Marijuana: The Information Gap

Medicine, Public Health, Profits, and What it All Means for Treatment Providers

Aaron Weiner, PhD

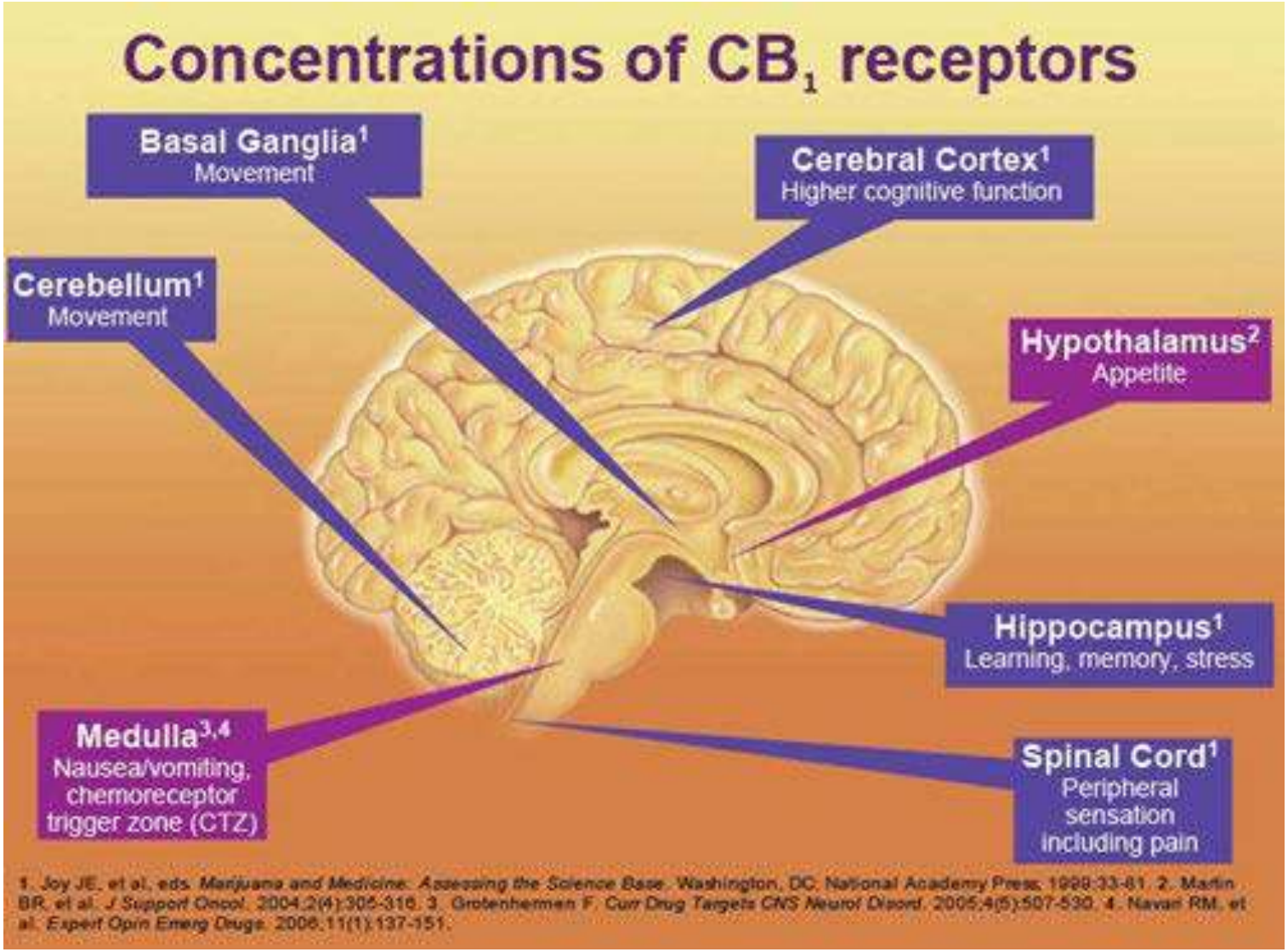
September 6, 2019

Aaron.Weiner@eehealth.org

What is marijuana?

- Plant with 500 chemical compounds, and 100 cannabinoids
- THC & CBD
- THC binds to CB1 receptors

Concentrations of CB_1 receptors



1. Joy JE, et al, eds. *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: National Academy Press; 1999:33-61. 2. Martin BR, et al. *J Support Oncol*. 2004;2(4):305-316. 3. Grotenhermen F. *Curr Drug Targets CNS Neurol Disord*. 2005;4(5):507-530. 4. Navari RM, et al. *Expert Opin Emerg Drugs*. 2006;11(1):137-151.

What is marijuana?

- Plant with 500 chemical compounds, and 100 cannabinoids
- THC & CBD
- THC binds to CB1 receptors
- Most-used substance behind alcohol & tobacco
- Number of routes of administration

(CDC, 2017)

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weedmap

LOL EDIBLES
CAP'N MUNCH
400 MG THC
LOL EDIBLES
Chronic Toast Crunch
400 MG THC
LOL EDIBLES
FROOTY LOOPYS
400 MG THC

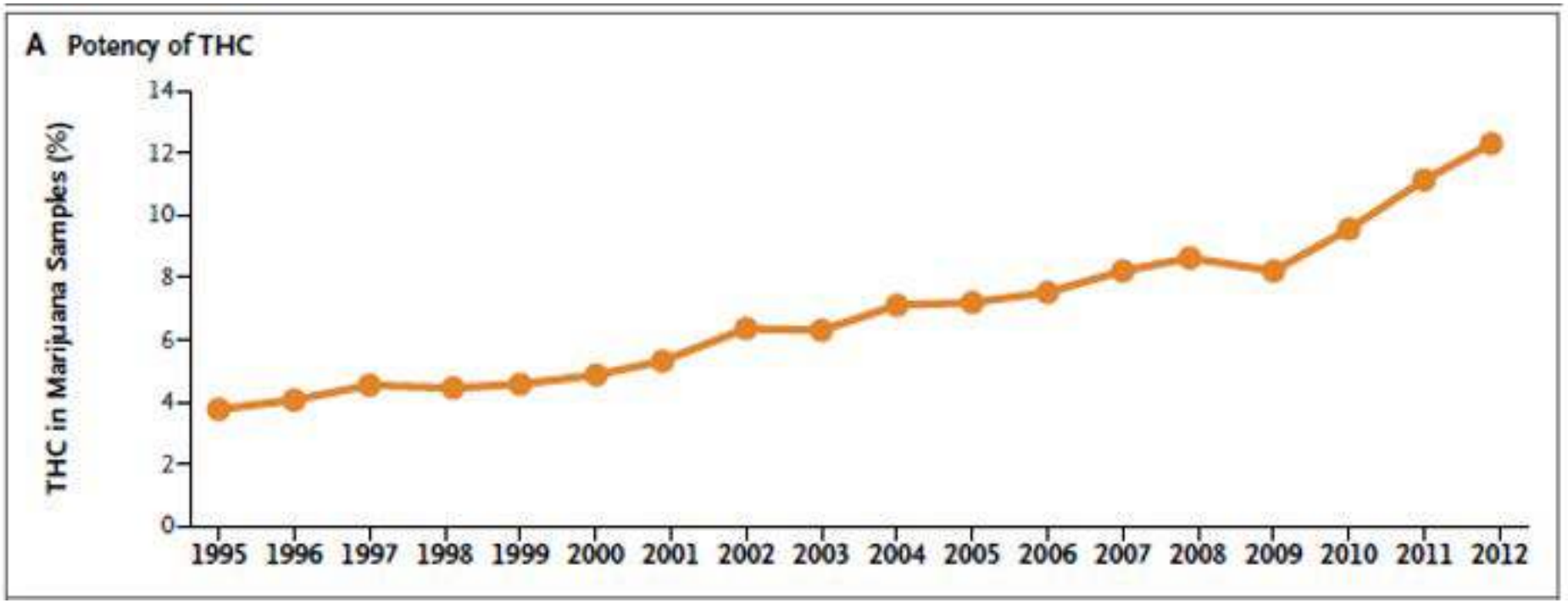
Rastaleers
Twixed
Munchy Way
Rasta Reese's
KeefKat
Puff-A-Mike Pattie
Buddahfinger
DouBIE PuPP OEO
Tri-Chrome CRUNCH

GANJAEATS
MAPLE SYRUP
Size: 8 oz 500 mg (31 mg per serving)
WWW.GANJAEATS.ORG

What is marijuana?

- Plant with 500 chemical compounds, and 100 cannabinoids
- THC & CBD
- THC binds to CB1 receptors
- Most-used substance behind alcohol & tobacco
- Number of routes of administration
- High variability of concentration

(CDC, 2017)



(Volkow et al., 2014)

What is marijuana?

- Plant with 500 chemical compounds, and 100 cannabinoids
- THC & CBD
- THC binds to CB1 receptors
- Most-used substance behind alcohol & tobacco
- Number of routes of administration
- High variability of concentration
- Addictive substance

(CDC, 2017)

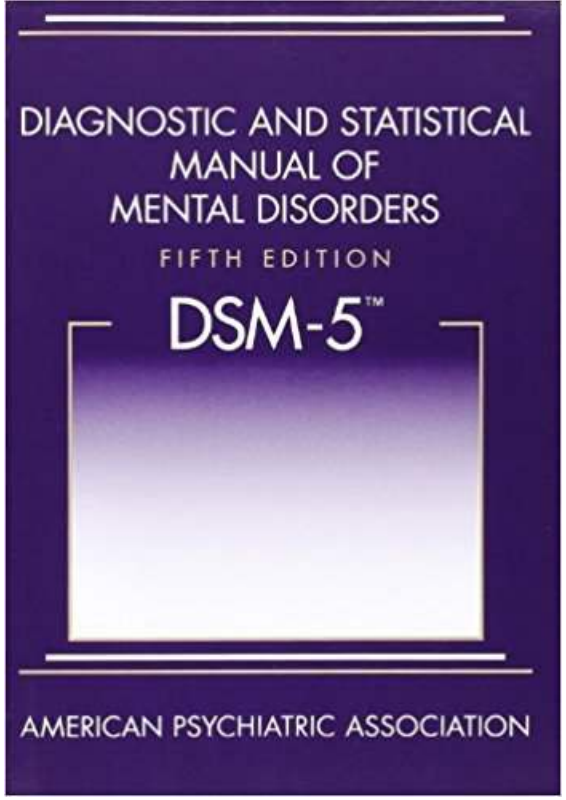
Reviews and Overviews

Review of the Validity and Significance of Cannabis Withdrawal Syndrome

Alan J. Budney, Ph.D.
John R. Hughes, M.D.
Brent A. Moore, Ph.D.
Ryan Vandrey, M.A.

The authors review the literature examining the validity and significance of cannabis withdrawal syndrome. Findings from animal laboratory research are briefly reviewed, and human laboratory and clinical studies are surveyed in more detail. Converging evidence from basic laboratory and clinical studies indicates that a withdrawal syndrome reliably follows discontinuation of chronic heavy use of cannabis or tetrahydrocannabinol. Common symptoms are primarily emotional and behavioral, although appetite change, weight loss, and physical discomfort are also frequently reported. The onset and time course of these symptoms appear similar to those of other substance withdrawal syndromes. The magnitude and severity of these symptoms appear substantial, and these findings suggest that the syndrome has clinical importance. Diagnostic criteria for cannabis withdrawal syndrome are proposed.

