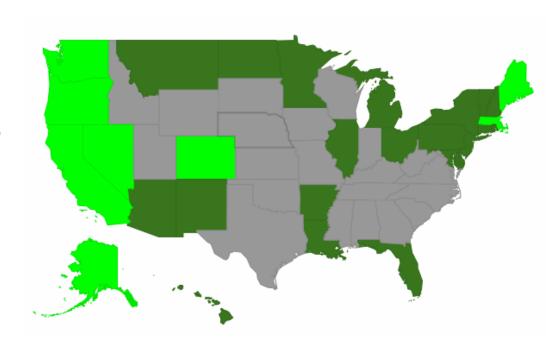# Marijuana and Health
MNCAMH June Webinar
June 9, 2017

Ken Winters, Ph.D.
Adjunct Faculty, Dept. of Psychology
University of Minnesota
&

Senior Scientist, Oregon Research Institute

winte001@umn.edu

Web-Based Resources

https://www.drugabuse.gov/publications/drugfacts/marijuana

www.learnaboutsam.org

http://norml.org/

View from 10,000 Feet

Policy Implications

Youth and Marijuana

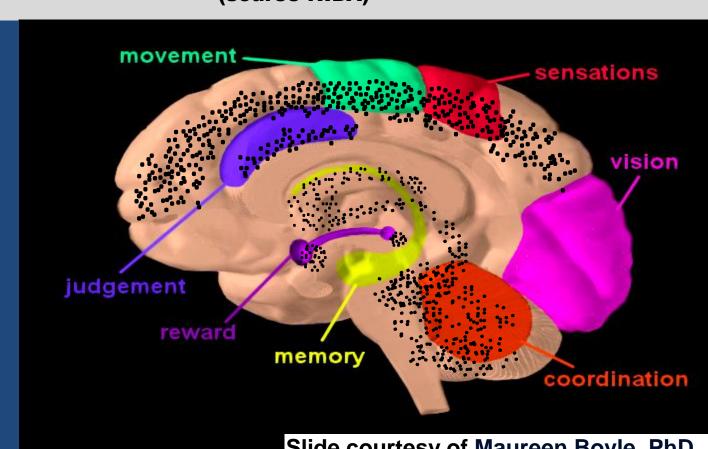Marijuana as Medicine

1. What is Marijuana?

- **Schedule 1 drug**
- **Contains over 400 chemicals**

  - **delta-9-tetrahydrocannabinol (THC)**

  - **delta-8-tetrahydrocannabinol**

  - **cannabidiol (CBD)**

  - **cannabinol**

  - **cannabichromene**

  - **cannabigerol**

  - **etc.**

Marijuana Binds Cannabinoid Receptors Located Throughout the Brain
(source NIDA)

- **Brain Development**
- **Memory & Cognition**
- **Motivational Systems & Reward**
- **Appetite**
- **Immunological Function**
- **Reproduction**
- **Movement Coordination**
- **Pain Regulation & Analgesia**

movement
sensations
vision
judgement
reward
memory
coordination

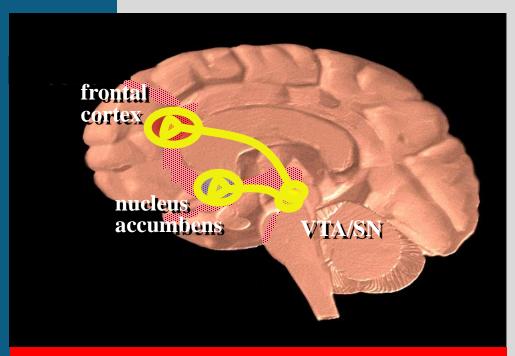**Slide courtesy of Maureen Boyle, PhD**

Cannabinoid receptors in our brains - why?
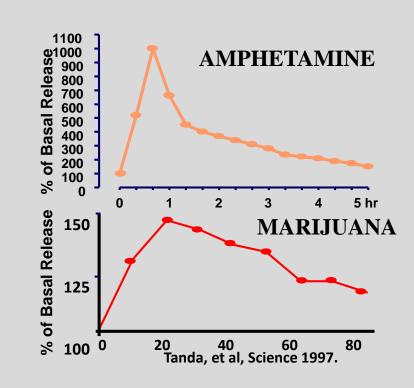
- **Animal studies show that without these receptors…**
  - **Experience more pain**
  - **Can't control appetite**
  - **More anxious**
  - **Less able to cope with stress**
- **These receptors are the main "volume" controls for neurotransmitters that affect pleasure, mood, pain, appetite, motivation, memory**

