

Cannabis Workshop: Changing Landscape of Marijuana (Cannabis): What's Real, What's Not???????

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ATTC Conference Workshop

Lebanon, NH

July 20, 2016



ADHERE: Addiction and Health Research
GEISEL SCHOOL OF MEDICINE



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Disclosures

Funded by *National Institute on Drug Abuse* -
NIH has supported my research and conference
attendance for about 25 yrs

Copy of Slides, Articles, or Other:

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Learning Objectives

1. Describe and discuss the potential impact of changes in cannabis laws and regulations
2. Describe the limitations of the evidence for cannabis as a therapeutic substance
3. Describe the primary concerns related to adolescents' use of cannabis, and how the changing landscape interacts with these issues

- THINK HARD ABOUT THESE ISSUES -

DO YOU THINK...

- Cannabis has addictive potential?
- Cannabis withdrawal is clinically important?
- Quitting Cannabis is relatively easy?

- Cannabis adversely impacts learning?
- Cannabis adversely impacts motivation?
- Cannabis adversely impacts decision-making?

- Cannabis has benefit for ADHD, PTSD, Anxiety?
- Cannabis has benefit for Epilepsy?
- Cannabis has therapeutic benefit for Pain?
- Cannabis use increases risk of psychosis?

DO YOU THINK ...

- Vaping is a safe way to use Cannabis?
- Eating is a safe way to use Cannabis?
- Cannabis is as dangerous as Alcohol?
- We should legalize Cannabis?
 - Medical? Recreational? Just One, Both?
- 18 year olds should be able to use Cannabis?

Reefer Madness 2015

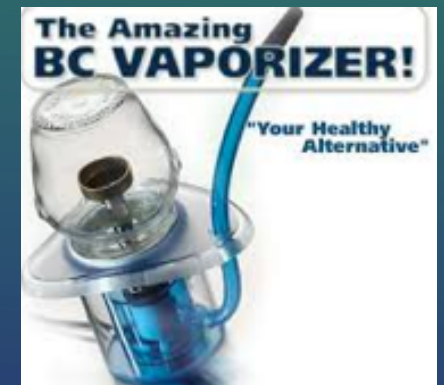
Cannabis Products: Smoking / Vaping



Reefer Madness: 2015 Edibles



Reefer Madness: 2015 Devices



Reefer Madness 2015: The Market



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Reefer Madness 2015: The Market



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A collage of images related to cannabis cooking, including a bowl of brownie batter, a bowl of brownies, a cannabis plant, a cup of coffee, a pizza, and a bowl of food. In the center is a black box with the text "WAKE AND BAKE a cookbook". A price tag in the bottom right corner says "\$24.99".

Wake & Bake: a cookbook

Are the Products What They Appear?

Vandrey et al. (2015)

- **Edible cannabis products (N=75) purchased from medical dispensaries**
- **3 quasi-randomly selected stores in San Francisco, Los Angeles, and Seattle**
- **State-approved patients given budget of \$400 to purchase variety of products**

	Accurate	Under	Over
#, % Products	12 (17%)	17(23%)	45 (60%)
THC, mg			
- label	15 - 200	20 - 1000	2 - 325
- actual	15 - 183	34 - 1246	<1 - 267
Discrepancy (Mean, SD) (Max)	-3 (4) 9	28 (13) 55	- 47 (29) -99



Current Marijuana “Laws”

- Legal “Medical” Marijuana: 24 States, plus Washington, D.C.
- At least 3 States have Pending legislation
- 5 States have legalized recreational use of cannabis
- Federal Status: **ILLEGAL**



Medical Marijuana Laws (USA)

“chaos”

- Fees to get “approval”: Range: \$15-\$200
- Reciprocal approvals with other States: n=6
- Minnesota and New York’s rules do not allow smoking of cannabis
- Allow dispensaries (n~15)
- Possession Limits Vary Tremendously:
 - 1oz – 24oz (n=19 states)
 - 30-60 day supply (n=5 states)
 - plants: (mature, immature, seedlings?)
 - Most States discuss plants and ounces, but don’t mention oils, wax, shatter, or even edibles
 - No mention of potency

Approved Medical Conditions across States

- Cachexia, cancer, chronic pain, epilepsy and other disorders characterized by seizures, glaucoma, HIV or AIDS, multiple sclerosis and other disorders characterized by muscle spasticity, and nausea, Hepatitis C, ALS, Crohn's disease, Alzheimer's disease, anorexia, arthritis, migraine, Parkinson's disease, **posttraumatic stress disorder**, decompensated cirrhosis, muscular dystrophy, severe fibromyalgia, spinal cord disease (including but not limited to arachnoiditis), Tarlov cysts, hydromyelia syringomyelia, Rheumatoid arthritis, fibrous dysplasia, spinal cord injury, traumatic brain injury and post concussion syndrome, Arnold-Chiari malformation and Syringomelia, Spinocerebellar Ataxia (SCA), Parkinson's Disease, **Tourette Syndrome**, Myoclonus, Dystonia, Reflex Sympathetic Dystrophy, RSD (Complex Regional Pain Syndromes Type I), Causalgia, CRPS (Complex Regional Pain Syndrome Type II), Neurofibromatosis, Chronic inflammatory Demyelinating Polyneuropathy, Chronic Inflammatory Demyelinating Polyneuropathy, Sjogren's Syndrome, Lupus, Interstitial Cystitis, Myasthenia Gravis, Hydrocephalus, nail-patella syndrome or residual limb pain; terminal illness with a life expectancy of under one year, **one or more injuries that significantly interferes with daily activities as documented by the patient's provider**, Huntington's disease

REVIEW

Open Access

Narrative review of the safety and efficacy of marijuana for the treatment of commonly state-approved medical and psychiatric disorders

Katherine A Belendiuk¹, Lisa L Baldini² and Marcel O Bonn-Miller^{3,4,5*}

Addiction Science & Clinical Practice (2015)

www.ncbi.nlm.nih.gov/pubmed/25896576

Belendiuk et al., 2015

Common conditions shared by > 80% of MML states:

- Alzheimer's disease
- Cachexia/wasting synd.
- Crohn's disease
- Glaucoma,
- HIV/AIDS,
- Severe & chronic pain- severe nausea.
- amyotrophic lateral sclerosis
- cancer
- epilepsy and seizures
- Hepatitis C
- MS / muscle spasticity
- **Post-traumatic stress disorder (PTSD)**

*... for the majority of these conditions, there is insufficient evidence to support the recommendation of medical marijuana at this time

California Society of Addiction Medicine

“Medical marijuana” is a flawed concept for 3 reasons:

A) administering any medication via drawing hot smoke into the lungs is inherently unhealthy;

B) although use of vaporizers, sprays, and tinctures solves problems inherent in smoking, treatment of illness without standardized dose or content of the medication remains a safety issue;

C) if the public wants to legalize marijuana, there is no reason to force physicians to be gatekeepers in a manner that enables liberal access to marijuana but generally fails to uphold accepted standards of practice for recommending a potentially addicting medication.

Challenges and Needs

Cannabis studied in context of illicit not medical use

Cannabinoids more so than cannabis studied

Highly variable plant(s) over 100 “active” compounds

Education needed for clinicians and patients

Data needed to determine effects, side-effects & risks

Seizures / Epilepsy

Animal studies

- anticonvulsant effects and reduce seizure-related mortality
- lower threshold for seizures; withdrawal increases convulsions

