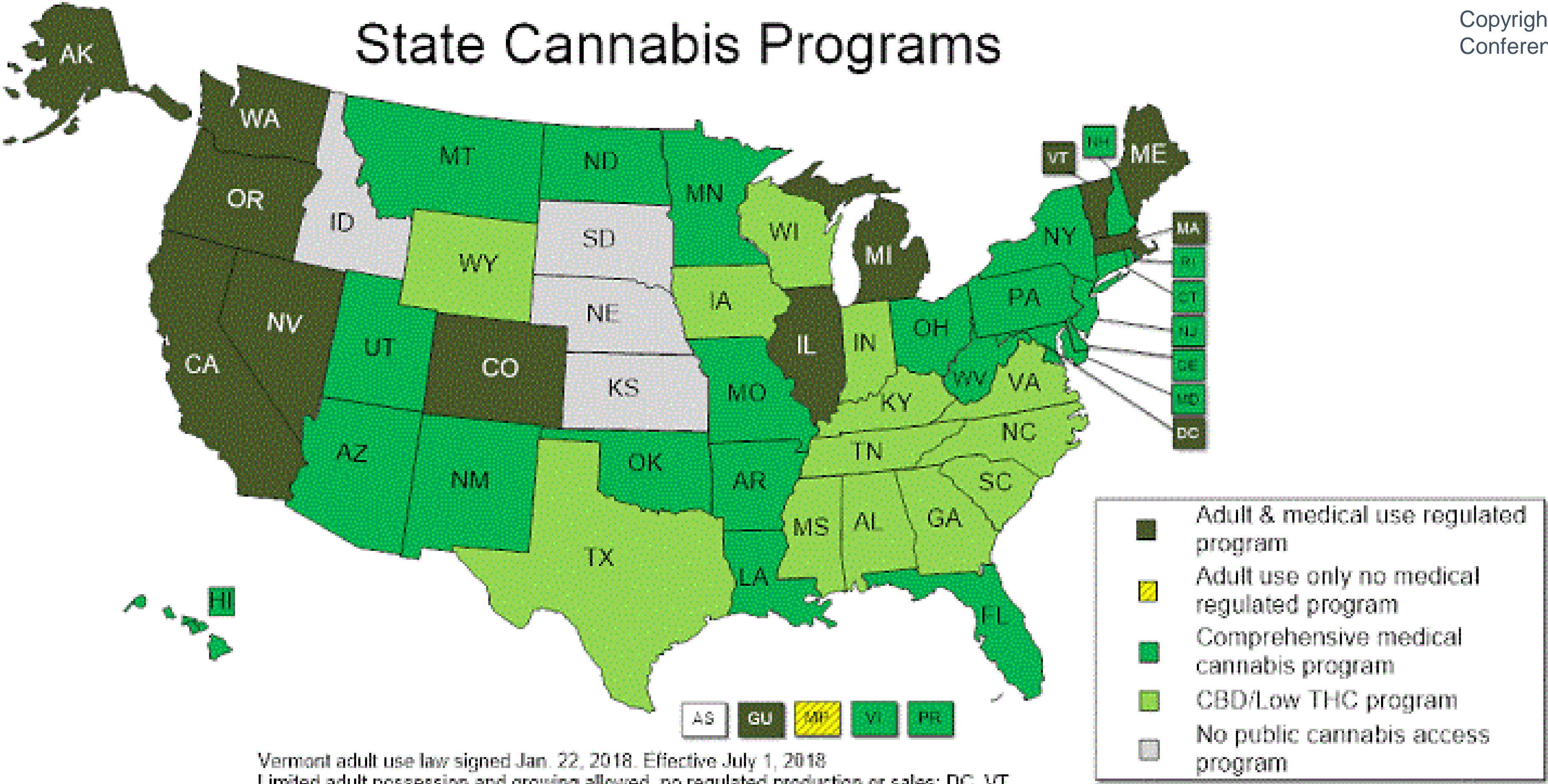

Copyright 2019 by National Conference of State Legislatures

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Cannabis – the world's favorite illicit substance