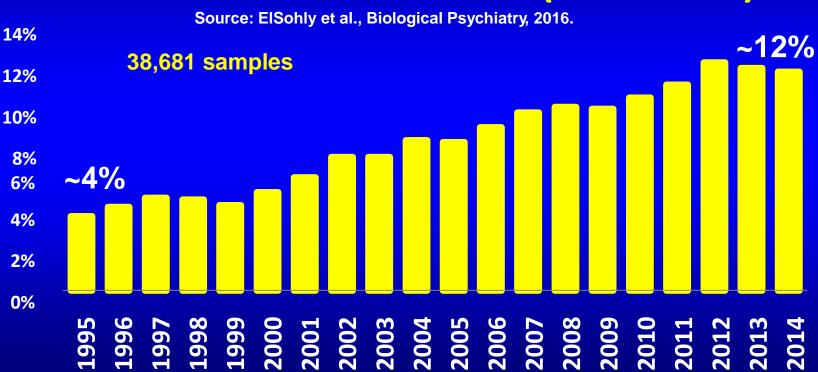Slide courtesy of Sion Kim, MD

The Reward Circuit

Drugs of abuse increase dopamine in the reward pathway region
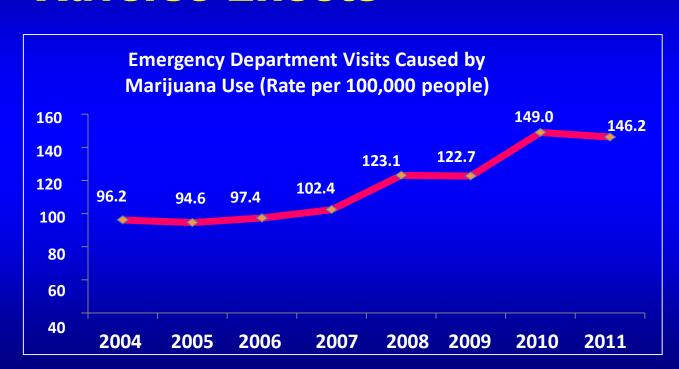
Slide courtesy of Maureen Boyle, PhD

Avg. % THC Content among Confiscated Cannabis Products in U.S. (1995-2014)

Source: ElSohly et al., Biological Psychiatry, 2016.

38,681 samples

~4%

~12%

Link Between THC Content and Adverse Effects

- **Paranoia**
- **Anxiety and panic**
- **Hallucinations**
- **Erratic mood swings**
- **Aggressive behavior**

Emergency Department Visits Caused by Marijuana Use (Rate per 100,000 people)

Year	Rate
2004	96.2
2005	94.6
2006	97.4
2007	102.4
2008	123.1
2009	122.7
2010	149.0
2011	146.2

2. Historical Perspective

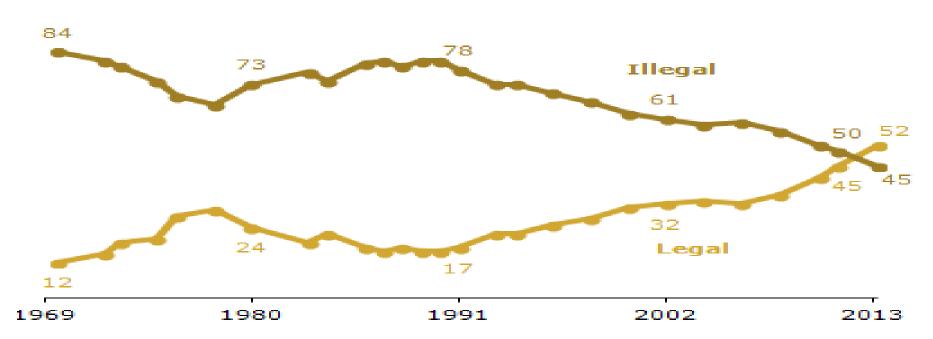- **Marijuana's popularity in recent times**
  - **40'- 50's:** tobacco use and alcohol popularized; illicit drugs dangerous; *Reefer Madness*
  - **60's – late 70's:** Woodstock generation; push for decriminalization or legalization; Cheech & Chong
  - **80's – early 90's:** crack epidemic; downturn in use of all illicit drugs
  - **1996 – current:** resumption of push for legalization; MJ as medicine (Compassionate Use Act); despite federal law, more than half states have pro-MJ laws
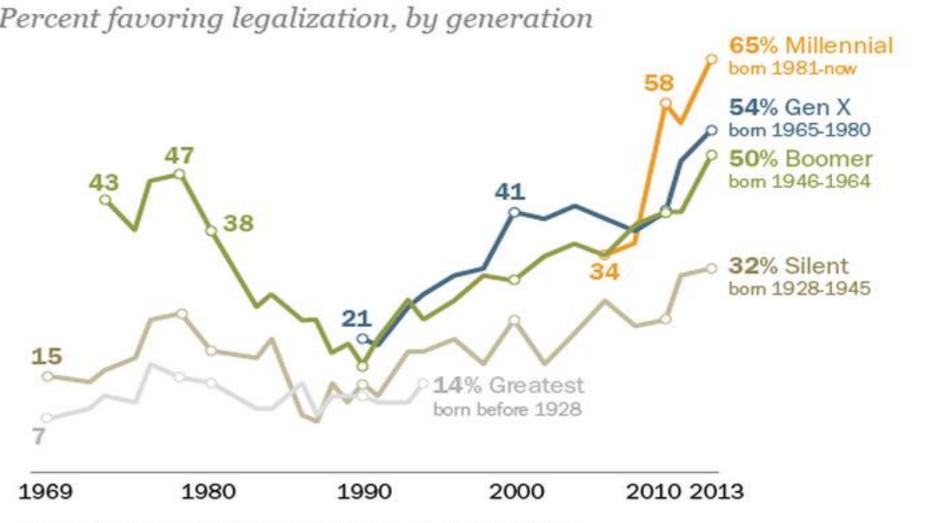
Support for Marijuana Legalization in the United States Has Reached Unprecedented Levels