Survey Studies

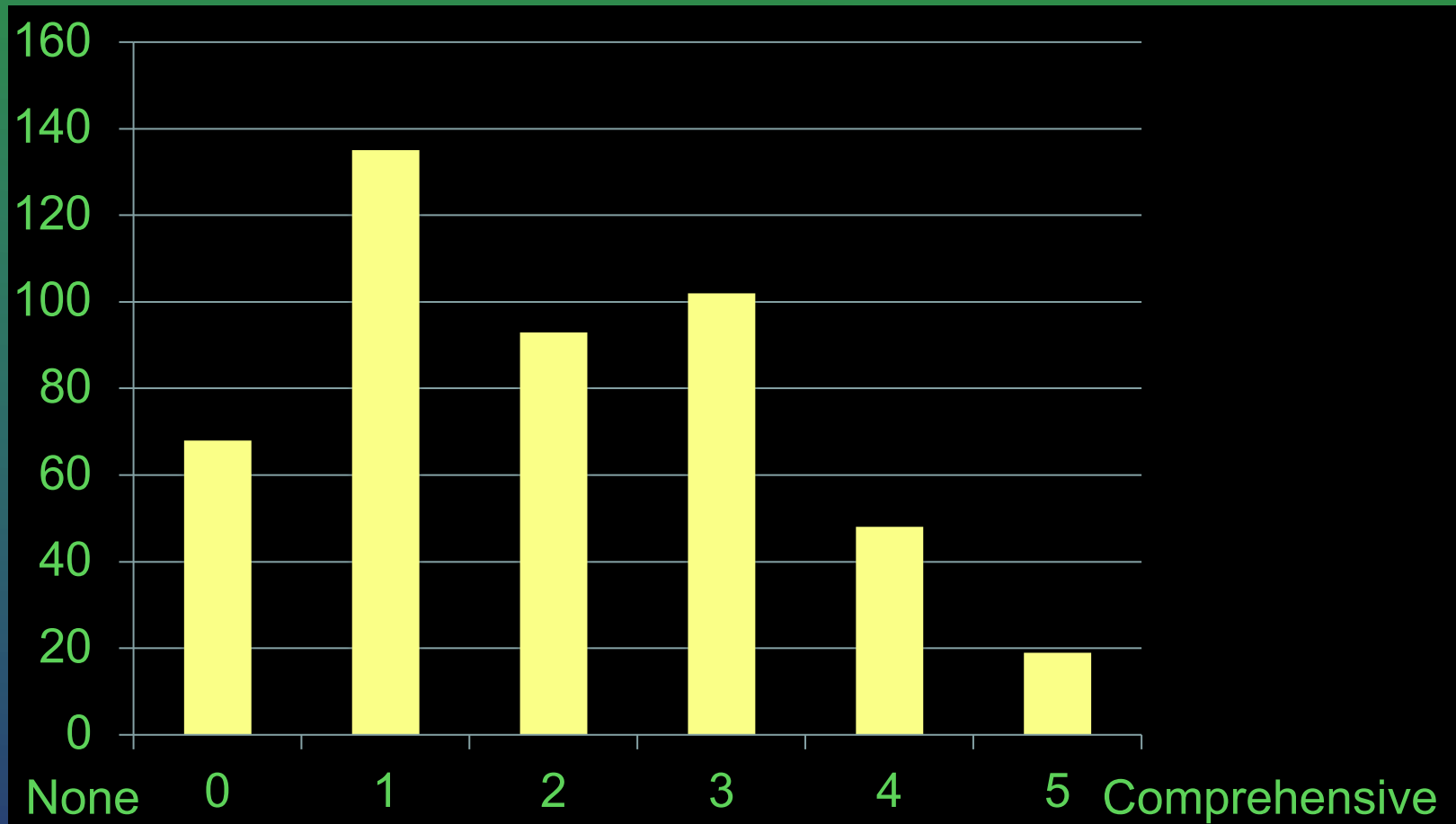
- 16-21 % of patients with epilepsy smoke cannabis
- some report positive effects and belief that it is therapeutic
- others reporting increased seizure frequency and intensity

RCTs (total of 48 patients) Cochrane Review (2014)

- only assess cannabidiol / no follow-up longer than 6 months
- reduction in seizure frequency (2 studies)
- no effect compared to placebo (1 study)

NH Medical Society Clinical Cannabis Survey

How would you rate your knowledge of marijuana/cannabis effects?



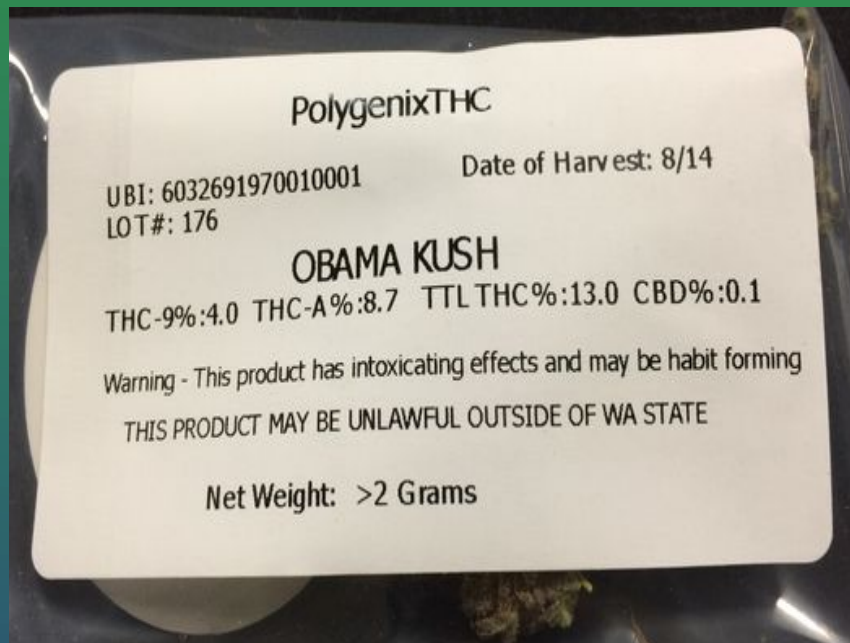
(Savage, 2014) www.nhms.org/content/reports-strategic-plans-surveys

Additional Suggested Reading:

Medical Marijuana: Review of the Science and Implications for Developmental-Behavioral Pediatric Practice

Hadland, SE, Knight, JR, Harris, SK. J Dev Behav Pediatr 36:115–123, (2015)

Recreational MJ Laws



Better / More Appropriate Alternative than
“Medical” Marijuana Legalization??



Changing World of Cannabis

What Will Legal / Regulatory Changes Bring

Potential for Positive and Negative Impact

- Higher Potency / New Products / New Delivery Systems
- Impact on Use, Attitudes, Perceived Risk
- Impact on Health, Public Safety
- **Addiction / Problematic Use**
- Science: Understanding of Cannabis

Impact on Addiction Science

**Windfall! Jackpot! Gold Mine!
Opportunities Abound!**

Science needed at all levels

- Define Safe Use
- Measure Intoxication
- Test Drug Interactions
- Prevention & Intervention
- Test Medical Applications
- Marketing / Labeling
- Dosing/Potency
- Methods of Admin.
- Reduction
- Product Content

How Science and Scientific Reporting Works



Little More About...

- Potency
- Methods of Administration
- Youth Consequences

Potency



Potency / Dose

Basic Behavioral and Clinical Pharmacology

- Potency (Dose) matters!

With Cannabis it's all about THC dose ...or is it?

- Cannabidiol?
- Over 100 compounds; over 70 phytocannabinoids

THC Potency

Lab studies have not gone **above 8% THC**, and only one study has gone that high.

- confiscated cannabis **averaged 12.8%** in 2012

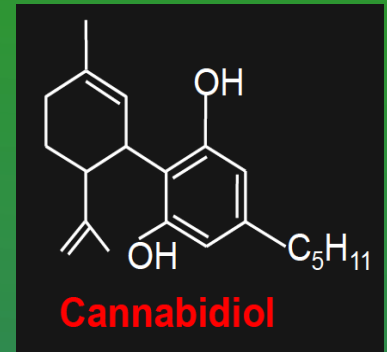
Existing data on lab and epidemiological studies capture results from use of much lower THC levels than now used

Need to learn more about higher % THC products!

Unlike alcohol, we do not have current norms on a standard dose (drink) and how much you can use before becoming “intoxicated”, or in medical danger

Unlike alcohol – different methods of administration

Cannabidiol (CBD)



Cannabis plants have varying amounts of CBD

Suggestive data that it *moderates effects of THC*

- Potential as an anxiolytic?
- Potential as an antipsychotic?
- Marketed (like marijuana) as a medication for multiple problems: e.g., epilepsy, SUDs!
- 1:1 ratio with THC in Sativex (approved medication)

Recent lab study suggests effects are not so clear?

- appeared almost inert when studied carefully in experienced cannabis users

Schubart et al. (2013); Neisink et al. (2013) Haney et al., (2015)



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QUIZ

Report in Medscape on an ongoing study of *cannabidiol* for children with epilepsy

What is wrong with this sentence?

“The US Food and Drug Administration (FDA) has given approval for studies to begin on a medicinal form of marijuana for the treatment of intractable epilepsy in children.”

Summary: Potency

- Cannabis is not just THC
- Need data on higher % THC
- Need data on Cannabidiol and THC/Cannabidiol
- Cannabis combination products ----
- What about with synthetic cannabinoids?
- How dose interacts with method of use

Route of Administration

Smoking vs. **Vaping vs. Eating**

Basic behavioral and clinical pharmacology route influences effects and thus interacts with with dose

- onset, timecourse, euphoric effects, adverse effects

Vaping Weed: A Guide For The Health-Conscious Pothead ...

www.buzzfeed.com/catferguson/vaping-weed ▾

May 28, 2015 - With the stigma of pot on the decline, people are increasingly turning to **vaping** to get high. Here's what you should know before you...

Vaping vs. smoking pot: What's safer, and is high the same?

www.thecannabist.co/2015/05/14/vaping-vs...vaping-marijuana/34906/ ▾

May 14, 2015 - Of the many ways one could consume **cannabis** — smoke it, eat it, **vape** it, dab it — much debate swirls around **vaping vs. smoking marijuana** ...