Image licensed from iStockphoto.com

Used by an estimated 3.9% of the world's population aged 15-64

Use in North America (within the past year) has increased 30-115% since 2002, to ~10-15% of adults

Varies notably by:

- Age
- Sex
- Education level
- Income

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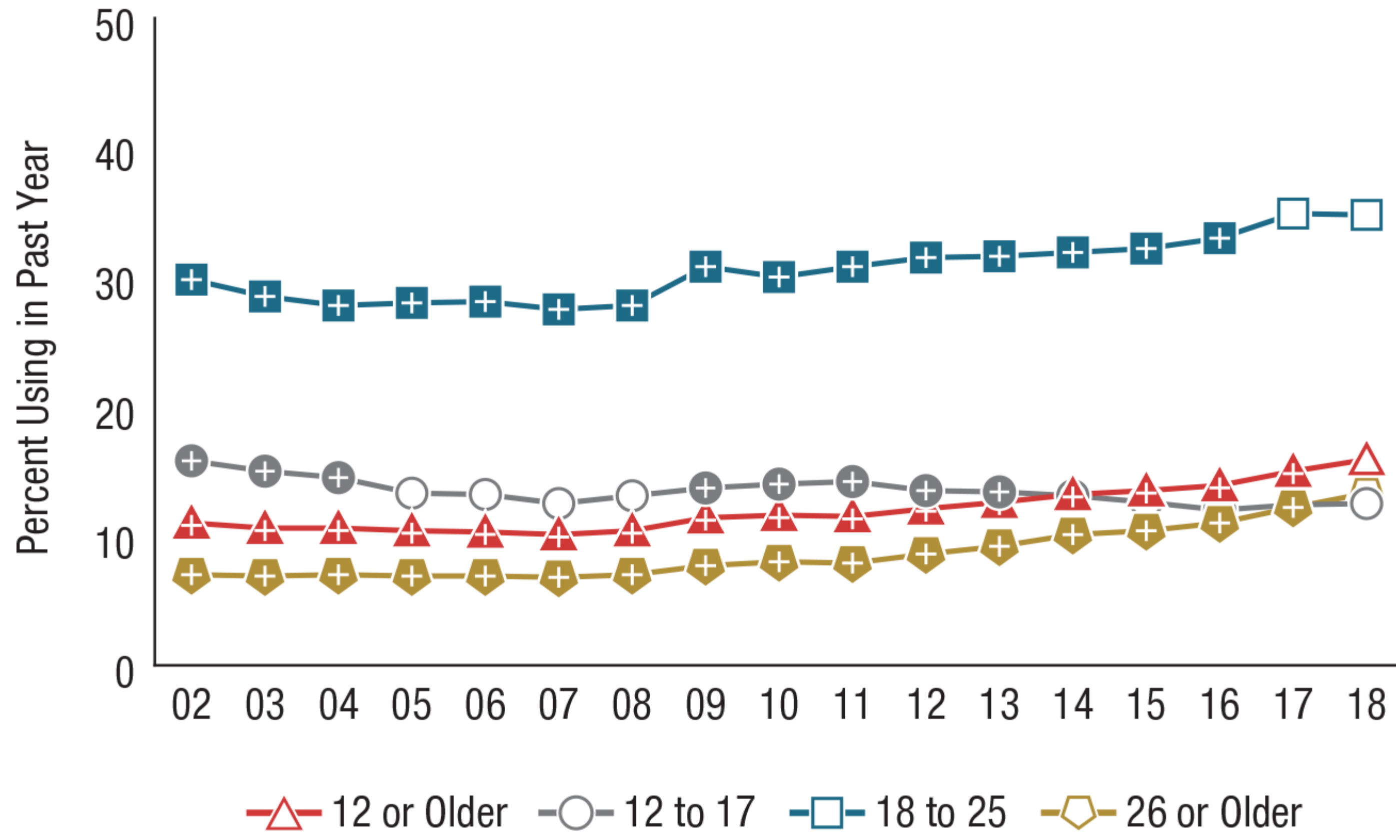
Past Year Marijuana Use among People Aged 12 or Older: 2002-2018