Views of Legalizing Marijuana: 1969-2013

% saying marijuana should be ...
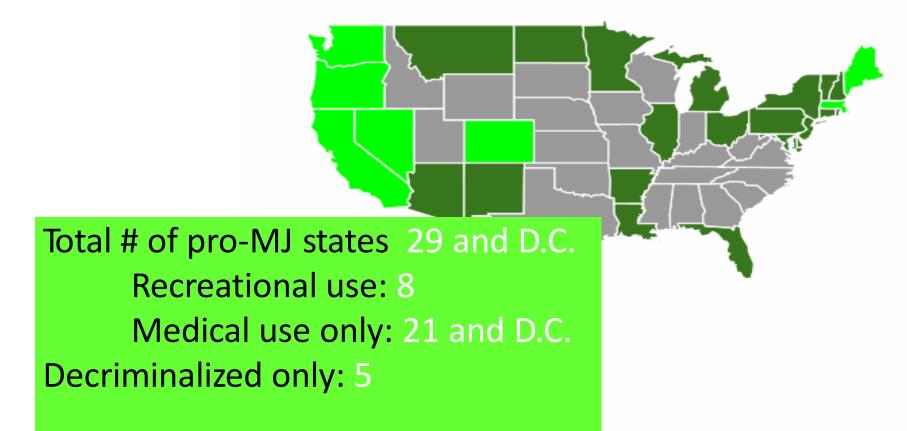
84

73

78

Illegal

61

50   52

45

12

24

17

32

Legal

45

1969   1980   1991   2002   2013

Percent favoring legalization, by generation

65% Millennial
born 1981-now

58

54% Gen X
born 1965-1980

50% Boomer
born 1946-1964

47

43

41

38

34

32% Silent
born 1928-1945

21

15

14% Greatest
born before 1928

7

1969   1980   1990   2000   2010 2013

Generational lines shown when significant sample is available.

**Marijuana and
Legalization, Nov., 2016**

Total # of pro-MJ states 29 and D.C.
Recreational use: 8
Medical use only: 21 and D.C.
Decriminalized only: 5

How did we get here?

- **Long-standing status in the drug culture**
- **Nature of the drug**
- **Civil libertarian views**
- **Free market capitalism**
- **Health benefits**
- **Political climate**

3. Health Issues
Overview from Three Recent Publications

Adverse Health Effects of Marijuana Use

Volkow, Baler, Compton, & Weiss, *NEJM*, 2014

Table 2. Level of Confidence in the Evidence for Adverse Effects of Marijuana on Health and Well-Being.

Effect	Overall Level of Confidence*
Addiction to marijuana and other substances	High
Abnormal brain development	Medium
Progression to use of other drugs	Medium
Schizophrenia	Medium
Depression or anxiety	Medium
Diminished lifetime achievement	High
Motor vehicle accidents	High
Symptoms of chronic bronchitis	High
Lung cancer	Low

Contemporary Health Issues on Marijuana (in press).
Editors: Sabet & Winters
Publisher: Oxford University Press

Health Topic	Conclusion
Brain structure/functioning	converging cross-sectional data suggestive that MJ affects multiple cognitive systems; longitudinal data inconclusive
Mental health	strong link for psychosis, less so for other disorders; candidate gene and early-onset use a contributor
Lung functioning	regular marijuana smoking is associated with symptoms of acute and chronic bronchitis; literature weakened by too few studies and confound of tobacco use often not controlled
Effects on driving	consistent relationship between the blood concentration of THC and driving impairment; early signs of impact on highway safety in CO and WA

Score Box for Negative Health

Nature of Evidence	# of Health Domains
Conclusive	0
Substantial	5
Moderate	6
Limited	7
No/Insufficient	7

<u>Strongest</u> **evidence that cannabis MJ is associated with…**

- **effectiveness for numerous medical conditions (e.g., chronic pain, some MS sym)**
- **increased risk of motor vehicle crashes**
- **increased risk for lung cancer**
- **lower birth weight of the offspring (maternal cannabis smoking)**
- **cognitive impairments (acute effects)**
- **development of schizophrenia or other psychoses; highest risk among heavy users**
- **development of problem cannabis use when early onset of use**

<u>Limited or no evidence</u> that cannabis is associated with…

- effectiveness for many other medical conditions (e.g., anxiety, PTSD)

- overdose deaths

- impaired academic achievement and education outcomes or social functioning

- likelihood of developing bipolar or anxiety disorders (except social anxiety disorder), or > in PTSD syms

- initiation of tobacco use

- changes in use of other licit and illicit substances
  - including opioid abuse

