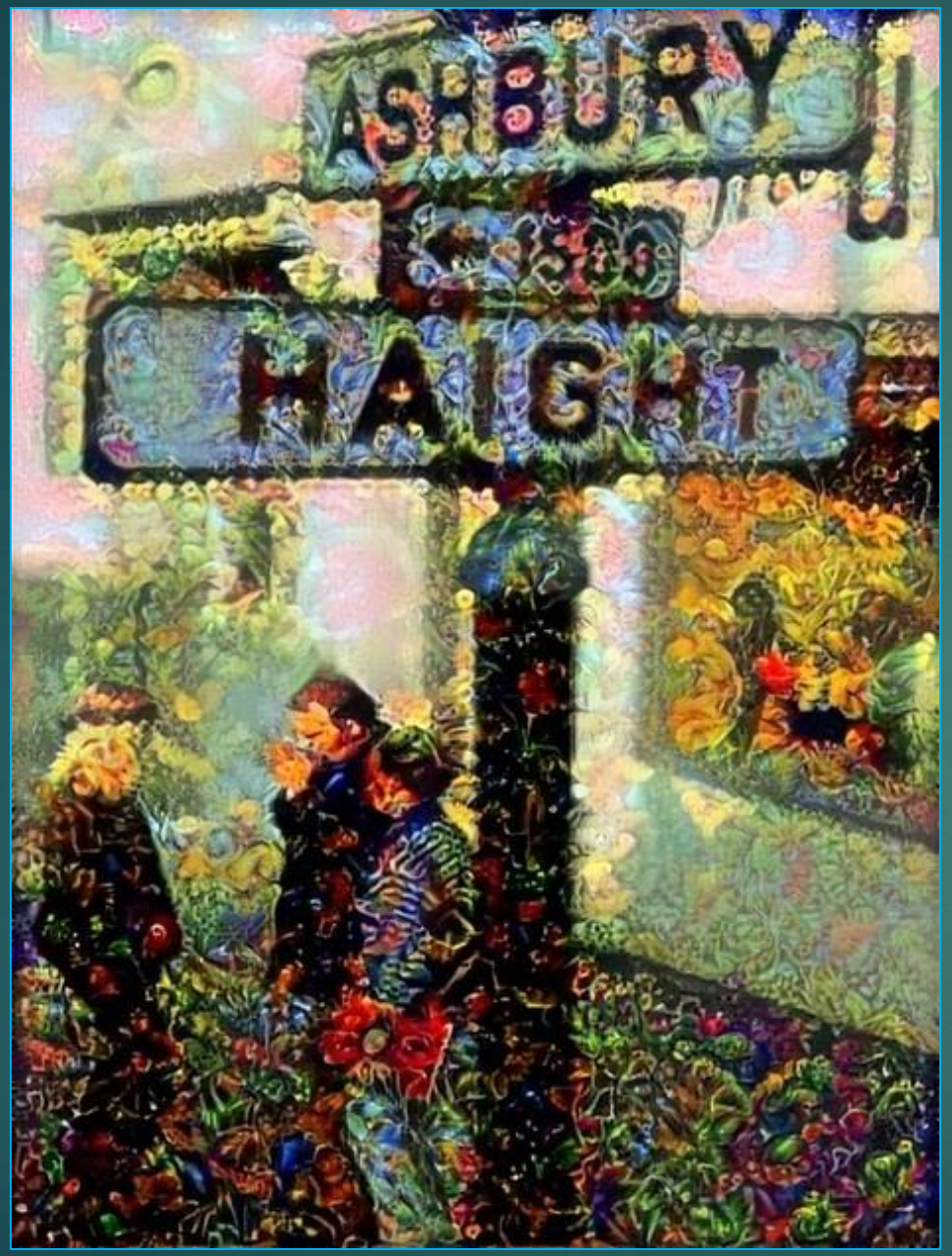

Cannabis Use and Cannabis Use Disorder in the Setting of Legalization

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Cannabis Question 1

FDA-approved indications include:

1. Insomnia related to PTSD
2. Glaucoma
3. Seizure disorder
4. N/V 2/2 to chemo, wasting related to HIV
5. Chronic pain/spasticity 2/2 multiple sclerosis

Cannabis Question 2

Past year use is highest in:

1. Age 12-17
2. Age 18-25
3. Age 26-35
4. Age 36-45

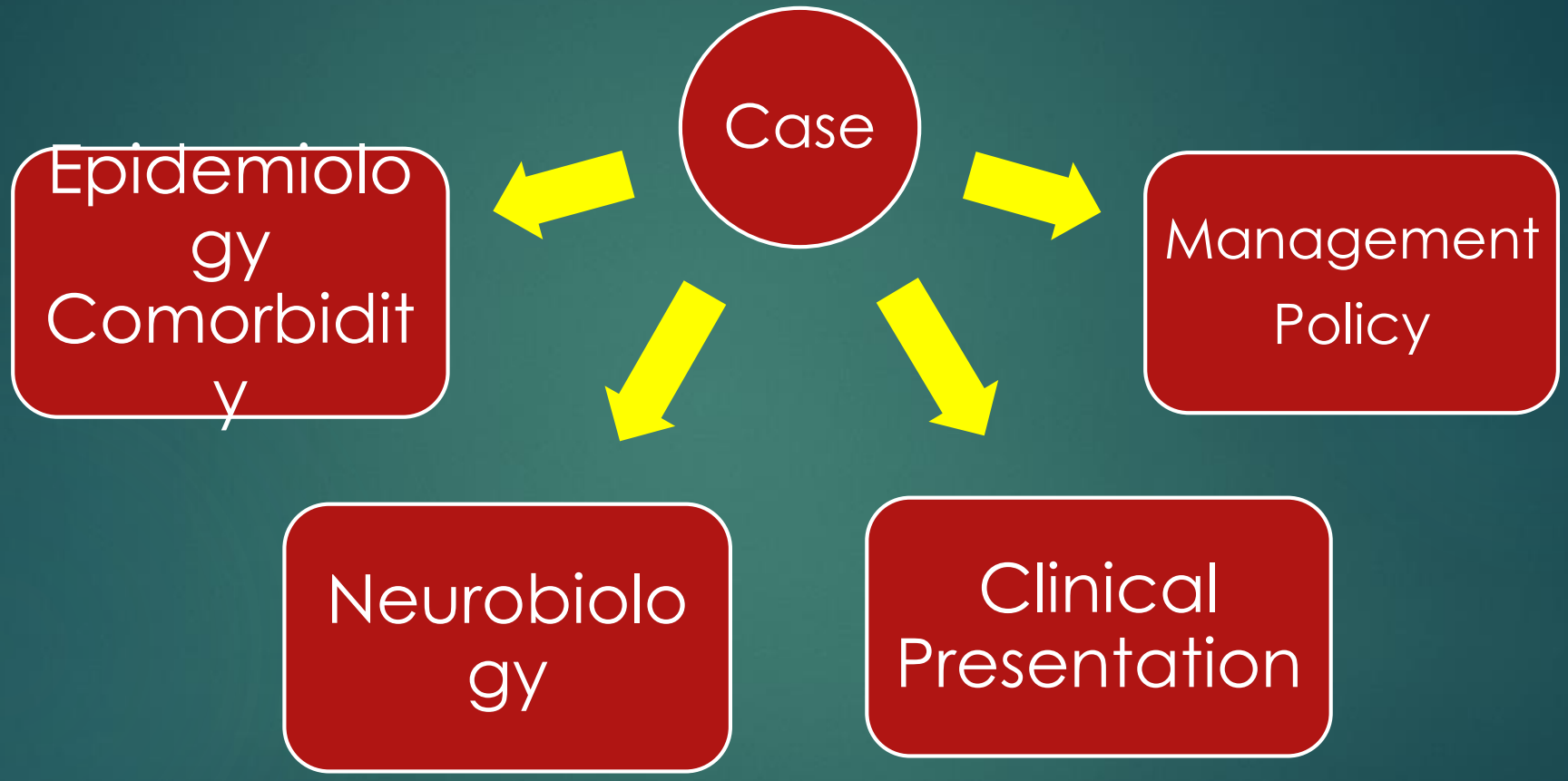
Cannabis Question 3

Risk of use disorder shown to be associated with:

1. Parental attitudes towards use
2. Early onset (adolescent) use
3. Route of administration
4. Regular/daily use

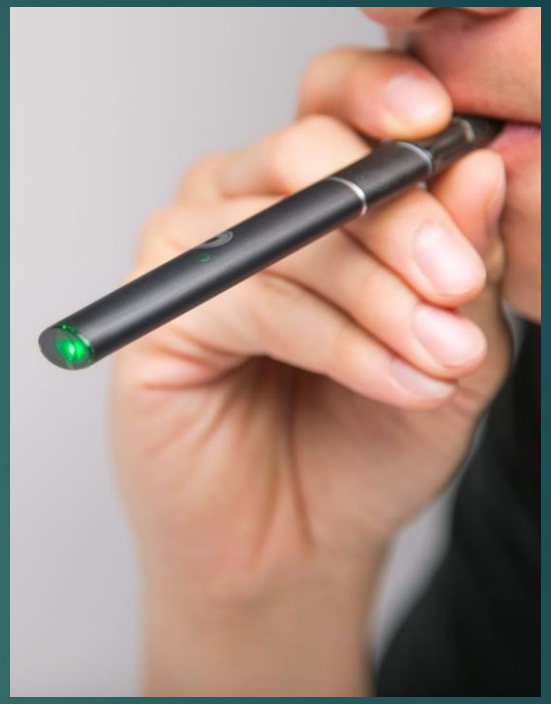
No conflicts of interest to disclose

Objectives


Case
Epidemiology Comorbidity
Management Policy
Neurobiology
Clinical Presentation

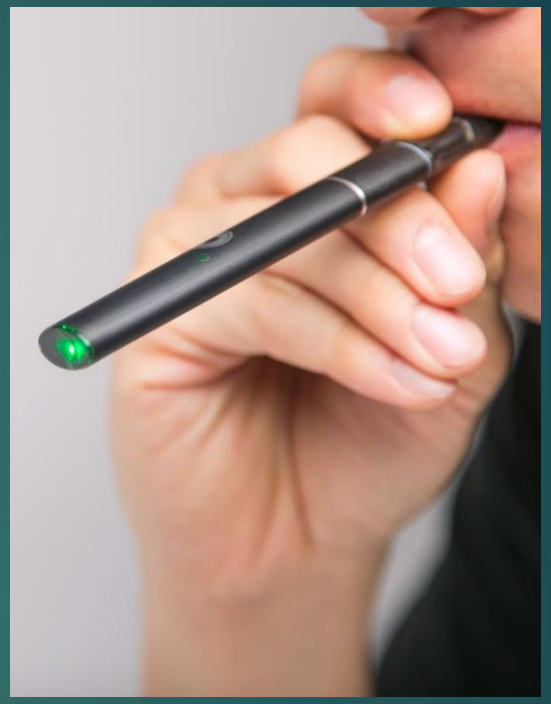
Case: TJ

- Forty-three yo navy veteran, PTSD, depression, MST, borderline traits, AUD (severe) in remission, impulse control/anger issues.
- Sertraline 300mg PO daily
- Prazosin 15mg PO QHS
- Quetiapine 300mg PO BID
- Trazodone 150mg PO QHS
- "Vapes" hash oil and consumes edible (brownie) daily.