Age	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
12 or Older	11.0+	10.6+	10.6+	10.4+	10.3+	10.1+	10.4+	11.4+	11.6+	11.5+	12.1+	12.6+	13.2+	13.5+	13.9+	15.0+	15.9
12 to 17	15.8+	15.0+	14.5+	13.3	13.2	12.5	13.1	13.7+	14.0+	14.2+	13.5+	13.4+	13.1	12.6	12.0	12.4	12.5
18 to 25	29.8+	28.5+	27.8+	28.0+	28.1+	27.5+	27.8+	30.8+	30.0+	30.8+	31.5+	31.6+	31.9+	32.2+	33.0+	34.9	34.8
26 or Older	7.0+	6.9+	7.0+	6.9+	6.9+	6.8+	7.0+	7.7+	8.0+	7.9+	8.6+	9.2+	10.1+	10.4+	11.0+	12.2+	13.3

+ Difference between this estimate and the 2018 estimate is statistically significant at the .05 level.

SAMHSA
Substance Abuse and Mental Health Services Administration

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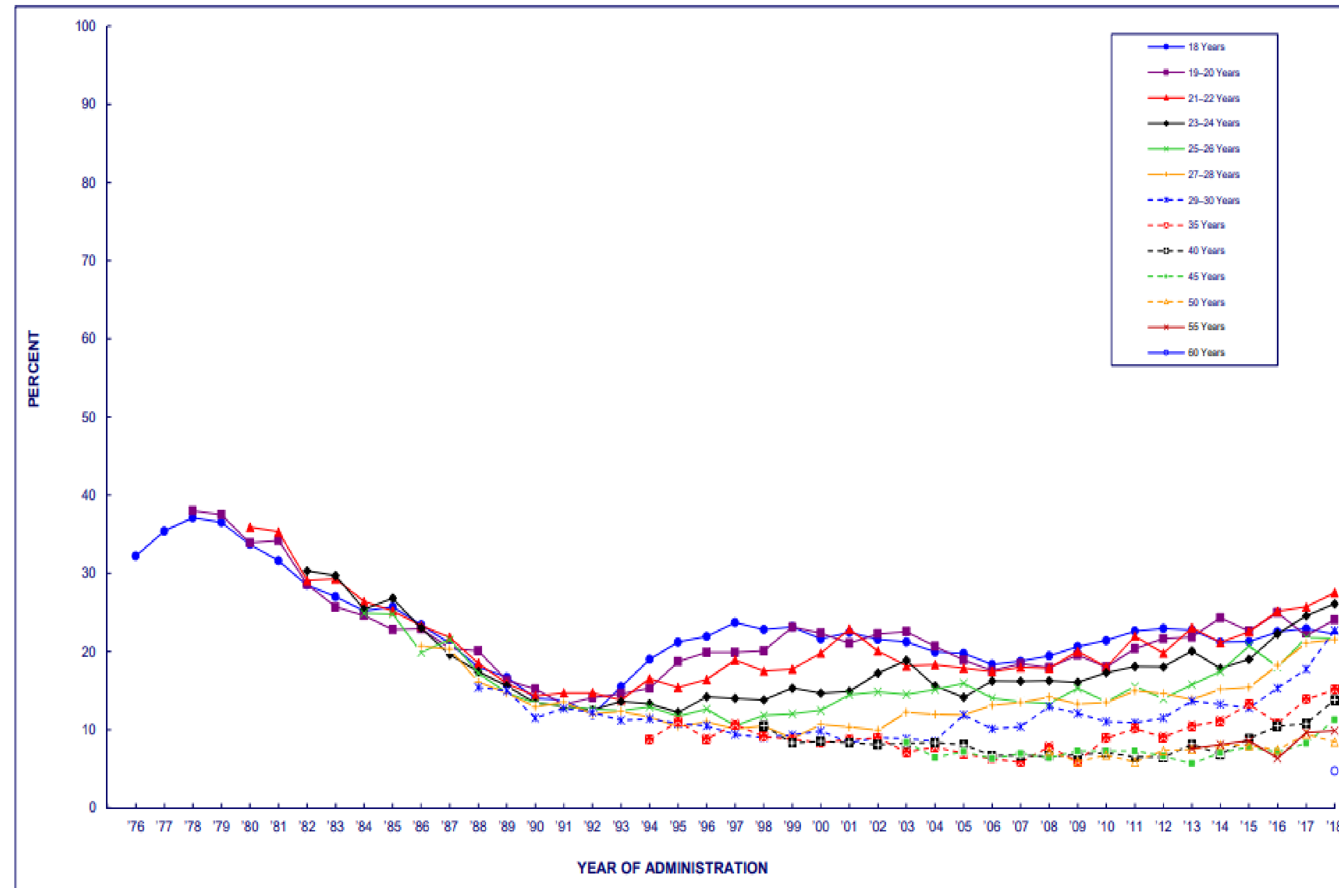
NATIONAL SURVEY RESULTS ON DRUG USE, 1975–2018

