RECOVERY RESEARCH INSTITUTE

RECOVERYANSWERS.ORG

Addiction, Opioids, Cannabis, and Youth

John F. Kelly, Ph.D.

MASC/MASS STATE CONVENTION, NOV 2017

ENHANCING RECOVERY THROUGH SCIENCE

RECOVERY RESEARCH INSTITUTE

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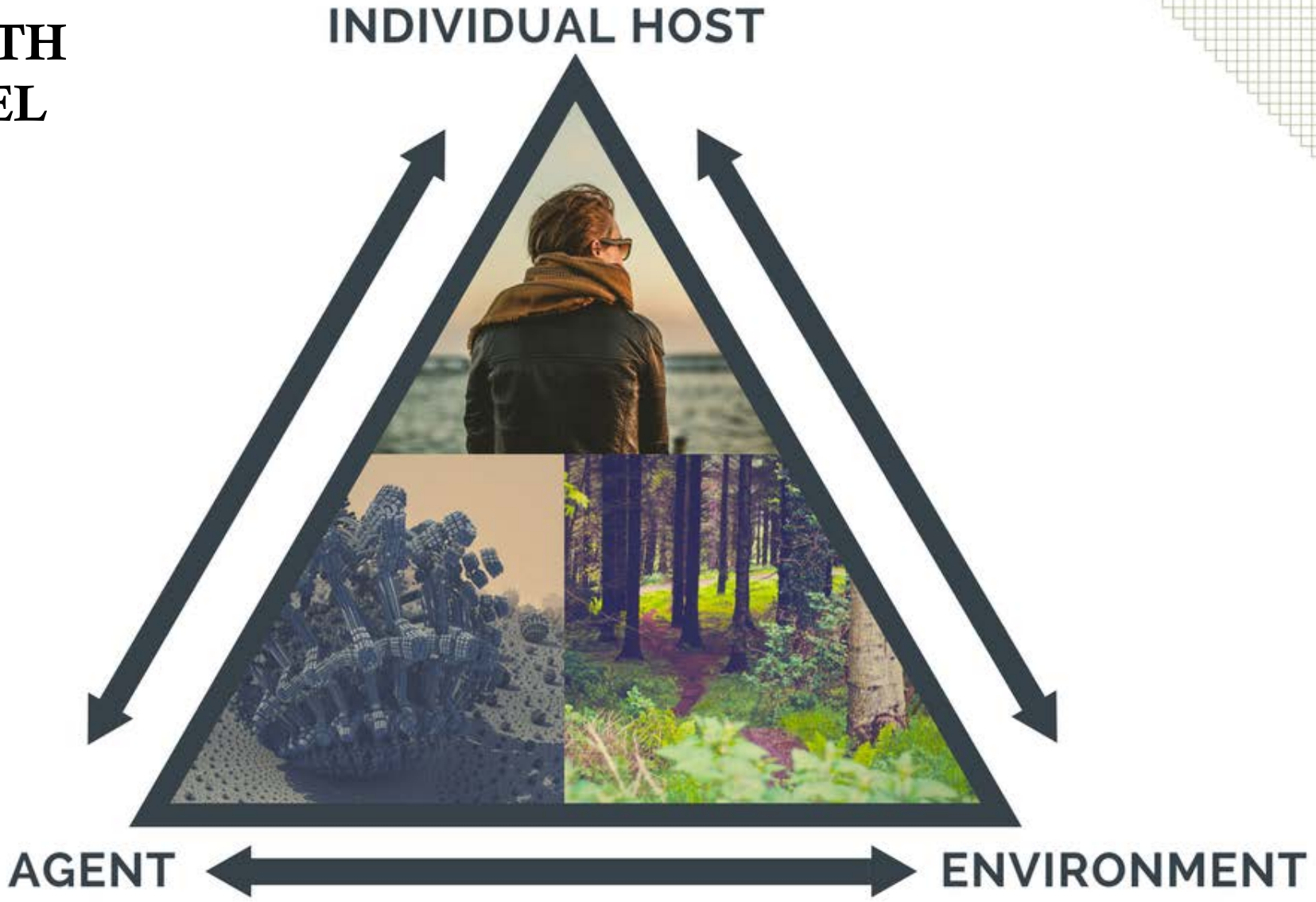
RECOVERY RESEARCH INSTITUTE MISSION:

To enhance the public health impact of addiction recovery science through the summary, synthesis, & dissemination of scientific findings & the conduct of novel research.

“Public Health Emergency”

PUBLIC HEALTH MODEL



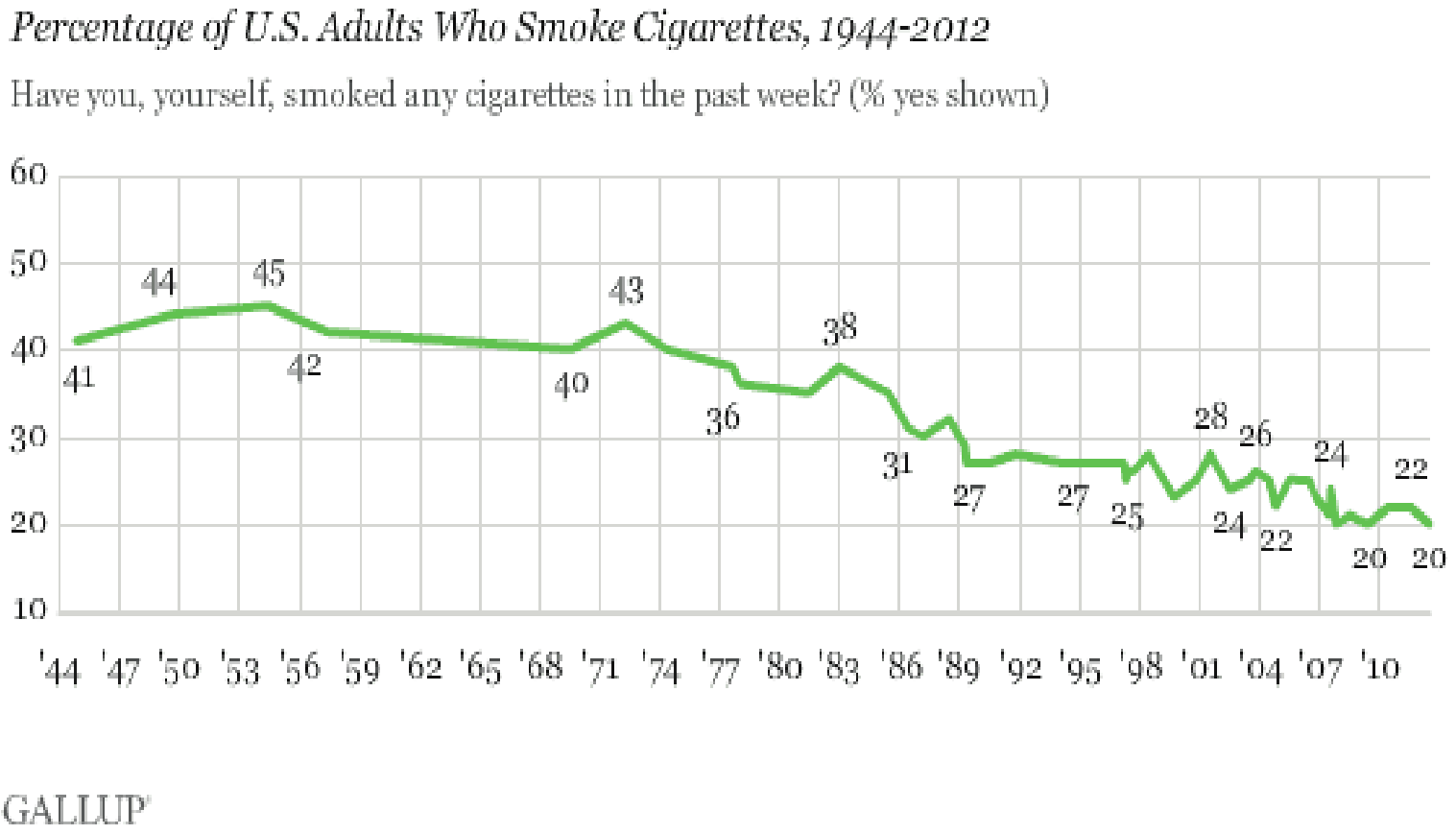
SUPPLY & DEMAND

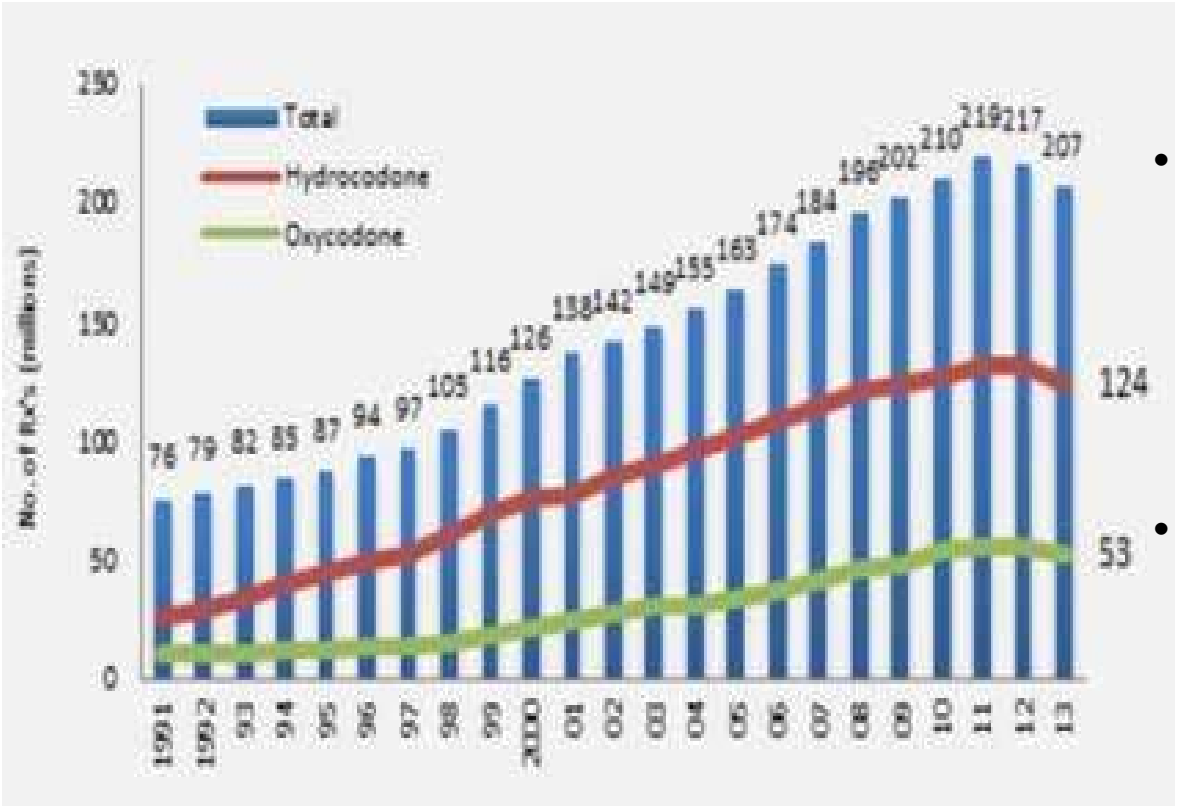
- Desirability
- Availability
- Accessibility
- Low Stigma
- Legal Status
- Cost

availability, accessibility, and price

prevention and treatment intervention

This is what we've seen with tobacco use…



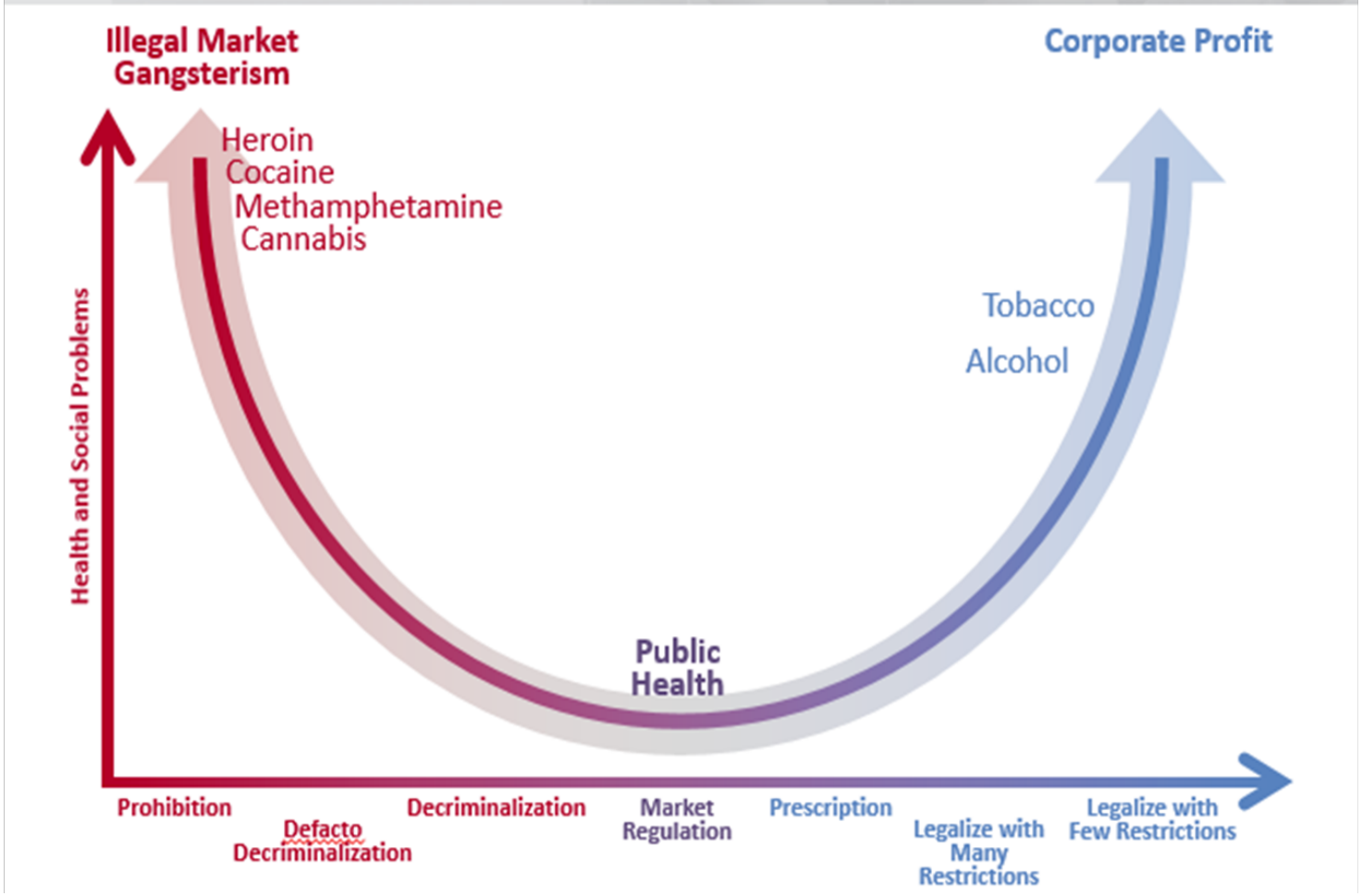


- United States biggest consumer globally of opioids, accounting for almost 100% of world total for hydrocodone (e.g., Vicodin) and 81% for oxycodone (e.g., Percocet).
- Number of prescriptions for opioids (like hydrocodone and oxycodone products) escalated from 76 million in 1991 to 207 million in 2013

International Narcotics Control Board Report 2008.External link, please review our disclaimer.. United Nations Pubns. 2009. p. 20