View from 10,000 Feet

Policy Implications
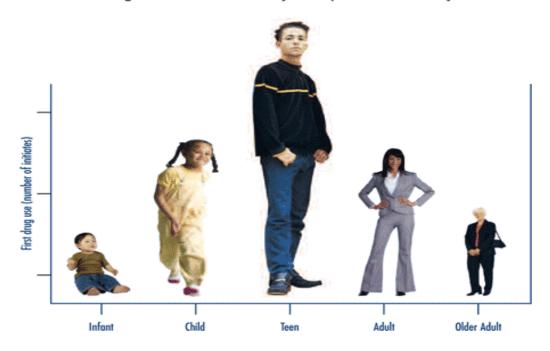
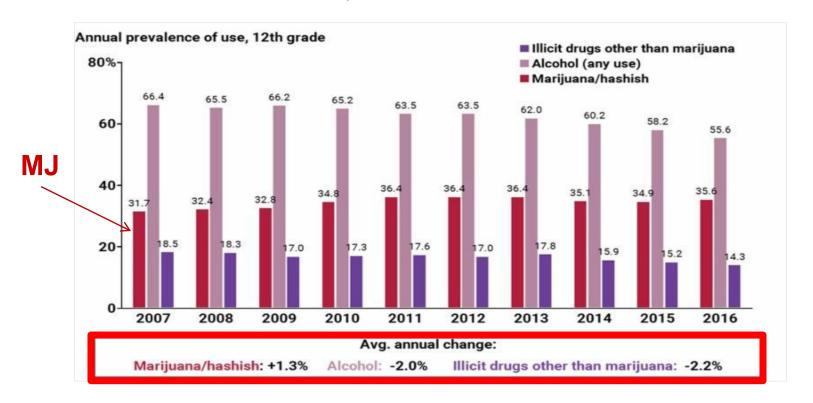**Marijuana as Medicine**

Youth and Marijuana

1. Youth and <u>Prevalence of Marijuana Use</u>

Drug abuse starts early and peaks in teen years

First drug use (number of initiates)

Infant   Child   Teen   Adult   Older Adult

MTFS, 2007- 2016 data

Annual prevalence of use, 12th grade

- Illicit drugs other than marijuana
- Alcohol (any use)
- Marijuana/hashish

MJ

Year	Marijuana/hashish	Alcohol	Illicit drugs other than marijuana
2007	31.7	66.4	18.5
2008	32.4	65.5	18.3
2009	32.8	66.2	17.0
2010	34.8	65.2	17.3
2011	36.4	63.5	17.6
2012	36.4	63.5	17.0
2013	36.4	62.0	17.8
2014	35.1	60.2	15.9
2015	34.9	58.2	15.2
2016	35.6	55.6	14.3

Avg. annual change:

Marijuana/hashish: +1.3%   Alcohol: -2.0%   Illicit drugs other than marijuana: -2.2%

MTFS, 2007- 2016 data

Annual prevalence of use, 12th grade

80%

Illicit drugs other than marijuana
Alcohol (any use)

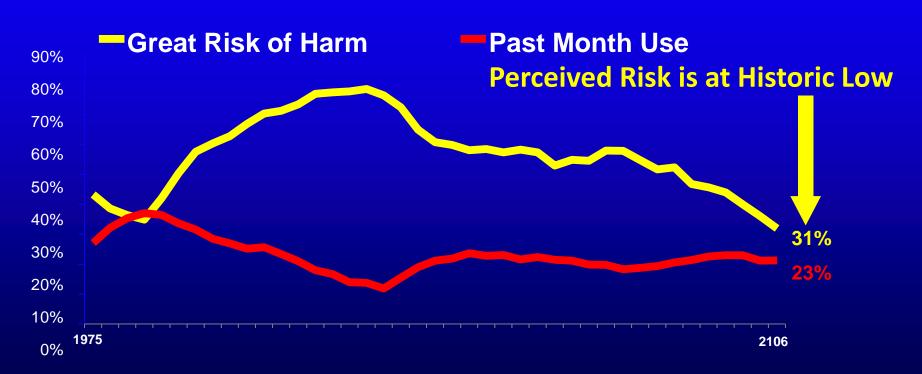**For 2016, for the three grades combined (8th, 10th and 12th), annual prevalence of marijuana showed a significant decline of 1.1 percentage points in 2016 compared to prior year.**

Avg. annual change:

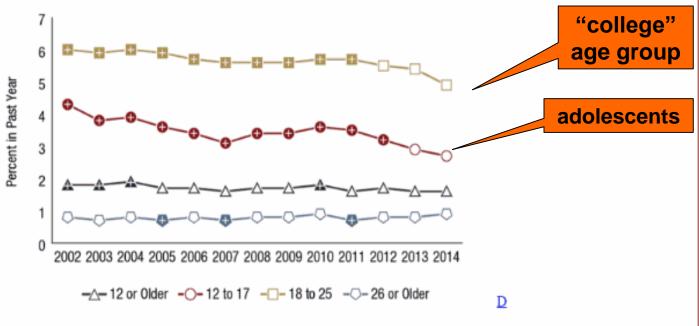+1.3%   -2.0%   -2.2%

Perceived Risk of Harm and Marijuana Use U.S.12ᵗʰ graders: MTFS, 1975-2016

Source: National Monitoring the Future Survey, 2016

Marijuana Use Disorder by Age Group
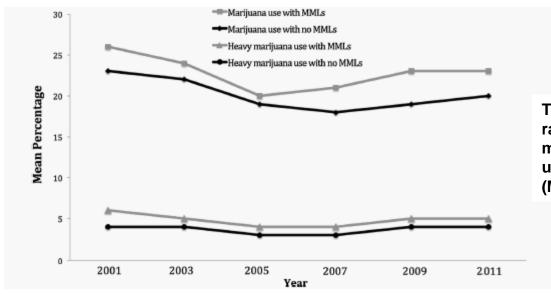## (NSDUH data)

Figure 35. Marijuana Use Disorder in the Past Year among People Aged 12 or Older, by Age Group: Percentages, 2002-2014

"college" age group

adolescents

— Difference between this estimate and the 2014 estimate is statistically significant at the .05 level.