FIGURE 5-3b
MARIJUANA
Trends in 30-Day Prevalence
among Respondents of Modal Ages 18 through 60, by Age Group



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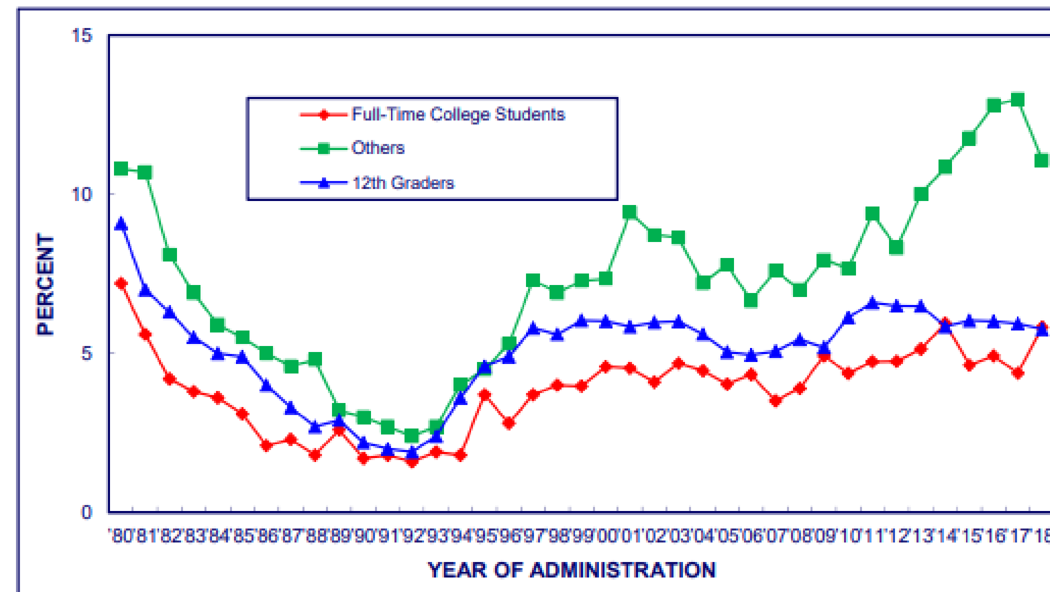
Cannabis use by income, insurance, and education

Per NESARC – past year use by income:

- 15.6% <$20,000
- 9.8% $20,000-34,999
- 8.4% $35,000-69,999
- 5.9% ≥ $70,000

Per insurance lab results, THC positive rates in 3.2% of screened applicants and are twice as high in low vs high face amounts



National Institute on Drug Abuse: National Institutes of Health

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Cannabis, a complex plant:
Different compounds and different effect on individuals . . .