Epidemiology

"Everyone smokes pot. Welcome to San Francisco."

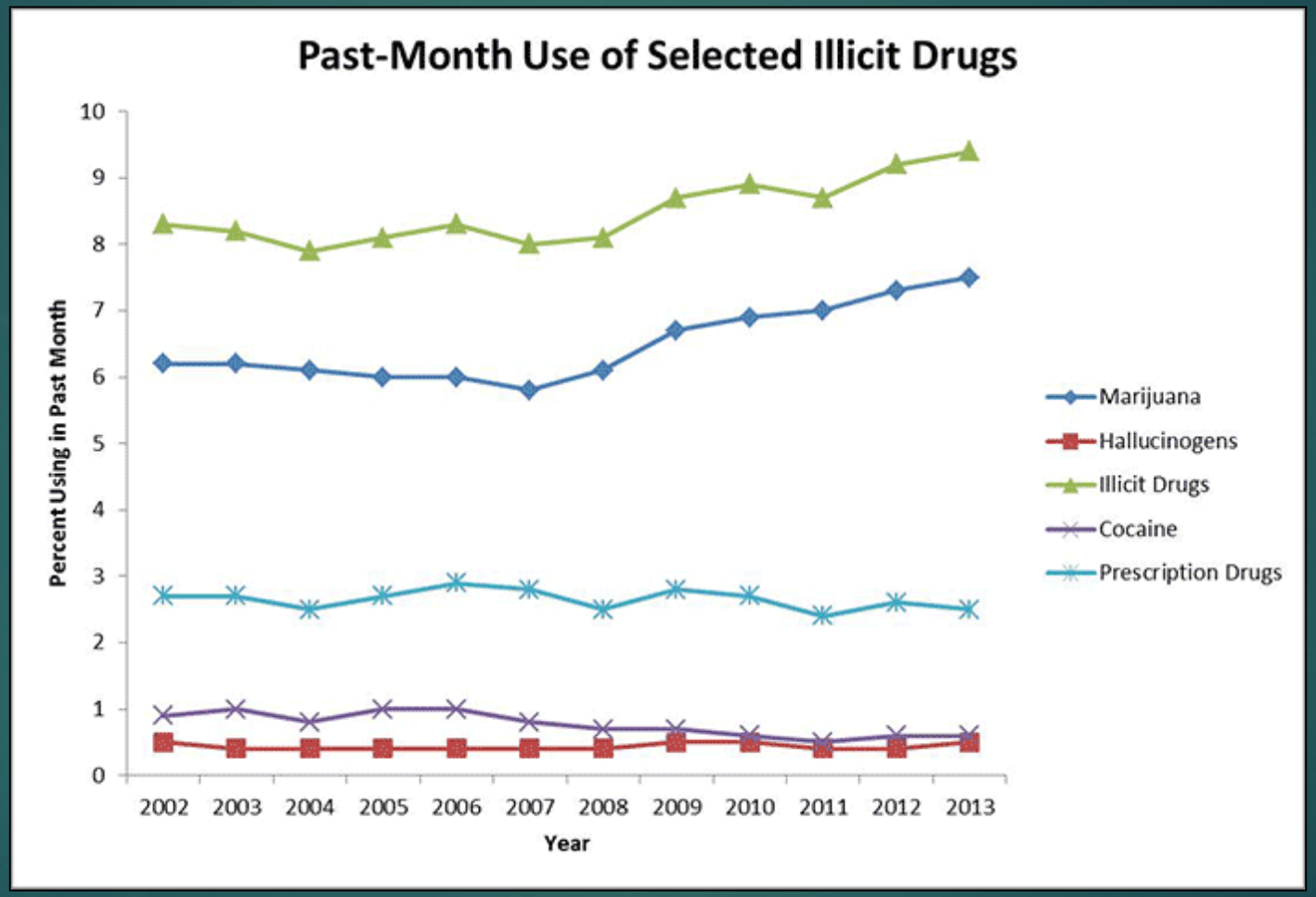


Epidemiology: Cannabis Use

- Most commonly used illegal substance worldwide
- Lifetime prevalence in U.S. 42-46%
- Past year use highest in young adults 18-25
- Past year CUD highest ages 21-26
- Abuse/dep: 1.5% (2001) → 2.9% (2012)
- Greater increases in use and CUD in MML states vs non-MML

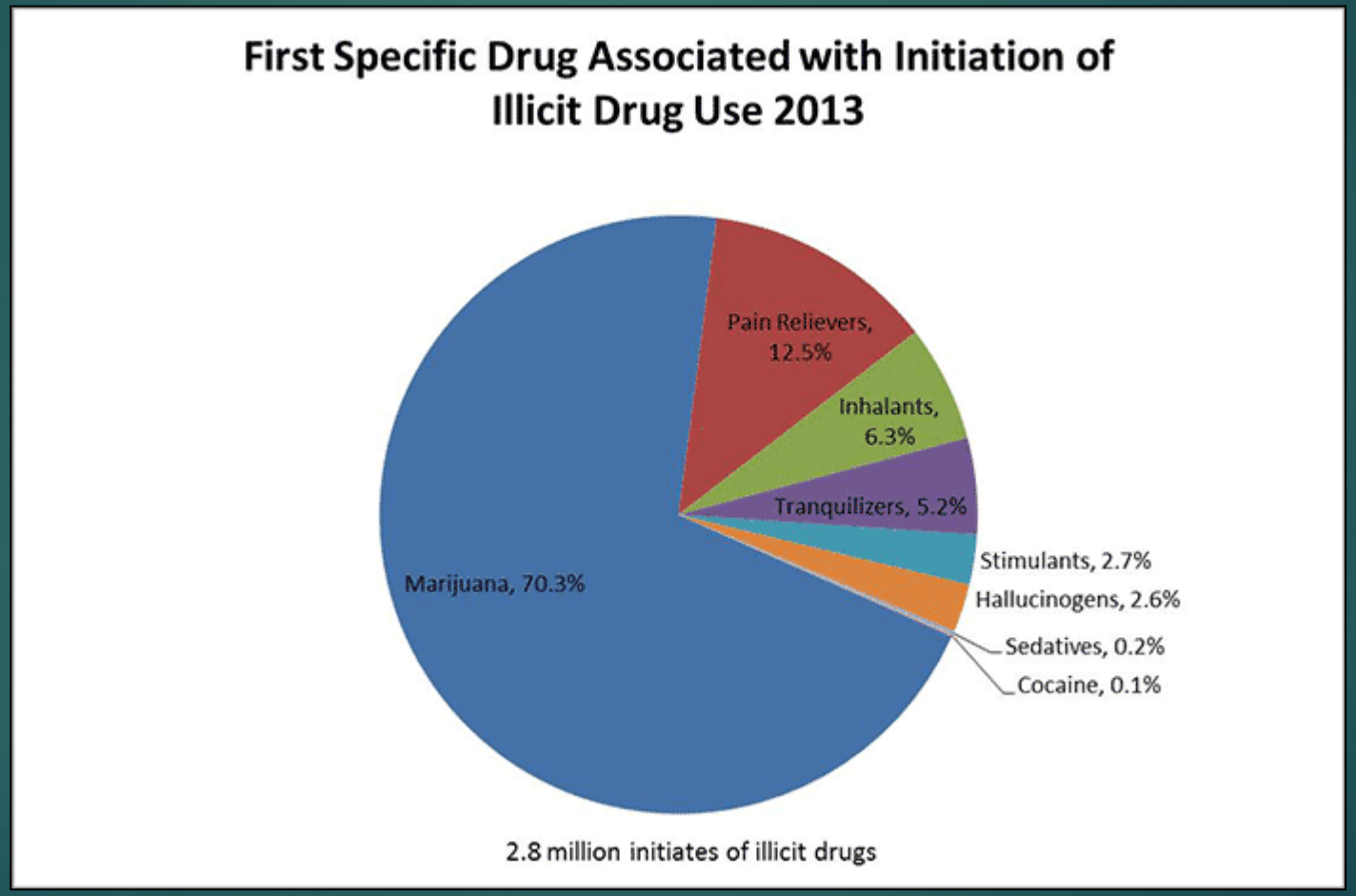
(Hasin JAMA 2017; DuPont 2014, UpToDate,)