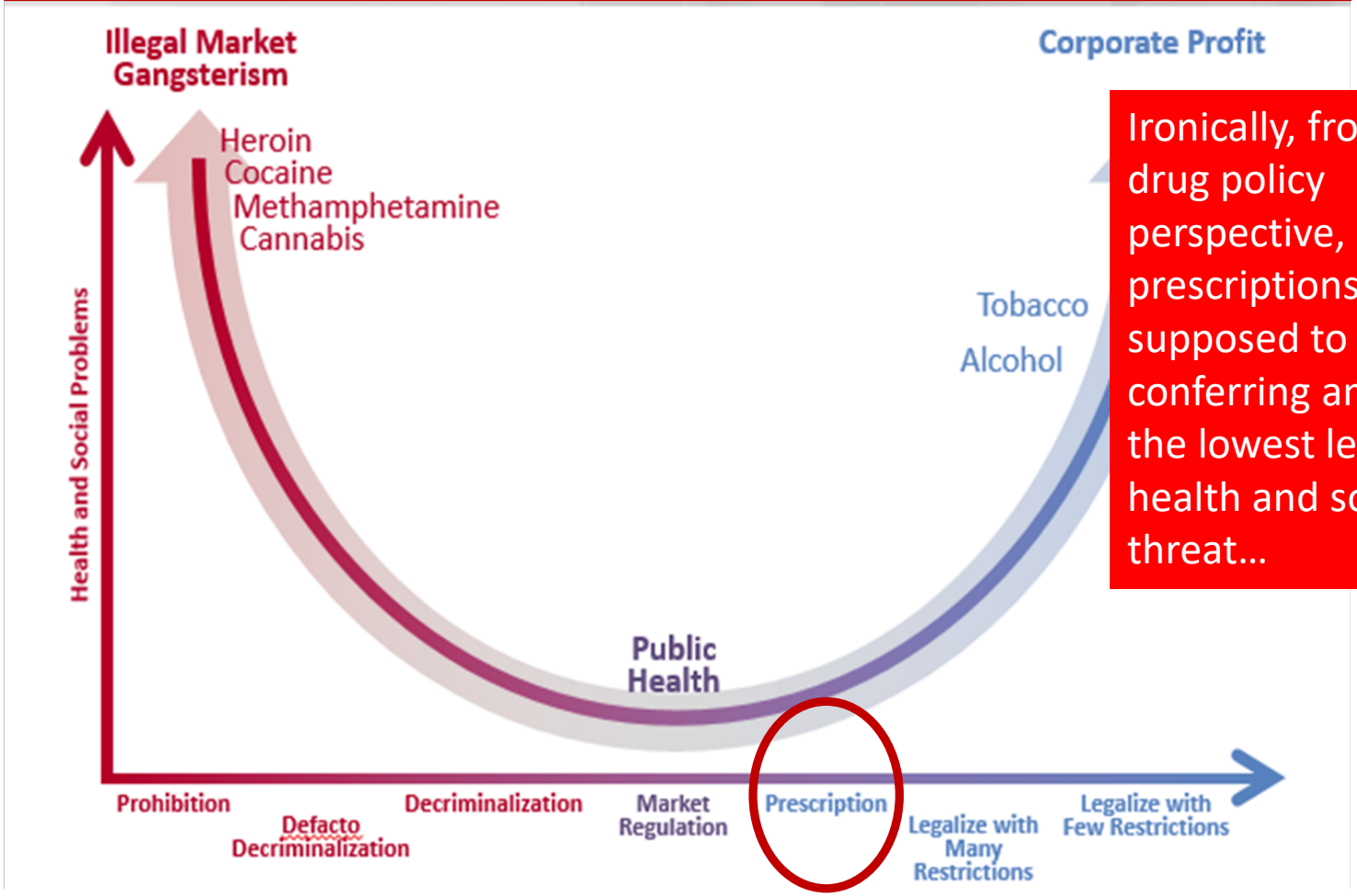
There are many different policy positions and strategies that one can take to address drugs in the population…

Degree of Problems Associated with Various Policy Approaches to Addressing the Drug Problem



There are many different policy positions and strategies that one can take to address drugs in the population…

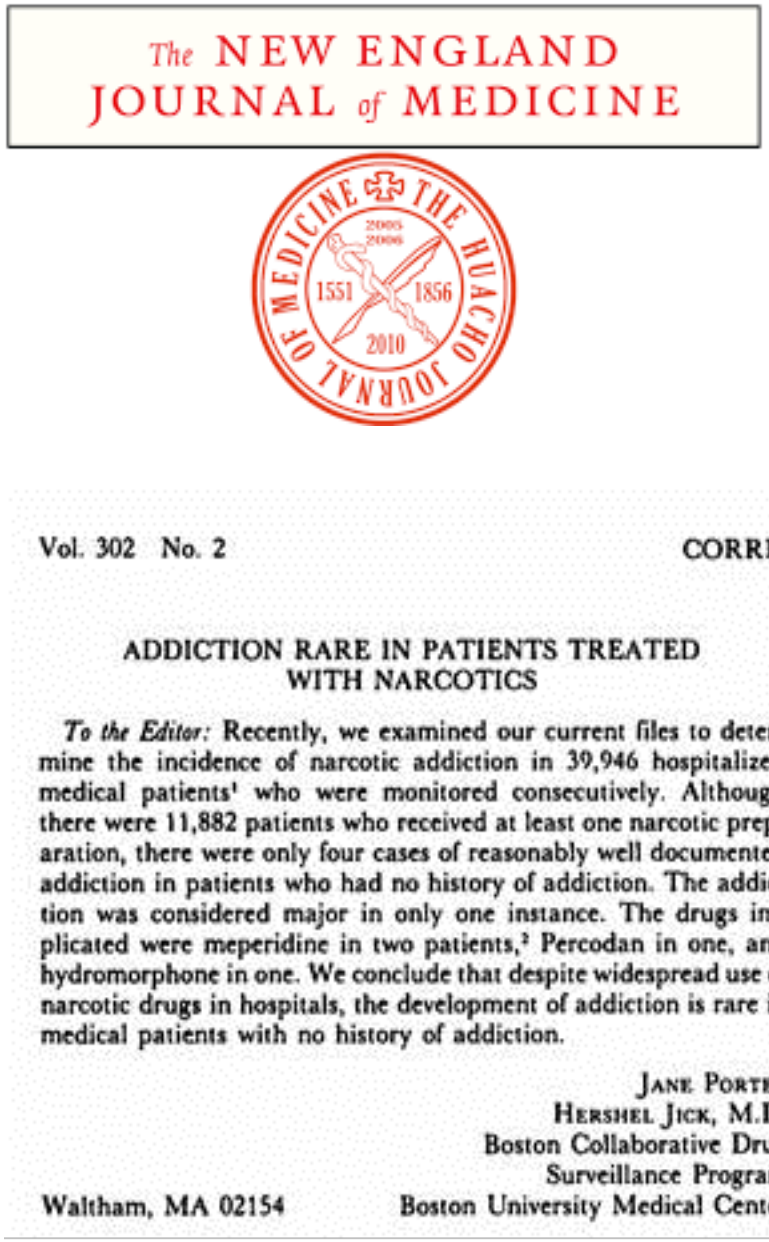
Degree of Problems Associated with Various Policy Approaches to Addressing the Drug Problem



Ironically, from a drug policy perspective, prescriptions are supposed to be safe conferring among the lowest levels of health and social threat…

Overprescribing: The 5th Vital Sign

- Unrelieved pain major, yet an avoidable, public health problem.
- 1997, collaborative project initiated to integrate pain assessment and management into standards
- 2001, all patient care organizations accredited by JCAHO - Pain Management becomes the 5th vital sign.
- Prescription opioids purported and perceived to be “safe” “non-addicting” …



The NEW ENGLAND JOURNAL of MEDICINE

Vol. 302 No. 2 CORRESPO

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Waltham, MA 02154 Boston University Medical Center

"I was sort of amazed. None of the companies came to talk to me about the letter or the use as an ad."

-Hershel Jick, NPR Interview, 2017

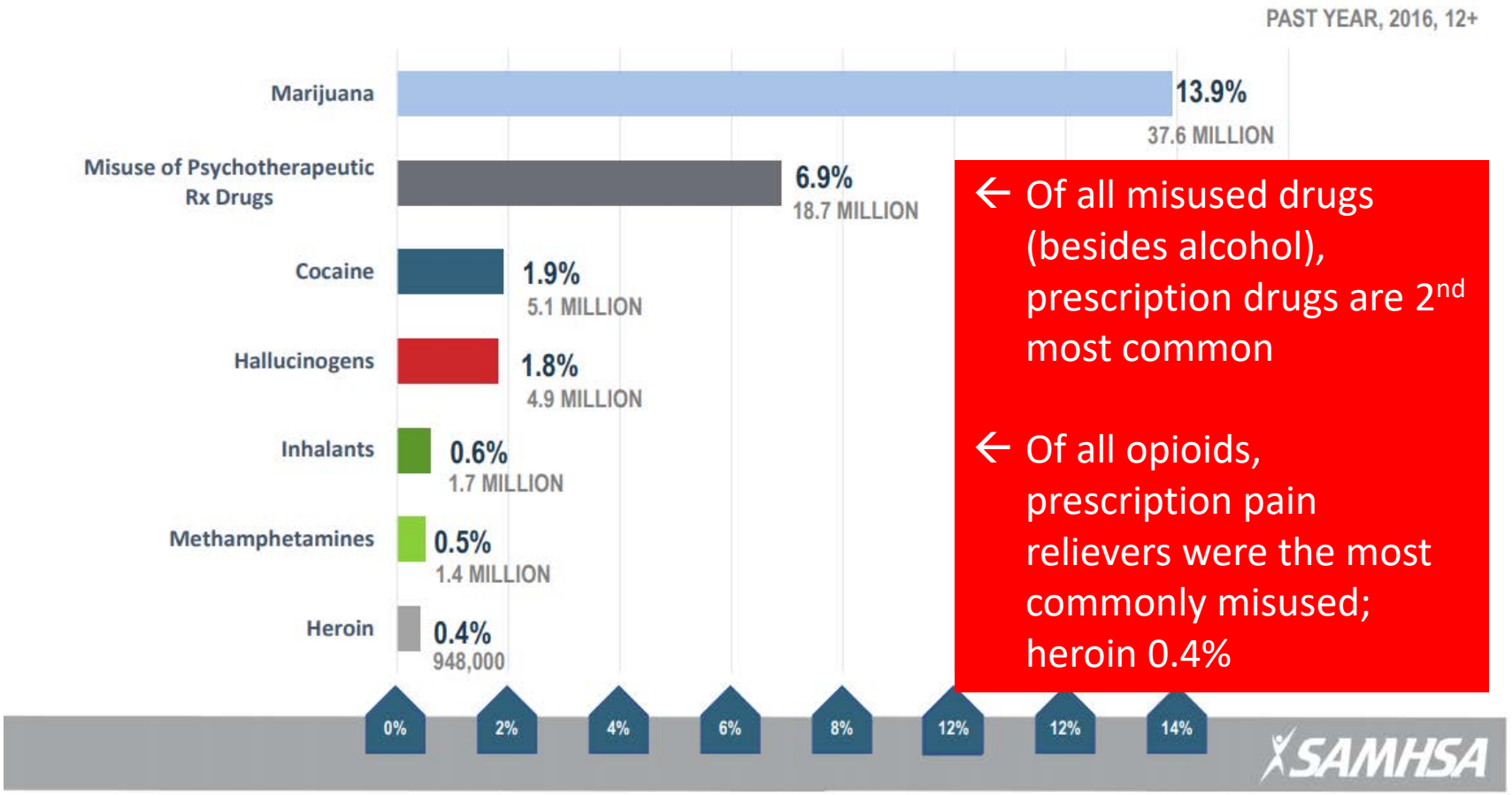
NPR: http://www.npr.org/sections/health-shots/2017/06/16/533060031/doctor-who-wrote-1980-letter-on-painkillers-regrets-that-it-fed-the-opioid-crisi

NEJM: http://www.nejm.org/doi/pdf/10.1056/NEJM198001103020221

How did we get here?
A perfect storm…

Powerfully seductive, addictive, legal, potentially lethal opioid medications, became too widely prescribed/ and available, easily accessible, promoted as “non-addictive” and safe, in an effort to treat the new “5th vital sign” (pain) with systematic encouragement and performance monitoring

NATIONAL TRENDS IN SUBSTANCE USE



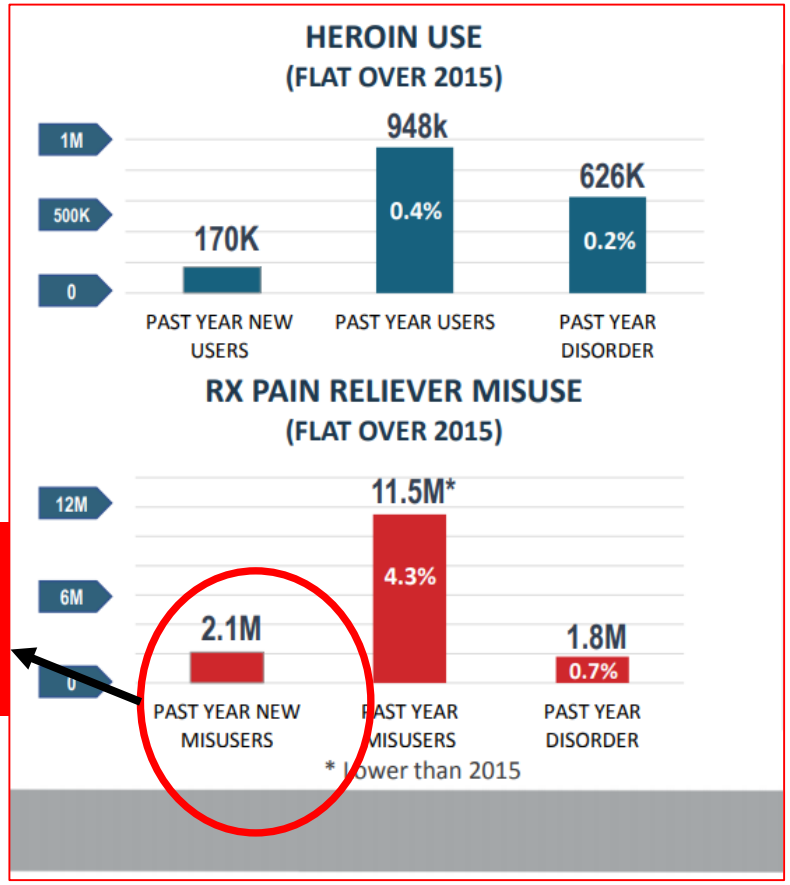
← Of all misused drugs (besides alcohol), prescription drugs are 2nd most common

← Of all opioids, prescription pain relievers were the most commonly misused; heroin 0.4%

NSDUH: https://www.samhsa.gov/sites/default/files/topics/data_outcomes_quality/nsduh-ppt-09-2017.pdf