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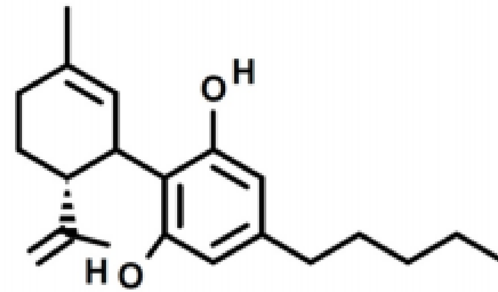
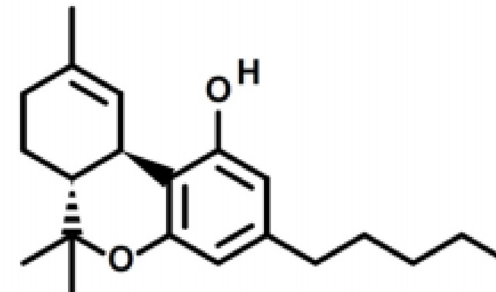
Cannabinoids

THC
tetrahydrocannabinol

CBD
cannabidiol



Cannabidiol



Delta-9-tetrahydrocannabinol (THC)

Alzghari et al. 2017. Open access - Cureus

Plus numerous other phytocannabinoids and terpenes…

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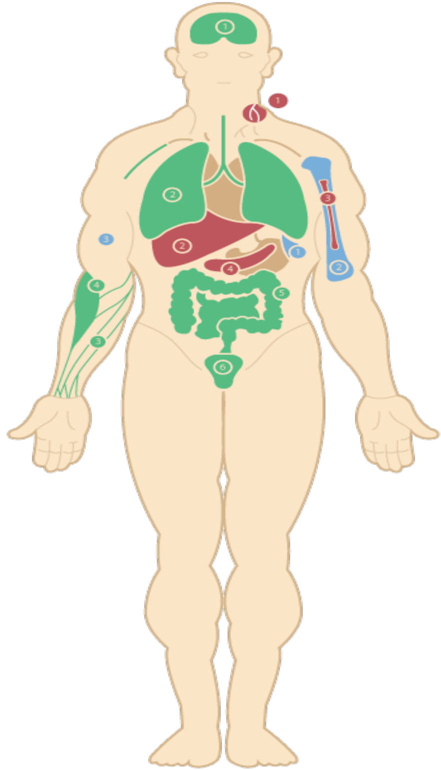
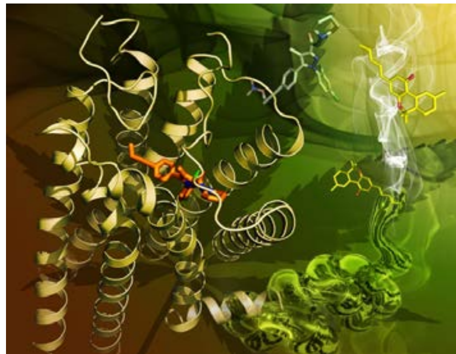
The endocannabinoid system (EC)





Structure of primary cannabinoid receptor
Yekaterina Kadyshevskaya, The Stevens Laboratory, USC

CB1 receptors are primarily found in the central nervous system and to a lesser extent in muscle, liver, adipose tissue

THC binding site - Psychoactive effects

CB2 receptors are found peripherally, primarily in immune system tissues as well as peripheral nerve terminals and GI tract

CBD binding site - No psychoactive effects

?Anti-inflammatory, ?Anti-cancer

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CBD

Up until December of 2018, CBD was federally classified as a Schedule I substance

Known to be effective for seizures, specifically in children with rare forms of childhood epilepsy who didn't respond to other medications

- A very selective crowd

Touted to be useful in numerous medical conditions

- Helpful in reducing some of the positive symptoms of schizophrenia as an adjunct of therapy

After that -- a very big gray zone

- Data otherwise is weak
- Some limited research done on anxiety but mostly in healthy volunteers who are made anxious
- Lacking are placebo-controlled studies with large numbers of ill patients and patients with anxiety disorders
- Is CBD really “safe”?

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The U.S. DEA has control over the legal production of marijuana for research

Patent #6630507 Dept of HHS

University of Mississippi, which is funded by the National Institute On Drug Abuse, is currently the only DEA-authorized marijuana supplier

- Researchers complain that this cannabis is low quality, contains mold, and is genetically more like hemp than cannabis

Image licensed from iStockphoto.com

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Medicinal vs Recreational Cannabis
(or is there any difference??)