Epidemiology: Cannabis Use



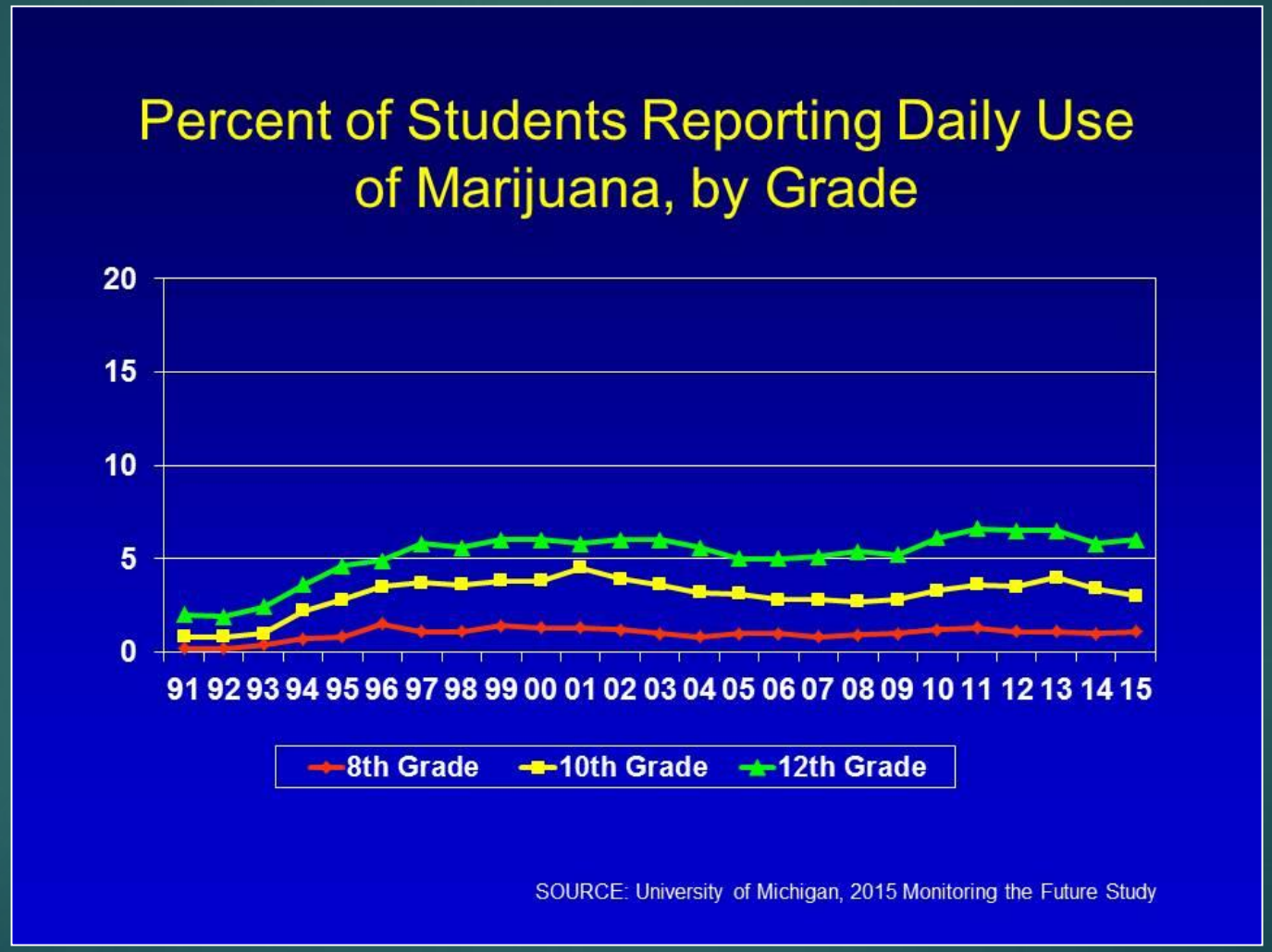
(SAMHSA NSDUH survey 2013)

Epidemiology: Cannabis Use



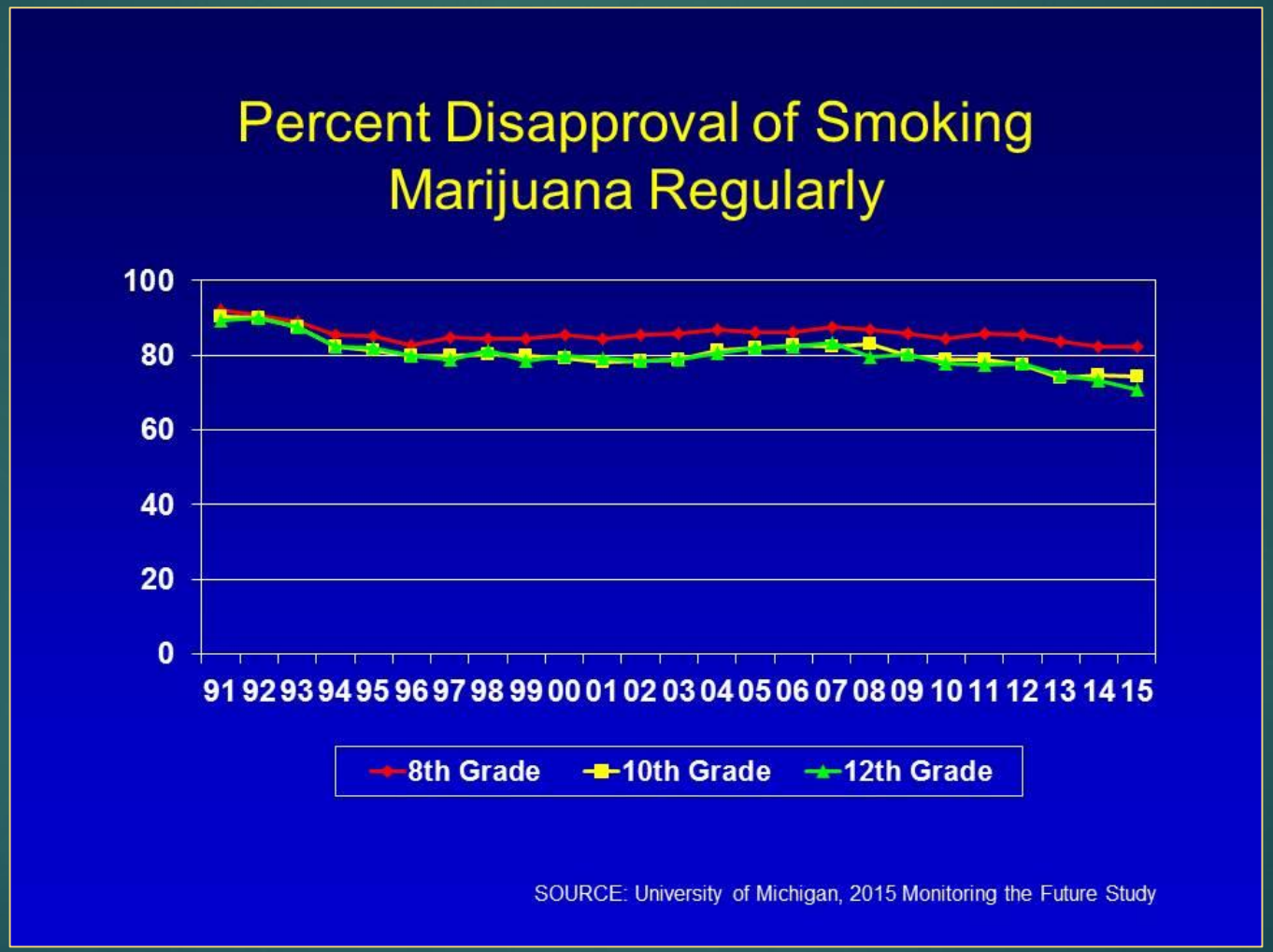
(SAMHSA NSDUH survey 2013)

Epidemiology: Cannabis Use



(UMich/NIDA MTF Study 2016)

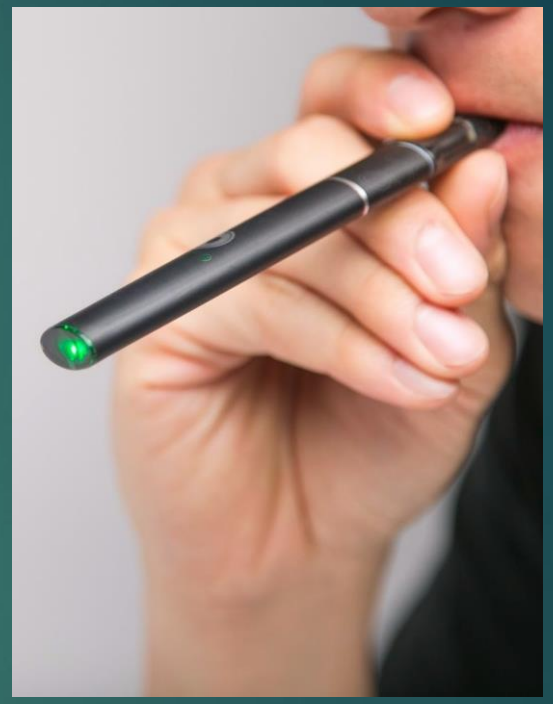
Epidemiology: Cannabis Use



(UMich/NIDA MTF Study 2016)

Comorbidity

"A lot of people with mental issues smoke pot."