EPIDEMIOLOGY & TRENDS: US

NATIONAL TRENDS



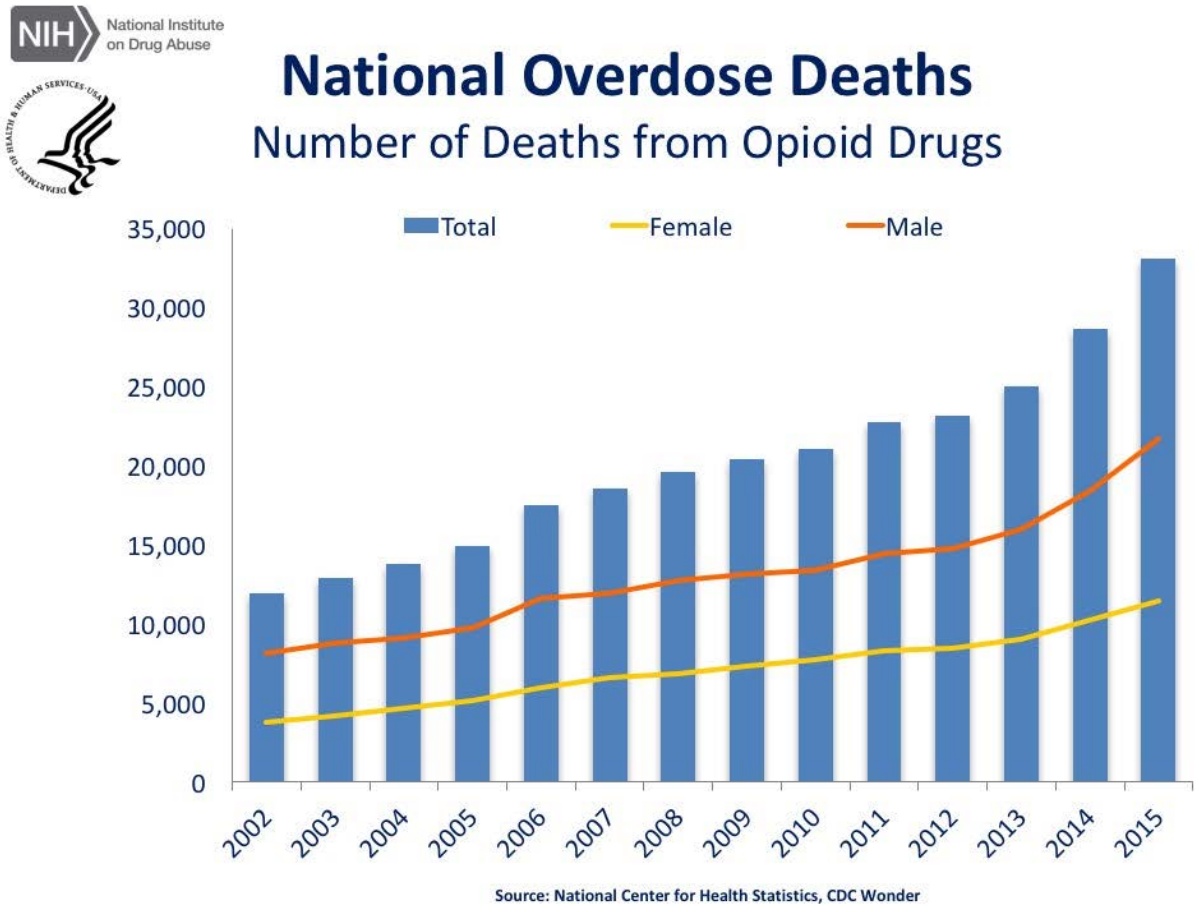
And we're still seeing lots of new misuse…

Rate of OD death 10x higher among individuals addicted to heroin compared to prescription opioids but prescription opioid use is 10x higher than heroin suggesting an equal need to reach and intervene with both groups assertively.

Rose's Theorem (prevention paradox): A large number of people exposed to a small risk can generate many more cases than a small number of people exposed to high risk (Rose, 1992).

NSDUH: https://www.samhsa.gov/sites/default/files/topics/data_outcomes_quality/nsduh-ppt-09-2017.pdf

NATIONAL OPIOID OD DEATHS: BY SEX



Almost a tripling in total number of OD deaths from ANY opioid drugs between 2002 and 2015

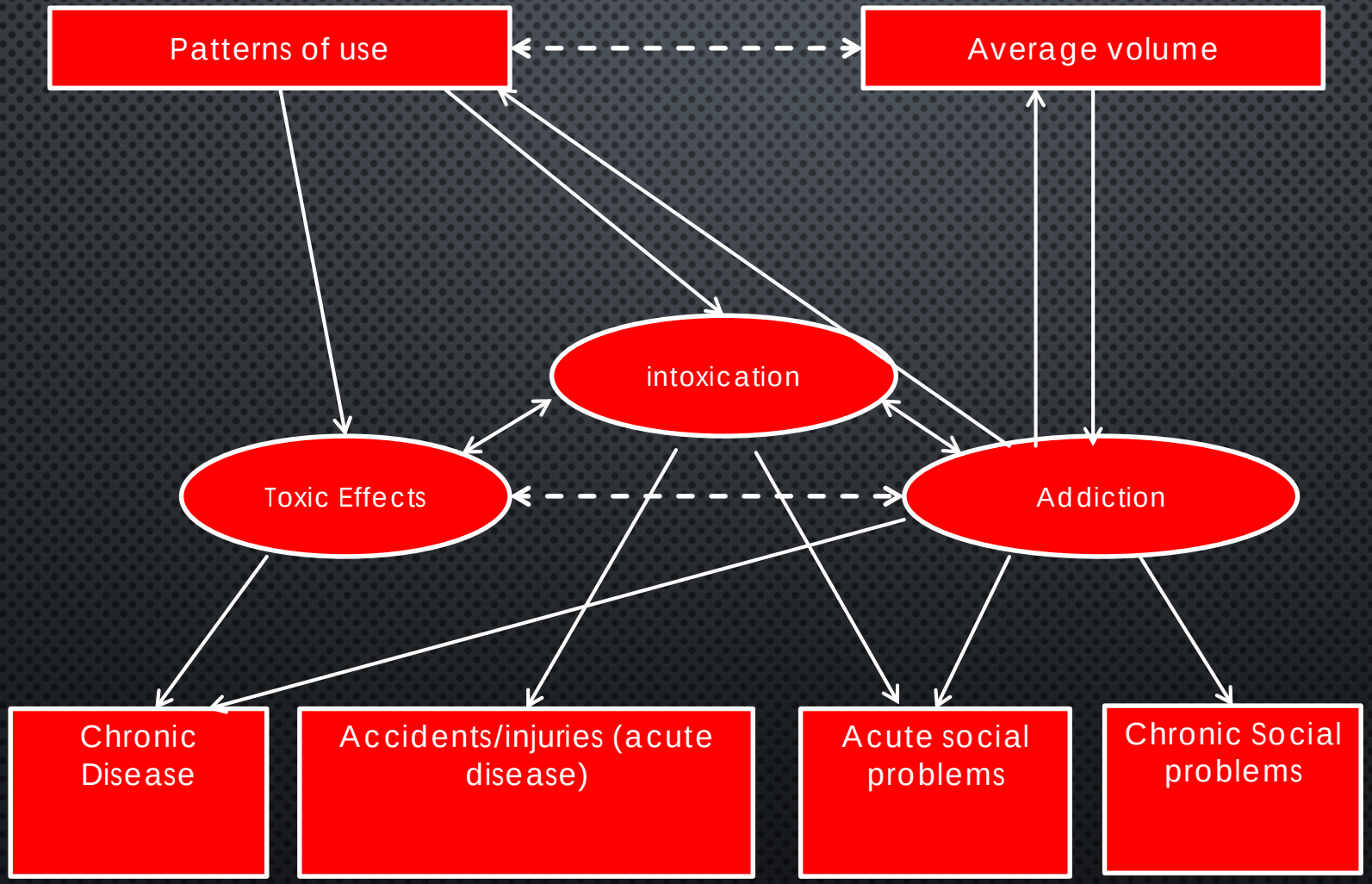
OPIOID OD represents about 62% of all OD deaths (excluding alcohol)

*Includes heroin, illicit synthetic opioids, and opioid analgesics

NIDA: https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates

Addiction is not the only pathway to harm....

Toxicity, Intoxication, and Addiction



Source: Babor et al, 2010

ADDICTION: THE RISK FACTORS

FACTORS THAT INCREASE THE LIKELIHOOD OF ONSET OR THE SPEED OF DEVELOPMENT OF A SUBSTANCE USE DISORDER.

GENETICS

Genetic predisposition can account for 40-60% of the risk of developing an addiction.

GENDER

Males are more likely than females to develop an addiction.

AGE AT FIRST USE

Starting substance use at an early age.

PSYCHOLOGICAL FACTORS

The prevalence of other mental health disorders, such as major depressive disorder, ADHD, or post-traumatic stress disorder, as well as personality traits such as high impulsivity & sensation seeking.

ENVIRONMENTAL INFLUENCES

Peer substance use, substance availability or access, exposure to traumatic events particularly physical, emotional or sexual abuse, media influences, etc.

FAMILY INVOLVEMENT

Lack of family involvement, support, or parental supervision, parent substance use.

HAVING 1 OR MORE OF THE ABOVE RISK FACTORS DOES NOT MEAN THAT SOMEONE WILL DEVELOP A SUBSTANCE USE DISORDER. THE PRESENCE OF RISK FACTORS INCREASES THE ODDS THAT ONE WILL DEVELOP SUBSTANCE USE DISORDER, & THE MORE RISK FACTORS PRESENT, THE GREATER THE LIKELIHOOD.

FOR MORE INFORMATION VISIT: www.recoveryanswers.org

(NIDA, MAYO CLINIC)

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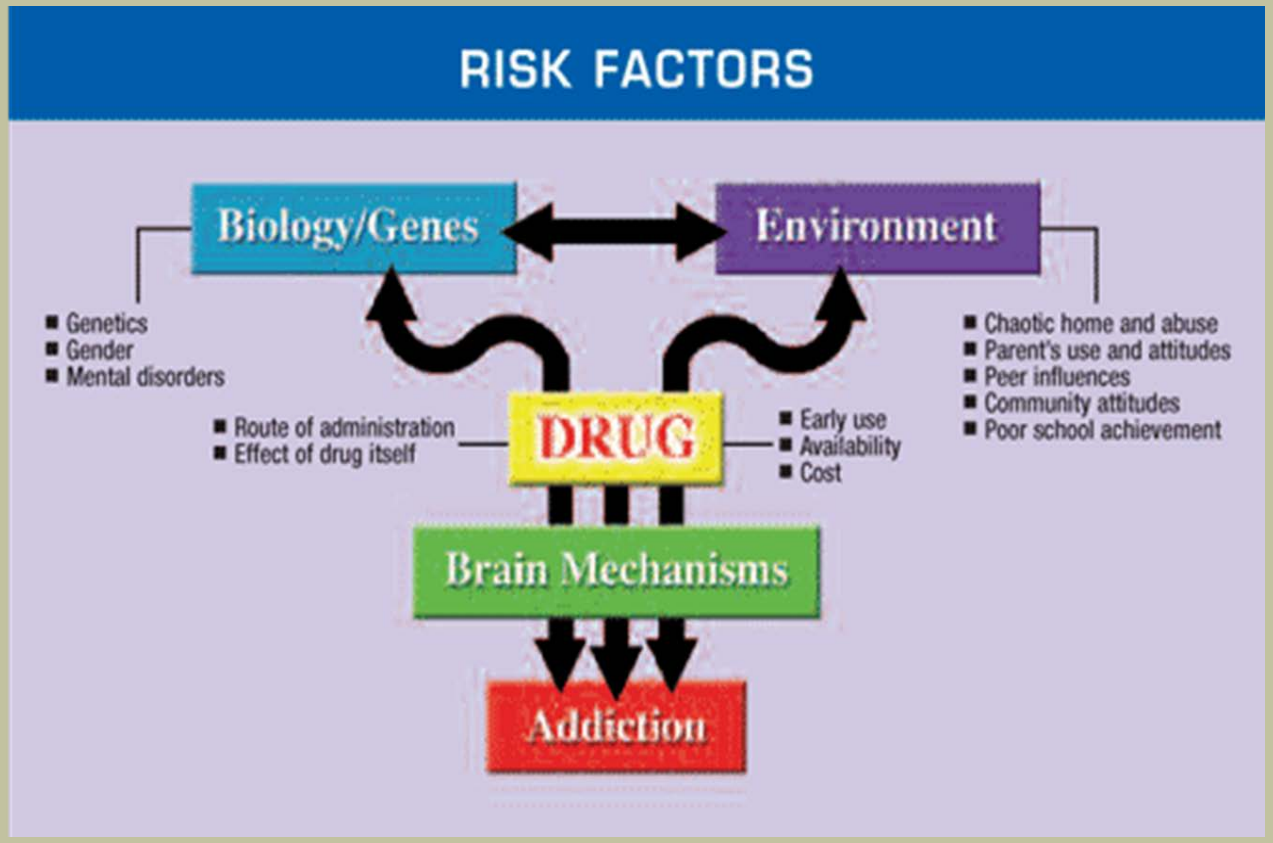
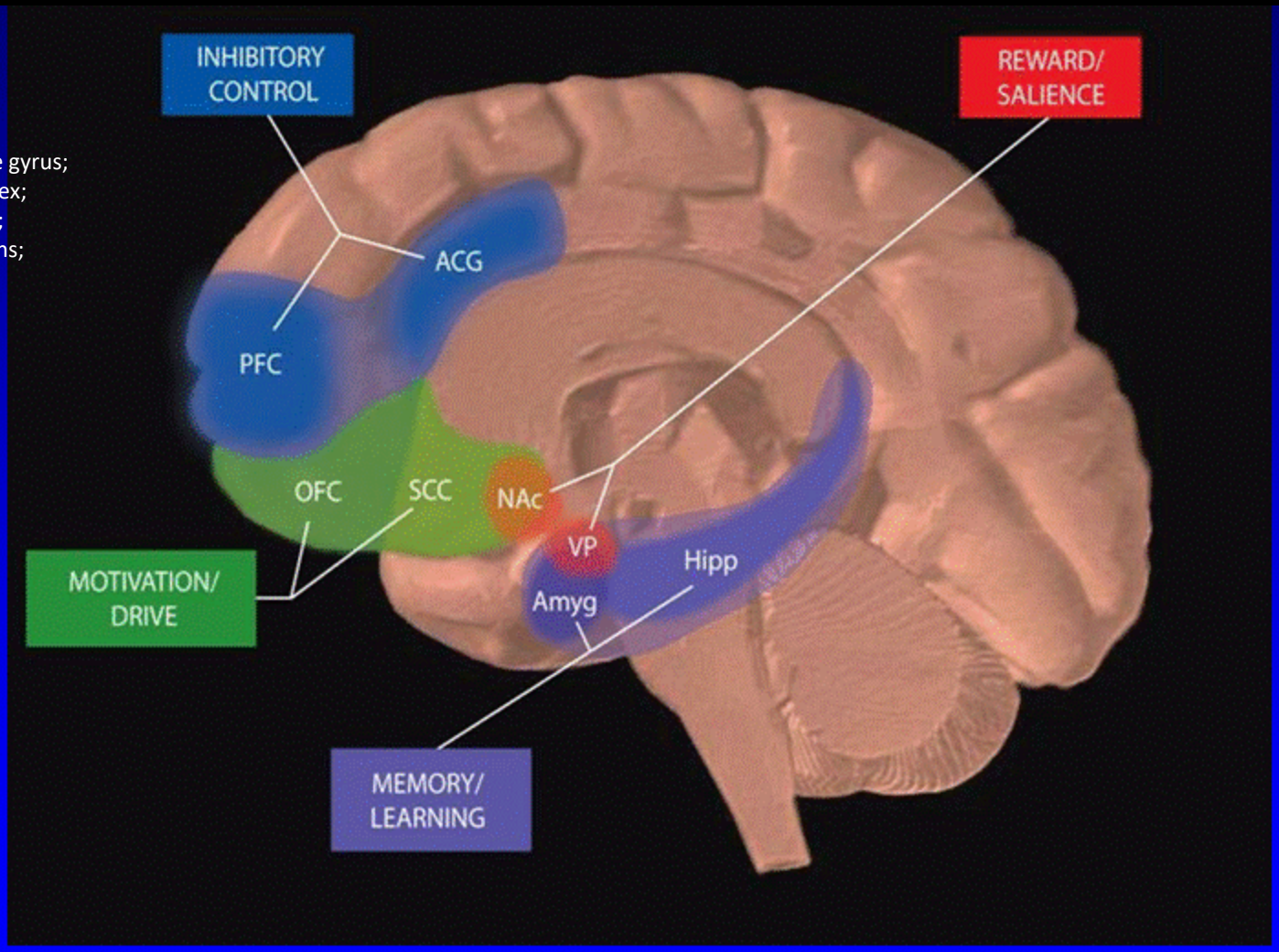
Addiction is a complex multi-factorially determined illness…