Why vaping is the dumbest thing ever - The Cannabist

www.thecannabist.co/2014/11/25/vaping-dumbest-thing-ever/23719/ ▾

Nov 25, 2014 - A drive around Denver, where recreational **cannabis** sales have ... An increasing number of **vaping**-focused stores compete for money and ...

Why vaping is the dumbest ... - Product reviews - Liquid pot

5 Marijuana Vaporizers Offering a Better, Healthier High

www.cheatsheet.com/.../5-marijuana-vaporizers-offering-a-better-healthi... ▾

Jun 25, 2015 - And as users began to swap out liquid nicotine for liquid pot, the rise of **marijuana vaping** has begun, too. The e-cigs, which traditionally are the ...

Vaping

“Vaping” is the slang term for the vaporization of substances (e.g., flavors, nicotine, or cannabis products) whereby liquid, oil, or plant material is heated to a temperature that releases an aerosolized mixture of water vapor and active ingredients (e.g., nicotine in e-cigs and THC in cannabis), which is then inhaled.

Avoids combustion of the substance and the inhaling of smoke, which contains carbon monoxide and other by-products of combustion.

Vaping: Knowns and Unknowns

Benefits

- Clear harm reduction impact with respect to respiratory / lungs / carcinogenic factors.
- Facilitate use of cannabis for medical purposes (titrate, no combustible smoke, etc.).

Concerns

- long-term effects of frequent vaping are unknown.
- may have a positive impact on cannabis initiation, problem development and maintenance?
 - better tasting, more efficient high, more discreet use, combined with flavors or nicotine, attractive packaging, part of an evolving vaping culture, perceived as safe

(Budney et al., 2015 *Addiction*)

Facebook Survey Study

(almost under review)

- Distributed to pro-cannabis interest groups

- NORML, Legalize Marijuana, Medical Marijuana

- Popular music associated with such groups


Liked / Interest marijuana

N= 2932



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You are invited to participate in a brief and anonymous marijuana use survey.



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Cannabis Use Characteristics

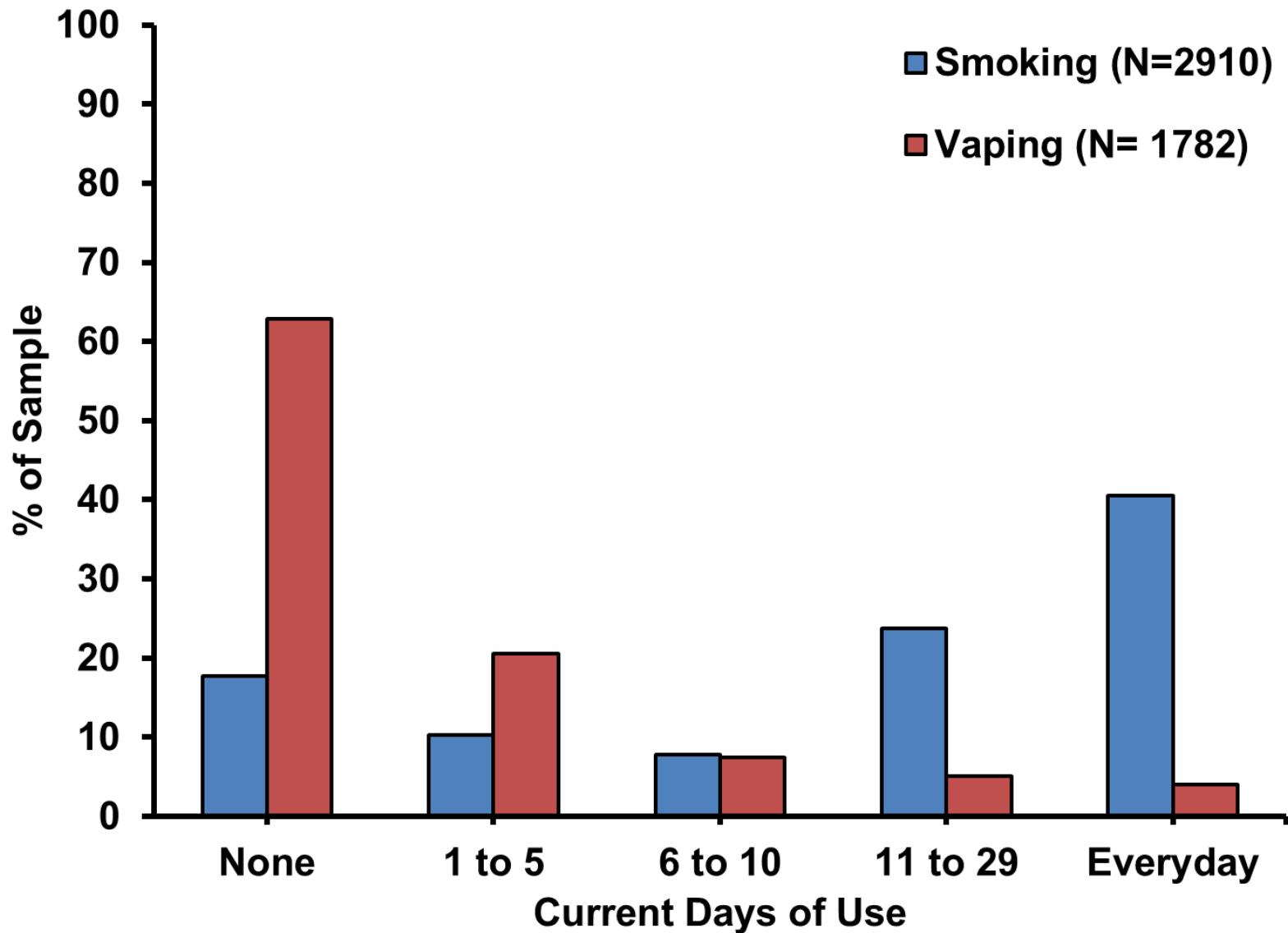
	% of Sample
Lifetime Prevalence	
Smoking	99.6%
Vaping	61.3%
Age of initiation	M (SD)
Smoking	15.6 (4.1)
Vaping	24.2 (12.2)

Daily cannabis smokers were more likely to report vaping compared to occasional smokers (73% vs. 41%, $p < .001$)

Reasons for vaping

- More safe for my health
- Better taste/less harsh
- Better effects
- Discreet
- Cool?

Current (past 30 days) Cannabis Use



High School (5 in CT): E-cigs and Cannabis Vaping

(Morean et al., 2015)

Lifetime Use (%)	Total n= 3847	E-cig Users n=1075	Cannabis Users n=1123	Dual Users n=724
e-cigs	27.9	----	64.5	----
cannabis	29.2	67.3	----	----
use e-cigs to vape	5.4	18.0	18.4	26.5

Differed by School and Age (younger more likely)

Youth Concerns: Vaping Culture

- FLAVORS, NICOTINE, CANNABIS, CAFFEINE
 - Earlier Initiation? Combine Products
 - Initiation by Youth at Lower Risk?
 - More frequent use?
 - More problematic use?
 - Health Concerns?



Edibles

- Onset much slower, eventually similar effects
 - “overdose” concerns
- Increase access and ease of use
- Discreet
- Reinforcing taste in addition to drug effect

Edibles: Concerns

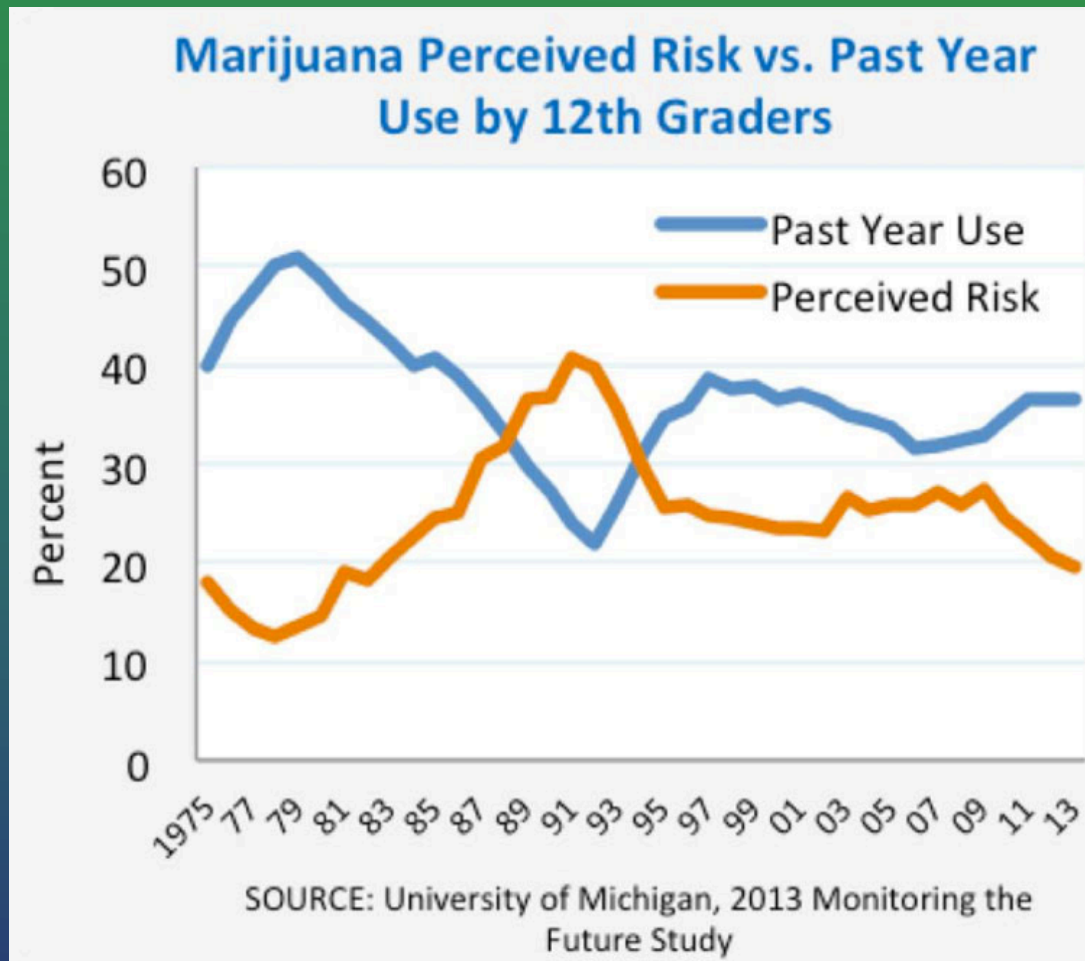
Labels related to dose and onset of effects?