Comorbidity: SUD

- N = 34653 NESARC respondents.
- Interviewed 2001-02, 2004-05.
- Cannabis use

→ SUD (OR 6.2)

→ CUD (OR 9.5)

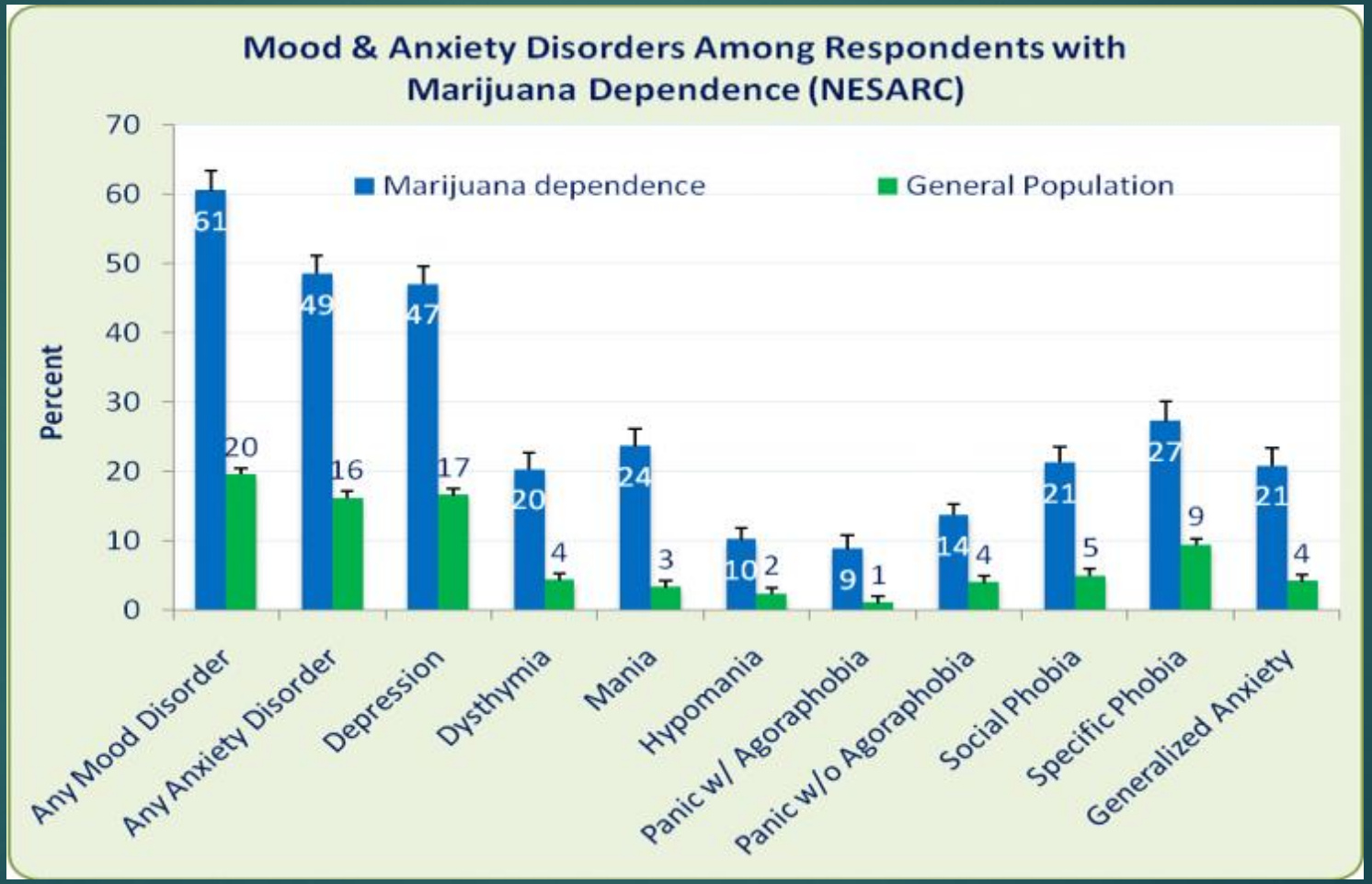
→ AUD (OR 2.7)

→ Nicotine dep (OR 1.7)

Not significant: new mood or anxiety dx.

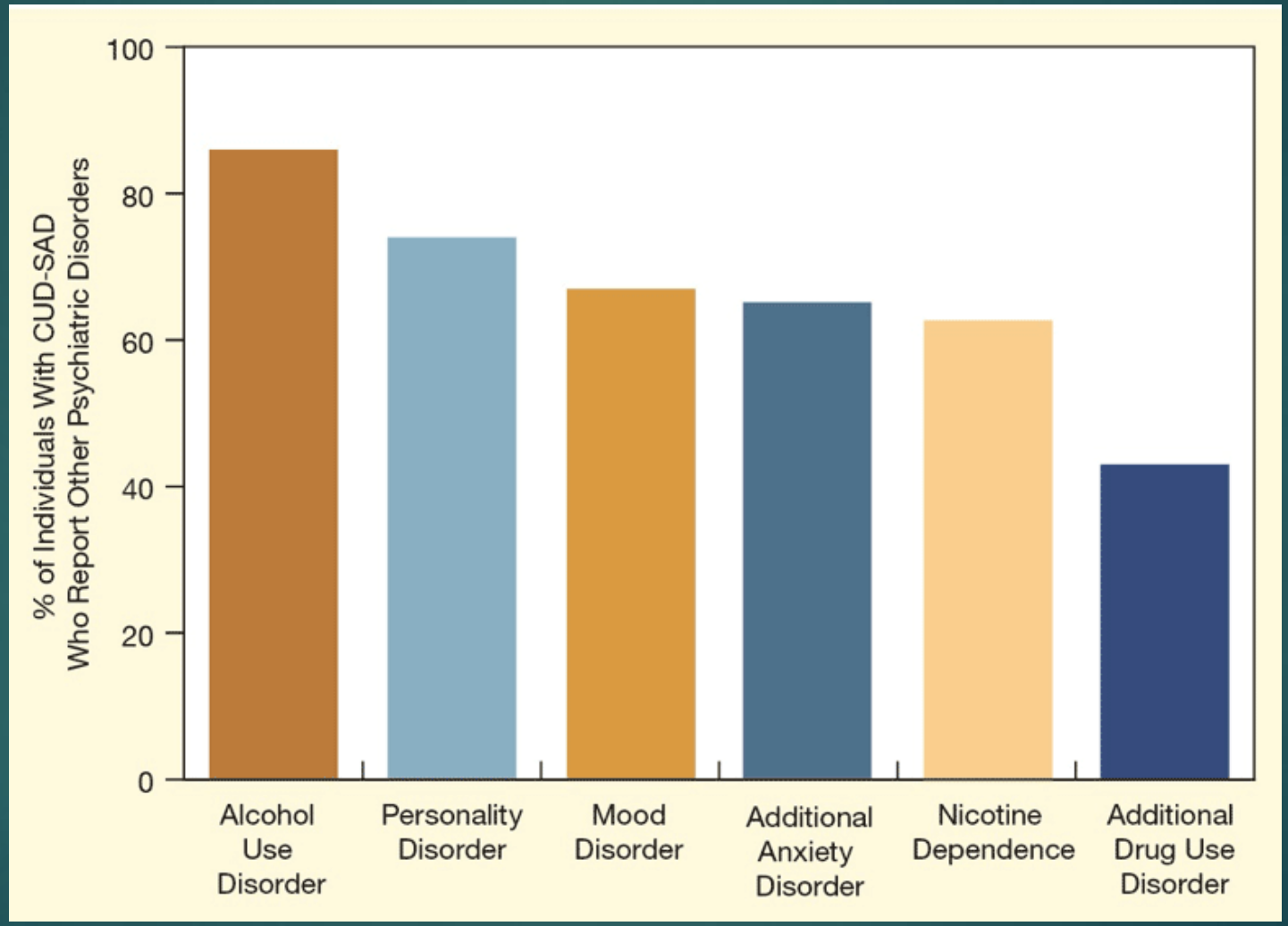
(Blanco 2016, JAMA)

Comorbidity: Mood and Anxiety



(NESARC 2014)

Comorbidity: Sub-populations?



(Buckner 2012, Drug Alc Dep)

Comorbidity: Adolescents

Among n = 462 Adolescent Cannabis Users	
Substance use diagnosis	***OR Dependent vs. Non-dependent***
Alcohol abuse	**2.09(1.14,3.82)**
Alcohol dependence	**1.18(0.64,2.19)**
Opioid abuse	**0.37(0.13,1.05)**
Opioid dependence	**0.76(0.43,1.35)**
Stimulant abuse	**1.74(0.38,8.05)**
Stimulant dependence	**0.82(0.21,3.18)**
Cocaine abuse	**1.14(0.31,4.22)**
Cocaine dependence	**2.25(0.50,10.13)**
Benzodiazepine abuse	**0.77(0.23,2.52)**
Benzodiazepine dependence	**1.58(0.34,7.37)**
Hallucinogen dependence	**1.56(0.18,13.61)**

(Zaman 2015, J Addict Med)

Comorbidity: Adolescents

Among n = 462 Adolescent Cannabis Users	
Psychiatric diagnosis	***OR Dependent vs. Non-dependent***
Any depressive disorder	**1.41(0.69,2.89)**
Bipolar disorder	**1.25(0.26,6.02)**
Mood Disorder NOS	**1.84(1.00,3.37)**
ADHD	**2.06(1.08,3.92)**
Any behavioral disorder	**2.43(0.82,7.16)**
Psychosis	**0.62(0.06,6.91)**
Any psychiatric disorder	**2.15(1.22,3.78)**
≥2 psychiatric disorders	**1.96(1.12,3.41)**

(Zaman 2015, J Addict Med)

Cannabis and Psychosis:

- Increased risk of psychotic outcome
- Dose dependent risk
- Speeds psychosis onset by 7 years
- Higher paranoia, hospitalizations
- Lower brain volume