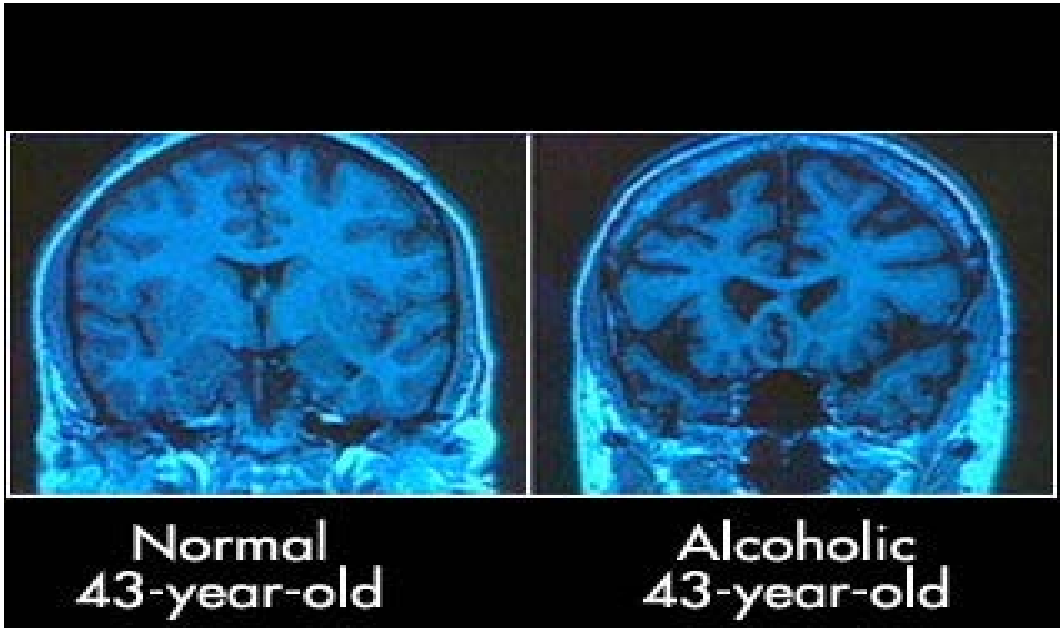
Addiction is a result of neurological changes …

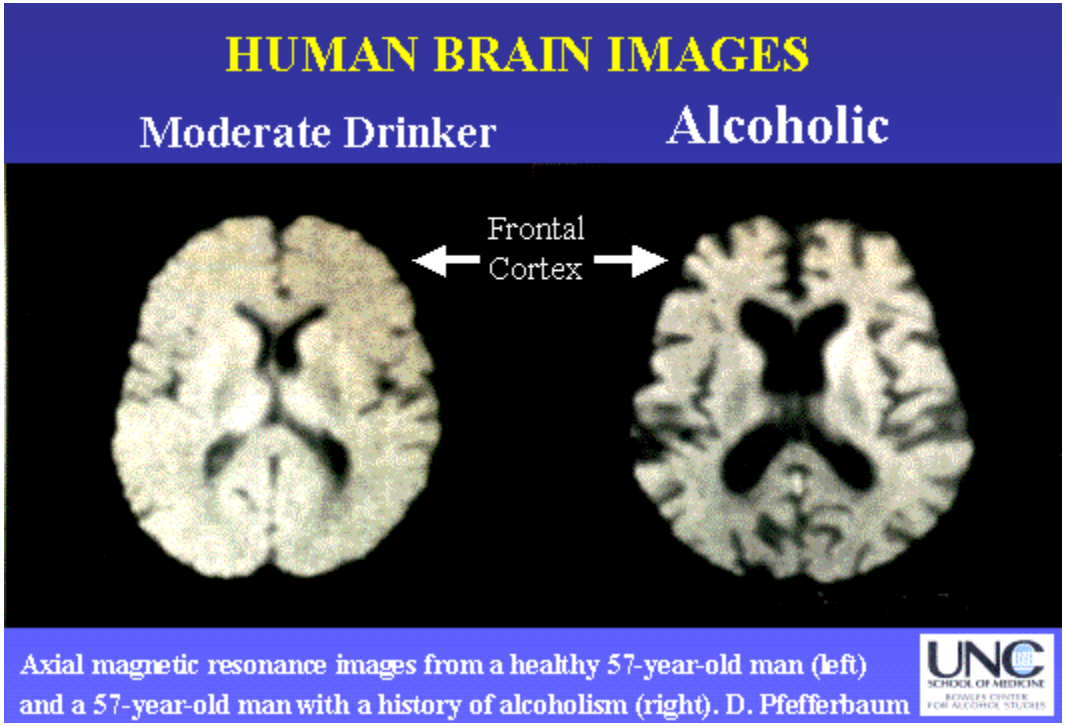
Key:
PFC – prefrontal cortex;
ACG – anterior cingulate gyrus;
OFC – orbitofrontal cortex;
SCC – subcallosal cortex;
NAc – nucleus accumbens;
VP – ventral pallidum;
Hipp – hippocampus;
Amyg – amygdala.



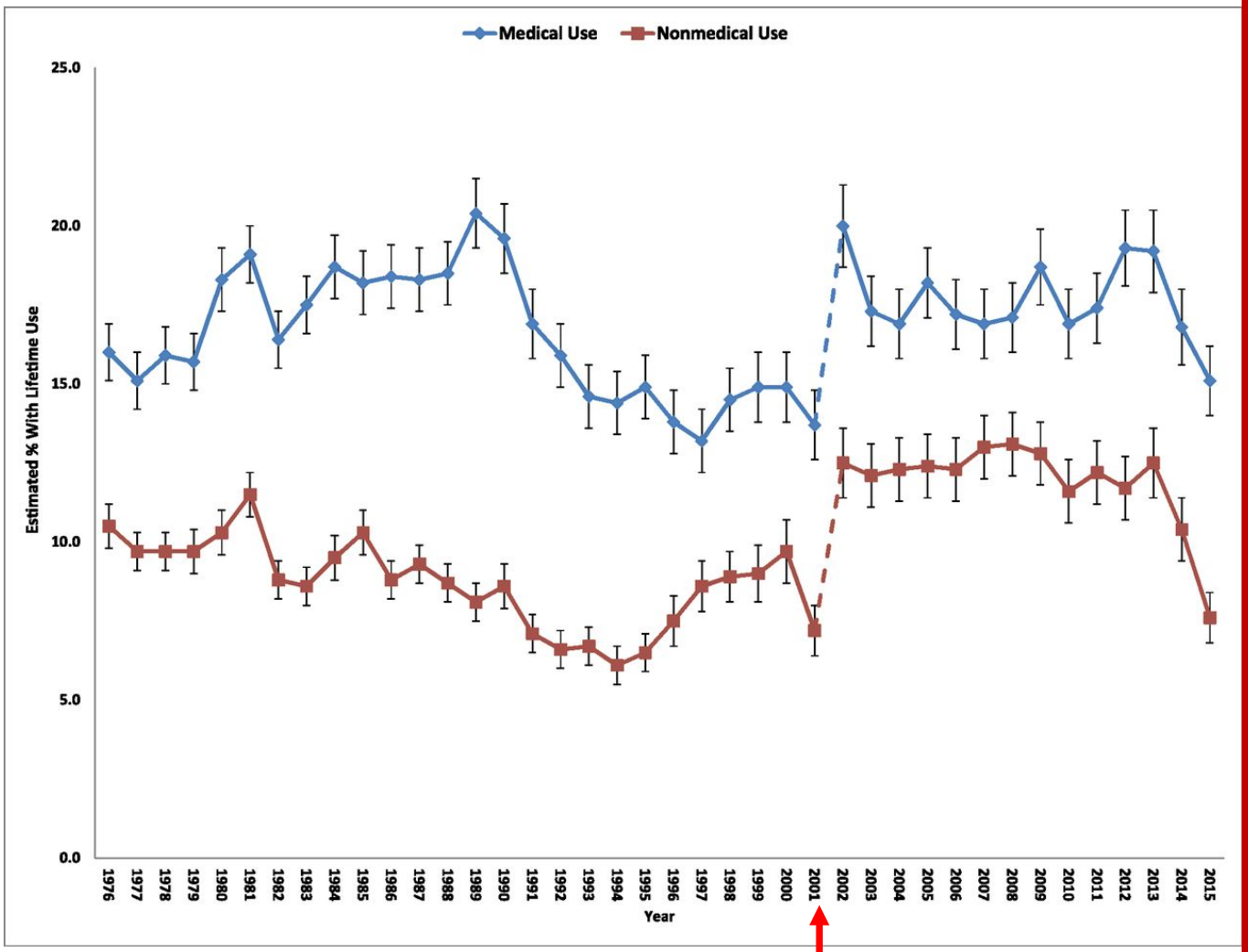
All of these brain regions must be considered in developing strategies to effectively treat addiction

NIDA


Normal
43-year-old
Alcoholic
43-year-old


HUMAN BRAIN IMAGES
Moderate Drinker
Alcoholic
Frontal
Cortex
Axial magnetic resonance images from a healthy 57-year-old man (left) and a 57-year-old man with a history of alcoholism (right). D. Pfefferbaum
UNC
SCHOOL OF MEDICINE

Trends in lifetime medical and nonmedical use of prescription opioids among high school seniors, 1976–2015.



Sean Esteban McCabe et al. Pediatrics
doi:10.1542/peds.2016-2387

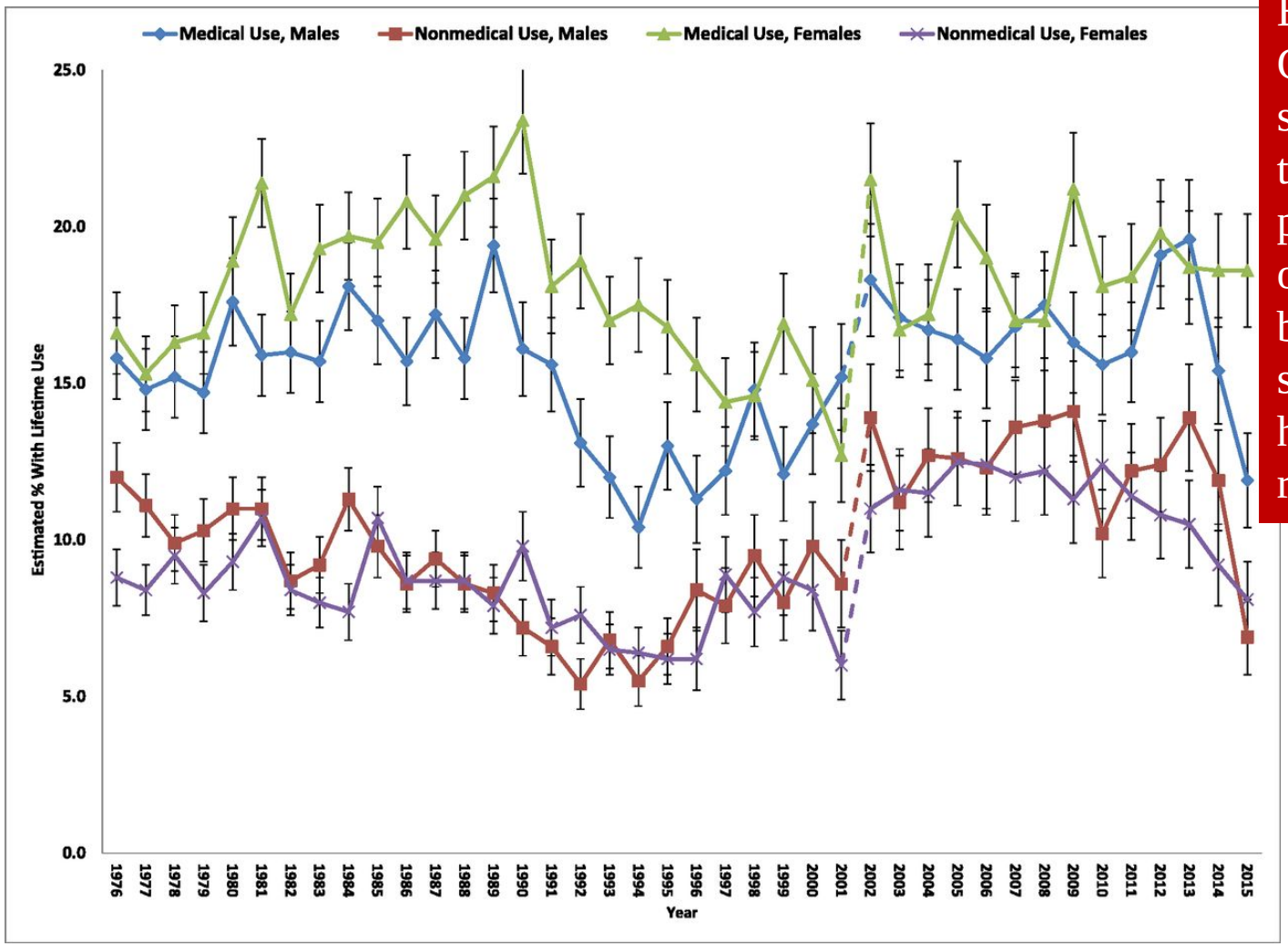
Joint Commission requirement to address pain

About 10-15% of HS seniors misuse Prescription opioids

(General adult population =5%)

Non-medical Use has largely Followed trends in medical Use.

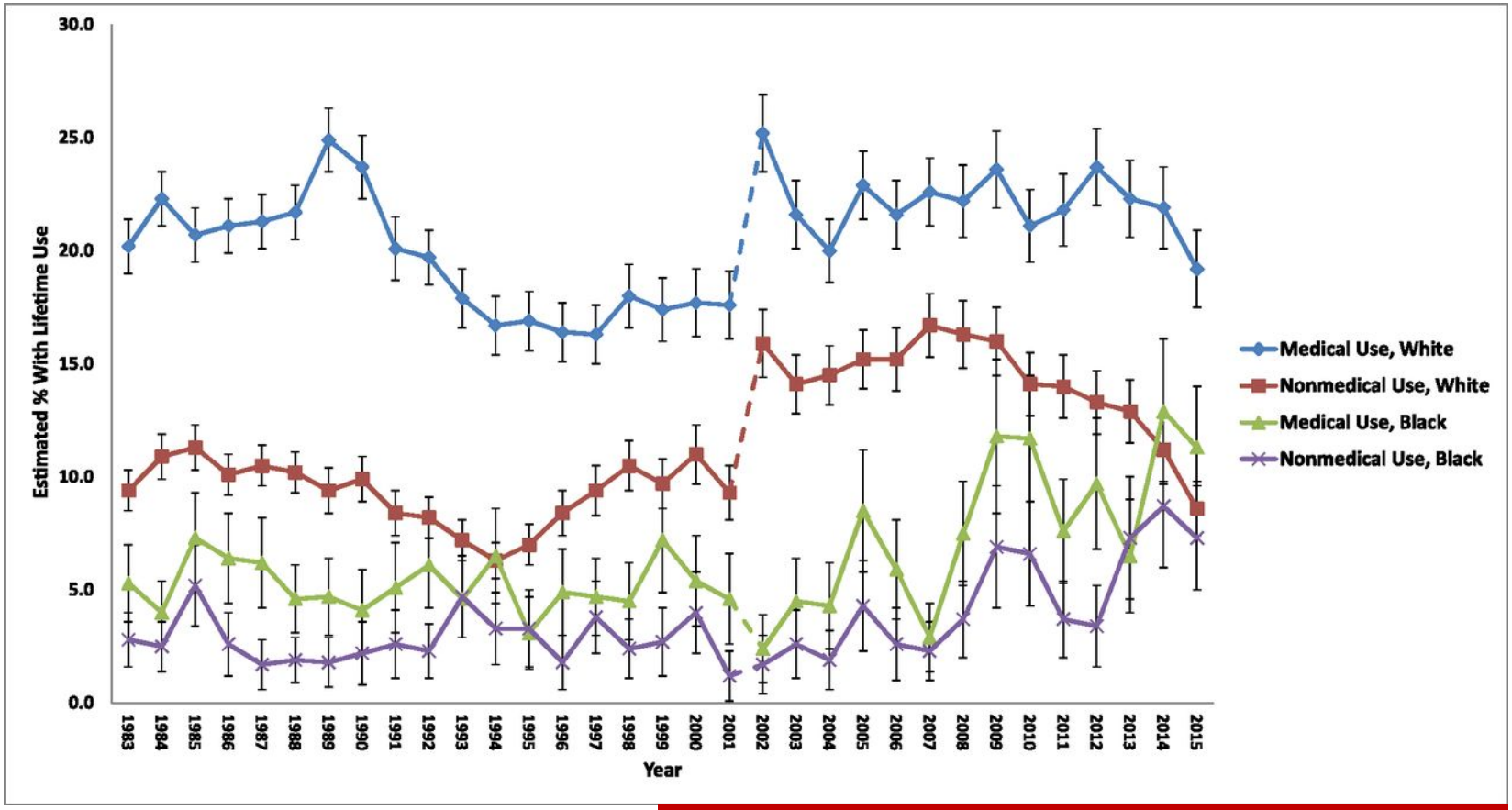
Trends in lifetime medical and nonmedical use of prescription opioids among high school seniors by sex, 1976–2015.