(Am J Psychiatry 2004; 161:1967–1977)



The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

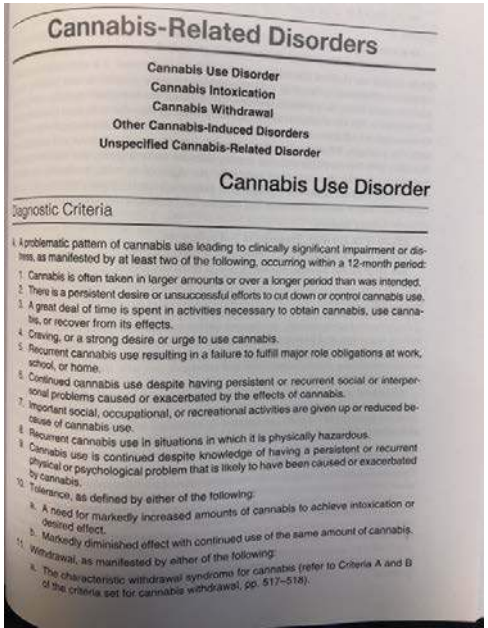
Dan L. Longo, M.D., *Editor*

Adverse Health Effects of Marijuana Use

Nora D. Volkow, M.D., Ruben D. Baler, Ph.D., Wilson M. Compton, M.D., and Susan R.B. Weiss, Ph.D.

Effects of long-term or heavy use

Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*


Cannabis-Related Disorders

Cannabis Use Disorder
Cannabis Intoxication
Cannabis Withdrawal
Other Cannabis-Induced Disorders
Unspecified Cannabis-Related Disorder

Cannabis Use Disorder

Diagnostic Criteria

A. 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 (refer to Criteria A and B of the criteria set for cannabis withdrawal, pp. 517–518).

What is marijuana?

- Plant with 500 chemical compounds, and 100 cannabinoids
- THC & CBD
- THC binds to CB1 receptors
- Most-used substance behind alcohol & tobacco
- Number of routes of administration
- High variability of concentration
- Addictive substance
  - Approximately 30% of active users have a SUD
  - 1:10 adults, 1:6 adolescents
- Well-studied detrimental impact on behavioral health and functioning

(CDC, 2017)

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Is this medicine?

- In Illinois since 2013, Ohio 2019
- Not approved by the FDA, nor prescribed/dispensed like medicine
  - **Medicine**: Marinol, Sativex, and Epidiolex

NDC 0051-0021-21
60 Capsules
2.5 mg
C III
MARINOL®
(DRONABINOL)
See Package Insert for Complete Prescribing Information.
MARINOL® (Dronabinol) Capsules should be packaged in a well-closed container and stored in a cool environment between 8° and 15°C (46° and 59°F) and alternatively could be stored in a refrigerator. Protect from freezing.
Mfg. by
Banner Pharmacaps, Inc.
High Point, NC 27265
Marketed by
UNIMED
PHARMACEUTICALS, INC.
NDC 0051-0021-21
60 Capsules
2.5 mg
MARINOL® C III
(DRONABINOL)
Capsules
℞ only
UNIMED

EPIDIOLEX
EPIDIOLEX® (cannabidiol)
100mg/ml Oral Solution
100ml
Oral Solution

Sativex
Spray zur Anwendung in der Mundhöhle
2,7 mg Delta-9-Tetrahydrocannabinol / 2,5 mg Cannabidiol
3 x 10-ml-Sprühflaschen
Zur Anwendung in der Mundhöhle
GW pharmaceuticals
Almirall

Is this medicine?

- In Illinois since 2013, Ohio 2019
- Not approved by the FDA, nor prescribed/dispensed like medicine
  - **Medicine**: Marinol, Sativex, and Epidiolex
  - **Not medicine**: Buying whatever you like from a dispensary, using it however you want
  - Also consider: physicians are not pushing for this

Therapeutic Uses for Marijuana

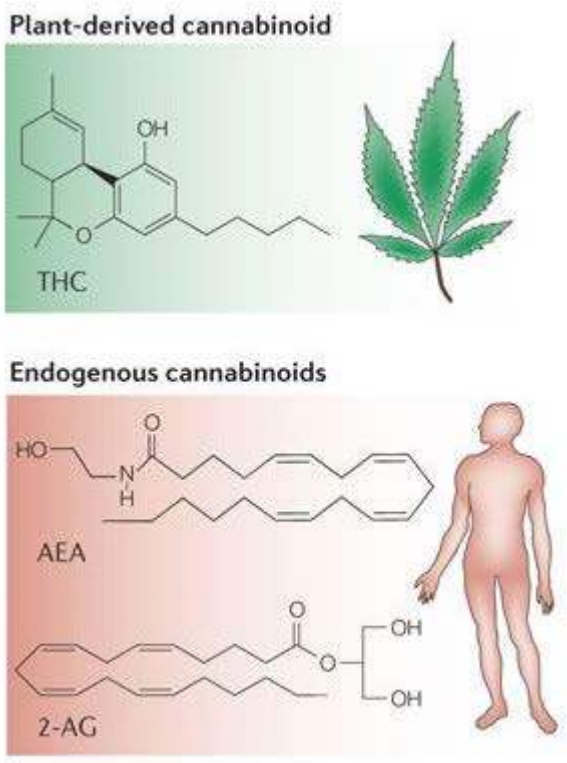
- What does quality research show it is good for?
  - Appetite stimulation
  - Nausea suppression
  - Some types of pain
  - MS spasticity (cannabinoids only)
  - Short-term sleep outcomes (cannabinoids only)
  - Good reference: National Academy of Sciences
- In Illinois, it is approved (by the legislature) for **51** conditions…starting at age 18 (Ohio 21)

Qualifying Conditions

- AIDS
- Amyotrophic Lateral Sclerosis (ALS)
- Alzheimer's disease
- Cancer
- Chronic Traumatic Encephalopathy
- Crohn's Disease
- Epilepsy or another seizure disorder
- Fibromyalgia
- Glaucoma
- Hepatitis C
- Inflammatory Bowel Disease,
- Multiple Sclerosis
- Pain that is either chronic and severe or intractable
- Parkinson's Disease
- Positive status for HIV
- Post-Traumatic Stress Disorder
- Sickle Cell Anemia
- Spinal Cord Disease or injury
- Tourette's Syndrome
- Traumatic Brain Injury
- Ulcerative Colitis

Endogenous Cannabinoids vs. Exogenous Manipulation

- Theory
  - Endocannabinoid system impacts many different diseases
  - Manipulate the same receptors, get the desired effect
- Reality
  - Hit & Miss



(Nature, 2012)

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 Belendiuk[1], Lisa L Baldini[2] and Marcel O Bonn-Miller[3,4,5*]

Abstract

The present investigation aimed to provide an objective narrative review of the existing literature pertaining to the benefits and harms of marijuana use for the treatment of the most common medical and psychological conditions for which it has been allowed at the state level. Common medical conditions for which marijuana is allowed (i.e., those conditions shared by at least 80 percent of medical marijuana states) were identified as: Alzheimer's disease, amyotrophic lateral sclerosis, cachexia/wasting syndrome, cancer, Crohn's disease, epilepsy and seizures, glaucoma, hepatitis C virus, human immunodeficiency virus/acquired immunodeficiency syndrome, multiple sclerosis and muscle spasticity, severe and chronic pain, and severe nausea. Post-traumatic stress disorder was also included in the review, as it is the sole psychological disorder for which medical marijuana has been allowed. Studies for this narrative review were included based on a literature search in PsycINFO, MEDLINE, and Google Scholar. Findings indicate that, for the majority of these conditions, there is insufficient evidence to support the recommendation of medical marijuana at this time. A significant amount of rigorous research is needed to definitively ascertain the potential implications of marijuana for these conditions. It is important for such work to not only examine the effects of smoked marijuana preparations, but also to compare its safety, tolerability, and efficacy in relation to existing pharmacological treatments.

Keywords: Cannabis, Medical marijuana, Marijuana, Medicine, Treatment, Alzheimer's disease, ALS, Cachexia, Cancer, Crohn's disease, Epilepsy, Seizures, Glaucoma, Hepatitis C virus, HCV, HIV, AIDS, Multiple sclerosis, MS, Pain, Nausea, Vomiting, Post-traumatic stress disorder, PTSD

Medical Marijuana

There is no or insufficient evidence to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for:

- Cancers, including glioma (cannabinoids) (4-2)
- Cancer-associated anorexia cachexia syndrome and anorexia nervosa (cannabinoids) (4-4b)
- Symptoms of irritable bowel syndrome (dronabinol) (4-5)
- Epilepsy (cannabinoids) (4-6)
- Spasticity in patients with paralysis due to spinal cord injury (cannabinoids) (4-7b)
- Symptoms associated with amyotrophic lateral sclerosis (cannabinoids) (4-9)
- Chorea and certain neuropsychiatric symptoms associated with Huntington's disease (oral cannabinoids) (4-10)
- Motor system symptoms associated with Parkinson's disease or the levodopa-induced dyskinesia (cannabinoids) (4-11)
- Dystonia (nabilone and dronabinol) (4-12)
- Achieving abstinence in the use of addictive substances (cannabinoids) (4-16)
- Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis (cannabidiol) (4-21)

- What about glaucoma?

AMERICAN GLAUCOMA SOCIETY

Summary: Although marijuana can lower the intraocular pressure (IOP), its side effects and short duration of action, coupled with a lack of evidence that it use alters the course of glaucoma, preclude recommending this drug in any form for the treatment of glaucoma at the present time.

- PTSD…

Is this medicine?

- Should lawmakers really be deciding what society calls “medicine?”
  - Public health implications? Perceived risk?
- Why are we doing an end-around the FDA?
  - And what are the consequences?

Healthcare before science?

- "I don't think we have the time to wait for those beautiful trials to come out in ten or twenty years. We have people dying now."

  Leslie Mendoza-Temple, MD

  Former Chair, Illinois Medical Cannabis Advisory Board

Source: As States Embrace Cannabis As Opioid Alternative, Science Lags Behind Policy, Illinois Public Media 2018

Why do clinical trials matter?