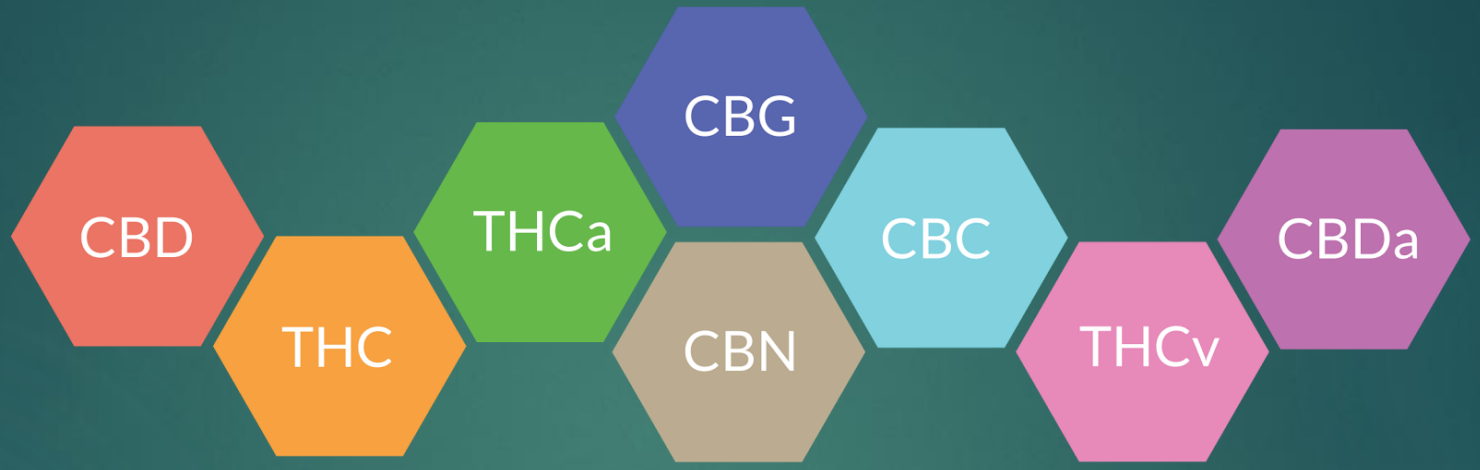
(Moore 2007, Lancet)

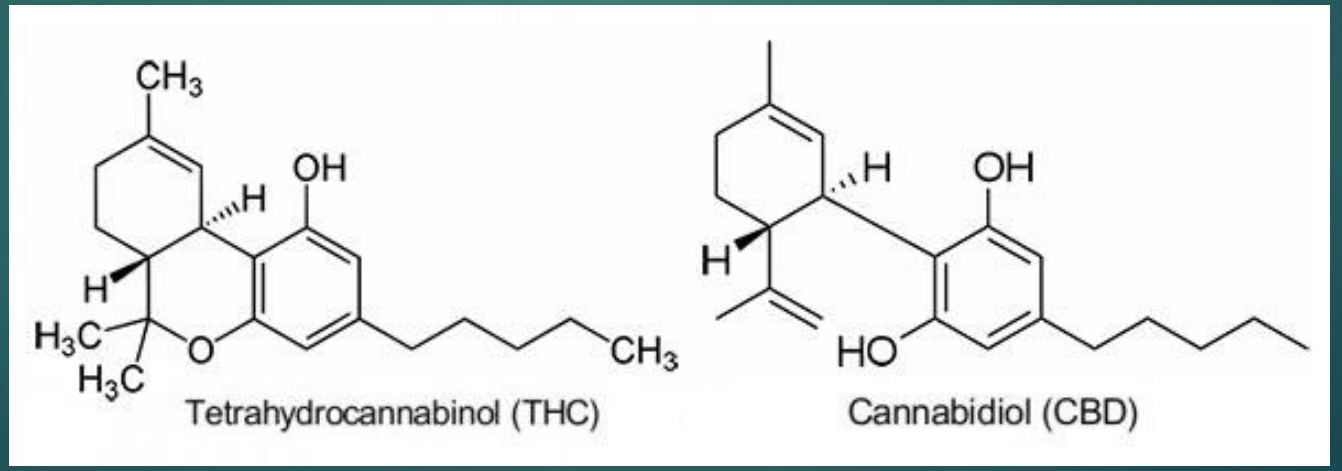
Neurobiology

"It's labeled like a medication. So I know exactly what I'm getting."