Boys and Girls show similar trends in prevalence of use with boys slightly higher in recent years

Sean Esteban McCabe et al. Pediatrics
doi:10.1542/peds.2016-2387

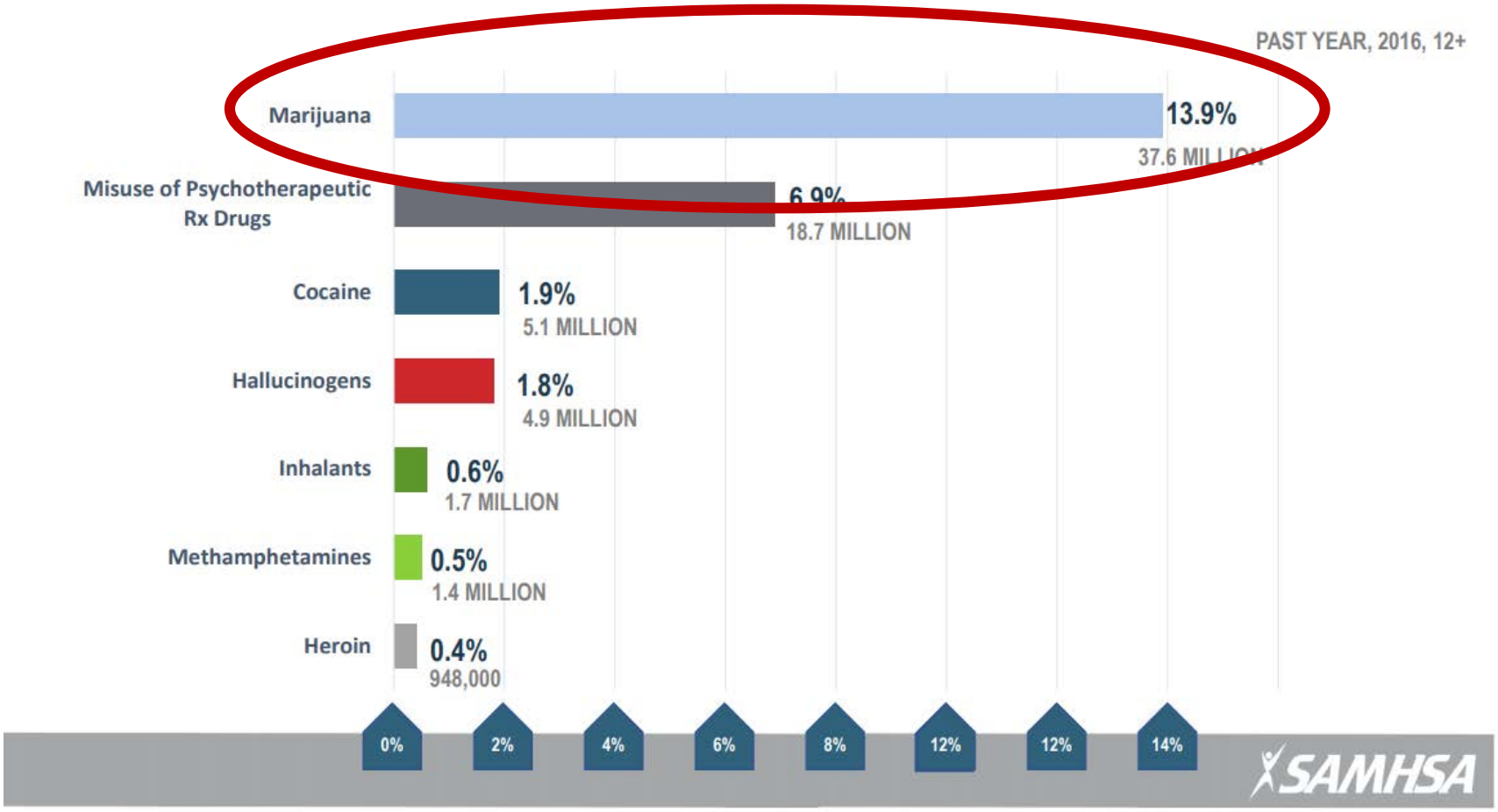
Trends in lifetime medical and nonmedical use of prescription opioids among US high school seniors by race, 1983–2015.



Rates of medical use and nonmedical use substantially higher among White than Black individuals

Sean Esteban McCabe et al. Pediatrics
doi:10.1542/peds.2016-2387

NATIONAL TRENDS IN SUBSTANCE USE



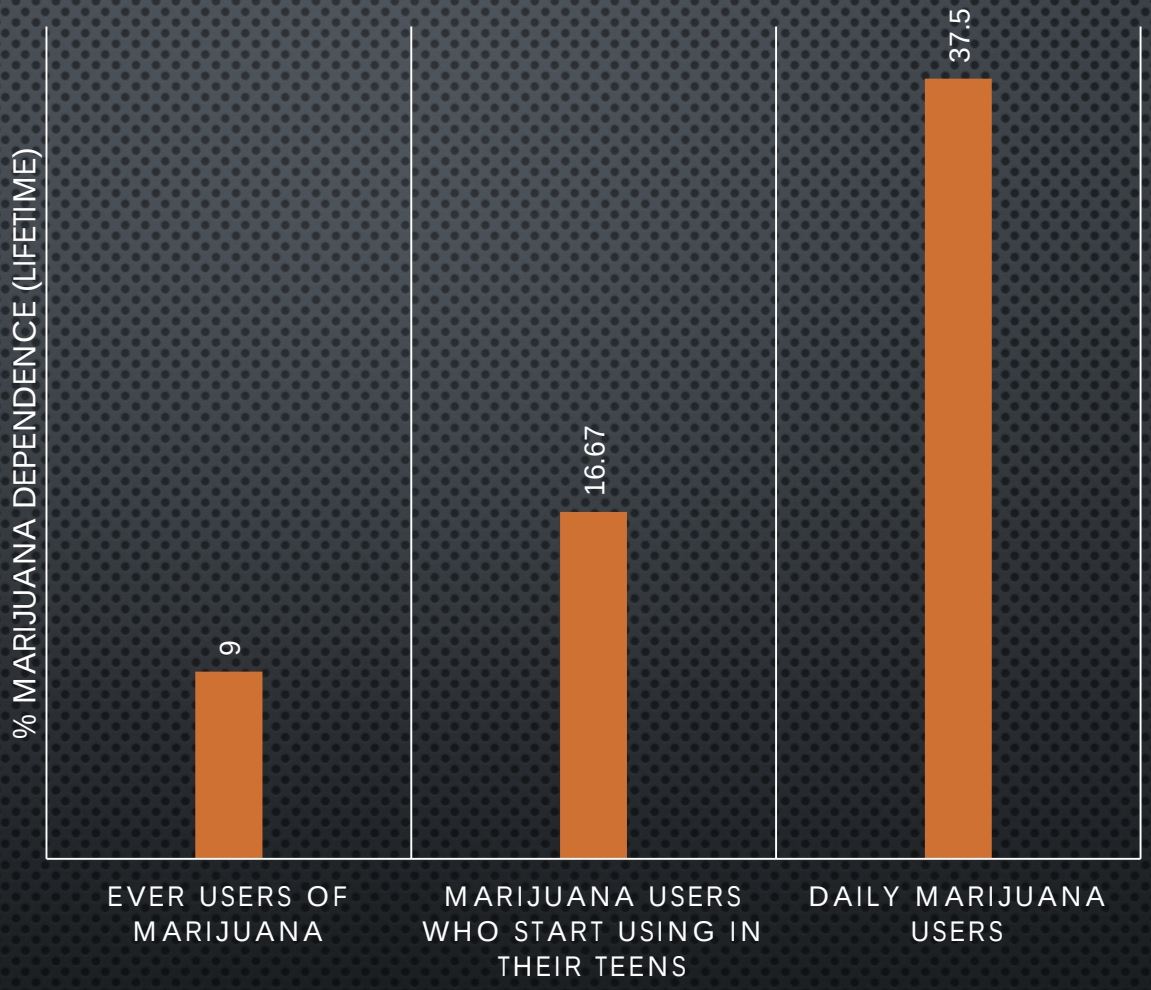
NSDUH: https://www.samhsa.gov/sites/default/files/topics/data_outcomes_quality/nsduh-ppt-09-2017.pdf

Addiction

ADDICTIVENESS OF MARIJUANA

"ADOLESCENTS, ESPECIALLY TROUBLED ONES, AND PEOPLE WITH PSYCHIATRIC DISORDERS (INCLUDING SUBSTANCE ABUSE) APPEAR MORE LIKELY THAN THE GENERAL POPULATION TO BECOME DEPENDENT ON MARIJUANA… "

-- INSTITUTE OF MEDICINE



Anthony, J.; Warner, L.A.; and Kessler, R.C. *Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey.* Exp Clin Psychopharmacol 2:244–268, 1994;

Hall, W.; and Degenhardt, L. *Adverse health effects of non-medical cannabis use.* Lancet 374:1383–1391, 2009;

Hall, W. *The adverse health effects of cannabis use: What are they, and what are their implications for policy?* Int J of Drug Policy 20:458–466, 2009

Original Investigation

Prevalence of Marijuana Use Disorders in the United States Between 2001-2002 and 2012-2013

Deborah S. Hasin, PhD; Tulshi D. Saha, PhD; Bradley T. Kerridge, PhD; Risë B. Goldstein, PhD, MPH; S. Patricia Chou, PhD; Haitao Zhang, PhD; Jeesun Jung, PhD; Roger P. Pickering, MS; W. June Ruan, MA; Sharon M. Smith, PhD; Boji Huang, MD, PhD; Bridget F. Grant, PhD, PhD

IMPORTANCE Laws and attitudes toward marijuana in the United States are becoming more permissive but little is known about whether the prevalence rates of marijuana use and marijuana use disorders have changed in the 21st century.

OBJECTIVE To present nationally representative information on the past-year prevalence rates of marijuana use, marijuana use disorder, and marijuana use disorder among marijuana users in the US adult general population and whether this has changed between 2001-2002 and 2012-2013.

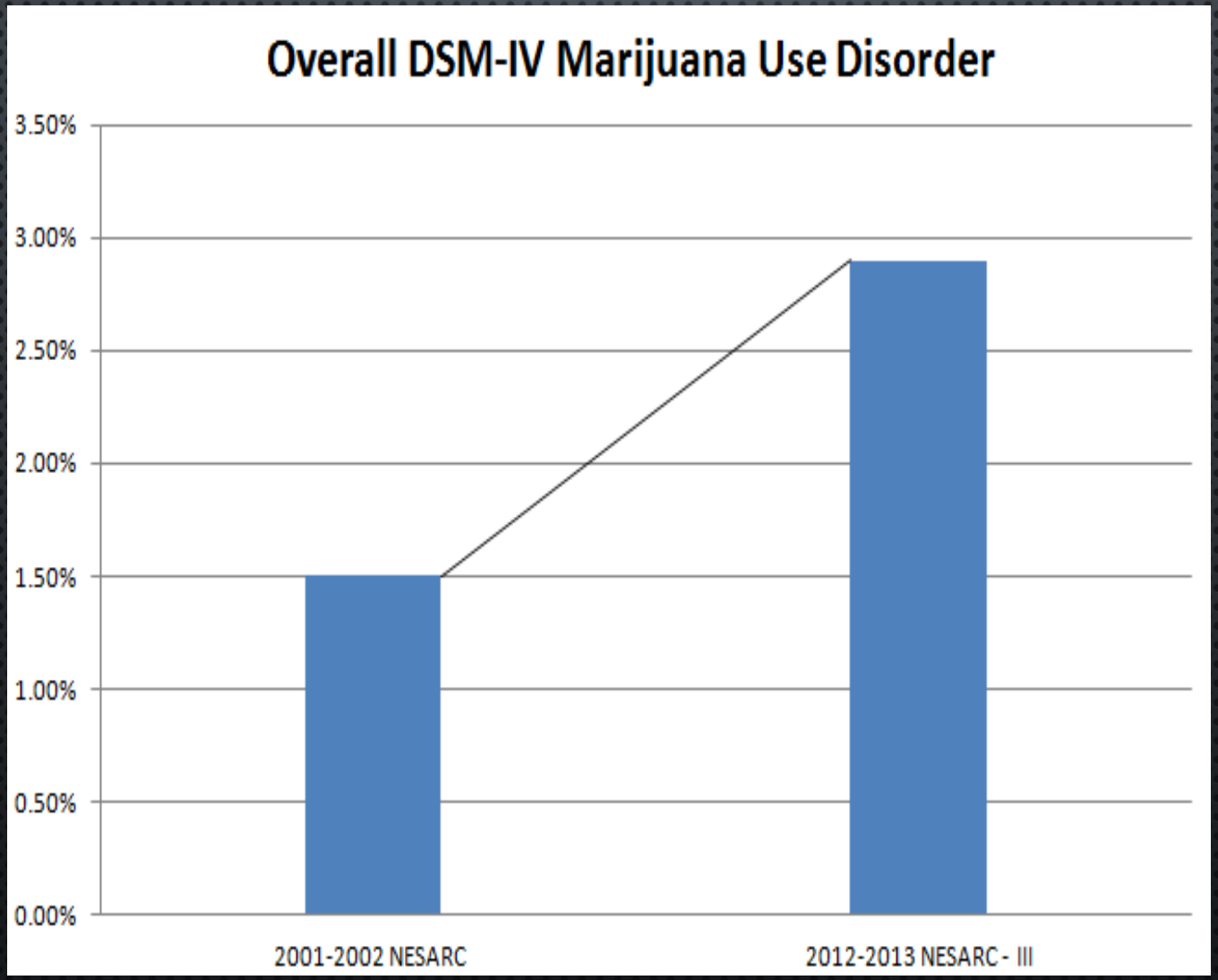
DESIGN, SETTING, AND PARTICIPANTS Face-to-face interviews conducted in surveys of 2 nationally representative samples of US adults: the National Epidemiologic Survey on Alcohol and Related Conditions (data collected April 2001-April 2002; N = 43 093) and the National Epidemiologic Survey on Alcohol and Related Conditions–III (data collected April 2012-June 2013; N = 36 309). Data were analyzed March through May 2015.