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Ratio THC:CBD defines the psychoactive potential

Breeders-Growers have created strains that amplify the THC content

- 1990s average 4%
- 2014 average 12%
- 2019 average 25%
- MJ extract (hash oil) 50-80%

Can also contain pesticides, heavy metals, aspergillus, butane, other drugs

Pharmaceutical preparations/"therapeutic pot" THC:CBD

Often 1:1, or 2.5:1, or even 0:1 (pure CBD)

Nearly 10% of users in the U.S. report using it for medicinal purposes

Substantial overlap between recreational and medicinal use however

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CBD and THC

Image licensed from iStock.com

Most studies have looked at cannabis containing both THC and CBD

Some evidence that the substances work better in tandem

Varying results in the literature as to effectiveness:

- A 2017 VA review: limited evidence that THC-CBD (1:1 to 2:1 ratio) may alleviate neuropathic pain
- A 2017 NASEM review: "conclusive or substantial evidence" that cannabis is effective in treating chronic pain, nausea and vomiting after chemotherapy and MS-related muscle spasms
- A 2018 systematic review: "It seems unlikely that cannabinoids are highly effective medicines for chronic non-cancer pain"

Risks???

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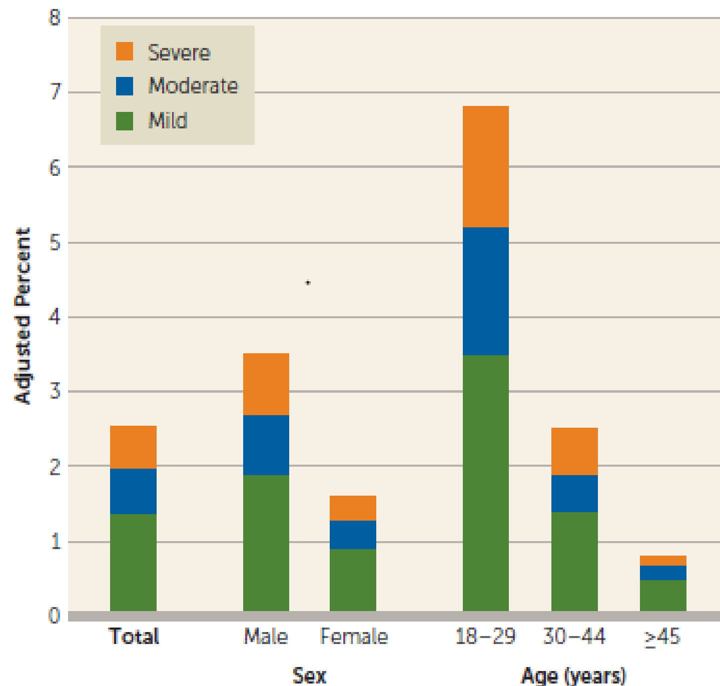
Cannabis use disorder (CUD)



DSM-5: MJ dependence and abuse = *cannabis use disorder*

- Associated with other substance use, psychiatric disorders, and cannabis-induced psychotic disorder
- Per 2013 NESARC III: One-year prevalence in U.S. of 2.5% (but <1% at age >26 or income >$70,000)

Conflicting data whether cannabis use, and use disorder, is increasing (NESARC III) or stable (NSDUH)

Approximately 9% of all users become dependent at some time in their life; 17% if started in teens

- Compared to 67.5% for nicotine

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Can marijuana cause schizophrenia?