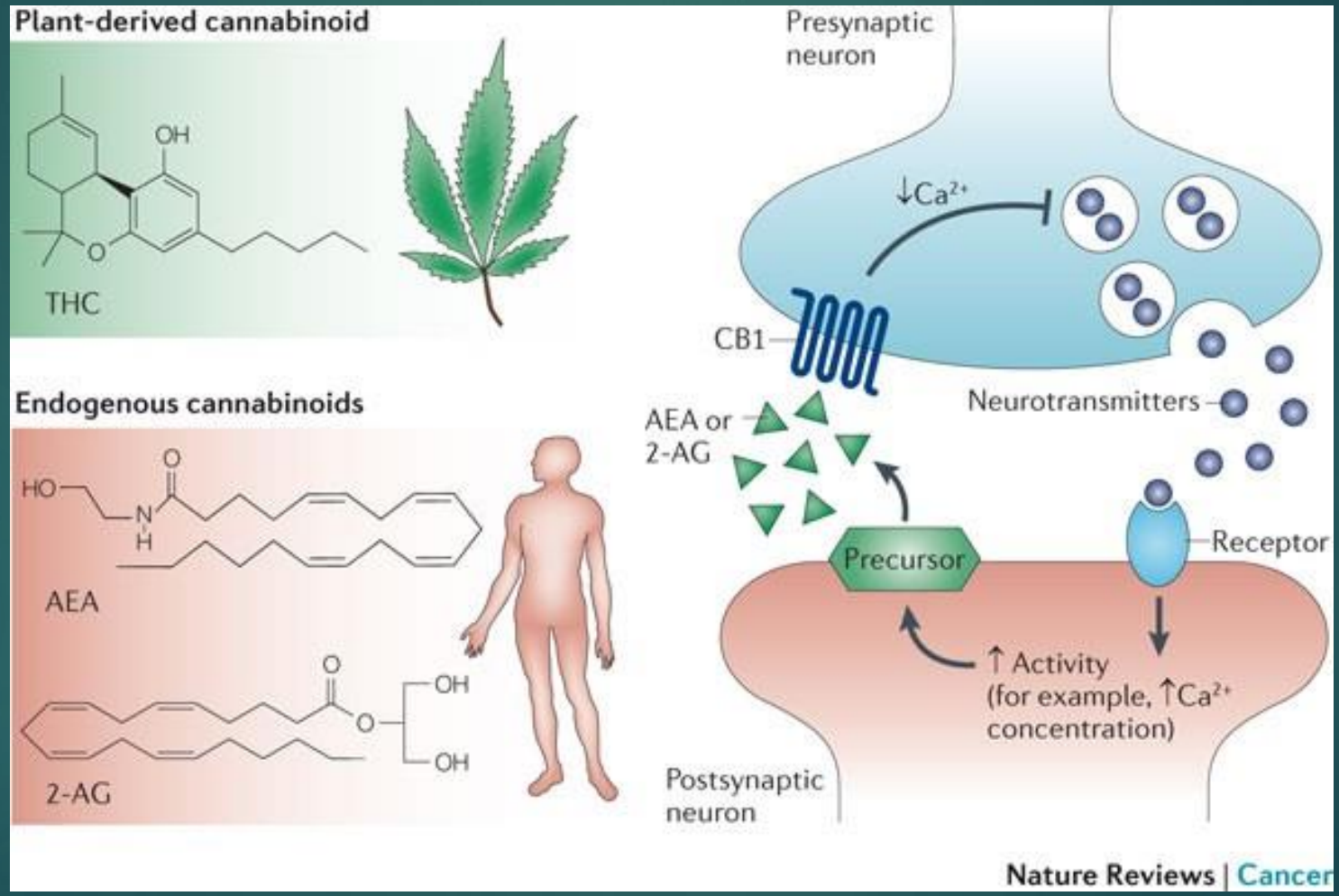
Trichomes

Chemical Composition



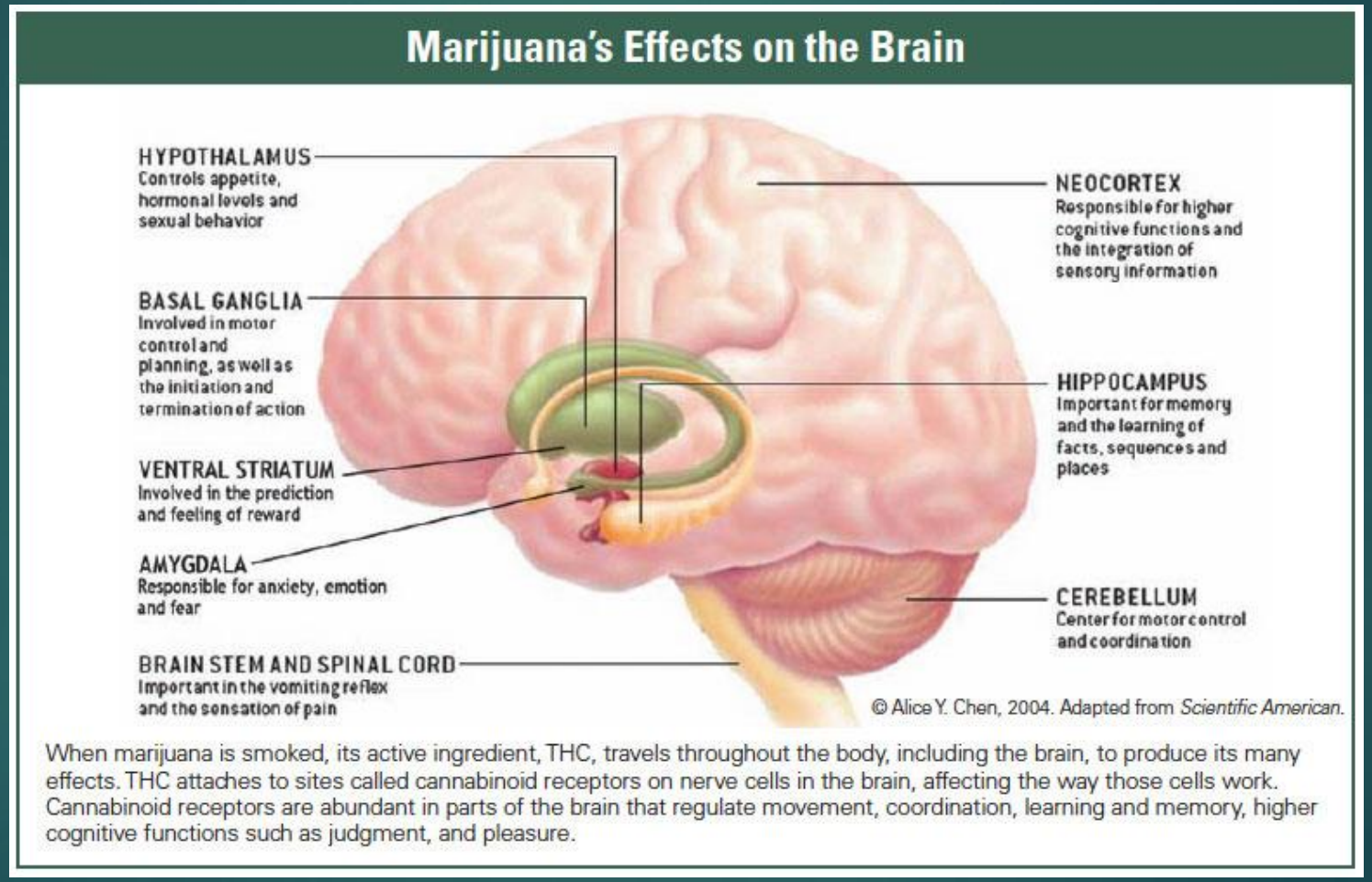


Neurobiology



(Nature)

Neurobiology

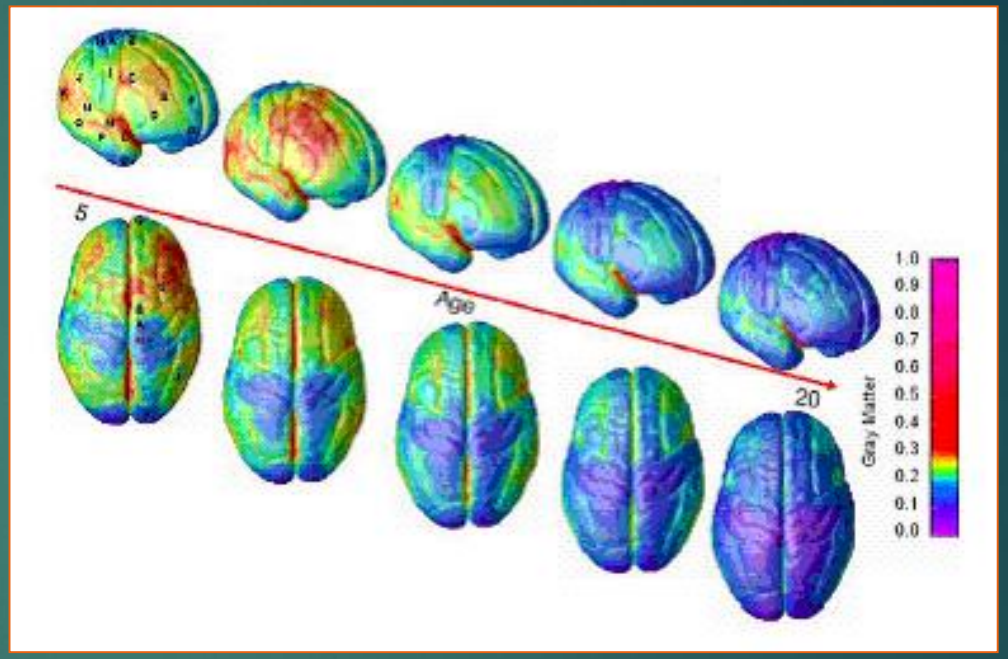


(NIDA/Scientific American)

Neurobiology

Brain matures (myelinates) from back to front

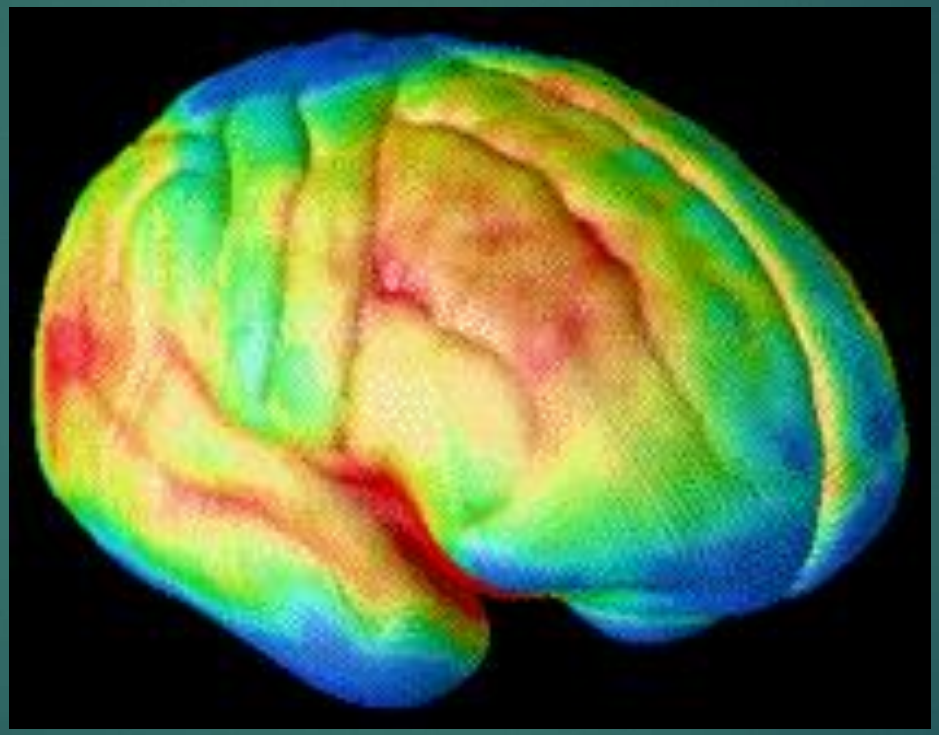
- 12-14 Cerebellum (motor)
- 14-18 Limbic (social or emotional)
- 18-26 Frontal (thinking or cognition)



(Dev Cog Neurosci. Paul Thompson, PhD/UCLA, in Gogtay, et al, PNAS 2004)

Adapted from D.Pating, SFVAMC 11/16

Neurobiology



(Paul Thompson, PhD/UCLA, 2004)

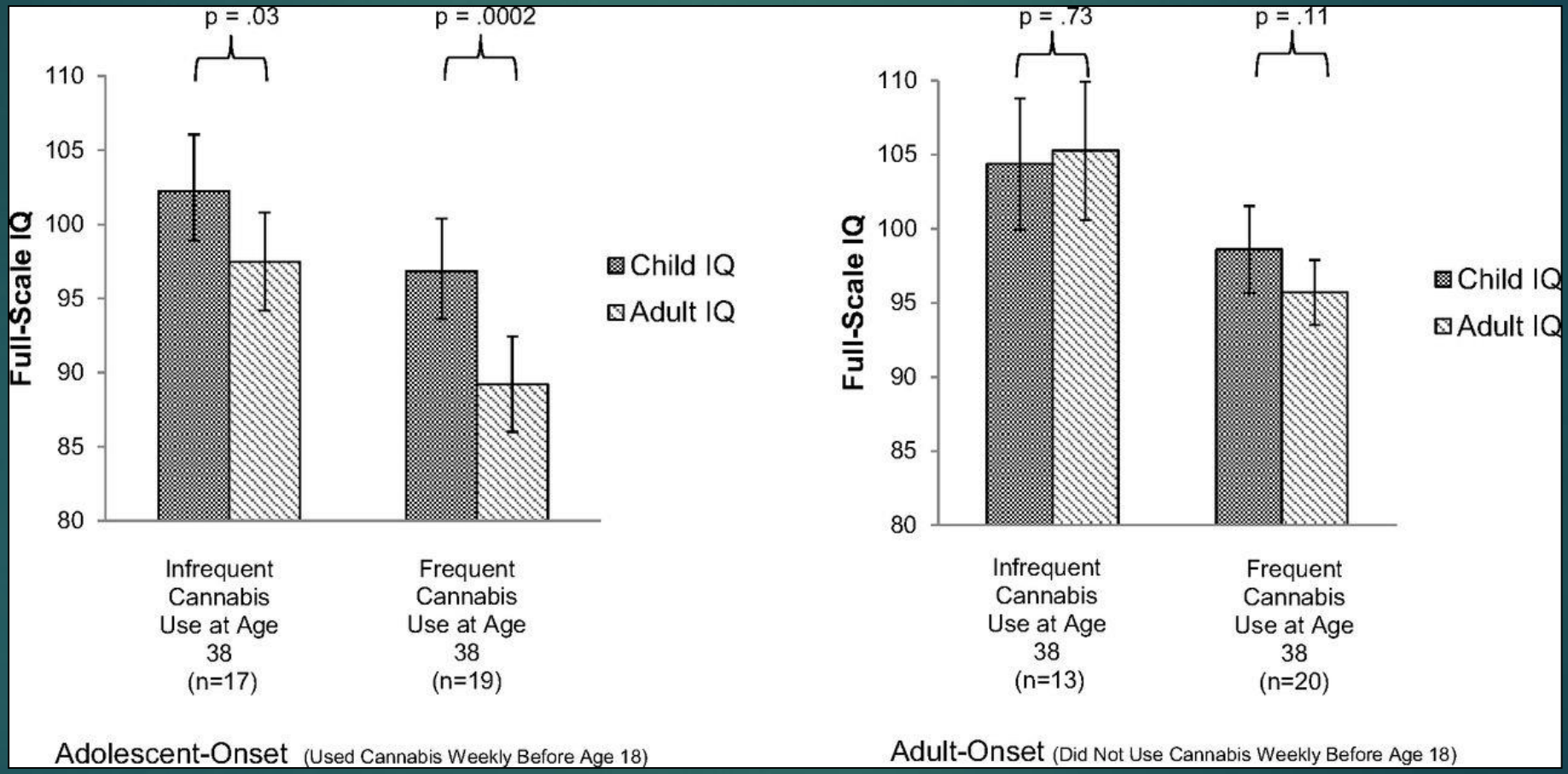
Adapted from D.Pating, SFVAMC 11/16

Cognition

Summary of Research Findings on the Effects of Cannabis on Executive Functions			
Executive Function	Acute Effects	Residual Effects	Long-Term Effects
Attention/Concentration	Impaired (light use) Normal (heavy use)	Mixed findings	Largely normal
Decision Making and Risk Taking	**Mixed findings**	**Impaired**	**Impaired**
Inhibition/Impulsivity	Impaired	Mixed findings	Mixed findings
Working Memory	Impaired	Normal	Normal
Verbal Fluency	Normal	Mixed findings	Mixed findings
Note: Acute = 0-6 hours after use; Residual = 7hr -20d after use; Long-term = ≥3wks.			