- Why are all these cannabis products needed?
 - alcohol lollipops, alcohol in chocolate?
 - caffeine???
- What is their purpose.... Marketing to youth, easier to ingest, sell as much as possible?
- Child protective packaging?

“The unfortunate aspect of this (*cannabis*) arms race is that they’re finally turning the drug into everything the U.S. government once said it was....It used to be we could say the government exaggerated the threat of this ‘crazy weed,’ but these new potent strains (*and methods of use*) belie that.”

Robert *MacCoun*, behavioral scientist, marijuana policy expert U.C. Berkeley

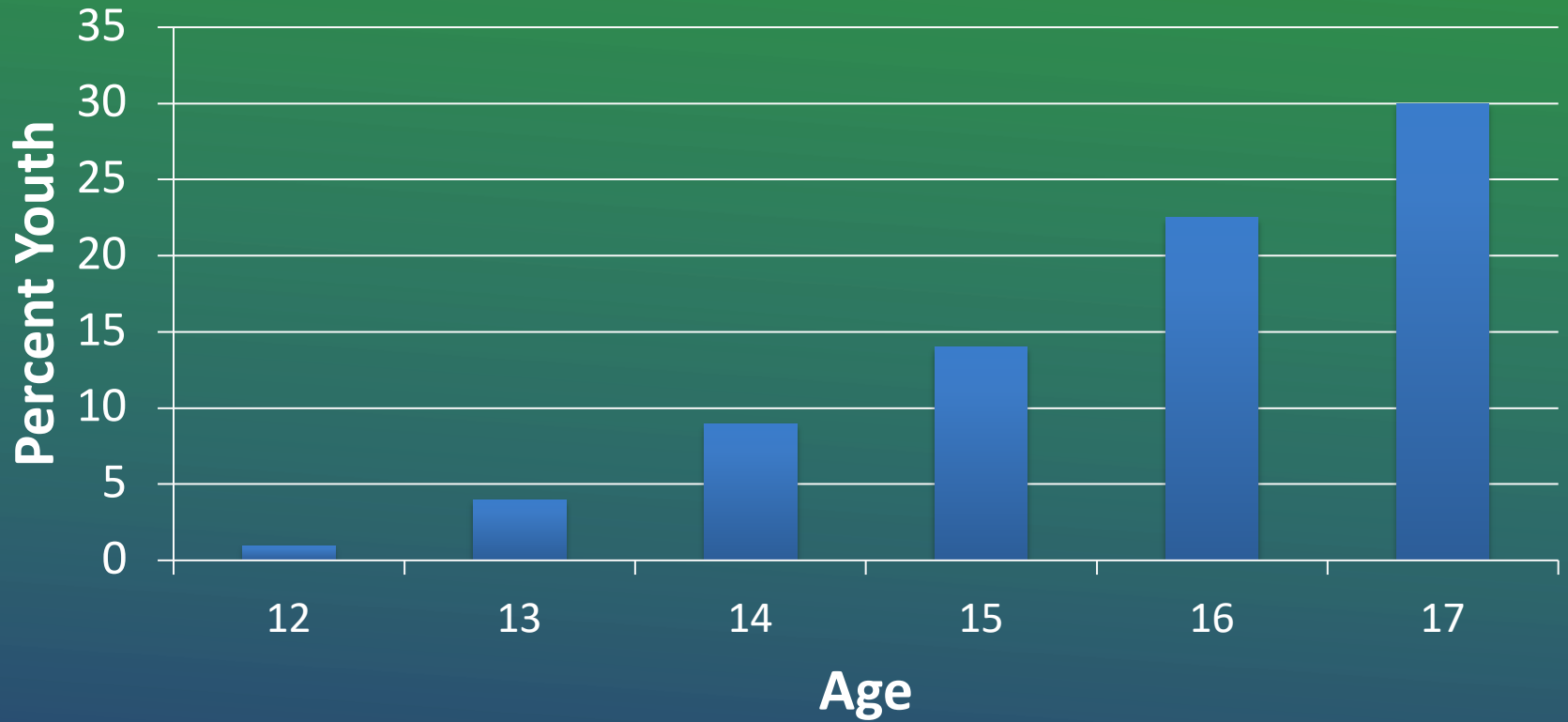
National Data: Risk – Use ?



Concerns about Youth Cannabis Use

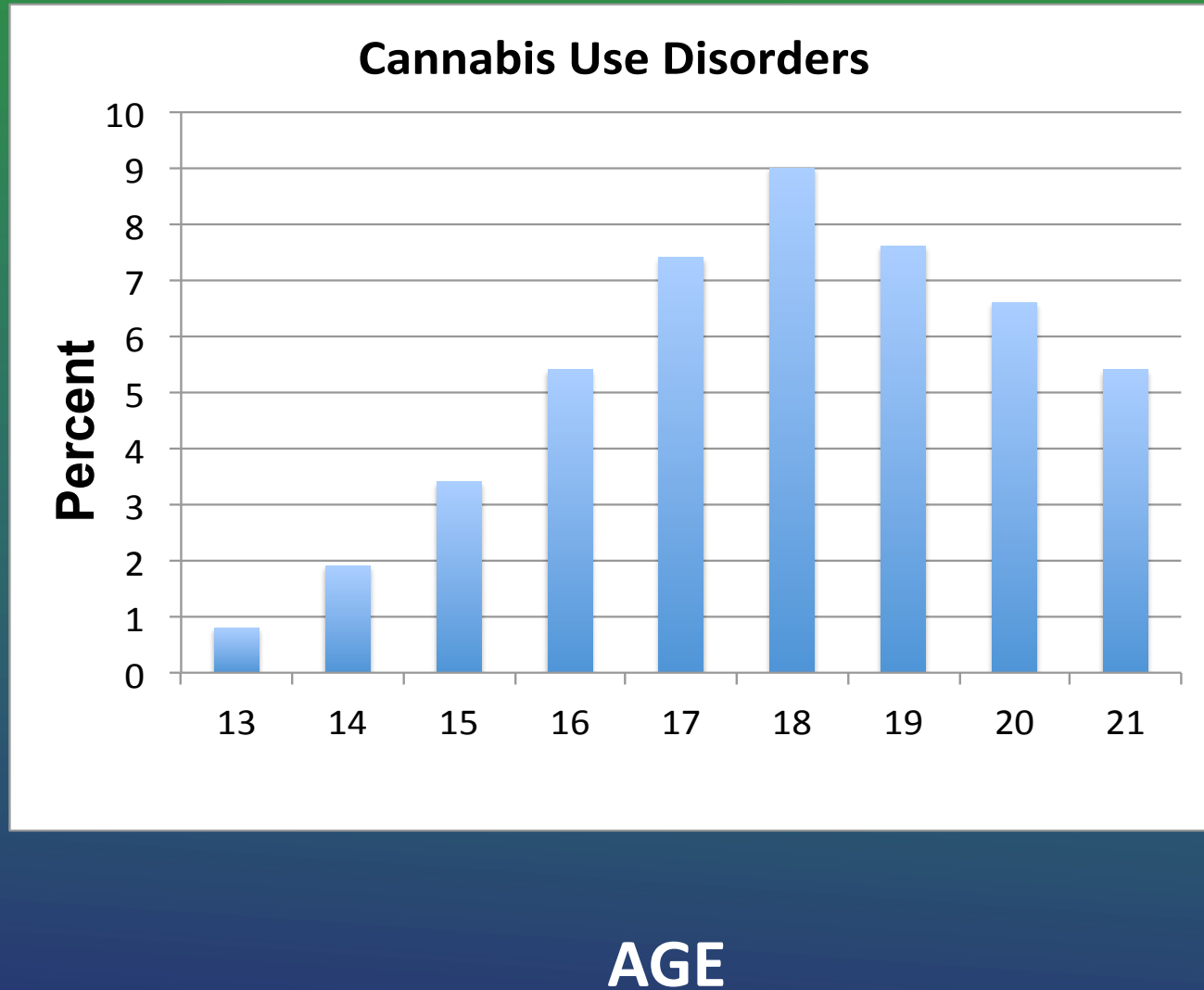
- Poor academic performance
- Interferes with brain development
- Increased risk of accidents
- Relationship problems
- Health/mental health problems
- Delinquent behavior
- High risk sexual behavior
- Gateway / Associated with use of Multiple Substances
- Addiction / Use Disorders / Problematic Use