Marijuana Legalization and Medical Marijuana Laws (MML) (Johnson et al., 2017)

- **Youth Risk Behavior Survey (YRBS) data collected during 1991–2011 from 45 states (N = 715,014) to examine MML effects.**
- **After correcting for year and state effects, no increase in rates of marijuana 30-day use or heavy use among adolescents.**
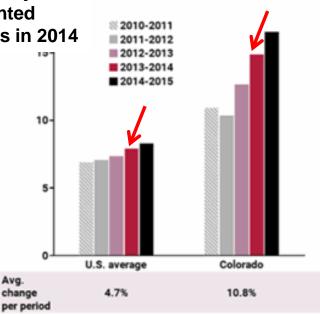

Trends in unadjusted prevalence rates of adolescent past-30-day marijuana and heavy marijuana use by state medical marijuana law (MML) status, 2001–2011.
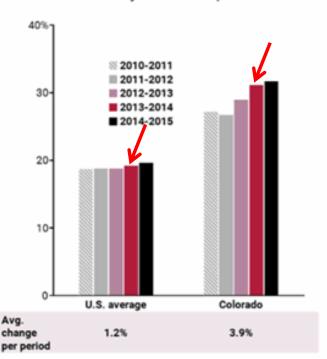
Since legalization, pot use in Colorado has steadily climbed, well outpacing the national average

Colorado legalized marijuana in 2012 and implemented legal marijuana stores in 2014

Percentage of population ages <u>12 and up</u> who used marijuana in the past month

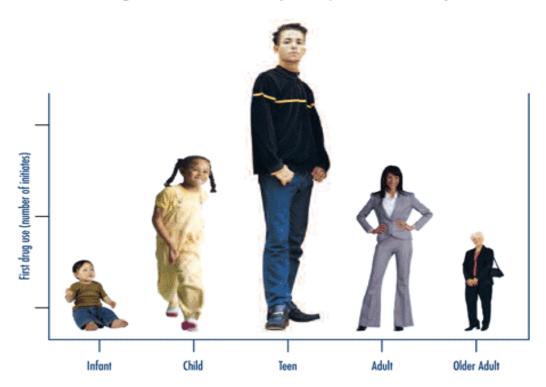Percentage of population ages <u>18 to 25</u> who used marijuana in the past month

Avg. change per period	4.7%	10.8%

Avg. change per period	1.2%	3.9%

2. Early Marijuana Use and <u>Risk for Cannabis Use Disorder</u>

Drug abuse starts early and peaks in teen years

First drug use (number of initiates)

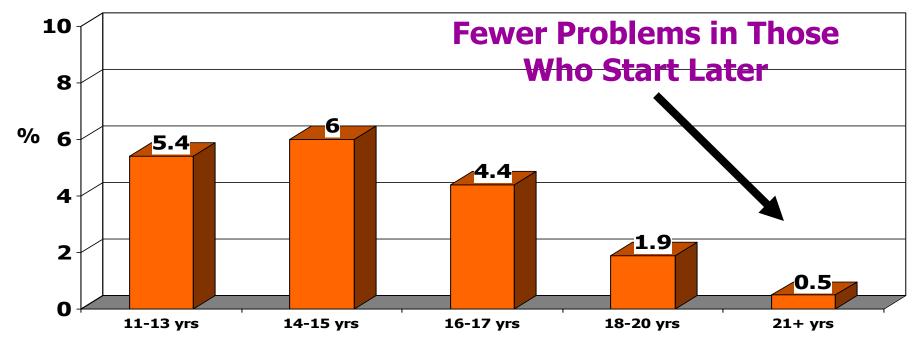Infant   Child   Teen   Adult   Older Adult

Early Marijuana Use and <u>Risk for Cannabis Use Disorder</u>

- **Research estimates indicate that 9% of people using marijuana will become dependent on it lifetime.**

- **However, among teens who start using marijuana, the risk is much higher of eventually becoming dependent.**

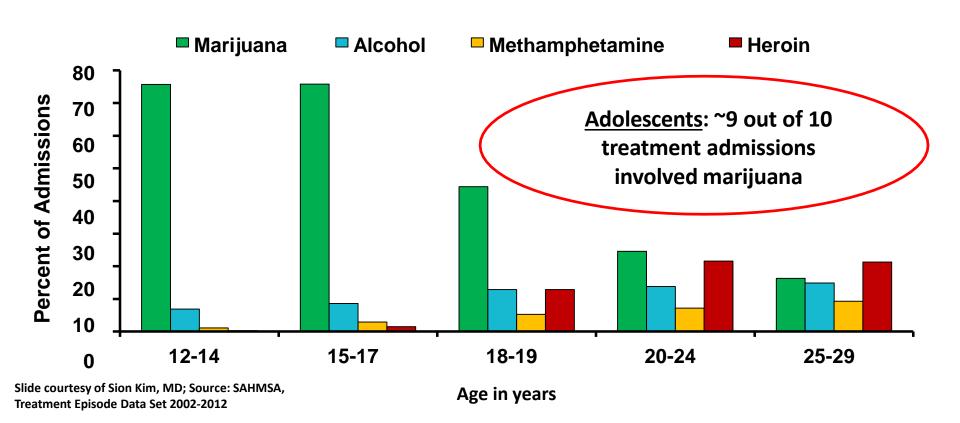- **Relative risk rate depends on how early in the teen years.**

https://www.drugabuse.gov/publications/research-reports/marijuana/marijuana-addictive