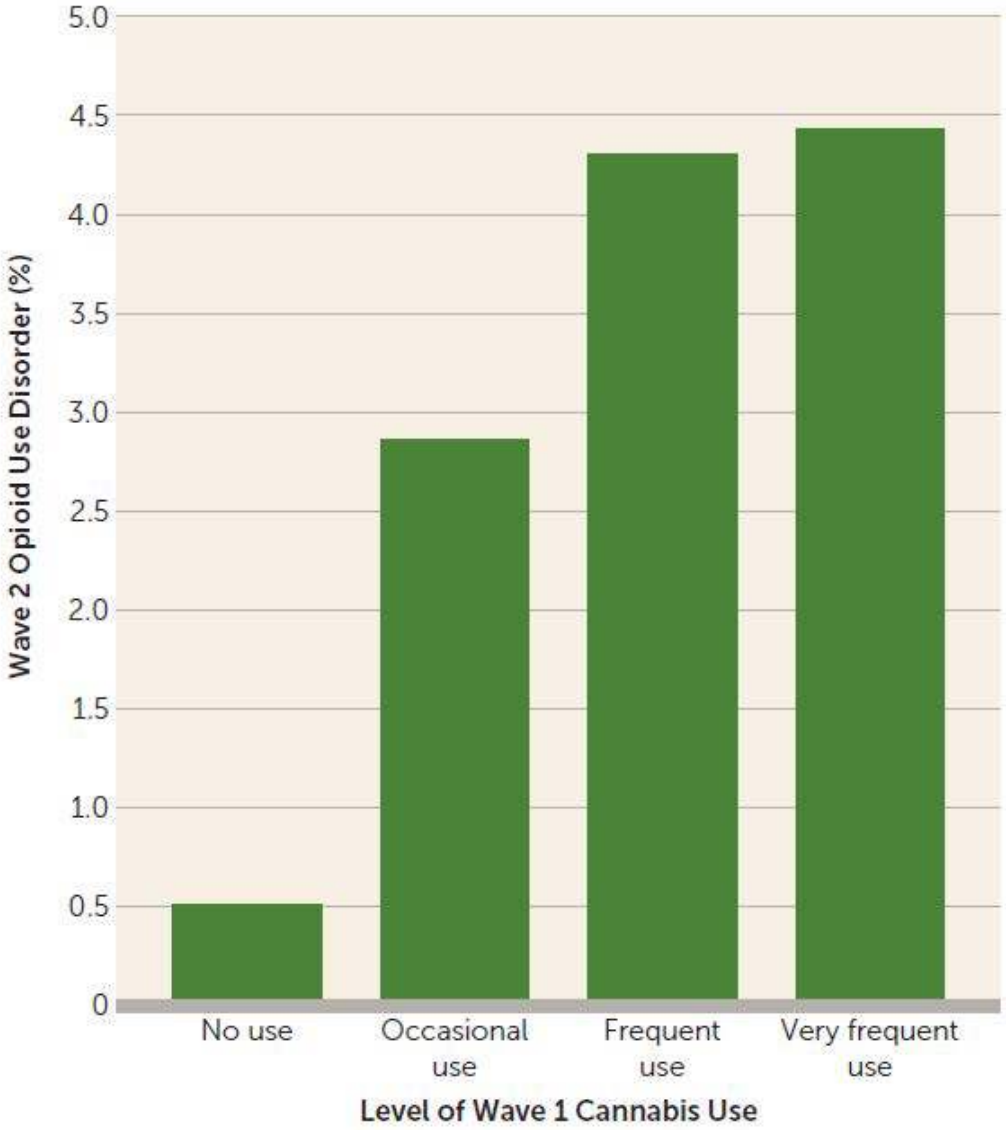
THE THALIDOMIDE TRAGEDY: LESSONS FOR DRUG SAFETY AND REGULATION

By: Bara Fintel, Athena T. Samaras, Edson Carias

Jul 28, 2009

Many children in the 1960's, like the kindergartner pictured above, were born with phocomelia as a side effect of the drug thalidomide, resulting in the shortening or absence of limbs. (Photo by Leonard McCombe//Time Life Pictures/Getty Images)

FIGURE 1. Level of Wave 1 Cannabis Use and Incident Wave 2 Prescription Opioid Use Disorder in the NESARC[a]



[a] NESARC=National Epidemiological Survey on Alcohol and Related Conditions; wave 1 was conducted in 2001 and 2002, and wave 2 in 2004 and 2005.

Opioid Substitute?

Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: findings from a 4-year prospective cohort study

Lancet Public Health 2018; 3: e341–50

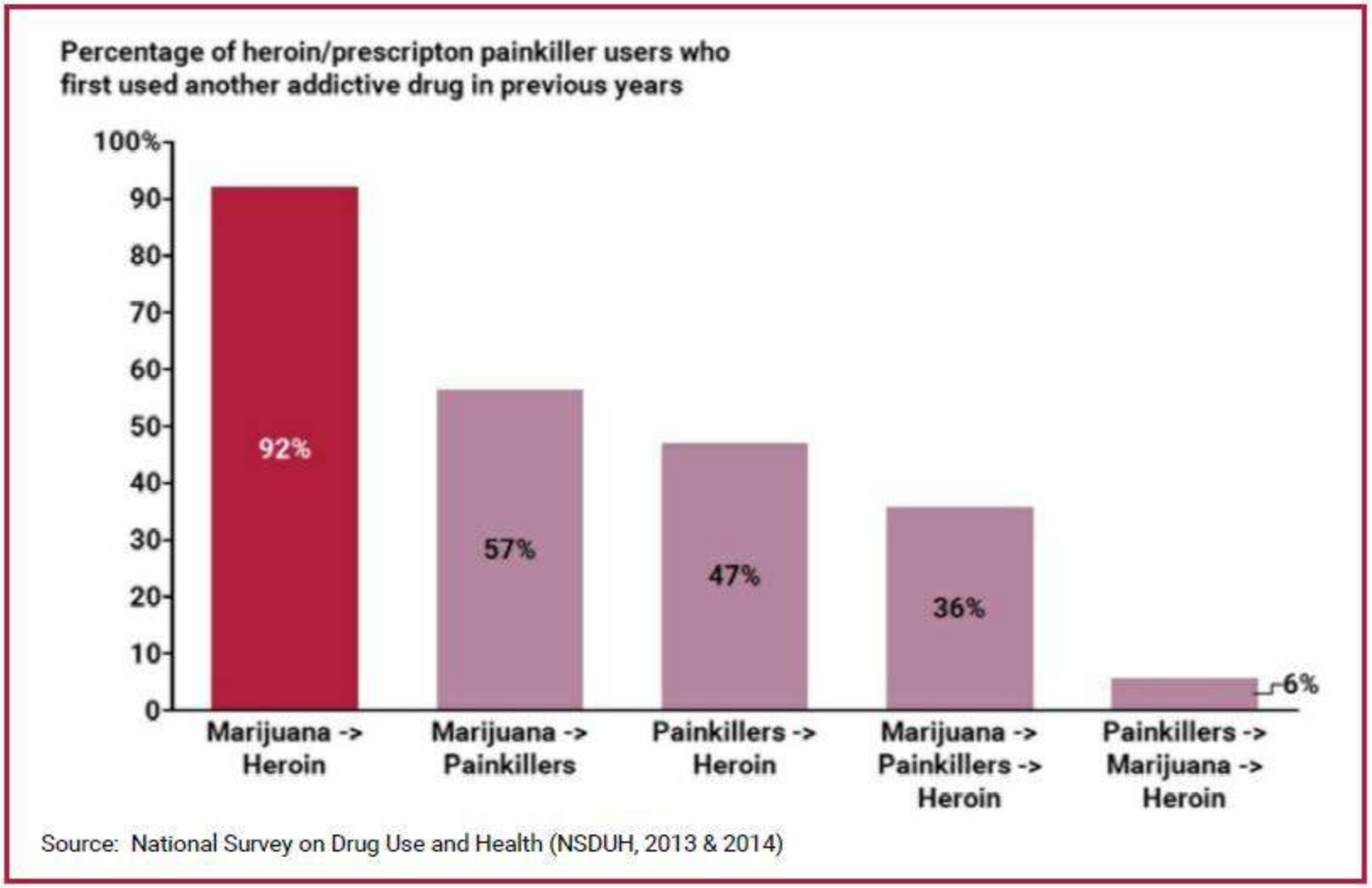
Gabrielle Campbell, Wayne D Hall, Amy Peacock, Nicholas Lintzeris, Raimondo Bruno, Briony Larance, Suzanne Nielsen, Milton Cohen, Gary Chan, Richard P Mattick, Fiona Blyth, Marian Shanahan, Timothy Dobbins, Michael Farrell, Louisa Degenhardt

Interpretation Cannabis use was common in people with chronic non-cancer pain who had been prescribed opioids, but we found no evidence that cannabis use improved patient outcomes. People who used cannabis had greater pain and lower self-efficacy in managing pain, and there was no evidence that cannabis use reduced pain severity or interference or exerted an opioid-sparing effect. As cannabis use for medicinal purposes increases globally, it is important that large well designed clinical trials, which include people with complex comorbidities, are conducted to determine the efficacy of cannabis for chronic non-cancer pain.

Medical Marijuana Users are More Likely to Use Prescription Drugs Medically and Nonmedically

Theodore L. Caputi, BS and Keith Humphreys, PhD

J Addict Med • Volume 12, Number 4, July/August 2018


Percentage of heroin/prescripton painkiller users who first used another addictive drug in previous years
100%
90
80
70
60
50
40
30
20
10
0
92%
57%
47%
36%
6%
Marijuana -> Heroin
Marijuana -> Painkillers
Painkillers -> Heroin
Marijuana -> Painkillers -> Heroin
Painkillers -> Marijuana -> Heroin
Source: National Survey on Drug Use and Health (NSDUH, 2013 & 2014)

PNAS Proceedings of the National Academy of Sciences of the United States of America

Association between medical cannabis laws and opioid overdose mortality has reversed over time

Chelsea L. Shover, Corey S. Davis, Sanford C. Gordon, and Keith Humphreys

PNAS June 25, 2019 116 (26) 12624-12626; first published June 10, 2019 https://doi.org/10.1073/pnas.1903434116

et al.'s analysis through 2017. Not only did findings from the original analysis not hold over the longer period, but the association between state medical cannabis laws and opioid overdose mortality reversed direction from −21% to +23% and remained positive after accounting for recreational cannabis laws. We also uncovered no evidence that either broader (recreational) or more restrictive (low-tetrahydrocannabinol) cannabis laws were associated with changes in opioid overdose mortality. We find it unlikely that medical

A little "dab" will do ya' in: a case report of neuro-and cardiotoxicity following use of cannabis concentrates

Shannon S. Rickner[a], Dazhe Cao[a], Kurt Kleinschmidt[a] and Steven Fleming[b]

[a]Division of Medical Toxicology, Department of Emergency Medicine, Parkland Memorial Health and Hospital System and University of Texas Southwestern Medical Center, Dallas, TX, USA; [b]Gulfstream Diagnostics, Dallas, TX, USA

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Cannabis-induced psychosis associated with high potency "wax dabs"

Joseph M. Pierre [a,b,*], Michael Gandal [a], Maya Son [c]

[a] Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA, Los Angeles, California
[b] Department of Veterans Affairs, VA Greater Los Angeles Healthcare System, Los Angeles, CA
[c] College of Medicine, University of Vermont, Burlington, VT

Smoking strong marijuana daily increases risk of psychosis, study finds

CBS NEWS

MARCH 20, 2019 / 11:44 AM / CBS/AP

Psychotic Disorders as Function of THC dose, Frequency of Use
11 Sites, 6 Nations in Europe, Brazil: 3 of the cities

The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI):A multicentre case control study

Di Forti et al

www.thelancet.com/psychiatry
Published online March 19, 2019

If high-potency cannabis were no longer available:

- 12·2% of cases of first-episode psychosis could be prevented across 11 cities
- 30·3% prevented London
- 50·3% prevented Amsterdam

ER visits linked to marijuana rose at Colorado hospital after legalization, study finds

People who consume marijuana edibles may be ingesting unsafe levels because they don't feel the immediate high, researcher says.

March 25, 2019, 4:30 PM CDT

By Shamard Charles, M.D.

NEWS

What messages are customers receiving?

Marijuana shops recommend products to pregnant women, against doctors' warnings

By Michael Nedelman, CNN

Updated 6:05 AM ET, Thu May 10, 2018

Obstetrics: *Original Research*

Recommendations From Cannabis Dispensaries About First-Trimester Cannabis Use

Betsy Dickson, MD, Chanel Mansfield, MPH, Maryam Guiahi, MD, MSc, Amanda A. Allshouse, MS, Laura M. Borgelt, PharmD, Jeanelle Sheeder, PhD, Robert M. Silver, MD, and Torri D. Metz, MD, MS

Is cannabis safe to take during pregnancy?

- "Different people opinions, kind of like alcohol; I used to be a bartender and it is legal to serve someone who is pregnant because it is up to them so you know. I am not here to tell you you should or should not use, does that make sense. I do know a lot of people that do use cannabis during their pregnancy though and for what they have found, there has not been side effects that they can see,"
- "I know a lot of doctors are recommending marijuana nowadays."
- "We have a girl that comes in and she is probably 6 months pregnant and she smokes bud but she does not smoke it as much as she did but she still does…she said her doctor said it was ok…she said the doctor said that but I am not a doctor…I know aspirin is ok for babies and that is pretty much what you are getting is an aspirin that is probably better."