Cannabis Use: Past Year



NHSDH 2012

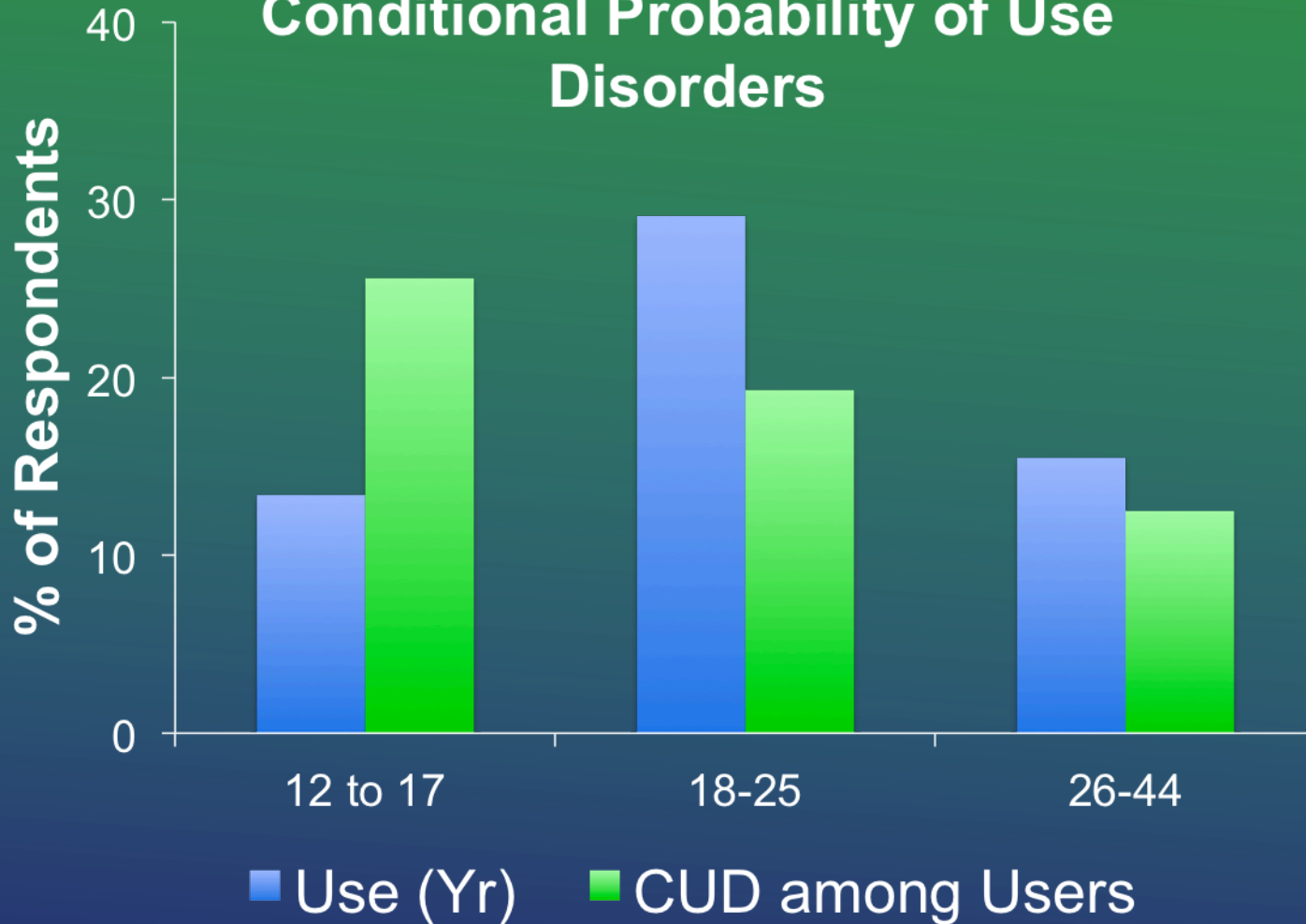
NSDUH 2012



NSDUH 2011

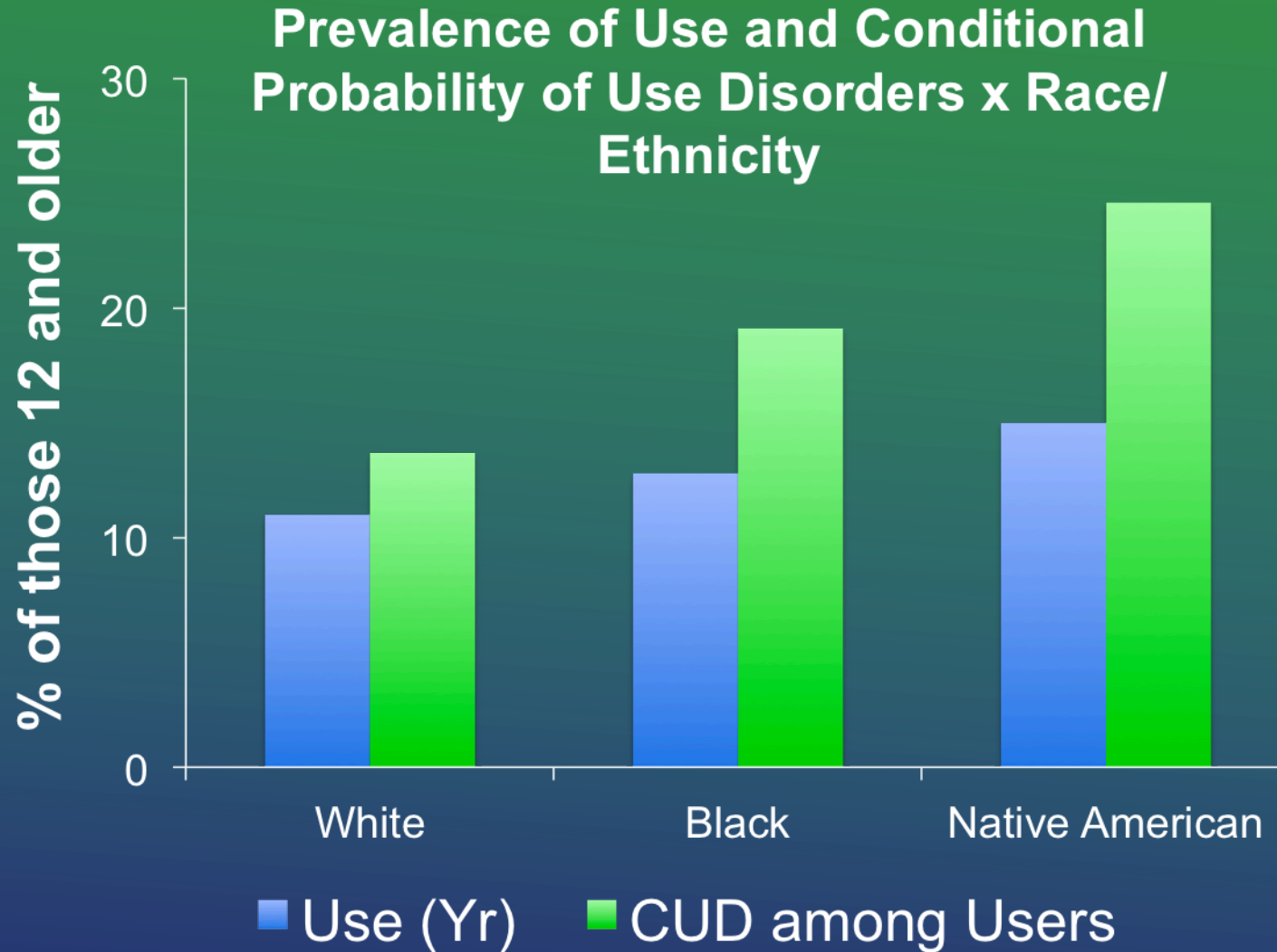
(Wu et al., 2013)