Percentages of Adult <u>Cannabis Dependence</u> as Function of Age of Onset of Use (National Household Survey on Drug Abuse, 2000-2001)

Fewer Problems in Those Who Start Later

Age of Cannabis Onset	%
11-13 yrs	5.4
14-15 yrs	6
16-17 yrs	4.4
18-20 yrs	1.9
21+ yrs	0.5
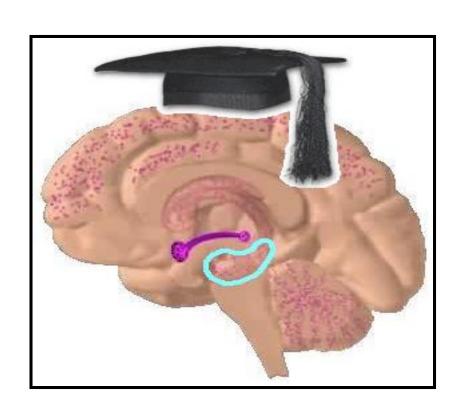
Treatment Admissions by Primary Drug

Slide courtesy of Sion Kim, MD; Source: SAHMSA, Treatment Episode Data Set 2002-2012

3. Effects of Adolescent Marijuana Use and <u>Cognitive Functioning</u>

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

- **Participants were members of the New Zeeland (Dunedin) Study, a prospective study of a birth cohort of 1,037 individuals followed from birth (1972/1973) to age 38 years.**

- **Cannabis use was ascertained in interviews at ages 18, 21, 26, 32, and 38 years.**

- **Neuropsychological testing was conducted at age 13 years, before initiation of cannabis use, and again at age 38 years, after a pattern of persistent cannabis use had developed.**
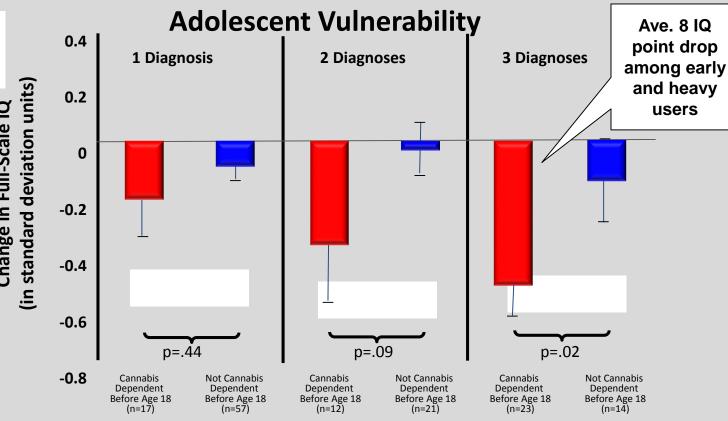
Marijuana and Cognitive Development

Major New Study Shows Heavy Marijuana Use Lowers IQ

Red = Early Onset

Blue = Later Onset

Adolescent Vulnerability

Ave. 8 IQ point drop among early and heavy users

Change in Full-Scale IQ (in standard deviation units)

1 Diagnosis   2 Diagnoses   3 Diagnoses

p=.44   p=.09   p=.02

Cannabis Dependent Before Age 18 (n=17)
Not Cannabis Dependent Before Age 18 (n=57)
Cannabis Dependent Before Age 18 (n=12)
Not Cannabis Dependent Before Age 18 (n=21)
Cannabis Dependent Before Age 18 (n=23)
Not Cannabis Dependent Before Age 18 (n=14)

National Institute on Drug Abuse

Source: Meier MH et al., PNAS Early Edition 2012.

Another Look: Two Longitudinal Twin Studies

Solid Line = non-user
Dashed line = user

ages 9-12 y

ages 17-20 y
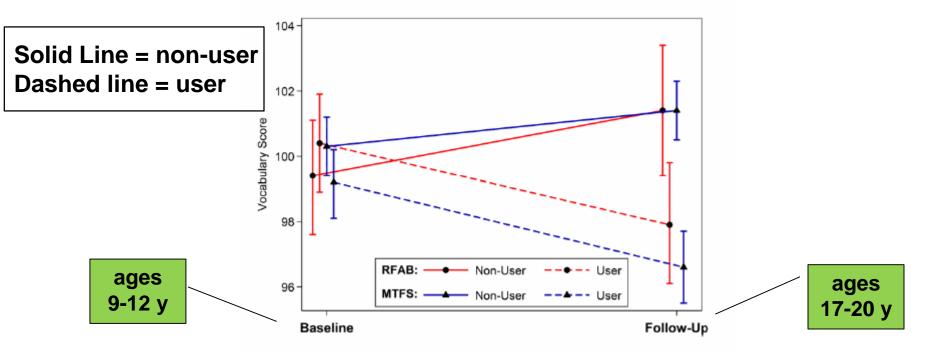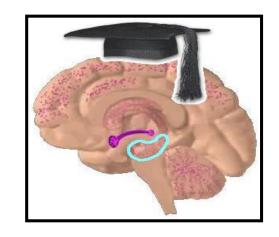
Fig. 1. Vocabulary score decline in marijuana users.