Drug Interactions

Drug Interaction Studies

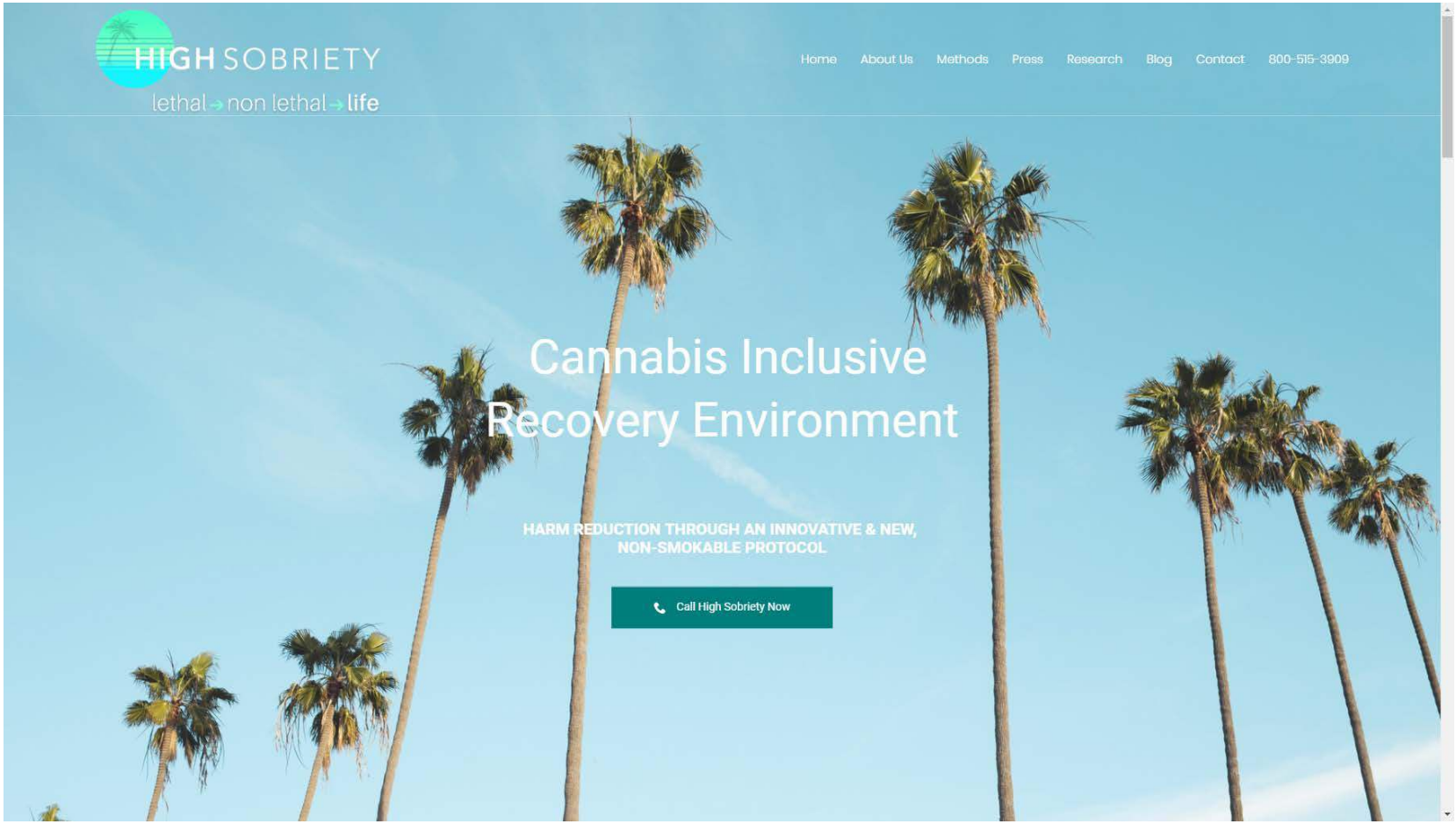
- **Warfarin**
  - THC and CBD increase warfarin levels (Yamaori et al 2012).
  - Frequent cannabis use has been associated with increased INR.
- **Alcohol**
  - Alcohol may increase THC levels (Hartman 2015).
- **Theophylline**
  - Smoked cannabis can decrease theophylline levels (Stout and Cimino 2014).
- **Indinavir or nelfinavir**
  - Smoked cannabis had no effect (Abrams et al 2003).
- **Docetaxel or irinotecan**
  - Cannabis infusion (tea) had no effect (Engels et al 2007).
- **Clobazam**
  - In children treated with CBD for epilepsy, CBD increased clobazam levels (Geffrey et al 2015).

- Studies are few and far between
- Frequent anecdotal reports that it may have an impact on psychiatric medications
  - Or at least is a confound

Implications for Treatment Centers

- Why not use pot? Some people do…

Transition Drug?



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Transition Drug?

- Why not smoke pot? Some people do…
  - Reasons why we generally recommend against:
    - Learning to cope without substances is a huge focus
    - Alignment with other patients / milieu issues
    - Triggering to other patients
- Does it actually work?

Transition Drug?

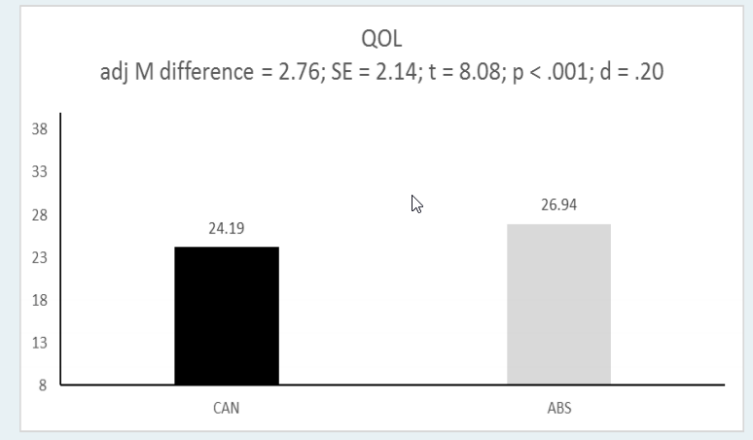
- 27% less likely to stay sober (Majarrad et al., 2014)

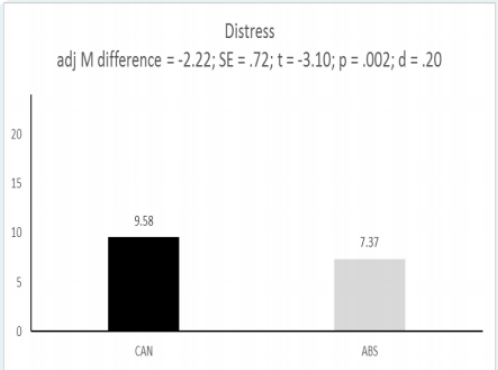
- Achieving abstinence in the use of addictive substances (cannabinoids) (4-16)

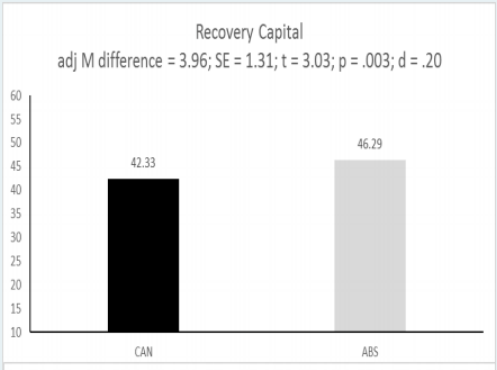
Cannabis as harm reduction?
Examining cannabis use in a national, probability-based sample of U.S. adults who have resolved a substance use problem

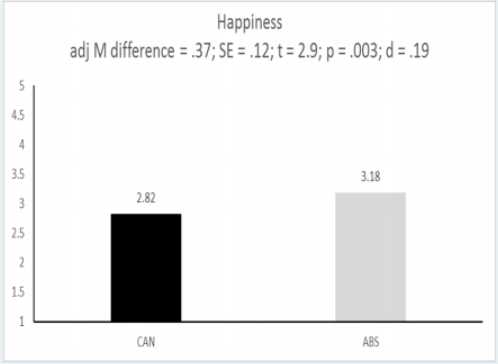
Brandon G. Bergman, PhD & John F. Kelly, PhD

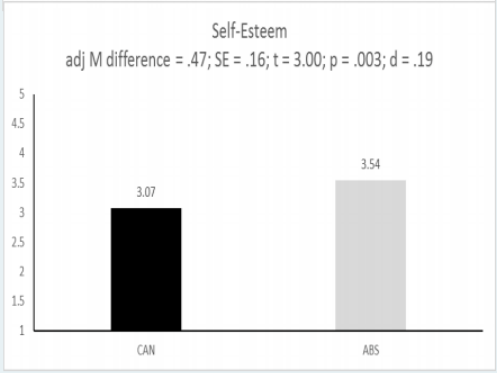
MASSACHUSETTS GENERAL HOSPITAL
HARVARD MEDICAL SCHOOL TEACHING HOSPITAL











Marijuana - Health and Safety Impact

- Negative health impact

Table 1. Adverse Effects of Short-Term Use and Long-Term or Heavy Use of Marijuana.

Effects of short-term use
Impaired short-term memory, making it difficult to learn and to retain information
Impaired motor coordination, interfering with driving skills and increasing the risk of injuries
Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases
In high doses, paranoia and psychosis
Effects of long-term or heavy use
Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)*
Altered brain development*
Poor educational outcome, with increased likelihood of dropping out of school*
Cognitive impairment, with lower IQ among those who were frequent users during adolescence*
Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*
Symptoms of chronic bronchitis
Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders

* The effect is strongly associated with initial marijuana use early in adolescence.

(Volkow et al., 2014)

Biological Psychiatry

The Role of Cannabinoids in Neuroanatomic Alterations in Cannabis Users

Valentina Lorenzetti, Nadia Solowij, and Murat Yücel

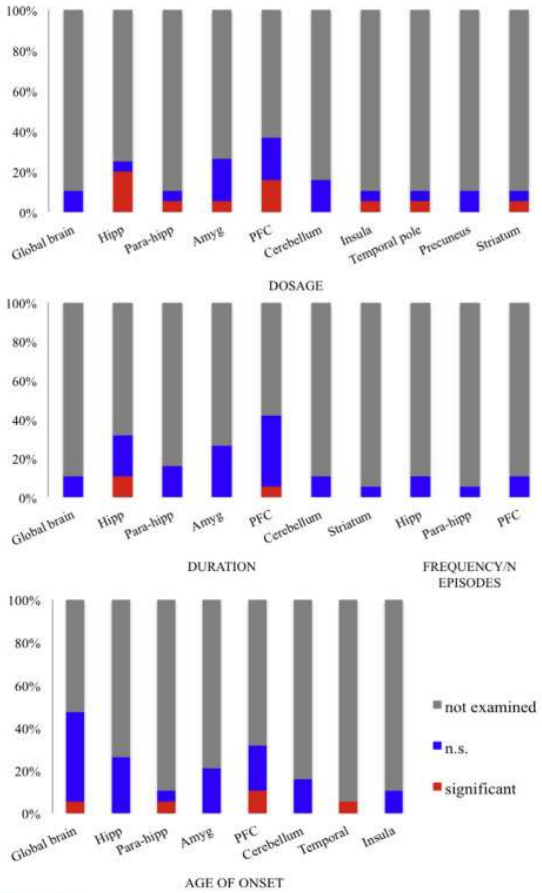


Figure 4. Percentage of studies reporting associations between regional neuroanatomy and cannabis use measures. Significant associations (red), nonsignificant associations (n.s.; blue), and associations unexamined (gray). Amyg, amygdala; Hipp, hippocampus; Para-hipp, parahippocampal gyrus; PFC, prefrontal cortex.