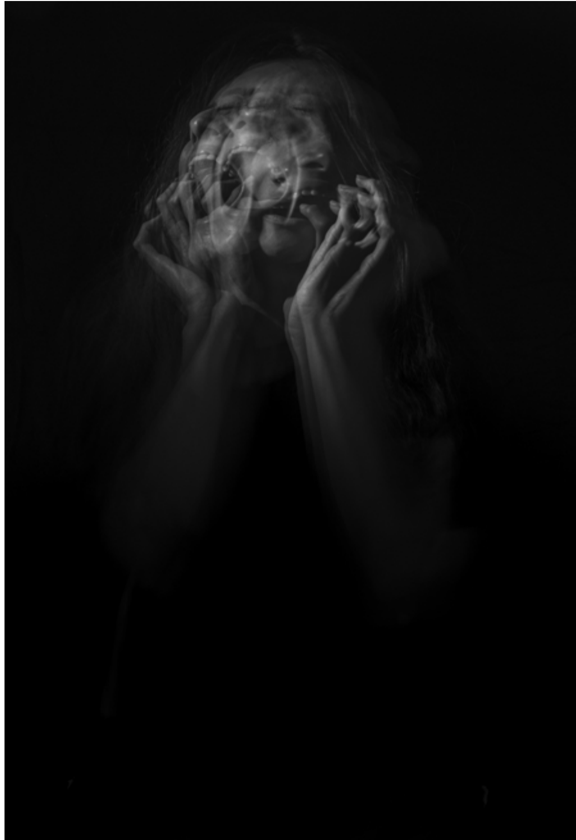

Photo by Camila Quintero Franco on Unsplash

Likely yes

- Early use (ages 15 to 18) is associated with the risk of psychotic disorders, even after controlling for many other factors
- Not likely to be ‘reverse causation’ or self-medication

Overall roughly doubles risk

Risk associated with multiple factors

- Early use (≤ 18yo) – effect on the developing brain
- Amount used and higher potency cannabis
- Pre-existing vulnerability (genetic, child abuse, psychiatric illness)

GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal influence of schizophrenia

Di Forti M, et al. Lancet Psychiatry (2019)
Eur Arch Psychiatry Clin Neurosci. 2009 October; 259(7): 413–431

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Risk of depression, anxiety, and suicidality in young adulthood

Systematic review and meta-analysis:

- 11 studies comprising 23,317 individuals were included in the quantitative analysis

The pooled odds ratio was 1.37 for depression and 3.46 for suicidal attempt

Biologic plausibility – known neuroanatomic alterations seen in early cannabis users

Image licensed from iStock.com

But remember – association does not mean causation!

Cannabis & MVA Risk: Meta-analysis

Pooled risk OR of 2.66

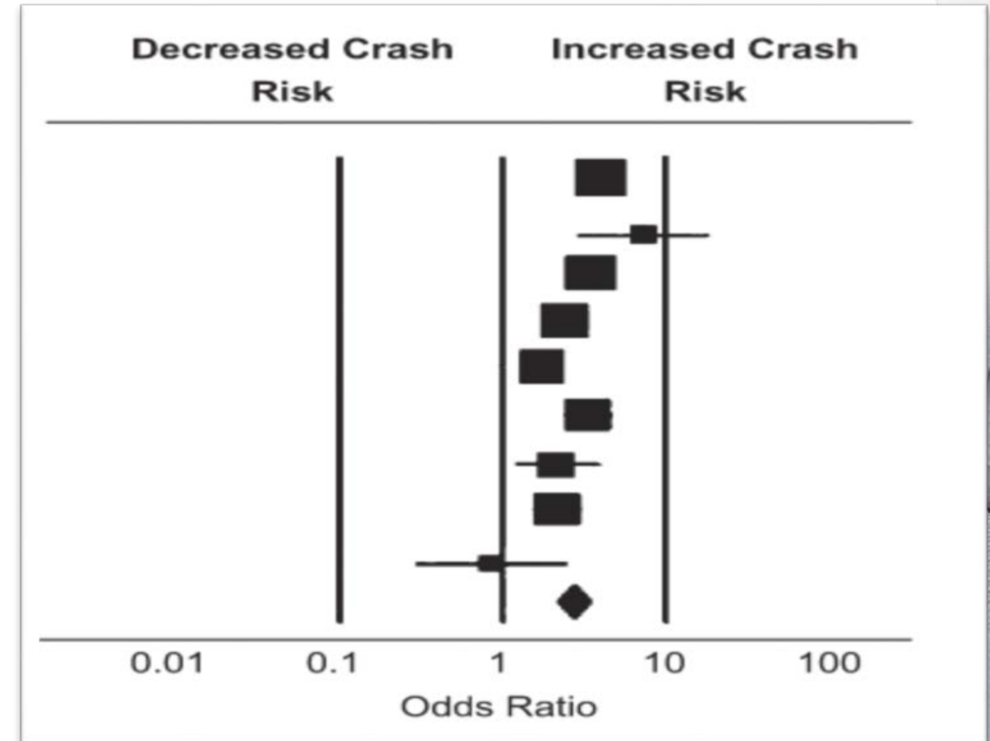
- other analyses with OR 1.5-2.0 range, including increasing risk with increasing THC levels