However, the cotwin control analysis revealed a different pattern of results. This analysis holds constant the potentially confounding influences of genetics and shared environment. Twin pairs that were discordant for marijuana use did not reveal significant differences in IQ change between MZ or DZ siblings, suggesting that familial confounds were responsible for the association between adolescent marijuana use and decline in IQ scores (Jackson et al., 2016).
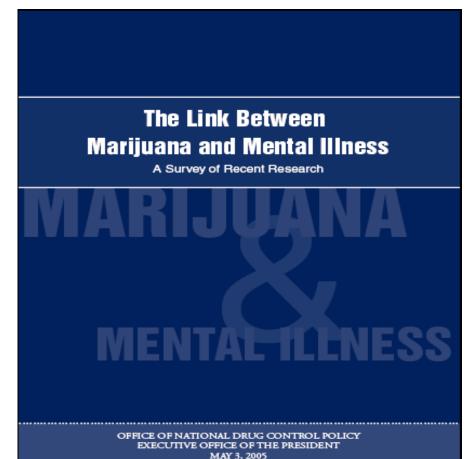
Sidebar: Marijuana Use and <u>Progress in College</u> (Arria et al., 2013, *Psychiatric Services*)

- **Marijuana use during year 1 of college significantly predicted discontinuous enrollment during the last 2 years of college but not earlier.**
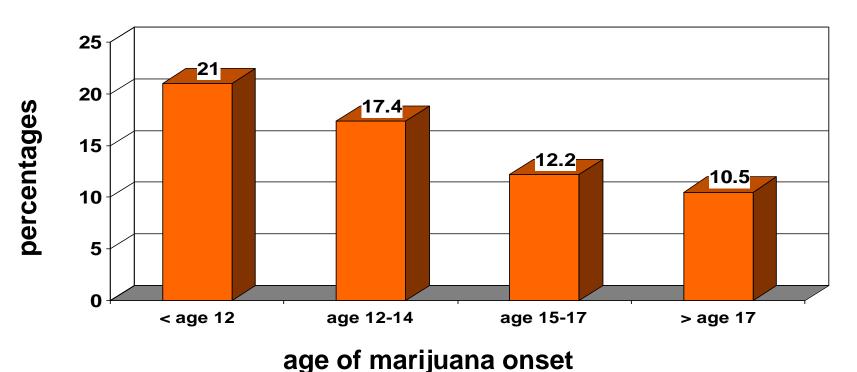

- **But problems with depression had a stronger relationship with discontinuous enrollment.**

4. Early Marijuana Use and <u>Risk for Mental Illness</u>

The Link Between Marijuana and Mental Illness

A Survey of Recent Research

MARIJUANA & MENTAL ILLNESS

OFFICE OF NATIONAL DRUG CONTROL POLICY
EXECUTIVE OFFICE OF THE PRESIDENT
MAY 3, 2005

Psychosis: Prevalence of Past Year Serious Mental Illness Among Lifetime Marijuana Users Aged 18+
(SAMHSA, 2005; data collected 2002-2003)

Miller's Review of the Marijuana and Mental Health Connection

Disorder	Cross-Sectional Data	Longitudinal Data
Schizophrenia	++	++
Bipolar	+	
Anxiety Disorders	+	+
Depressive Disorders	+	+
Risk of Suicide	+	
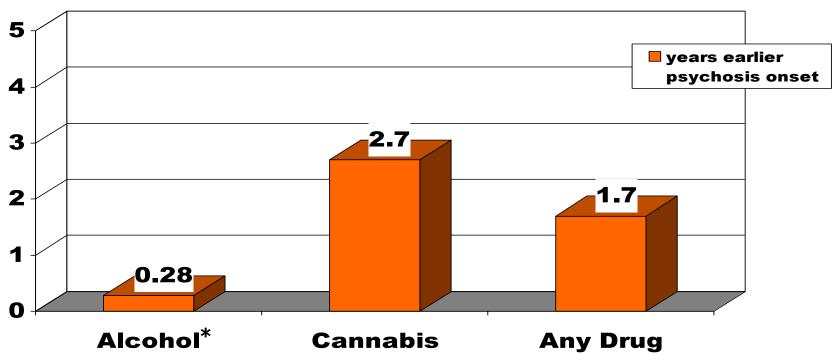
Key: ++ several studies; + a few studies

Miller, C. L. (in press). The impact of marijuana on mental health. In K.A. Sabet & K.C. Winters, *Contemporary health issues on marijuana.* NY: Oxford Press.

Miller's Review of the Marijuana and Mental Health Connection

Disorder	Cross-Sectional Data	Longitudinal Data
Schizophrenia*	++	++
Bipolar	+	
Anxiety Disorders	+	+
Depressive Disorders	+	+
Risk of Suicide	+	

Yellow box = risk greater when MJ use onset during youth.   * Risk may be linked to those with certain genetic variant of the AKT1 gene.

Miller, C. L. (in press). The impact of marijuana on mental health. In K.A. Sabet & K.C. Winters, *Contemporary health issues on marijuana.* NY: Oxford Press.

Drug Use and Age at Onset of Psychosis Based on a Meta-Analysis (Large et al., 2011)

mean years earlier of age at onset of psychosis compared to non-drug using controls
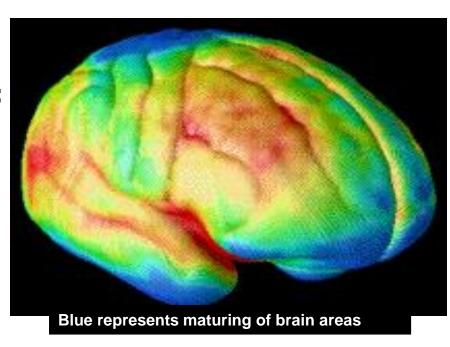
* = nonsig. with controls

1. View from 10,000 Feet

Youth and Marijuana

Why?