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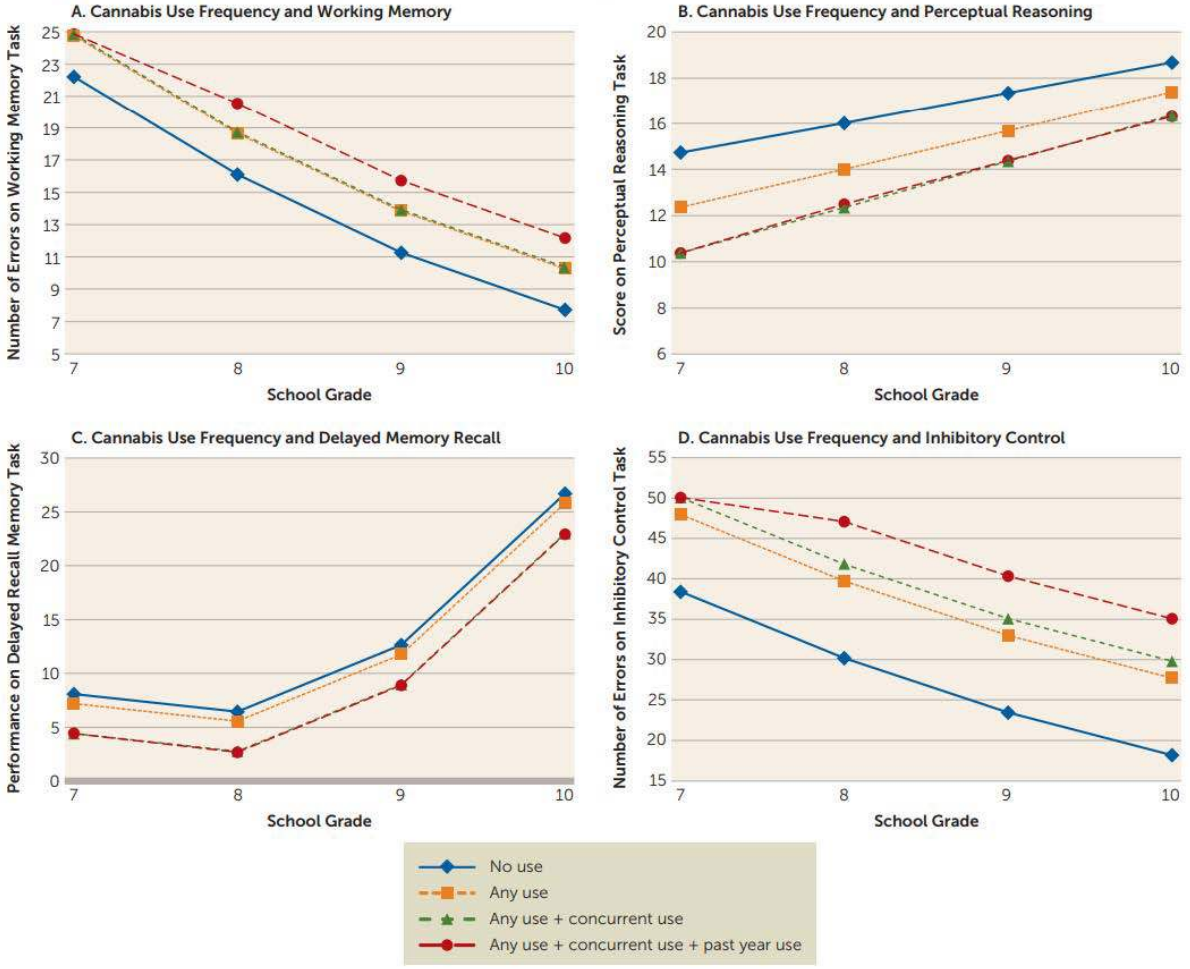
A Population-Based Analysis of the Relationship Between Substance Use and Adolescent Cognitive Development

Jean-François G. Morin, B.A., Mohammad H. Afzali, Ph.D., Josiane Bourque, M.Sc., Sherry H. Stewart, Ph.D., Jean R. Séguin, Ph.D., Maeve O'Leary-Barrett, Ph.D., Patricia J. Conrod, Ph.D.

FIGURE 2. Between-Subject and Within-Subject (Concurrent and Lagged) Relationships Between Cannabis Use Frequency and Working Memory Errors, Perceptual Reasoning Performance, Delayed Memory Recall Performance, and Inhibitory Control Errors[a]



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Drivers of Brain Aging

In the largest known brain imaging study, scientists from Amen Clinics, Google, John's Hopkins, UCLA, and UC San Francisco evaluated **62,454 brain SPECT scans** of indivivduals from nine months old to 105 years of age to investigate factors that accelerate brain aging.

128 brain regions studied to predict the chronological age of a patient

Accelerated Aging Prediction

Schizophrenia	4 years
Cannabis Abuse	2.8 years
Bipolar Disorder	1.6 years
ADHD	1.4 years
Alcohol Abuse	0.6 years

Aging SPECT scans

"We can now link clinical diagnoses and addictions to premature aging of the brain. Better treatment of these disorders can slow or even halt brain aging.

The cannabis abuse result was especially important, as our culture is starting to view marijuana as a harmless substance. These findings invite us to rethink its effects on the brain."

~ Daniel G. Amen, MD, founder of Amen Clinics

Caption: Drivers of Brain Aging. Credit: Daniel G. Amen

Vaping appears to be making hundreds of people sick. No one knows exactly why.

The mysterious spike in respiratory illnesses is a reminder that e-cigarettes may be more dangerous than they seem.

By Julia Belluz | @juliaoftoronto | julia.belluz@voxmedia.com | Sep 3, 2019, 2:20pm EDT

City of Milwaukee urges residents to stop vaping 'immediately'; 89% of Wisconsin sick cite THC

First death linked to vaping reported in Illinois

24 August 2019

Another death is linked to vaping, the 1st tied to a pot shop

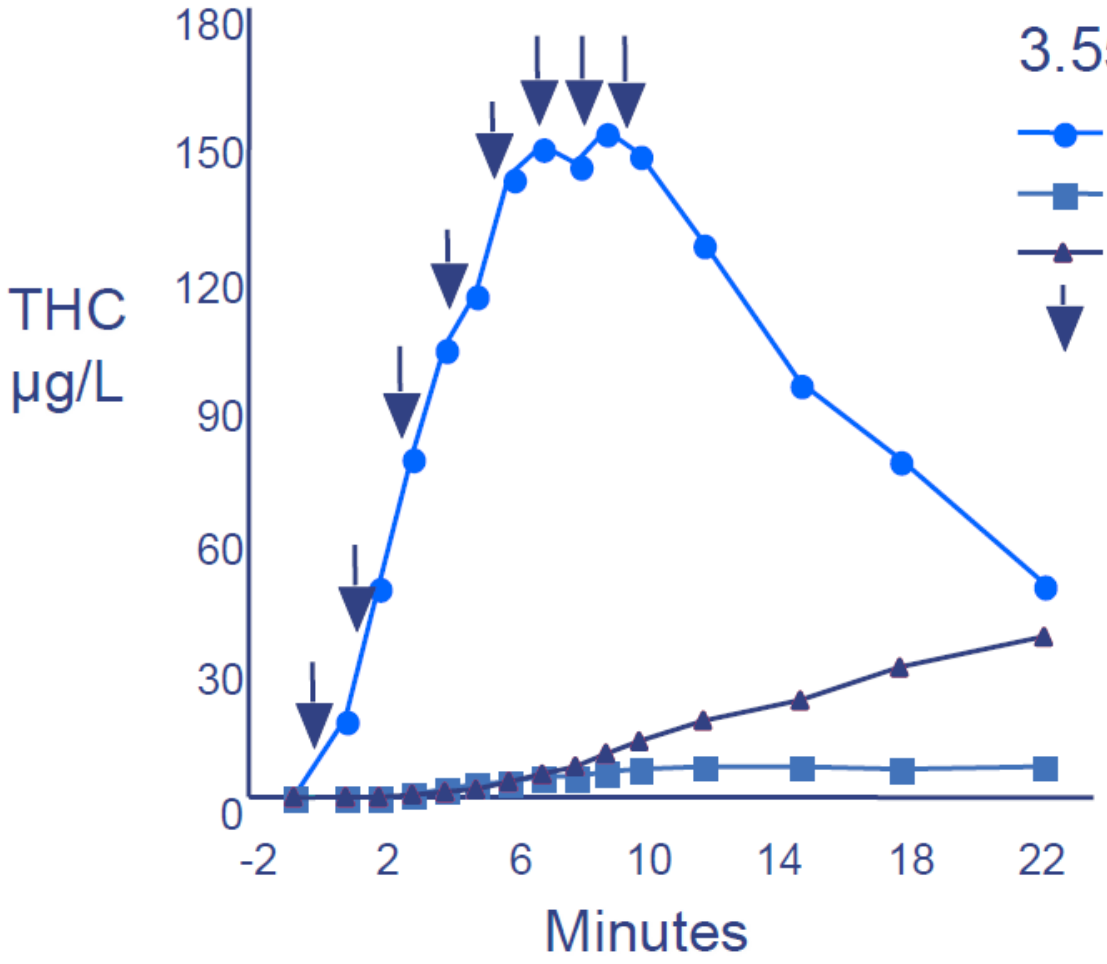
Gillian Flaccus Associated Press

Published 8:55 a.m. ET Sep. 5, 2019 | **Updated 10:16 a.m. ET Sep. 5, 2019**

Marijuana - Health and Safety Impact

- Negative health impact
- Impaired motor function
  - Traffic safety concerns
  - Detection concerns