Psychomotor impairment lasts for 12 to 24 hours due to accumulation of marijuana in adipose tissue

- and awareness of this decreases in a few hours

Risk appears to be less than that seen with alcohol

5.2% higher rate in CO, WA, and OR compared with neighboring states that did not legalize retail sales



Asbridge M, et al. BMJ 2012;344:e536 doi: 10.1136
Hartmann RL, Huestis MA. Clin Chem. 2013 March ; 59(3)
Rogeberg O, Elvik R. Addiction. 2016 Aug;111(8):1348-59
HLDI Bulletin. Recreational marijuana and collision claim frequencies. 2018;35(8):1-14.

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Cannabis: pros and cons

Good evidence for:
- MS - Decreased pain and spasticity
- Parkinson's - Decreased tremor, rigidity, and pain
- ALS - Improved appetite and decreased pain and spasticity

Limited or no evidence of benefits for:
- General pain control
- Insomnia
- Decreased opioid risk

Valid concerns of:
- Addiction for some (~10%)
- Psychosis in vulnerable youth
- Increased MVA risk
- Impairment in work, school, and relationships

Questionable increased risk for:
- Lung disease
- Cancer
- MI/Stroke
- As a "gateway drug"

Unequivocal finding of comorbidity with psychiatric conditions and with alcohol, tobacco, and illicit drug abuse.
Cannabis is used primarily for its intoxicating effects – and therein lies the main risk

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Mortality risk of cannabis use

Clinical literature has found little to indicate an independent mortality risk except for the increased MVA risk and possibly a small increase in lung cancer risk.

- Risk appears to be primarily in the company it keeps

Kaiser and NHANES population studies:

- Small, but not significant increased risk in someone who admits to using marijuana in the last month, controlled for other aspects of their medical history

kimzy-nanney-b2haCjfk_cM-unsplash_Cannabis

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Insurance population results

Insurance lab studies of applicants testing positive for THC found that much of the mortality of marijuana is mediated by the concomitant use of cigarettes.

When controlled for smoking status, plus age and sex (but not other effects of underwriting), the hazard ratios were:

- CRL*
  - 1.21
- ExamOne**
  - ~1.0 for women
  - 1.97 for men THC(+) only, 3.06 cotinine (+) only, and 3.97 if both (+)

➢ Risk higher in younger ages
➢ THC(+) also correlated some with most other drugs of abuse

Courtesy of: *Dr Steven Rigatti, Rigatti Risk Analytics, LLC; **Brian Lanzrath, Director of Analytics, ExamOne

What's the market doing?

Rate as tobacco?

- Not very well justified by these data

Majority of carriers (by ~3:1):

- Assess based on quantity used and distinguish between recreational and medicinal use
- But do not distinguish between legal and illicit use and do not test for THC

Are we attuned to the messages out there?

Millions of Marijuana users were afraid to pee in a cup

A lot of Untapped Green When It Comes to Cannabis

I Smoke Marijuana! Can I Get Life Insurance?

Images courtesy of Giggleinsurance.com

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High points

1. Cannabis use (especially frequent recreational use?) is *associated* with excess mortality risk
   - Heavily influenced by comorbid factors – alcohol, smoking, substance use, mental health issues, risky behaviors

     But are you always able to pick those up in underwriting?!?
   - Added risk for those with underlying respiratory disease such as asthma or COPD
   - MVA and psychosis risk but otherwise no clear direct mortality connection

2. Younger applicants portend higher risk – see #1

3. There are no long-term studies on edibles - mortality also likely heavily influenced by comorbids

This is a continuously evolving landscape – stay alert!

QUESTIONS???

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Thank you!

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