(Crean 2011, J Addict Med)

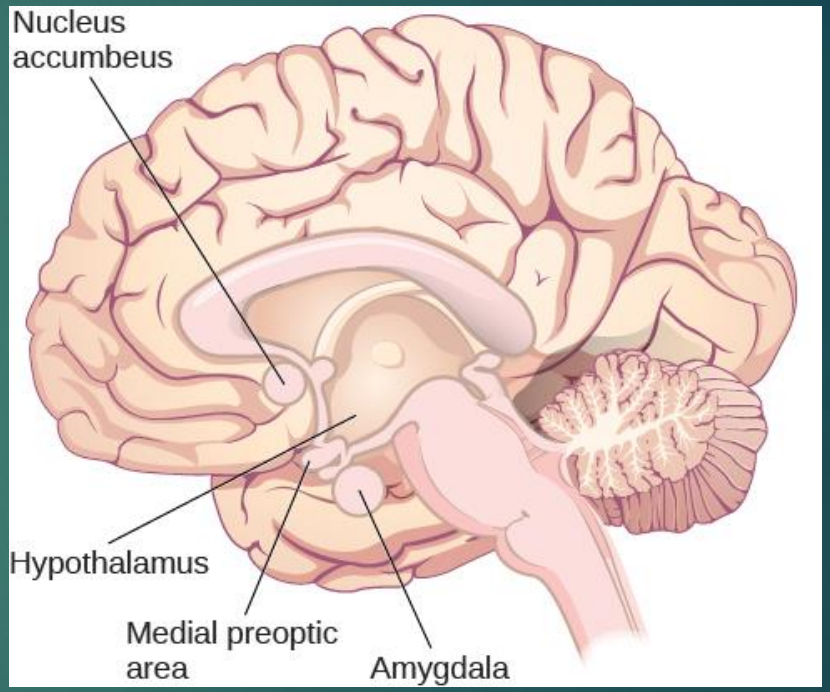
Adolescent Use and Cognition



(Meier 2012, PNAS)

Adolescent Use and Cognition

- Age of onset, frequency, amount affect cog performance
- Earlier onset <-> More use, poorer cog
- Structural, functional differences in brains of users
- Conclusion: **Exposure during vulnerable period → altered brain development**



(Batalla 2013, PLoS One; Gruber 2012, Psychol Addict Beh)

Adolescent Use and Outcomes

Age- and dose-dependent impact on:

- High-school completion
- Attainment of university degree
- Cannabis dependence
- Illicit drugs
- Suicide attempt
- Depression
- Welfare dependence

(Silins 2014, Lancet Psychaitry)

Preparations

Preparations	Description
Marijuana[a]	Dried plant product consisting of leaves, stems, and flowers; typically smoked or vaporized
Hashish	Concentrated resin cake that can be ingested or smoked
Tincture[a]	Cannabinoid liquid extracted from plant; consumed sublingually
Hashish oil	Oil obtained from cannabis plant by solvent extraction; usually smoked or inhaled; butane hash oil (sometimes referred to as "dabs"), for example
Infusion[a]	Plant material mixed with nonvolatile solvents such as butter or cooking oil and ingested

[a] These preparations are available from state-approved medical marijuana dispensaries.

(Hill 2015, JAMA)

Pair tied to butane hash oil explosion in Astoria accused of assault

4 Updated on May 5, 2017 at 4:57 PM, Posted on May 5, 2017 at 4:04 PM

Two men involved in a butane-related explosion in Astoria last fall were arraigned in Clatsop County Court Friday on felony assault charges, including one that comes with a mandatory 70 month sentence. *(Danny*

(The Oregonian)

Dispensaries

Preparations

Preparations

Preparations

Labeling (in)accuracy

Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products FREE

Ryan Vandrey, PhD[1]; Jeffrey C. Raber, PhD[2]; Mark E. Raber[2]; Brad Douglass, PhD[3]; Cameron Miller, MS[3]; Marcel O. Bonn-Miller, PhD[4]

[+] Author Affiliations

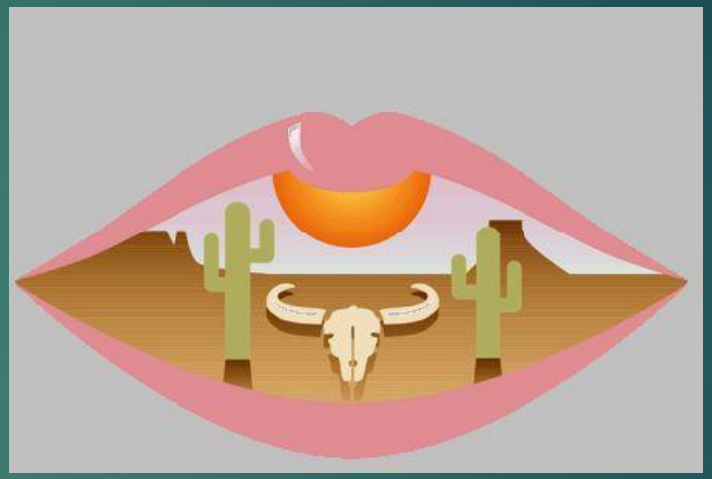
JAMA. 2015;313(24):2491-2493. doi:10.1001/jama.2015.6613.

Addiction to Cannabis

"You can't really get hooked on it like the other stuff."

Cannabis intoxication

Impairment + 2 symptoms within 2 hours



(DSM 5)

By MICHELLE MILLER / CBS NEWS / July 13, 2016, 7:14 PM

Synthetic marijuana overdose turns dozens into "zombies" in NYC

113 Comments / Share / Tweet / Stumble / Email

NEW YORK -- We were reminded again of the nightmare of drug abuse Tuesday when synthetic marijuana seemed to turn people into zombies on a New York City street.

It was a bizarre scene: Dozens of people with blank stares stumbling around a Brooklyn neighborhood. Brian Arthur live-streamed it on Facebook.

"As I was walking up a block, I see anybody laying out on the floor, and everybody's just stumbling all over the place," Arthur said. "It looked like a scene out of a zombie movie."

Emergency workers sent 33 people to area hospitals, saying they appeared to be under the

(CBS news reports)

Cannabis withdrawal

Three within 1 week:

- Irritability, anger or aggression
- Anxiety
- Sleep difficulty
- Decreased appetite or w/l
- Restlessness
- Depressed mood
- At least one: abd pain, shakiness/ tremors, sweating, fever, chills, or headache

(DSM 5)

Cannabis Withdrawal Scale

		Not at all						Moderately				Extremely	Negative Impact on daily activity (0 – 10)
1	The only thing I could think about was smoking some cannabis	0	1	2	3	4	5	6	7	8	9	10	
2	I had a headache	0	1	2	3	4	5	6	7	8	9	10	
3	I had no appetite	0	1	2	3	4	5	6	7	8	9	10	
4	I felt nauseous (like vomiting)	0	1	2	3	4	5	6	7	8	9	10	
5	I felt nervous	0	1	2	3	4	5	6	7	8	9	10	
6	I had some angry outbursts	0	1	2	3	4	5	6	7	8	9	10	
7	I had mood swings	0	1	2	3	4	5	6	7	8	9	10	
8	I felt depressed	0	1	2	3	4	5	6	7	8	9	10	
9	I was easily irritated	0	1	2	3	4	5	6	7	8	9	10	
10	I had been imagining being stoned	0	1	2	3	4	5	6	7	8	9	10	
11	I felt restless	0	1	2	3	4	5	6	7	8	9	10	
12	I woke up early	0	1	2	3	4	5	6	7	8	9	10	
13	I had a stomach ache	0	1	2	3	4	5	6	7	8	9	10	
14	I had nightmares and/or strange dreams	0	1	2	3	4	5	6	7	8	9	10	
15	Life seemed like an uphill struggle	0	1	2	3	4	5	6	7	8	9	10	
16	I woke up sweating at night	0	1	2	3	4	5	6	7	8	9	10	
17	I had trouble getting to sleep at night	0	1	2	3	4	5	6	7	8	9	10	
18	I felt physically tense	0	1	2	3	4	5	6	7	8	9	10	
19	I had hot flashes	0	1	2	3	4	5	6	7	8	9	10	

(Allsop 2011, PLoS One; NIDA)