THC, 11-OH-THC & THCCOOH Plasma Concentrations After Smoking Cannabis



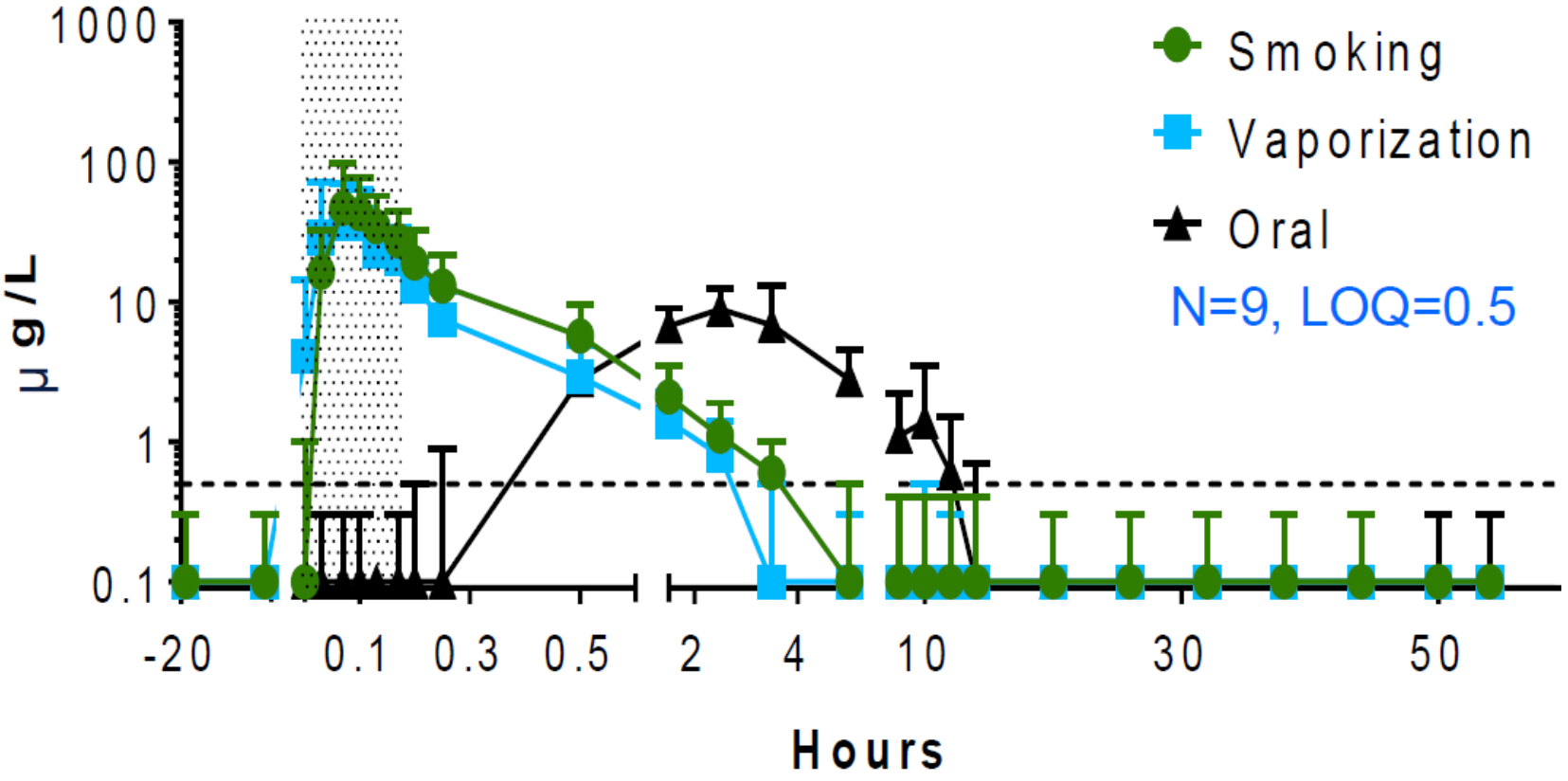
3.55% THC

THC
11-OH THC
THCCOOH
Inhale
N = 6

THC detected 3 - 27 h
THCCOOH 2 – 7 days
LOQ 0.5 µg/L

Huestis et al
J Anal Toxicol 1992

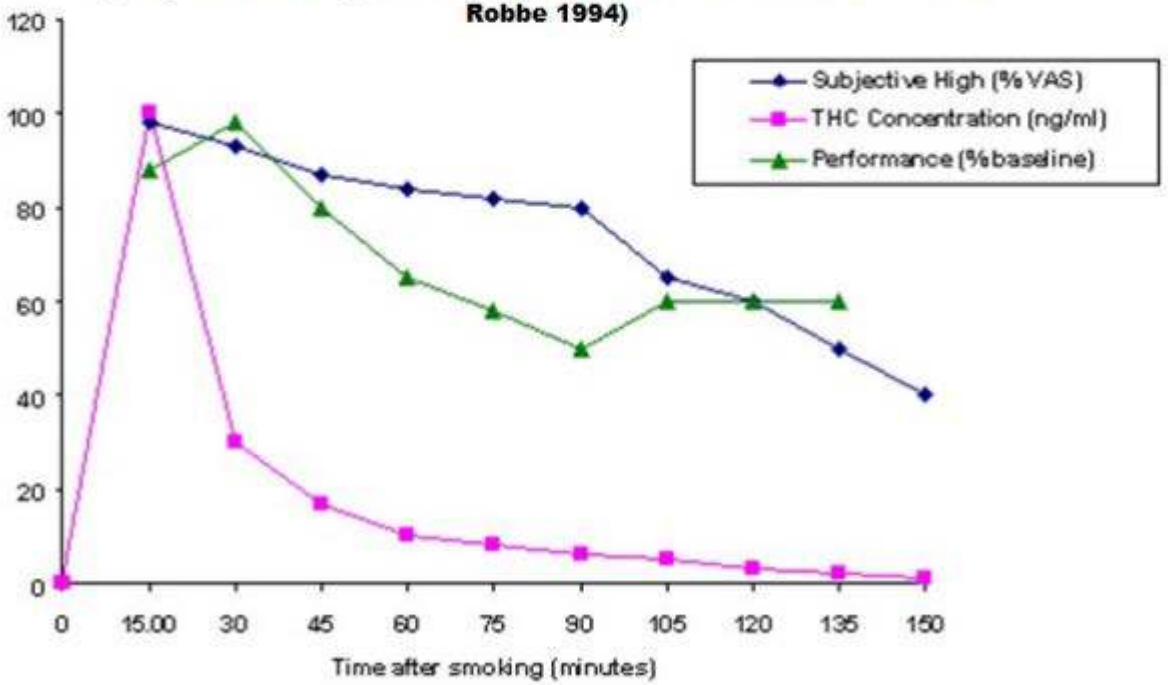
Mean Blood THC Concentrations in Occasional Smokers After 50.6 mg THC by 3 Administration Routes



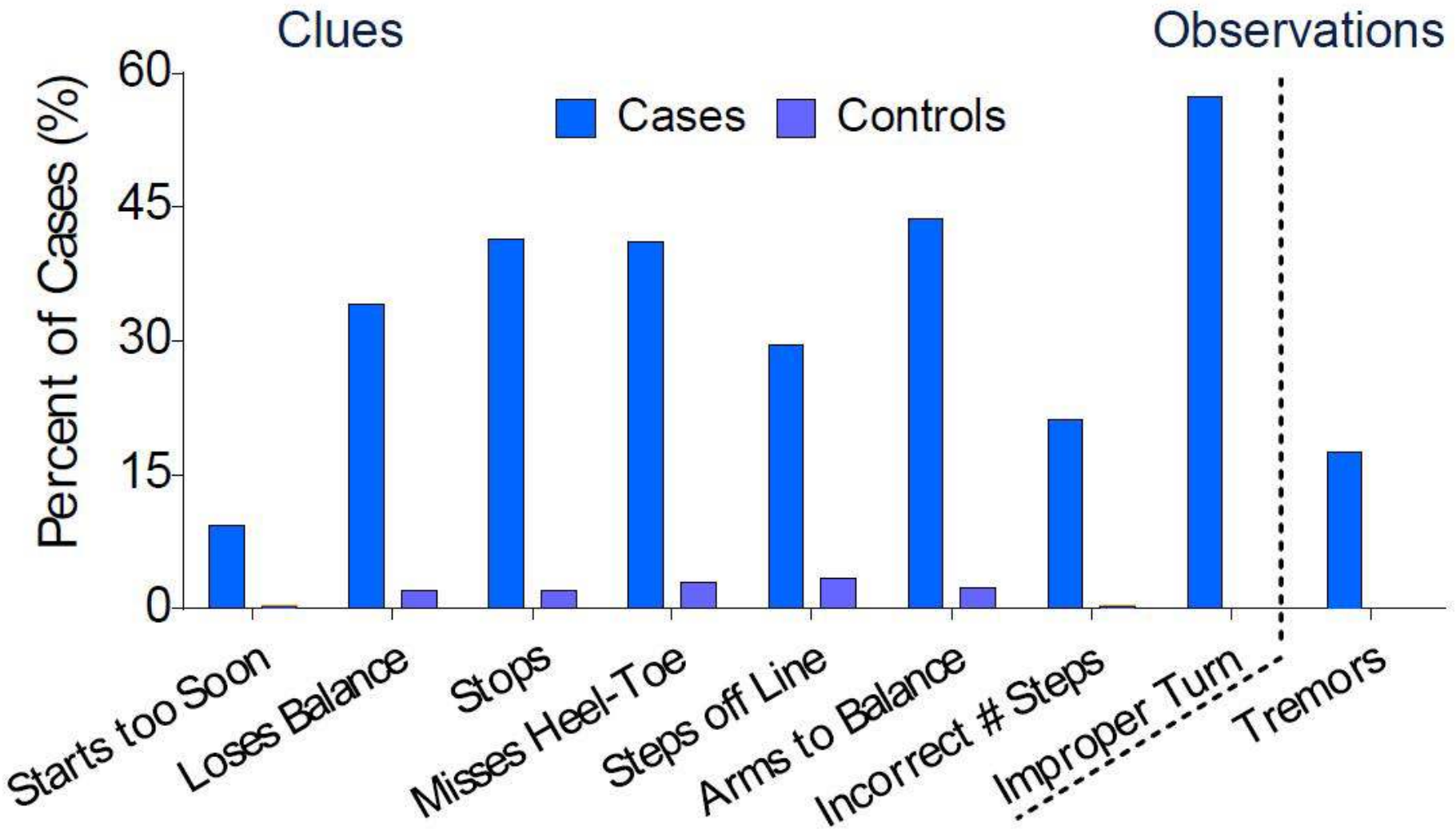
Traffic Safety Concerns

Figure 4

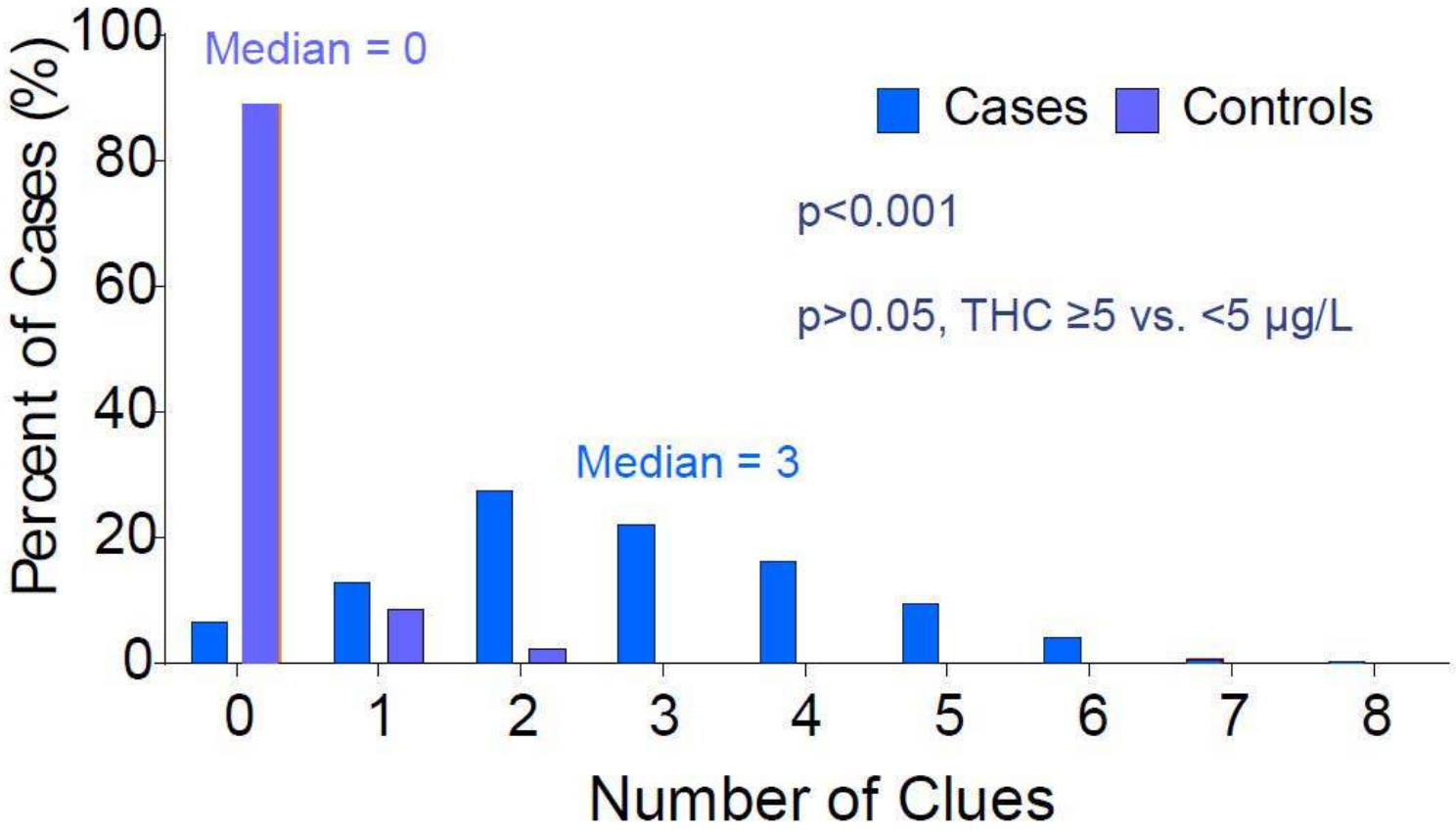
Time Course of Standardized THC Concentration in Plasma, Performance Deficit and Subjective High after Smoking Marijuana (Adapted from Berghaus et al. 1998, Sticht and Käferstein 1998 and Robbe 1994)



Walk And Turn Clues & Observations



Number of WAT Clues
≥2 considered "Impaired"



Medical Cannabis Patients Driving While High

Driving under the influence of cannabis among medical cannabis patients with chronic pain

Erin E. Bonar[a,b,*], James A. Cranford[a], Brooke J. Arterberry[a,c], Maureen A. Walton[a,b], Kipling M. Bohnert[a,d], Mark A. Ilgen[a,d]

In the past 6 months…

- 56.4% endorsed driving within 2h of use
- 50.5% endorsed driving while “a little high”
- 21.5% endorsed driving while “very high”
- US base rate 16+ for driving high in the past year: 4.3%

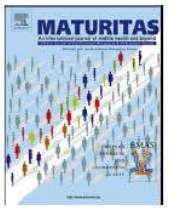
What about retirees or older adults?