MAIN OUTCOMES AND MEASURES Past-year marijuana use and *DSM-IV* marijuana use disorder (abuse or dependence).

RESULTS The past-year prevalence of marijuana use was 4.1% (SE, 0.15) in 2001-2002 and 9.5% (SE, 0.27) in 2012-2013, a significant increase ($P < .05$). Significant increases were also found across demographic subgroups (sex, age, race/ethnicity, education, marital status, income, urban/rural, and region). The past-year prevalence of *DSM-IV* marijuana use disorder was 1.5% (0.08) in 2001-2002 and 2.9% (SE, 0.13) in 2012-2013 ($P < .05$). With few exceptions, increases in the prevalence of marijuana use disorder between 2001-2002 and 2012-2013 were also statistically significant ($P < .05$) across demographic subgroups. However, the prevalence of marijuana use disorder among marijuana users decreased significantly from 2001-2002 (35.6%; SE, 1.37) to 2012-2013 (30.6%; SE, 1.04).

CONCLUSIONS AND RELEVANCE The prevalence of marijuana use more than doubled between 2001-2002 and 2012-2013, and there was a large increase in marijuana use disorders during that time. While not all marijuana users experience problems, nearly 3 of 10 marijuana users manifested a marijuana use disorder in 2012-2013. Because the risk for marijuana use disorder did not increase among users, the increase in prevalence of marijuana use disorder is owing to an increase in prevalence of users in the US adult population. Given changing laws and attitudes toward marijuana, a balanced presentation of the likelihood of adverse consequences of marijuana use to policy makers, professionals, and the public is needed.

PAST YEAR *DSM-IV* MARIJUANA USE DISORDER




Toxic
Effects

Experimental and Clinical Psychopharmacology
2012, Vol. 20, No. 5, 420–429

1064-1297/12/$1

Residual Effects of Cannabis Use on Neurocognitive Performa Prolonged Abstinence: A Meta-Analysis

Amy M. Schreiner and Michael E. Dunn
University of Central Florida

1. First Analysis (k=33)

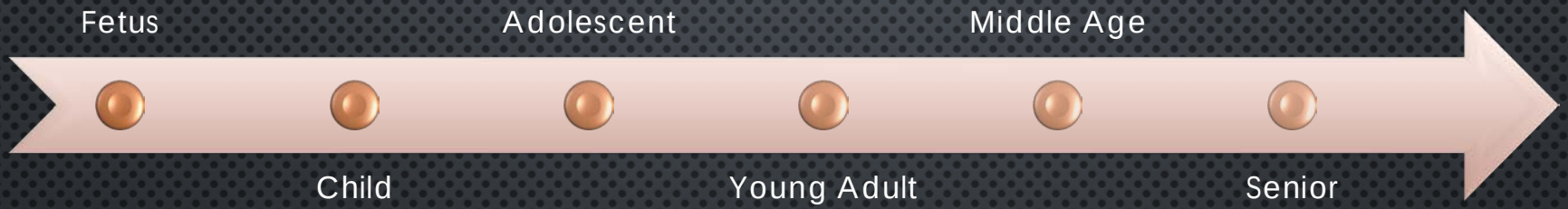
Results: Neurocognitive deficits in most domains of functioning present early during abstinence

2. Second Sub-Analysis (k-13)

Results: Not present after 25 or more days of abstinence

3. … but what about among youth?

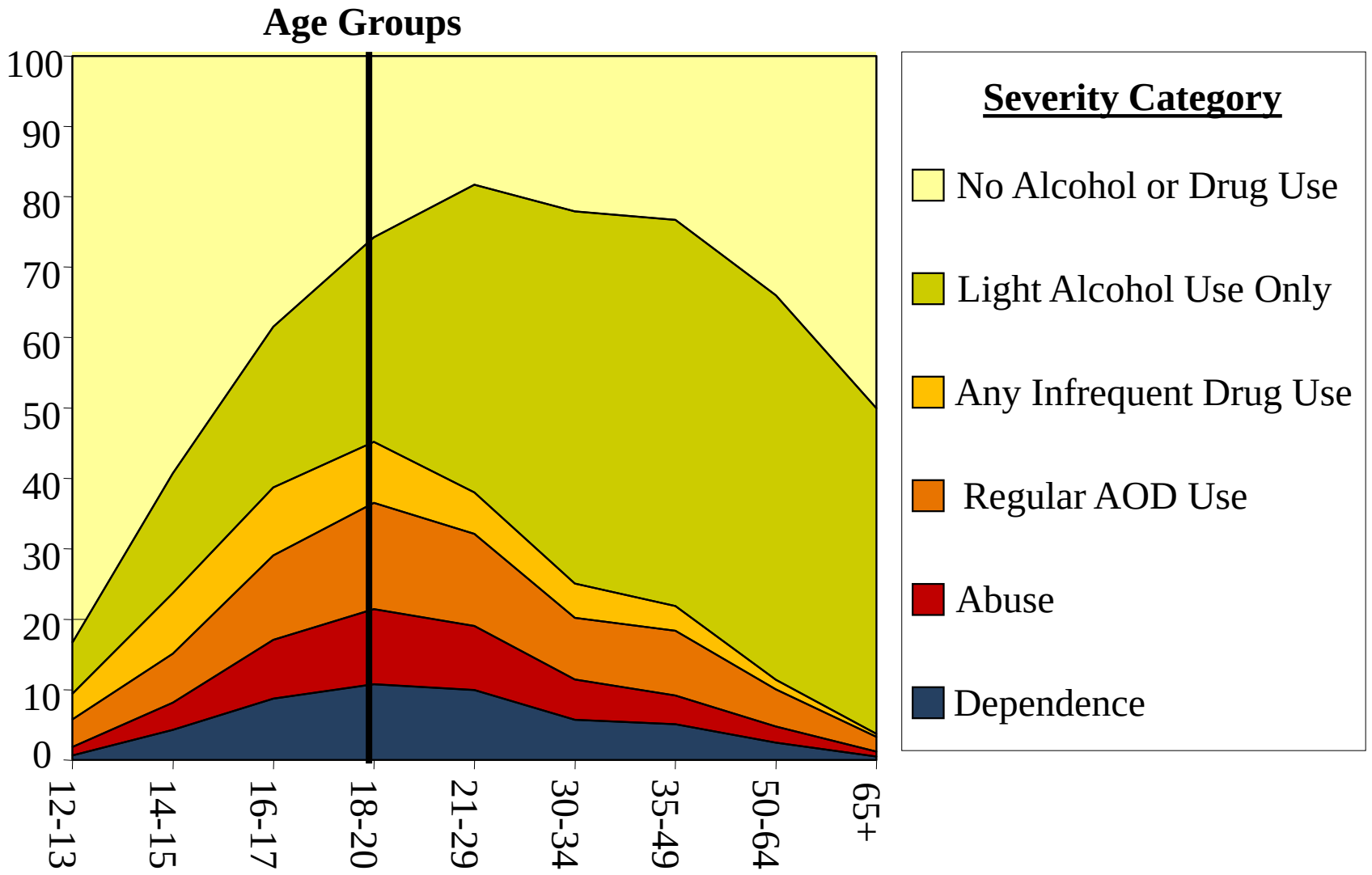
A LIFE COURSE PERSPECTIVE



The life course perspective has the advantage of recognizing developmental stages as factors facilitating or inhibiting change and continuity, and/or protective and risk factors, that may differ across the life span (Hser & Anglin, 2008).

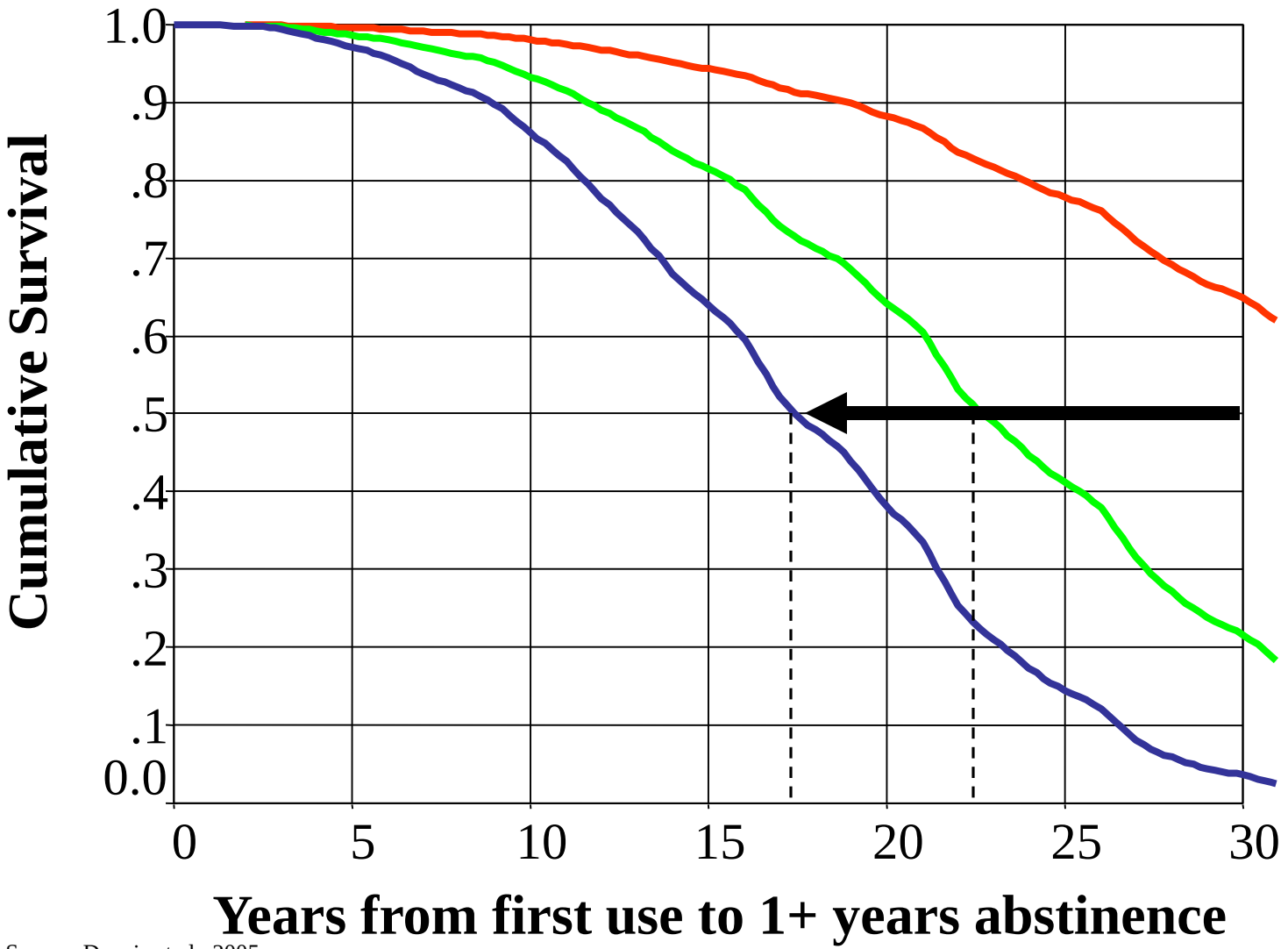

90%
OF INDIVIDUALS WITH SUBSTANCE USE DISORDERS
BEGAN SMOKING, DRINKING, OR USING OTHER DRUGS BEFORE THE AGE OF 18.

Clinician's Illusion vs Epidemiologist's Illusion

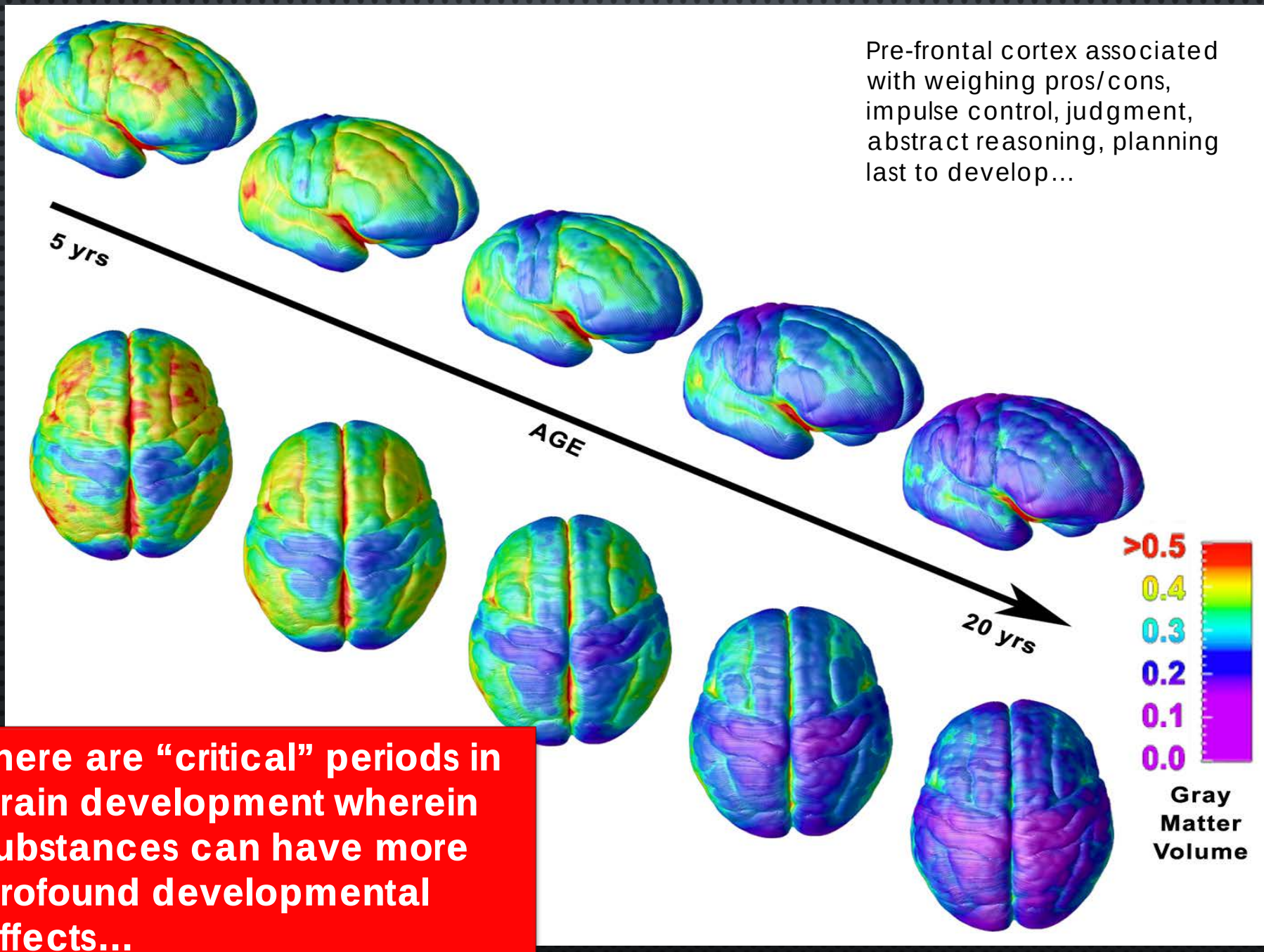


NSDUH and Dennis & Scott

Earlier Intervention Lessens Impact and Duration of SUD



Source: Dennis et al., 2005


Pre-frontal cortex associated with weighing pros/cons, impulse control, judgment, abstract reasoning, planning last to develop…
5 yrs
AGE
20 yrs
>0.5
0.4
0.3
0.2
0.1
0.0
Gray Matter Volume
There are “critical” periods in brain development wherein substances can have more profound developmental effects…