Cannabis Use Disorder

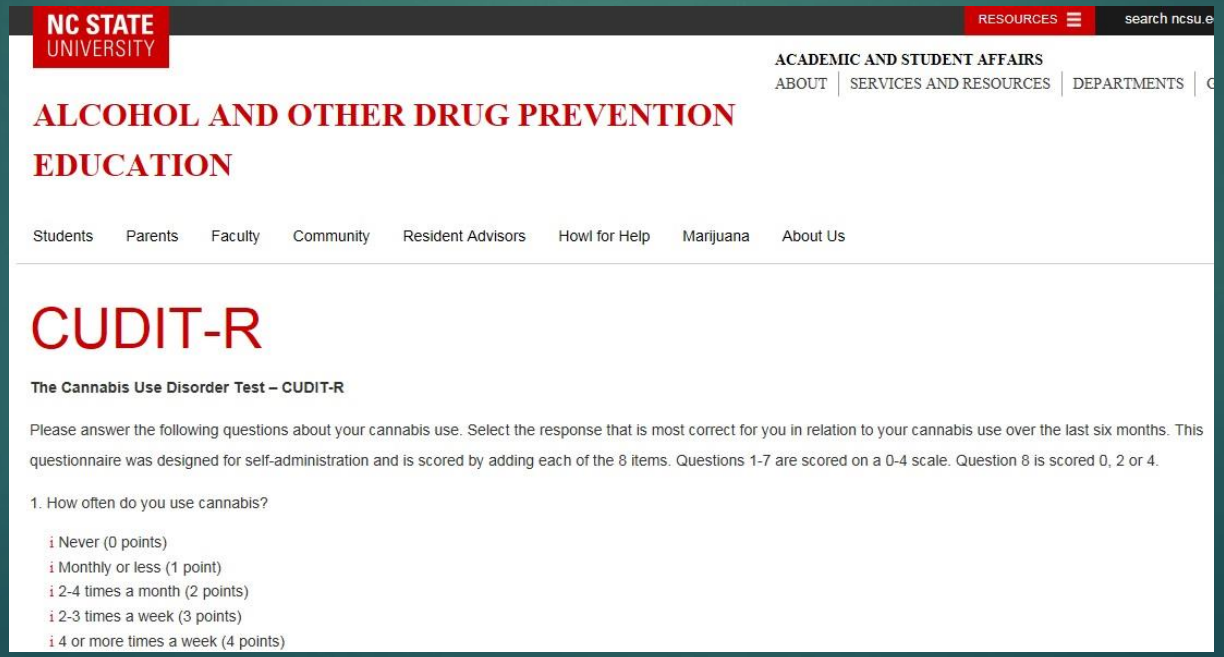
Two within 12 months:

- **Larger amounts, longer than intended**
- Persistent/unsuccessful cut down
- **A great deal of time spent**
- Cravings
- **Failure at major obligations**
- Persistent social/interpersonal impairment.
- Important activities reduced
- Recurrent use in hazardous situations
- **Use despite consequences**
- Tolerance
- Withdrawal

(DSM 5)

CUDIT-R

- Eight questions, 0-4 points each.
- Scores ≥ 8 = hazardous cannabis use.
- Scores ≥ 12 = possible CUD, speak with expert.



(NIDA/NC State Univ.)

Use to Addiction

All users → 9% addicted.

Adolescent users → 17% addicted.

Daily users → 25-50% addicted.

(NIDA Drug Facts 2012)

Case: TJ

Travelled to Iowa

Five days after cessation:

- Anxiety/outbursts
- Insomnia
- Tremors
- Insomnia
- PTSD symptoms/isolation → home

Treatment: Pharmacology

- Mason BJ 2012: RCT, n=50
  - Gabapentin 1200mg daily vs Placebo
  - Gabapentin = less +UDS, decreased w/d
- Gray KM 2012: RCT, n=116 adolescents
  - NAC 1200mg BID vs Placebo
  - NAC = more negative UDS

(Mason 2012, Gray 2012)

Treatment: Pharmacology

- Levin FR 2011: RCT, n=156,
  - Dronabinol 20mg BID vs Placebo
  - Dronabinol = higher retention, decreased w/d
- Allsop DJ 2014: RCT, n=51
  - Nabiximols (~80mg:80mg TCH:CBD) vs Placebo
  - Nabiximols = higher retention, decreased w/d

(Levin 2011, Allsop 2014)

Treatment: Behavioral

No one best modality, good evidence for:

- Cognitive Behavioral Therapy
- Motivational interviewing
- + Contingency Management
- Group therapy

(DuPont 2014, UpToDate)

Case: TJ- Outcome

"I don't want to stop. It's a good treatment for my PTSD. But we can keep an eye on it."

"Medical" Marijuana

Psychiatric:

- ✓ APA 2013: No current psychiatric indications, but more study warranted

Non-psychiatric:

- ✓ Nausea, vomiting related to chemo
- ✓ Anorexia/Wasting related to HIV

(APA 2013; Abramowicz 2017 JAMA)

“Medical” Marijuana

- Epilepsy
  - Early evidence for childhood, rx-resistant epilepsy
  - Insufficient evidence for other seizure d/o
- Specific pain syndromes
  - Chronic pain: 6 studies, n =325
  - Neuropathic pain: 6 studies, n = 396
- Spasticity from Multiple Sclerosis
  - Twelve studies, n=1600

(Abramowicz 2017 JAMA ; Hill 2015 JAMA)


LET'S GET IT RIGHT, CALIFORNIA:
Adult Use of Marijuana Act
Join the AUMA coalition to pass the consensus statewide ballot measure to control, regulate and tax adult use of marijuana while protecting kids.
Your Email Address
Zip Code
SUBMIT

Cannabis Question 1

FDA-approved indications include:

1. Insomnia related to PTSD
2. Glaucoma
3. Seizure disorder
4. N/V 2/2 to chemo, wasting related to HIV
5. Chronic pain/spasticity 2/2 multiple sclerosis

Cannabis Question 1

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Cannabis Question 2

Past year use is highest in:

1. Age 12-17
2. Age 18-25
3. Age 26-35
4. Age 36-45

Cannabis Question 2

Past year use is highest in:

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Cannabis Question 3

Risk of use disorder shown to be associated with:

1. Parental attitudes towards use
2. Early onset (adolescent) use
3. Route of administration
4. Regular/daily use

Cannabis Question 3

Risk of use disorder shown to be associated with:

1. Parental attitudes towards use
2. Early onset (adolescent) use
3. Route of administration
4. Regular/daily use

Take home points

- Increasing prevalence with legalization
- Risky for adolescent brain
- High rates of comorbidity
- THC, CBD, other compounds
- Intoxication, withdrawal, use disorder
- Early use, daily use → poorer outcomes
- Some medical, no psychiatric indications
- Legalization → adolescent protection? Study?

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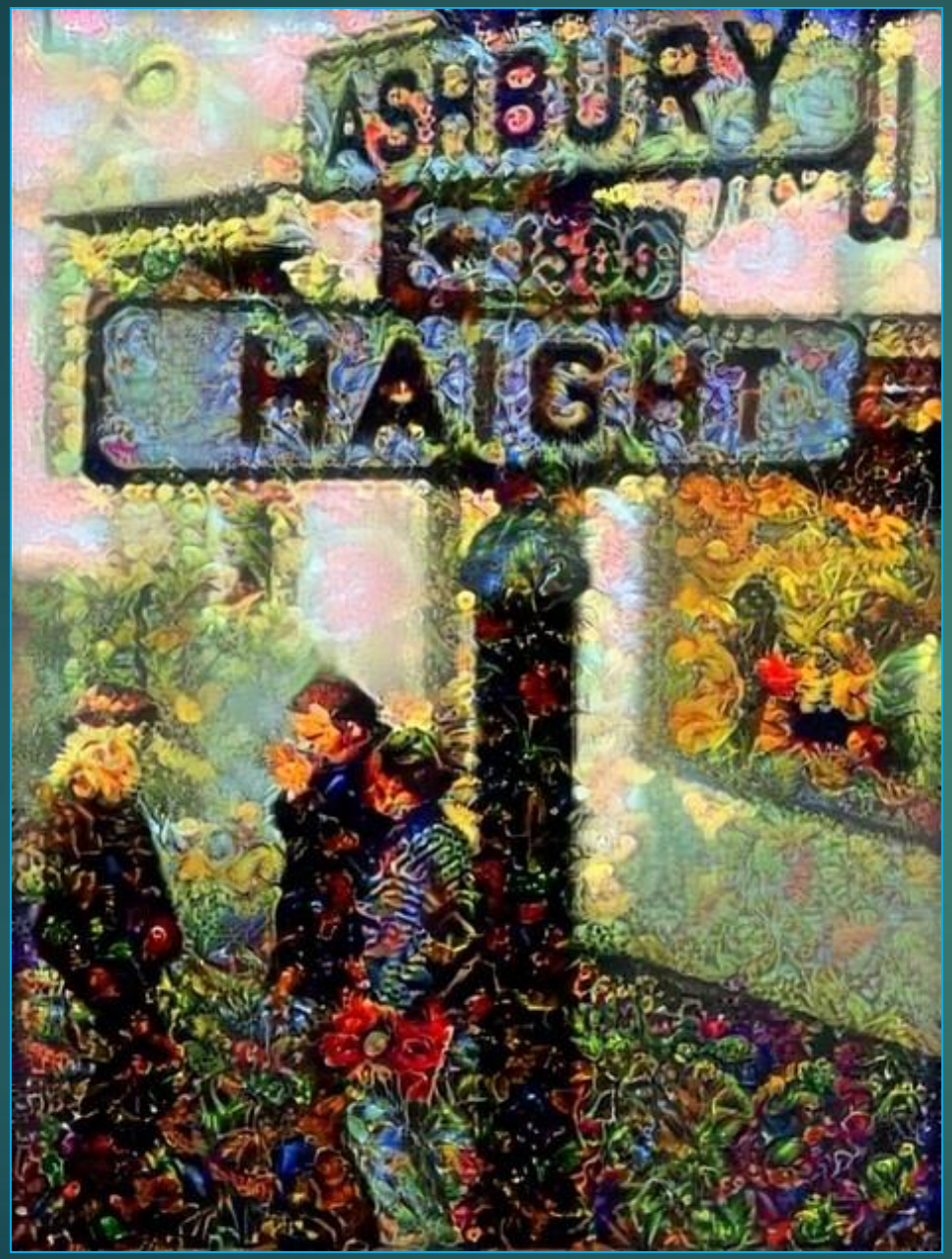

Thank You!

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