Maturitas 118 (2018) 56–59

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas



Medical cannabis use in older patients: Update on medical knowledge

Olivier Beauchet[a,b,c,d,*]

[a] Department of Medicine, Division of Geriatric Medicine, Sir Mortimer B. Davis - Jewish General Hospital and Lady Davis Institute for Medical Research, McGill University, Montreal, Quebec, Canada
[b] Dr. Joseph Kaufmann Chair in Geriatric Medicine, Faculty of Medicine, McGill University, Montreal, Quebec, Canada
[c] Centre of Excellence on Longevity of McGill integrated University Health Network, Quebec, Canada
[d] Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore

- Quality data is scarce, but some trends have emerged
- Primary validated uses: chronic pain & during chemotherapy
  - Worth noting: average mg THC used per dose often less than 5, often in oils or tinctures.

4. Conclusions

Cannabis use is highly prevalent and is likely to increase due to the change in the perception of the risks associated with cannabis in the general population, including older adults. Cannabis for recreational use has been legalized even though it has been proved that cannabis can produce psychiatric adverse effects and can be addictive. In parallel, however, there is increasing evidence that cannabis is beneficial for a large range of medical conditions. There is a growing body of data showing the positive effects of medical cannabis use, but studies have had mixed results, and many of those studies have had small samples; moreover, there have been few randomized control trials. It is therefore difficult to reach a firm conclusion regarding the utility of this alternative therapy for patients. The lack of evidence is marked for older patients, few of whom have been examined. There is little information to guide medical cannabis prescription in this group of patients. There is a need for well controlled clinical trials to establish therapeutic efficacy, dose ranges and safety in older patients.

To Recap: Delivery System

- How is medicine approved for the public?
  - Replicated science, multi-phase FDA trials
- How is medicine prescribed?
  - Dose, frequency, type, concentration
- How is medicine produced?
  - Uniform, standardized
- Do we smoke any medicine you're aware of?
  - Or use bongs, butane torches, vape pens, etc.
- What demographic do the products appear to be marketed at?

Marketing

Have you ever looked at what product is actually being sold?

- Local Example / Another Local Example

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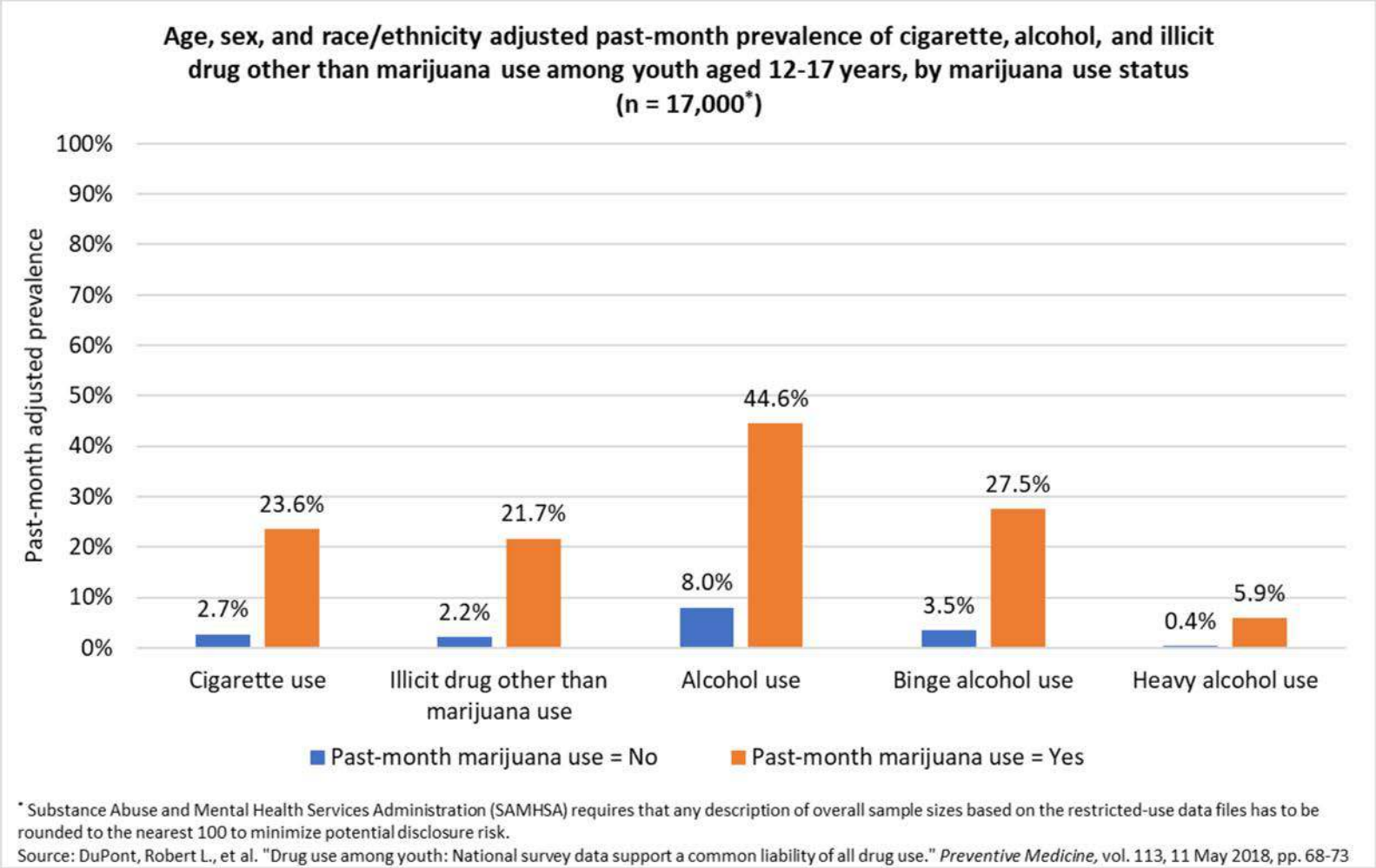
Gateway Drug?



* Substance Abuse and Mental Health Services Administration (SAMHSA) requires that any description of overall sample sizes based on the restricted-use data files has to be rounded to the nearest 100 to minimize potential disclosure risk.

Source: DuPont, Robert L., et al. "Drug use among youth: National survey data support a common liability of all drug use." *Preventive Medicine,* vol. 113, 11 May 2018, pp. 68-73

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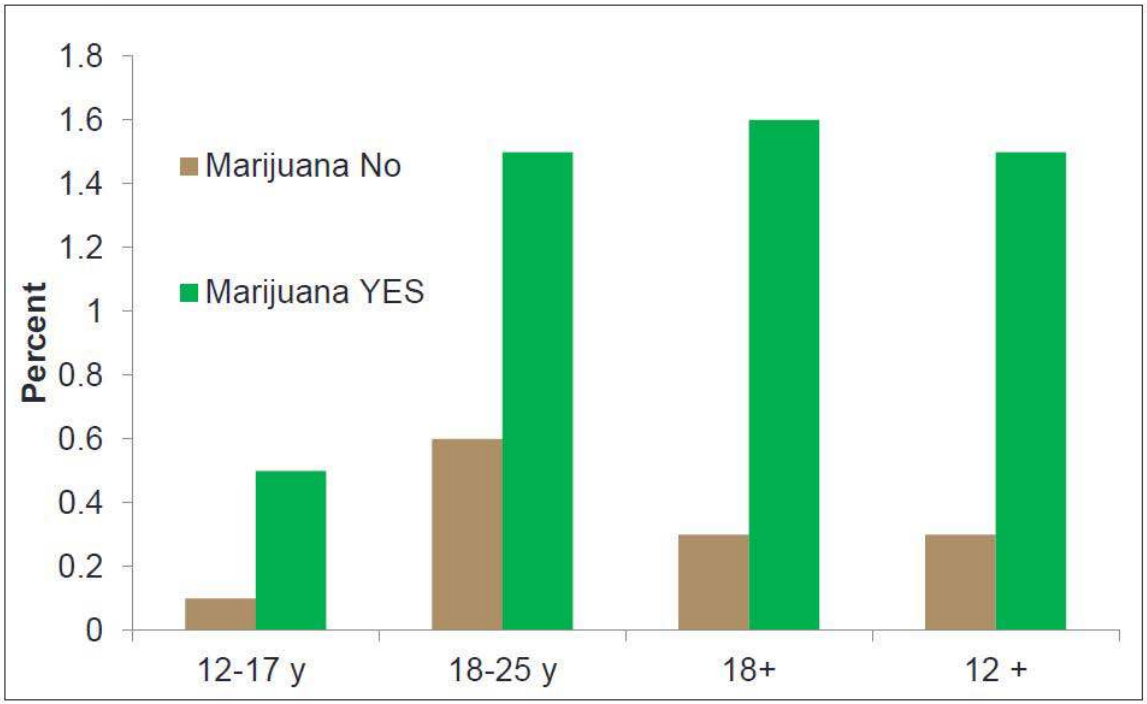
Gateway Drug?

Prevalence Of Heroin Use Among Marijuana Users in the US



SAMHSA's Center for Behavioral Health Statistics and Quality: NSDUH 2015

(DuPont, 2017)

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Gateway Drug?