Pharmacology & Therapeutics 148 (2015) 1–16

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

Associate editor: S. Andersen

Cannabis and adolescent brain development

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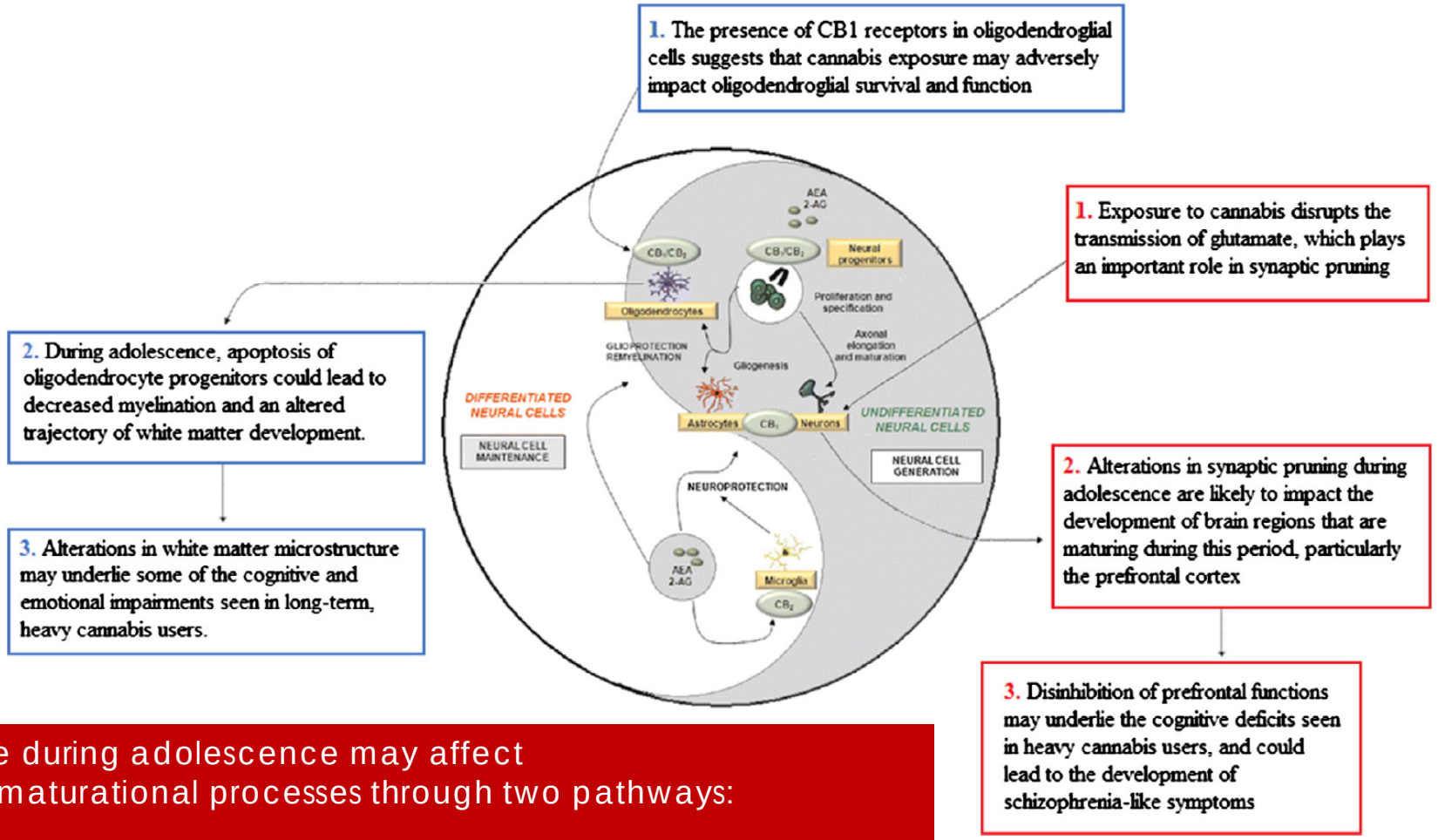
Brain development
Endocannabinoid
Cognition
Mental illness

ABSTRACT

Heavy cannabis use has been frequently associated with increased rates of mental illness and cognitive impairment, particularly amongst adolescent users. However, the neurobiological processes that underlie these associations are still not well understood. In this review, we discuss the findings of studies examining the acute and chronic effects of cannabis use on the brain, with a particular focus on the impact of commencing use during adolescence. Accumulating evidence from both animal and human studies suggests that regular heavy use during this period is associated with more severe and persistent negative outcomes than use during adulthood, suggesting that the adolescent brain may be particularly vulnerable to the effects of cannabis exposure. As the endocannabinoid system plays an important role in brain development, it is plausible that prolonged use during adolescence results in a disruption in the normative neuromaturational processes that occur during this period. We identify synaptic pruning and white matter development as two processes that may be adversely impacted by cannabis exposure during adolescence. Potentially, alterations in these processes may underlie the cognitive and emotional deficits that have been associated with regular use commencing during adolescence.



MJ use during adolescence may affect neuromaturational processes through two pathways:

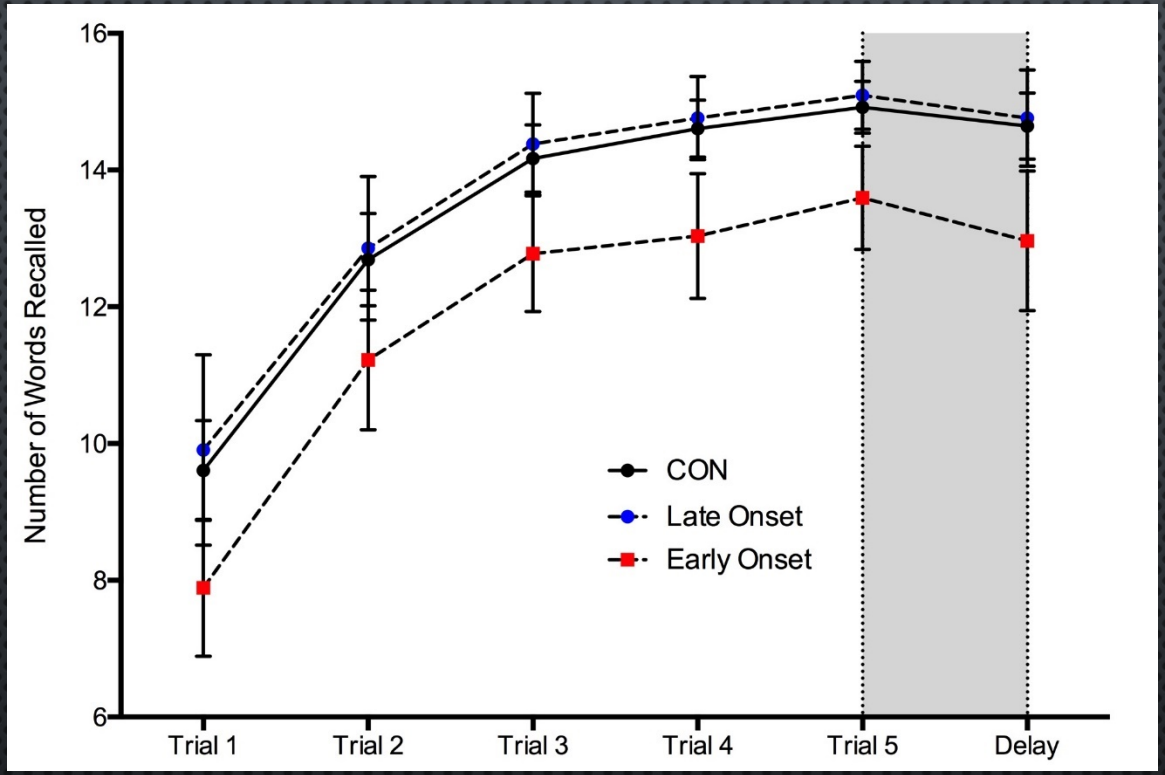
1. **Alters synaptic pruning** (via disrupting glutamate Transmission) leading to greater disinhibition in prefrontal regions leading to psychotic symptoms

2. **Decreased myelination altering development of white matter** leading to cognitive-emotional impairments

lls during prenatal and early post-natal stages of brain development (grey yang side) as uronal migration and axonal pathfinding, as well as the generation of glial cells, including functions of the endocannabinoid system and alter brain development: (i) by interfering

D.I. Lubman et al. / Pharmacology & Therapeutics 148 (2015) 1–16

Potential impact on academic achievement: Marijuana Users Show Worse Performance on a Memory Test



- **Early onset MJ users (<16), show impaired learning compared to non-users**
- **Could mean students using MJ regularly could have difficulty attending to and learning new information**

Schuster et al., 2016

PNAS PLUS

Persistent cannabis users show neuropsychological decline from childhood to midlife

Madeline H. Meier[a,b,1], Avshalom Caspi[a,b,c,d,e], Antony Ambler[e,f], HonaLee Harrington[b,c,d], Renate Houts[b,c,d], Richard S. E. Keefe[d], Kay McDonald[f], Aimee Ward[f], Richie Poulton[f], and Terrie E. Moffitt[a,b,c,d,e]

[a]Duke Transdisciplinary Prevention Research Center, Center for Child and Family Policy, [b]Department of Psychology and Neuroscience, and [c]Institute for Genome Sciences and Policy, Duke University, Durham, NC 27708; [d]Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC 27710; [e]Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; and [f]Dunedin Multidisciplinary Health and Development Research Unit, Department of Preventive and Social Medicine, School of Medicine, University of Otago, Dunedin 9054, New Zealand

Edited by Michael I. Posner, University of Oregon, Eugene, OR, and approved July 30, 2012 (received for review April 23, 2012)

Recent reports show that fewer adolescents believe that regular cannabis use is harmful to health. Concomitantly, adolescents are initiating cannabis use at younger ages, and more adolescents are using cannabis on a daily basis. The purpose of the present study was to test the association between persistent cannabis use and neuropsychological decline and determine whether decline is concentrated among adolescent-onset cannabis users. Participants

neuropsychological test performance after a period of abstinence from cannabis. There are two commonly cited potential limitations of this approach. One is the absence of data on initial, precannabis-use neuropsychological functioning. It is possible that differences in test performance between cannabis users and controls are attributable to premorbid rather than cannabis-induced deficits (17–20). A second limitation is re-

Even when recent MJ use was taken into account along with other confounds heavy use during **teen years** was associated with an 8 point drop in IQ

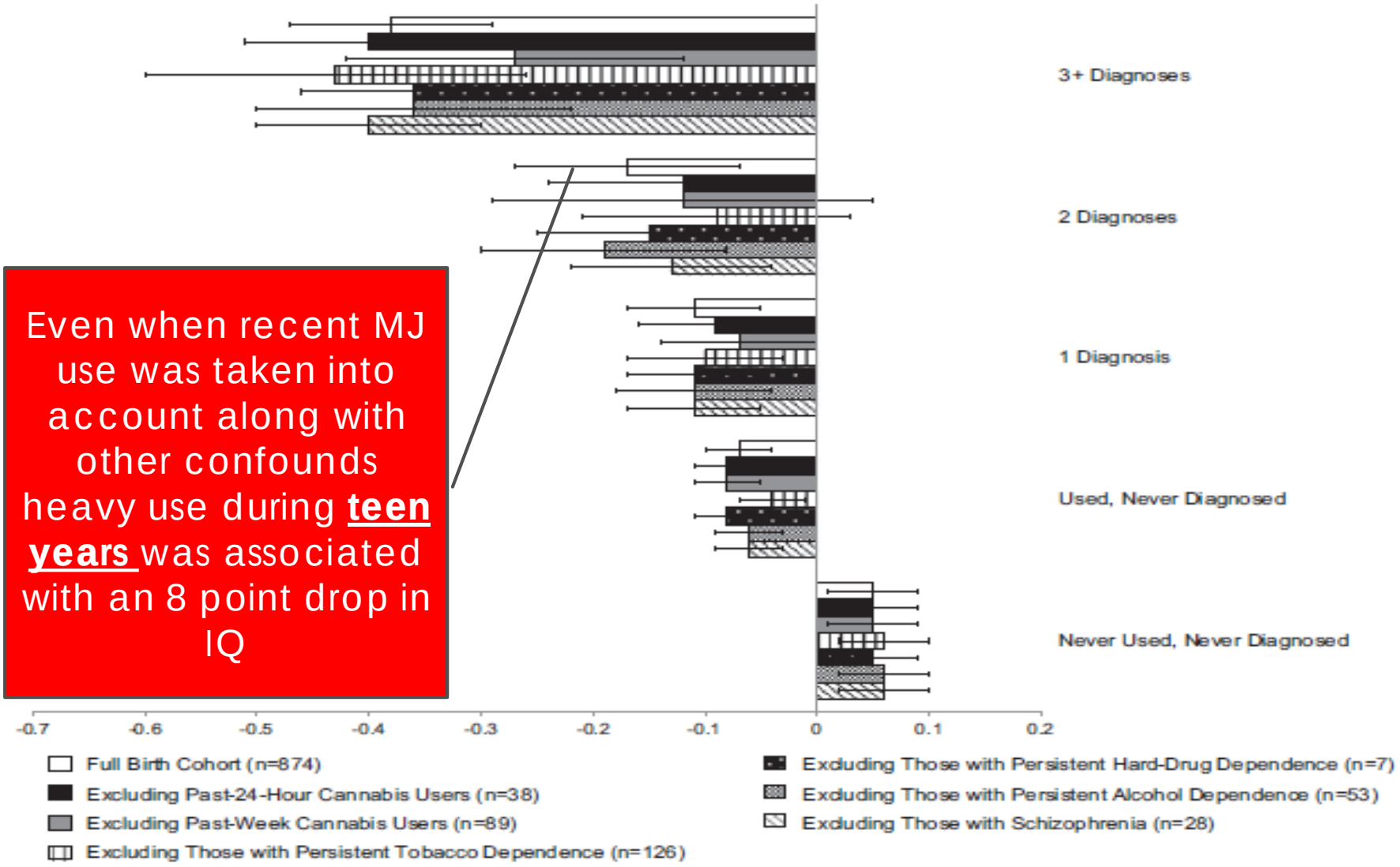
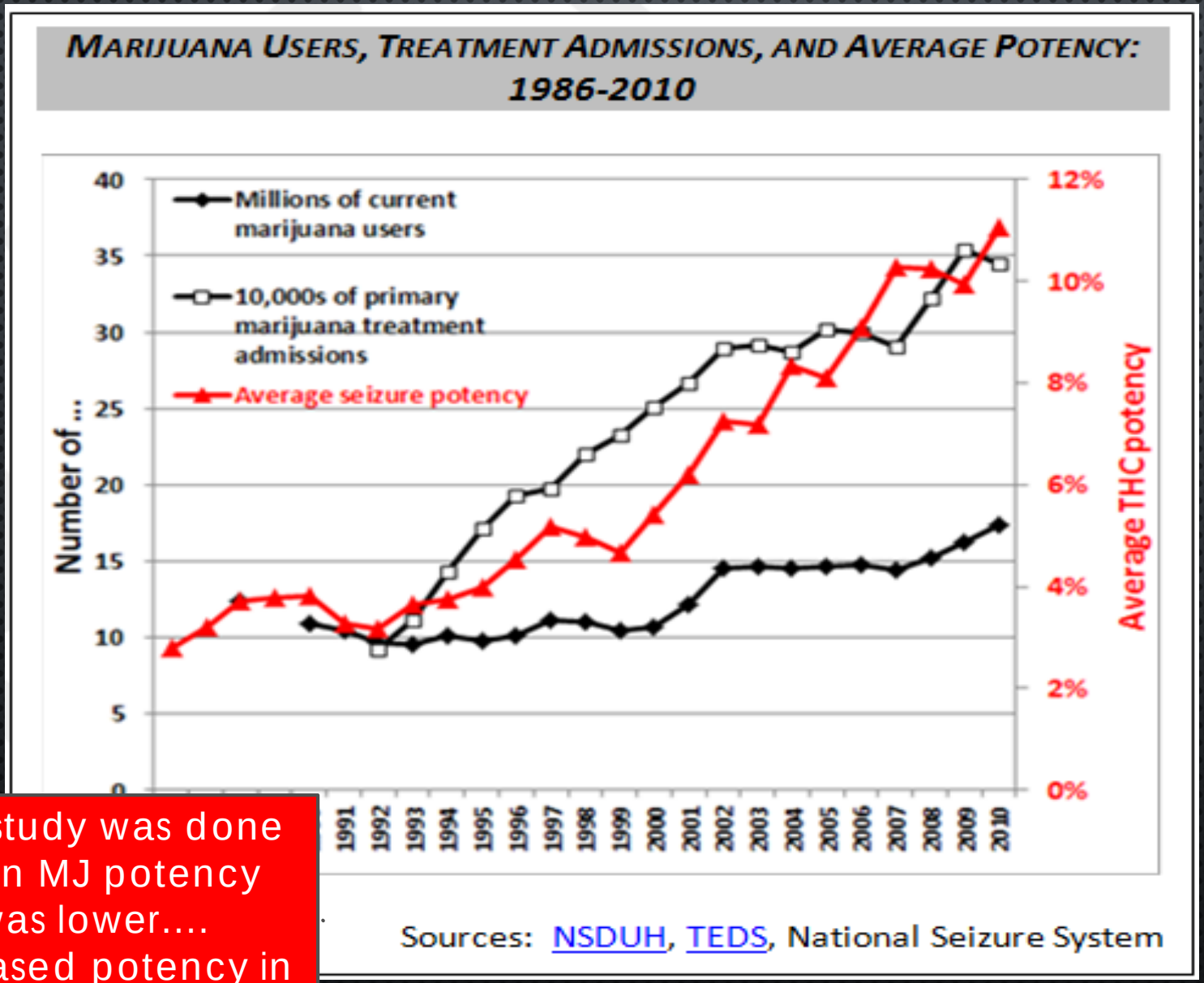