Early-Onset Marijuana Use May....

- **aggravate pre-existing neurobiological deficits in youth**

- **interact with pre-existing genetic predisposition**

- **alter normal neurobiological functioning in a non-risk youth**

- **contribute to exposure to accumulating psychosocial risk factors**

- **combination of the above**

Blue represents maturing of brain areas

Source: PHAS USA 2004 May 25; 101(21): 8174-8179. Epub 2004 May 17.

Adolescent Brain Cognitive Development National Longitudinal Study

Ten year longitudinal study of 10,000 children from age 10 to 20 years to assess effects of drugs on individual brain development trajectories
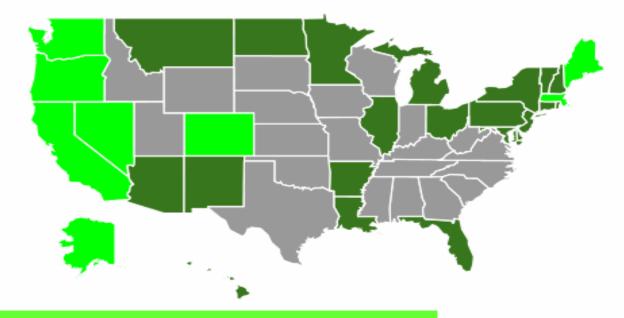

Slide courtesy of Maureen Boyle, PhD

Marijuana and Legalization, Nov., 2016

Total # of states with medical MJ law:

29 and D.C.

1. Is the Marijuana Plant Medicine?

National Academies of Sciences, Engineering, and Medicine (2017)

- **Credible reports by individuals and growing body of research that components of marijuana may be uniquely beneficial for some conditions.**

Score Box for Medicinal Value

Nature of Evidence	# of Conditons
Conclusive	0
Substantial	3
Moderate	1
Limited	6
No/Insufficient	-

2. Do We Need to Smoke it?

Challenges:

1. **When raw marijuana is smoked, it is difficult to standardize the dosage for the patient. No physician could legally take responsibility for "prescribing" raw marijuana.**

2. **The smoking of almost any plant material is associated with mouth, throat and lung cancer.**

3. **MJ plant consists of only two compounds (THC and CBD) among the 400 that are believed to have medicinal properties.**

4. **Easy to manufacture own supply with home cultivation and avoid regulations.**
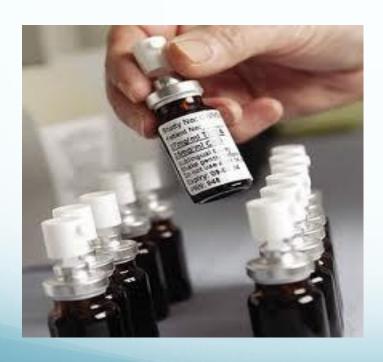
3. Getting FDA Approval

- **The FDA requires carefully clinical trials in hundreds to thousands of human subjects**
  - benefits?
  - risks?

- **Some progress to date**

Marijuana-Based Medicines

FDA Approved

- **Marinol (Dronabinol), Sindros, & Naboline**
  - **contains lab-made THC and is widely available at pharmacies as capsules or liquid to treat nausea/vomiting from cancer chemotherapy**

Not Yet

- **Epidiolex®**
  - **contains only cannabidiol (CBD), the presumed medicine in cannabis; for epilepsy**

- **Sativex® is in the process of being studied in the USA.**
  - **administered via an oral mouth spray; already approved in Canada and Europe; contains both THC and CBD**

Source: www.learnaboutsam.org

Marijuana-Based Medicines

Also 'Not Yet'

- **Oils (for vaporizing), many liquids, and patches (available in some states)**

View from 10,000 Feet

Policy Implications

Youth and Marijuana

Marijuana as Medicine

1. Will 'Big Tobacco' Tactics be Used in Legal States?

- **Heavy marketing/advertising**

- **Campaigns that minimize/ignore potential harm**

- **Campaigns that promote economic and social benefits**

- **Minimal regulations to optimize access**

2. Will 'Responsible' Policies be Employed?

- **Governance and compliance checks regarding access and distribution**

- **Regulation of edibles, candies**

- **Research on changes in use patterns and health effects of MJ use**

- **Comparison of extra tax revenue vs. social and health costs**

- **Assessment of effects on trafficking**

Source: www.learnaboutsam.org

3. Regulations for Medical Marijuana Can Be Rigorous

- **Minnesota's Medical MJ Law:**
  - **Only prescribed by MDs and limited to a few bona fide and specific disorders**

  - **Grown by the state; only usable in oil (for vaporizing), pill or liquid forms**

  - **Dispensed at only a handful of state-run clinics**

Final Comments:

Where will the U.S. go from here?

- **Likely that polices about marijuana will continue to be influenced by science, politics and free market capitalism.**

- **The recent trend, with some exceptions, is more legalization.**

The U.S. in a Few Years?

THANK YOU!

winte001@umn.edu

View from 10,000 Feet

Policy Imp

ch and
ijuana

Marijua
Medicine