Drug and Alcohol Dependence 194 (2019) 51–58

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

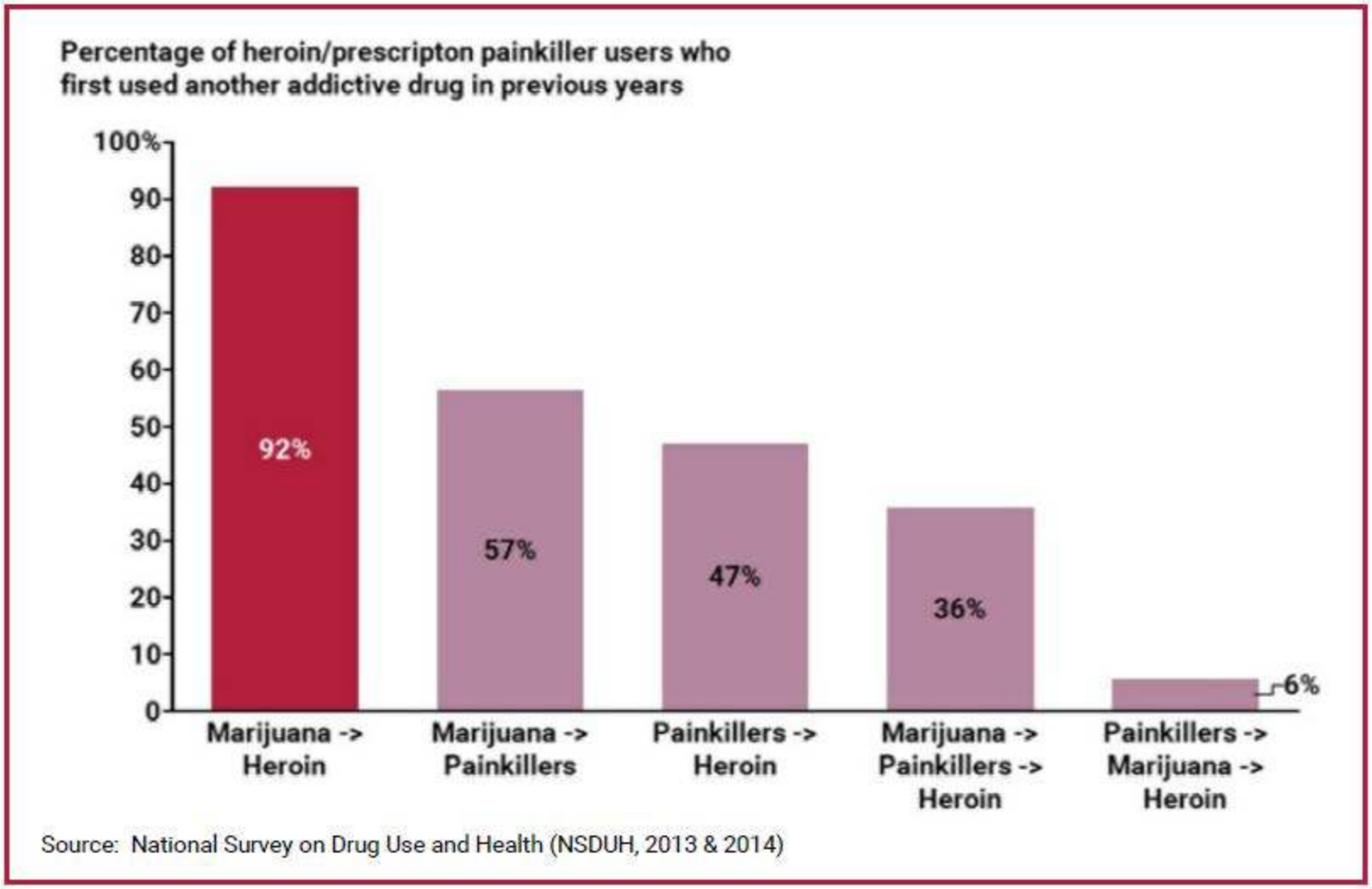
Full length article

Historical trends in the grade of onset and sequence of cigarette, alcohol, and marijuana use among adolescents from 1976–2016: Implications for "Gateway" patterns in adolescence

Katherine M. Keyes[a,b,*], Caroline Rutherford[a], Richard Miech[c]

[a] Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA
[b] Center for Research on Society and Health, Universidad Mayor, Santiago, Chile
[c] Institute for Social Research, University of Michigan, Ann Arbor, MI, USA

Conclusion: Marijuana is increasingly the first substance in the sequence of adolescent drug use. Reducing adolescent smoking has been a remarkable achievement of the past 20 years; those who continue to smoke are at higher risk for progression to marijuana use.


Percentage of heroin/prescripton painkiller users who first used another addictive drug in previous years
100%
90
80
70
60
50
40
30
20
10
0
92%
57%
47%
36%
6%
Marijuana -> Heroin
Marijuana -> Painkillers
Painkillers -> Heroin
Marijuana -> Painkillers -> Heroin
Painkillers -> Marijuana -> Heroin
Source: National Survey on Drug Use and Health (NSDUH, 2013 & 2014)

So what's this all about then?

- To review…
  - Lack of quality evidence to support most medical claims
  - Dispensing system that is unspecific and promotes self-medication
  - Selling concentrates that have up to 70% THC (93% in Illinois)
  - Low age for entry, products that can appeal to kids and young adults

- Do these ads look familiar?

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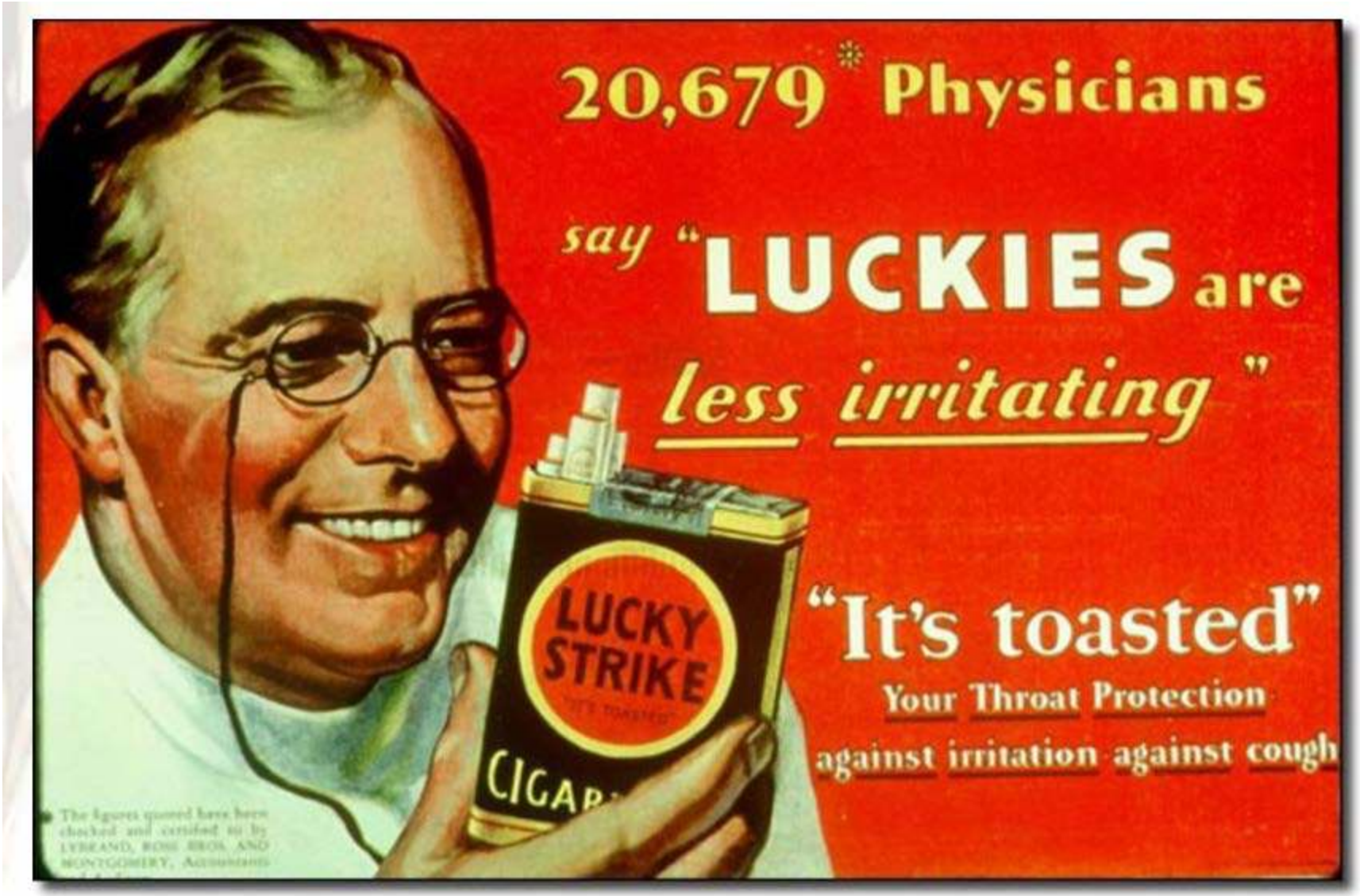
Every doctor in private practice was asked:
—family physicians, surgeons, specialists...
doctors in every branch of medicine—
"What cigarette do you smoke?"
According to a recent Nationwide survey:
More Doctors
Smoke Camels
than any other cigarette!
THE "T-ZONE" TEST WILL TELL YOU
CAMEL


20,679* Physicians
say "LUCKIES are
less irritating"
LUCKY STRIKE
"It's toasted"
Your Throat Protection
against irritation against cough
The figures quoted have been checked and certified to by LYBRAND, ROSS BROS. AND MONTGOMERY, Accountants

THE SHOCK OF FACING
what your figure may become
When Tempted
Reach for a
LUCKY
instead
"It's toasted"
THE SPIRIT OF YOUTH
carry on-avoid that future shadow
AVOID THAT FUTURE SHADOW
by refraining from over-indulgence
When Tempted
Reach for a
LUCKY
instead
LUCKY STRIKE
CIGARETTES
"It's toasted"
Your Throat Protection — against irritation — against cough.

NOW...Scientific Evidence on Effects of Smoking!

A MEDICAL SPECIALIST is making regular bi-monthly examinations of a group of people from various walks of life. 45 percent of this group have smoked Chesterfield for an average of over ten years.

After ten months, the medical specialist reports that he observed . . .

no adverse effects on the nose, throat and sinuses of the group from smoking Chesterfield.

First and Only Premium Quality Cigarette in Both Regular and King-Size

CONTAINS TOBACCOS OF BETTER QUALITY AND HIGHER PRICE THAN ANY OTHER KING-SIZE CIGARETTE

MUCH MILDER

CHESTERFIELD IS BEST FOR YOU

Copyright 1953, Liggett & Myers Tobacco Co.

Marijuana: Bottom Line

- Actual science-based therapeutic applications for cannabinoids are present, but limited
  - The distinction between marijuana and cannabinoids is critical
- The delivery system is not consistent with current models for healthcare, promoting speculative treatment, poor product choices, self-medication, and potential resale to youth
- There are numerous health & safety concerns related to marijuana use, particularly for youth and young adults
  - Addiction, brain development, achievement, psychosis, drug sequencing, vaping & road safety
- Our perspective has shifted on drugs before…

BAYER Pharmaceutical Products

HEROIN—HYDROCHLORIDE

is pre-eminently adapted for the manufacture of cough elixirs, cough balsams, cough drops, cough lozenges, and cough medicines of any kind. Price in 1 oz. packages, $4.85 per ounce; less in larger quantities. The efficient dose being very small (1-48 to 1-24 gr.), it is

The Cheapest Specific for the Relief of Coughs

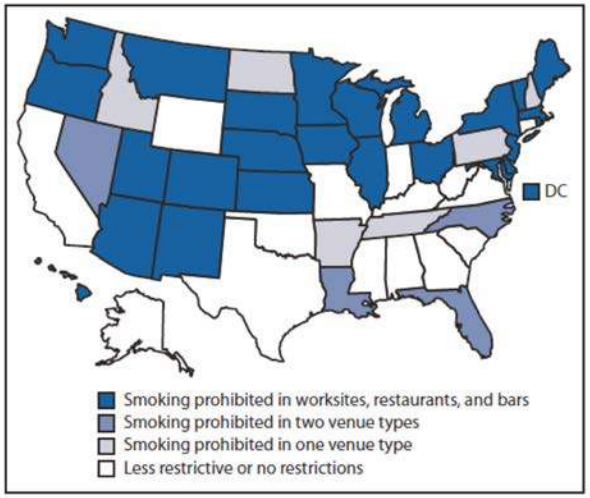
(In bronchitis, phthisis, whooping cough, etc., etc.)

WRITE FOR LITERATURE TO

FARBENFABRIKEN OF ELBERFELD COMPANY

SELLING AGENTS

P. O. Box 2160 40 Stone Street, NEW YORK


DC
Smoking prohibited in worksites, restaurants, and bars
Smoking prohibited in two venue types
Smoking prohibited in one venue type
Less restrictive or no restrictions

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- There are numerous health & safety concerns related to marijuana use, particularly for youth and young adults
  - Addiction, brain development, achievement, psychosis, drug sequencing, & road safety
  - Our perspective has shifted on drugs before…

…let's go in with eyes open this time.

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Thank You!