Prevalence of Cannabis Use and Conditional Probability of Use Disorders



NSDUH 2011

(Wu et al., 2013)



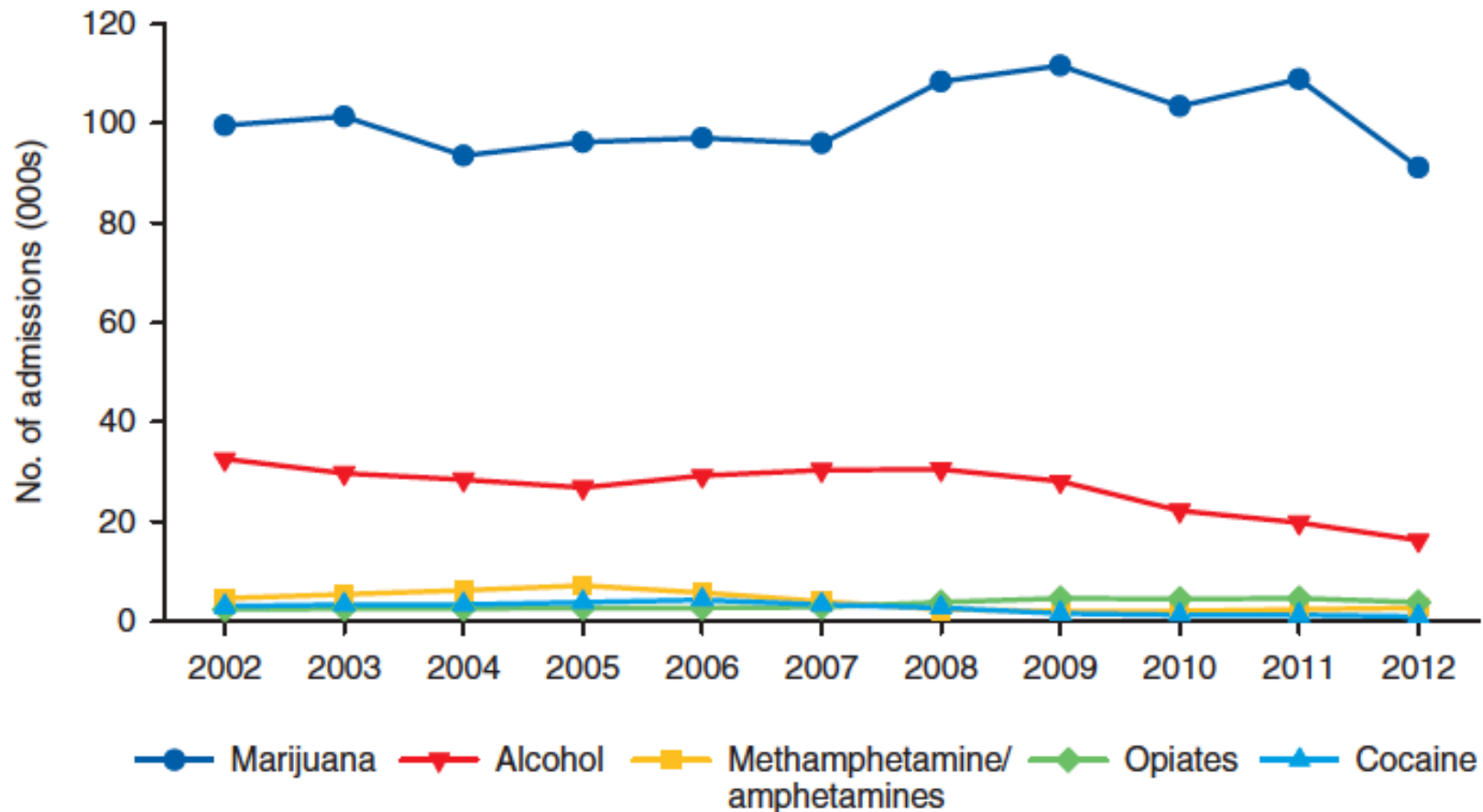
Epidemiology Take Homes

- Use and frequency are moving in an increasing direction, although not as clear for frequency
- Start paying attention to types of cannabis/cannabinoids and how they are administered
- Distinguish between use and problematic use
 - Examine full range of frequency
 - Look more carefully at more narrow age ranges
- Subgroups Differences (vulnerable populations)
 - Disadvantaged populations can least afford an increase in use/misuse

Adolescent Treatment Admissions

TEDS Data Set

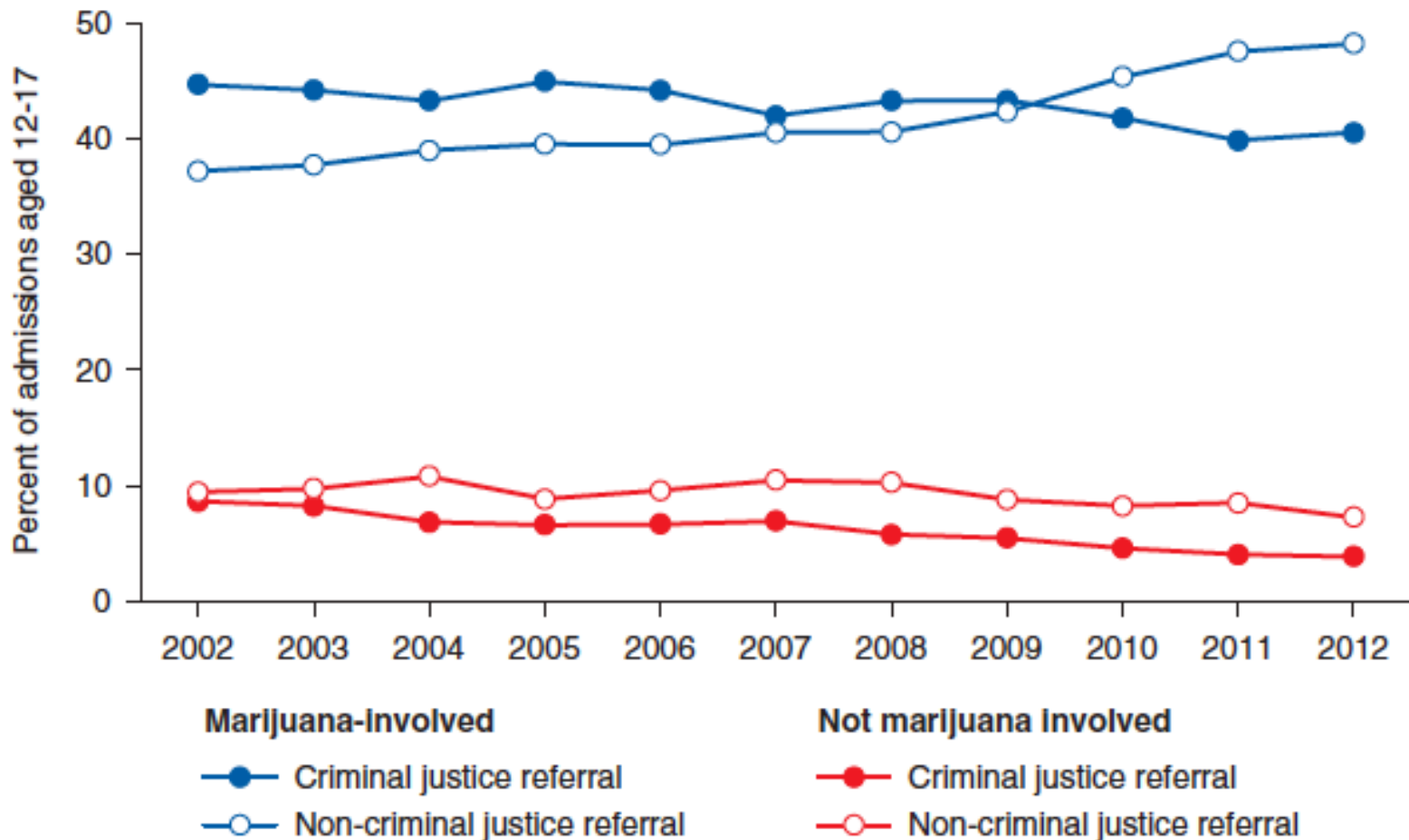
Figure 19. Adolescent admissions aged 12 to 17, by primary substance: 2002-2012



Admissions x Criminal Justice Involvement

TEDS Data Set

Figure 20. Adolescent admissions aged 12 to 17, by marijuana involvement and criminal justice/DUI source: 2002-2012



Health Services Take Home:

- Youth are using a substantial amount of substance use treatment services, most of which are related to problematic use of cannabis
- Legalization will not likely reduce this; may increase it?