Fig. 1. Ruling out alternative explanations. Shown is change in full-scale IQ (in SD units) from childhood to adulthood as a function of the number of study waves between ages 18 y and 38 y for which a study member met criteria for cannabis dependence. Change scores are presented for the full birth cohort and the cohort excluding (*i*) past 24-h cannabis users, (*ii*) past-week cannabis users, (*iii*) those with persistent tobacco dependence, (*iv*) those with persistent hard-drug dependence, (*v*) those with persistent alcohol dependence, and (*vi*) those with lifetime schizophrenia. Persistent tobacco, hard-drug, and alcohol dependence were each defined as dependence at three or more study waves. IQ decline could not be explained by other factors. Error bars = SEs.

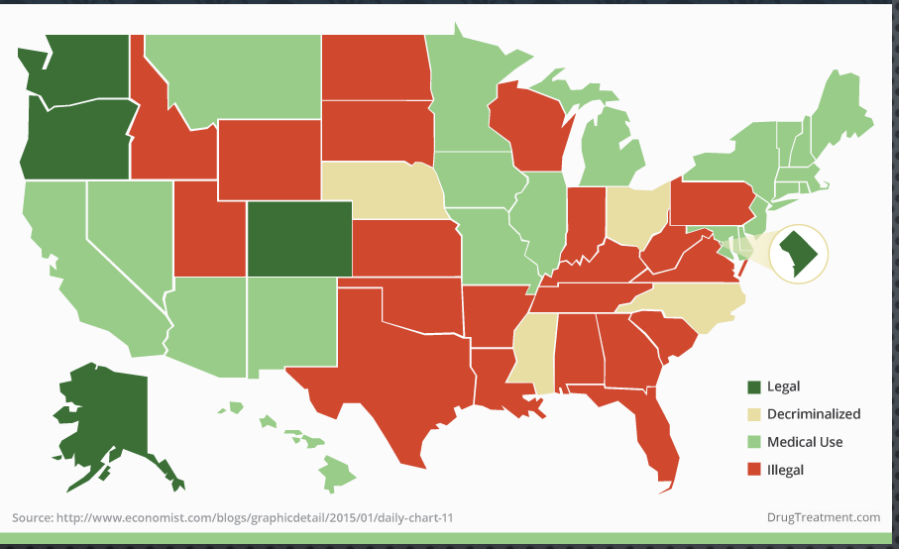
sizes, representing within-person IQ change as a function of tobacco, hard-drug, or alcohol dependence), and schizophrenia

What will be the effects of higher potency MJ?



That study was done when MJ potency was lower.... Increased potency in past 20 years

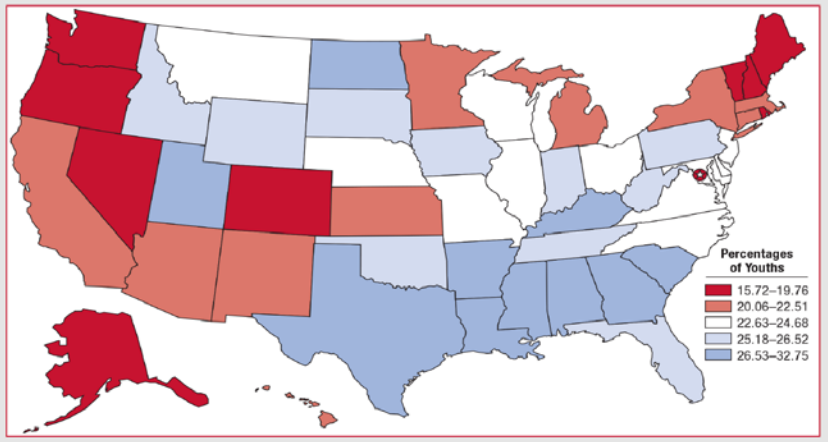
Legality of Marijuana in the United States



Source: http://www.economist.com/blogs/graphicdetail/2015/01/daily-chart-11

DrugTreatment.com

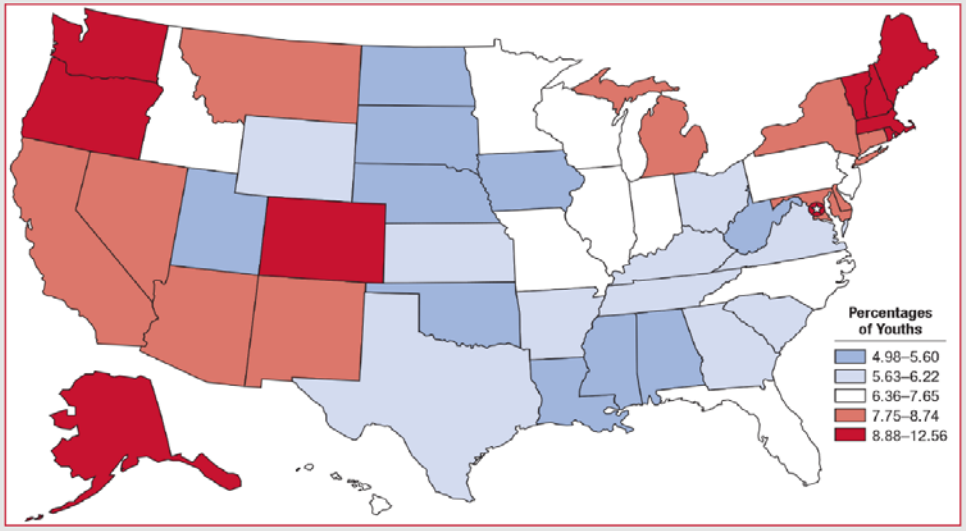
Figure 2. Perceptions of great risk of harm from smoking marijuana once a month among youths aged 12 to 17, by state: percentages, annual averages, 2013-2014



Source: SAMHSA, Center for Behavioral Health Statistics and Quality, National Surveys on Drug Use and Health (NSDUHs), 2013 and 2014.

Will legalization lead to Increased consumption of MJ?

Figure 1. Marijuana use in the past month among youths aged 12 to 17, by state: percentages, annual averages, 2013-2014



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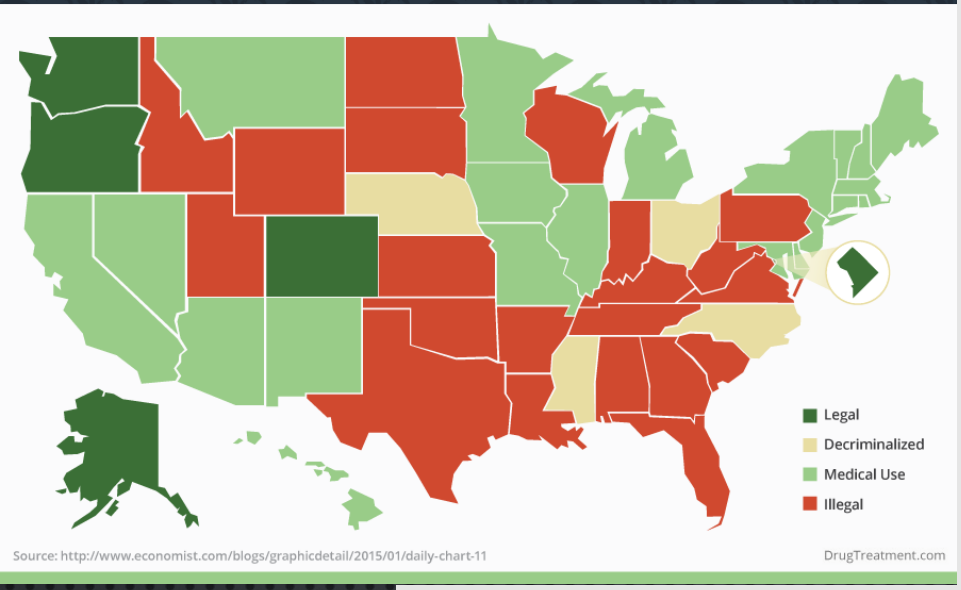
Legality of Marijuana in the United States



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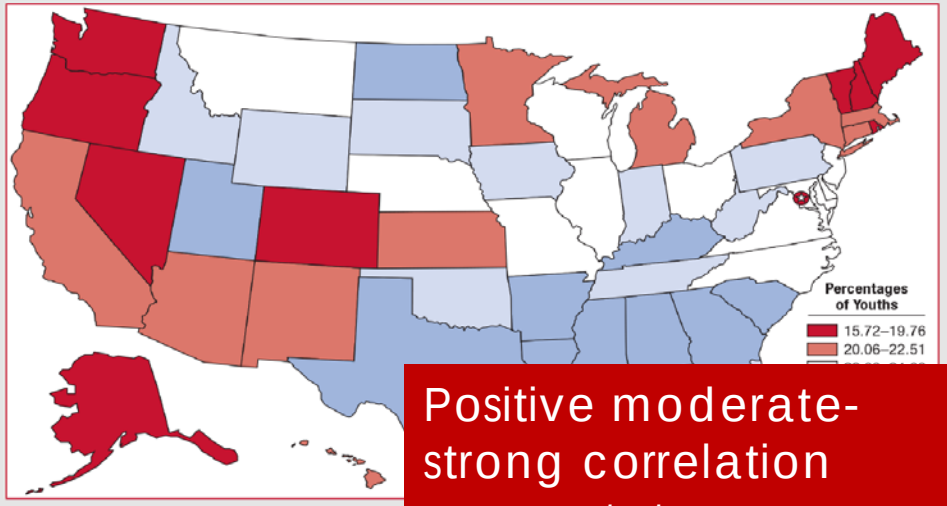

Source: SAMHSA, Center for Behavior

Positive moderate-strong correlation across states, between **less perceived harm** and legalization and "medicalization" of MJ

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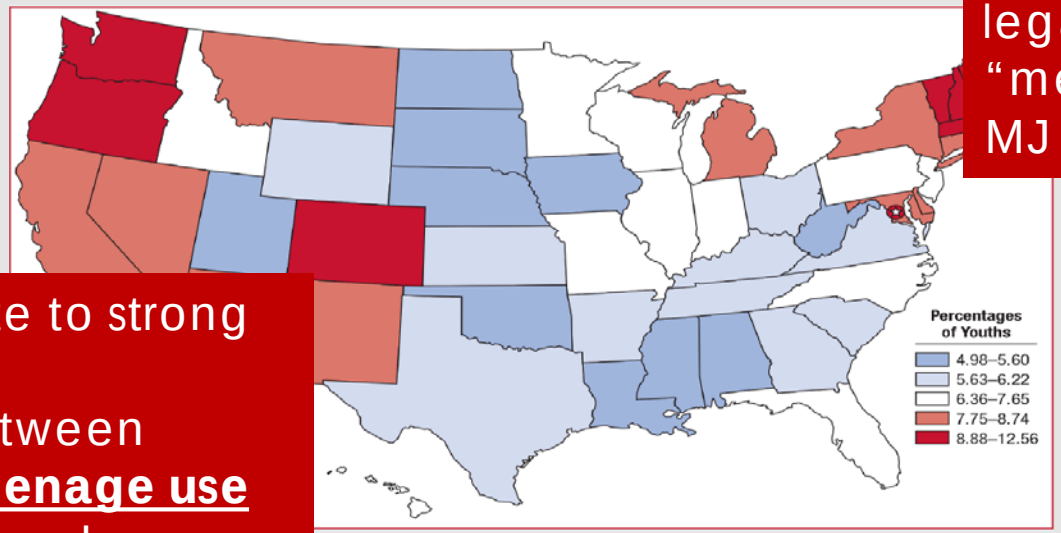

for Behavioral Health Statistics and Quality, National Surveys NSDUHs), 2013 and 2014.

Positive moderate to strong correlation across states, between **higher rates of teenage use** and legalization and "medicalization" of MJ

IMPACT OF EDIBLES?

The American Journal of Psychiatry

Cannabis Use and Risk of Prescription Opioid Use Disorder in the United States

Mark Olfson, M.D., M.P.H., Melanie M. Wall, Ph.D., Shang-Min Liu, M.S., Carlos Blanco, M.D., Ph.D.

Objective: The authors sought to determine whether cannabis use is associated with a change in the risk of incident nonmedical prescription opioid use and opioid use disorder at 3-year follow-up.

Method: The authors used logistic regression models to assess prospective associations between cannabis use at wave 1 (2001–2002) and nonmedical prescription opioid use and prescription opioid use disorder at wave 2 (2004–2005) of the National Epidemiologic Survey on Alcohol and Related Conditions. Corresponding analyses were performed among adults with moderate or more severe pain and with nonmedical opioid use at wave 1. Cannabis and prescription opioid use were measured with a structured interview (the Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV version). Other covariates included age, sex, race/ethnicity, anxiety or mood disorders, family history of drug, alcohol, and behavioral problems, and, in opioid use disorder analyses, nonmedical opioid use.

Results: In logistic regression models, cannabis use at wave 1 was associated with increased incident nonmedical prescription opioid use (odds ratio=5.78, 95% CI=4.23–7.90) and opioid use disorder (odds ratio=7.76, 95% CI=4.95–12.16) at wave 2. These associations remained significant after adjustment for background characteristics (nonmedical opioid use: adjusted odds ratio=2.62, 95% CI=1.86–3.69; opioid use disorder: adjusted odds ratio=2.18, 95% CI=1.14–4.14). Among adults with pain at wave 1, cannabis use was also associated with increased incident nonmedical opioid use (adjusted odds ratio=2.99, 95% CI=1.63–5.47) at wave 2; it was also associated with increased incident prescription opioid use disorder, although the association fell short of significance (adjusted odds ratio=2.14, 95% CI=0.95–4.83). Among adults with nonmedical opioid use at wave 1, cannabis use was also associated with an increase in nonmedical opioid use (adjusted odds ratio=3.13, 95% CI=1.19–8.23).

Conclusions: Cannabis use appears to increase rather than decrease the risk of developing nonmedical prescription opioid use and opioid use disorder.

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