Cannabis / Mental Illness: Positive Association

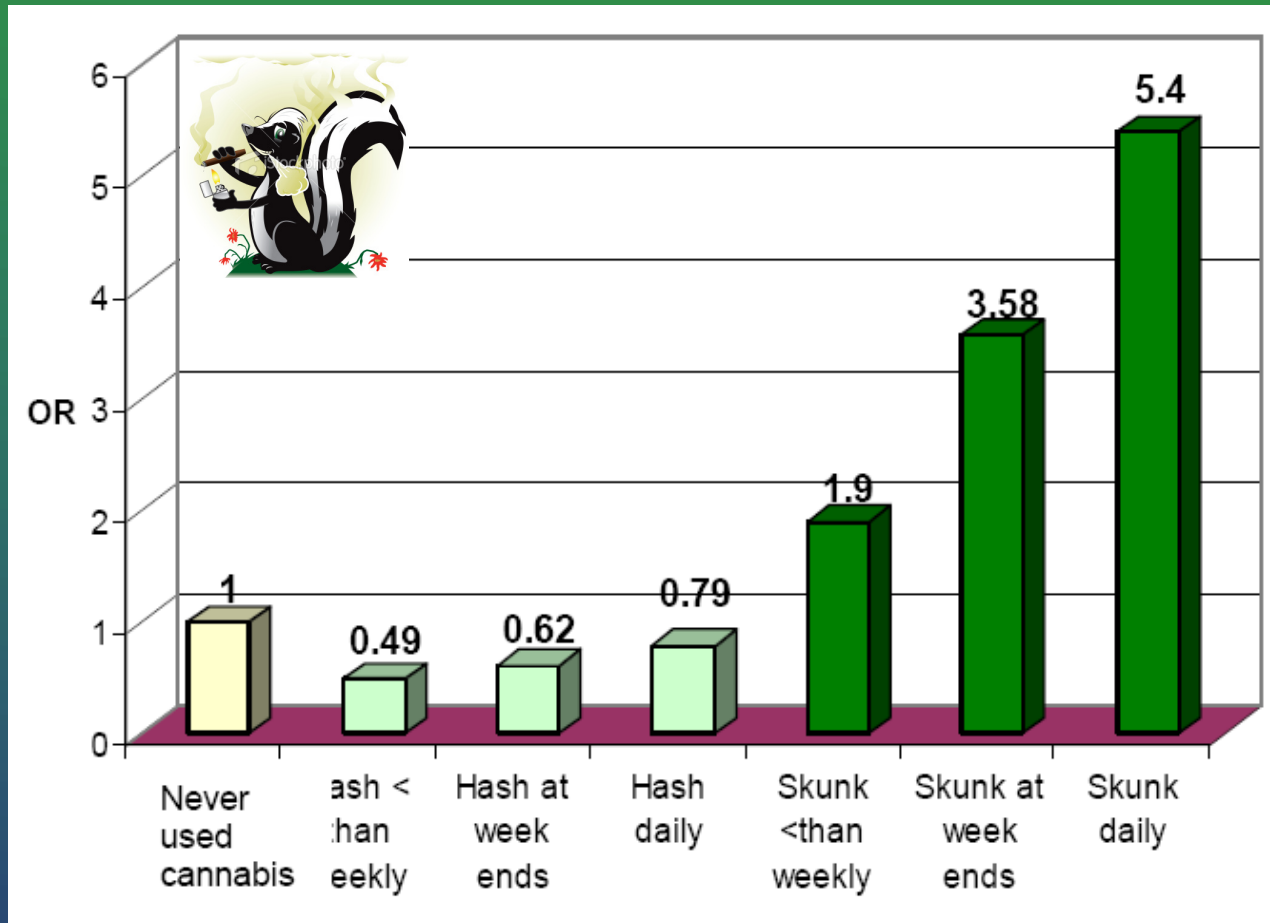
- Psychotic Disorders
- Affective Disorders
- Anxiety Disorders / PTSD
- ADHD

Causal Factor or Impact on Existing Illness?

Product of third variable

Risk of being a Psychotic Case

(OR adjusted for gender, age, ethnicity, Stimulants, level of Ed)



Frequent Use of High-Potency Cannabis May Drive the Increased Probability of Psychosis in Cannabis Users (Di Forti et al., 2014)

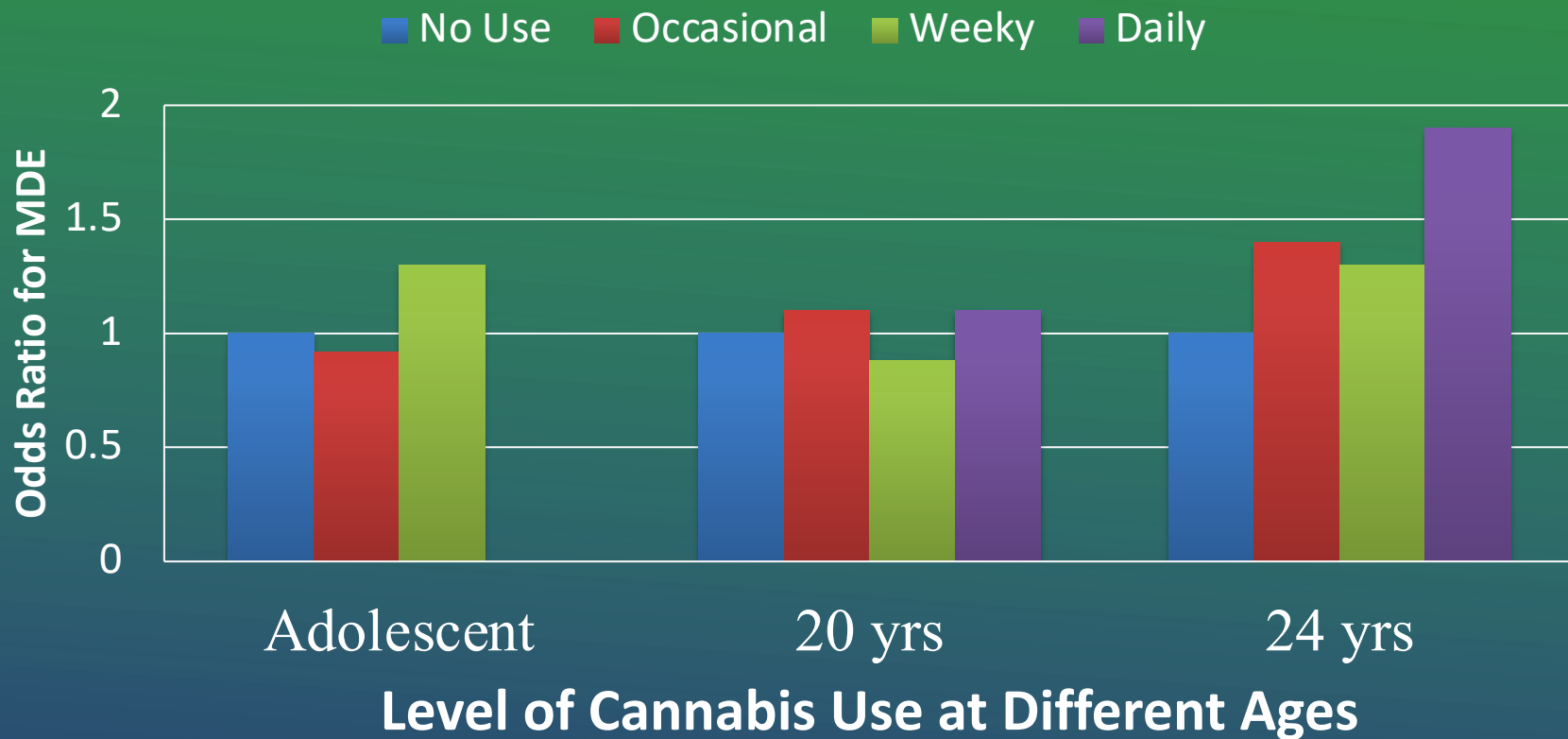
Suggested Reading:

Does Cannabis Cause, Exacerbate or Ameliorate
Psychiatric Disorders? An Over-simplified Debate
Discussed. M. Haney, A.E. Evins
Neuropsychopharmacology, August 2015

www.nature.com/npp/journal/vaop/naam/abs/npp2015251a.html

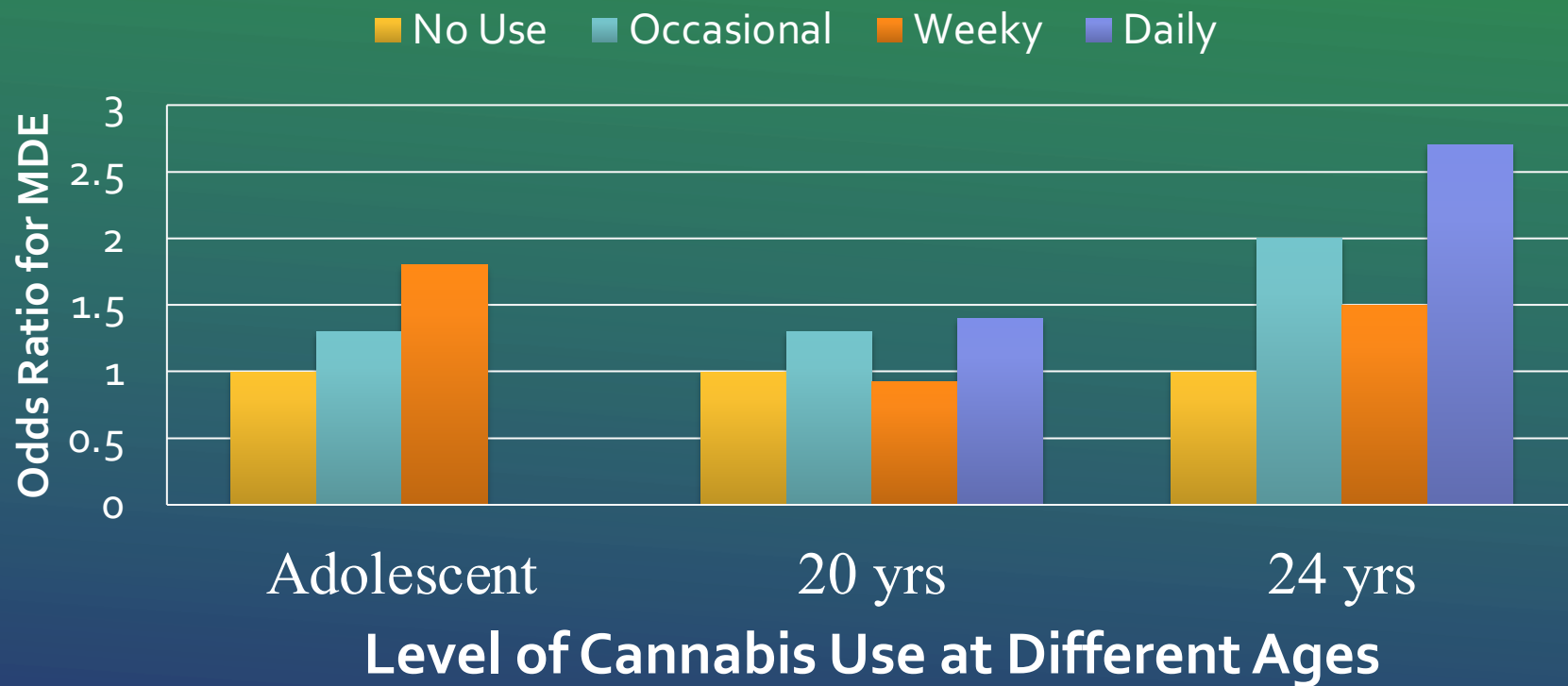
Australian Adolescent Health Cohort Study (n=1756)

Impact of Cannabis Use on MDE at Age 29



Australian Adolescent Health Cohort Study (n=1756)

Impact of Cannabis Use on Anxiety Disorder at Age 29



Cannabis and Mental Illness Summary

Cannabis use is associated with increased levels of mental illness; this relationship may be moderated by frequency of use and potency of the cannabis

Growing evidence that cannabis use may have causal impact on lowering of the age of onset of Psychotic Disorders; related to age of onset of cannabis use, frequency and potency.

* Probability of occurrence is “low” in low risk samples

Cannabis use can probably be considered a risk factor for poor outcomes in functioning across mental illnesses.

**Data do not support use of cannabis
to treat any type of mental illness**

Impact on Brain, Brain Development, Cognitive Functioning

SUGGESTED READINGS

Dare to delay? The impacts of adolescent alcohol and marijuana use onset on cognition, brain structure, and function. Lisdahl KM, Gilbert ER, Wright NE, et al. *Front Psychiatry*. 2013;4:53.

Medical Marijuana: Review of the Science and Implications for Developmental-Behavioral Pediatric Practice. Hadland, SE, Knight, JR, Harris, SK. *J Dev Behav Pediatr* 36:115–123, (2015)

The effects of regular cannabis use on neurocognition in adolescent and young adults. Lisdahl KM, Wright NE, Kirchner-Medina C, Maple KE, Shollenbarger S. *Curr Addict Rep*. 2014 1(2):144-156.

Regular Cannabis Use / Brain Summary

* Cannabis Use ~ abnormal brain structure/cognition

- Gray matter: Limbic (amygdala, hippocampus), reward (nucleus accumbens), cerebellum, parietal, PFC
- White matter: reduce integrity
- Cognitive: negative impact: IQ, verbal memory, psychomotor speed, complex attention, executive function (cognitive inhibition, decision-making)
 - small to medium effect sizes
 - *higher dose-exposed and early age onset ~ higher risk*

Limitations: Preexisting conditions, environment, genetics, sampling

Early Initiation = Bad

Table 1. Select Studies^a Demonstrating Changes in Cognition, Brain Structure, and Brain Function Associated with Cannabis Use in which Adolescent Onset Is Associated with Worsened Outcome

Reference	Cognitive	Brain Structure	Brain Function
Meier et al, 2012	↓ IQ		
Pope et al, 2003	↓ IQ		
Ehrenreich et al, 1999	↓ Attention		
Huestegge et al, 2002	↓ Visual search		
Fontes et al, 2011	↓ Executive functioning		
Solowij et al, 2012	↓ Executive functioning		
Churchwell et al, 2010		↓ Prefrontal cortex volume	
Gruber et al, 2011	↑ Impulsivity	↓ White matter integrity in prefrontal cortex	
Lopez-Larson et al, 2011		↓ Superior prefrontal cortex thickness	
Wilson et al, 2000		↓ Total gray matter, ↑ total white matter	
Becker et al, 2010a			↑ Left superior prefrontal cortex fMRI blood oxygen level dependent (BOLD) signal during working memory task
Gruber et al, 2012			↓ Anterior cingulate fMRI blood oxygen level dependent (BOLD) signal during inhibition task
Jager et al, 2010			↑ Prefrontal cortex MRI blood oxygen level dependent (BOLD) signal during novel stimuli presentation in working memory task

Prevention

- Prevention Messages??
 - Perceived Risk on the Decline -- Worrisome
 - Not as bad as alcohol (accidents, adverse events, etc.)
 - Putative “Medical” benefits are numerous
 - Vaping or Eating --- no respiratory issues

Some argue that maybe cannabis will replace or reduce alcohol consumption -- that would be a net benefit?

What Do We Tell Parents / Kids

- Communicate
- Clear Disapproval
- Not OK for teens; just like alcohol
- State the Concerns / Risks
- Does not matter if you used to do it or even if you currently use it
- Find a way to present risks / benefits information

Kushexpo.com



Irony is, as we move toward legalization cannabis appears to be on a trajectory towards becoming a class of substance with more potential for harm (enticing products including edibles, increased potency products, more efficient methods of delivery, and surely other modifications that will increase its allure).

Silver Lining

- stimulating thoughtful and important science and discourse related to cannabis and drug policy
- more objective, thoughtful contemplation of pros and cons

In the end, more rational policy and regulation...

One can only hope!

Take Home Messages

“The Times They are a Changing”

Science and Common Sense Policy is Needed Now
More than Ever

Educate yourself through traditional means:
read the scientific literature!

Thank you!!

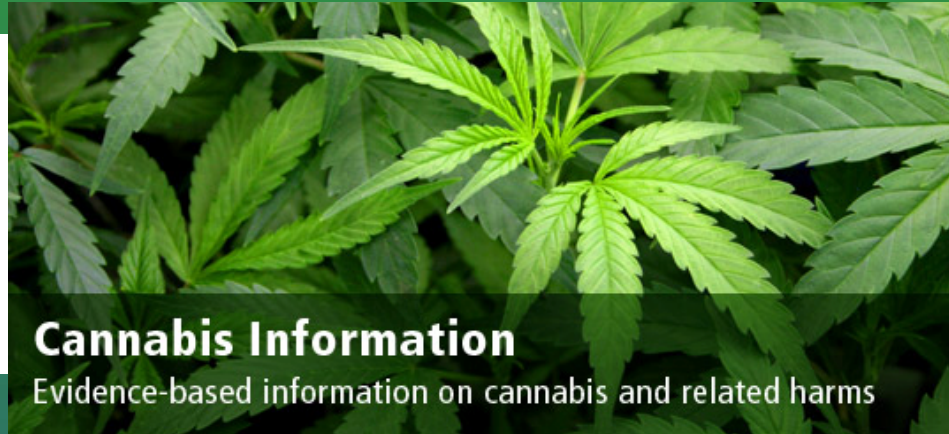
For your time and attention today!

To NIDA for funding my scientific endeavors

To my colleagues, trainees, and research staff, particularly:

Dustin Lee, Catherine Stanger, John Hughes, Ryan Vandrey
Jim Sargent, Ben Crosier, Jacob Borodosky, Mary Brunette, Gray
Norton, Samantha Auty, Jennifer Darsie, Lisa Marsch, Mark Milam,
Stanley See, Hao Yang, Bonita Bosnyat

ncpic.org.au



drugabuse.gov/drugs-abuse/marijuana

