MARIJUANA LEGALIZATION AND THE “ANSWER” TO OUR DRUG PROBLEMS

John F. Kelly, PhD
THE DRUG PROBLEM ...

"FOR EVERY COMPLEX PROBLEM THERE IS A SOLUTION THAT IS CLEAR, SIMPLE, AND WRONG"

—HENRY L. MENCKEN
WHAT IS MJ?

- **Is the common name for the Cannabis Sativa plant which contains psychoactive effects through a variety of cannabinoids, notably Delta-9 THC, and cannabidiol.**

- **Most commonly inhaled through the lungs, it produces mild euphoria, mood enhancement, relaxation; higher/regular use produces intoxication, slowed cognition/memory impairment (short-term memory/working memory) increased anxiety/paranoia/psychosis, hallucinations, addiction.**

- **Can increase the likelihood of accidents/MJ-related deaths but unlikely to produce OD related mortality directly.**

- **May be neurotoxic in higher doses; developing teen brain appears more susceptible to negative impacts than older adult users.**
Top 20 Drugs – Last 12 Months – Whole Sample (N=78,819)

MJ is popular around the world...
...and in the USA Second only to alcohol...

Top 20 Drugs – Last 12 Months – USA (N=6,500)

Global Drug Survey GDS2014©

*Denotes all types and preparations

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

Source: Canada Drug Policy Coalition, 2015
In most countries and the US, prohibition generally pertains to illegality in terms of manufacture, sale, or distribution (can also mean possession as in the US). Remains primary policy position for psychoactive drugs that have the potential to be misused, cause intoxication, addiction, and induce harms (other than alcohol, nicotine).
1. Often confused with legalization but very different.

2. Decriminalization means if you are caught in possession of small amounts for personal use, you do not incur a criminal penalty.

3. It is still illegal to use the drug.

4. The penalty, however, is typically nothing more than a modest fine, such as $100.

5. Multiple states have now passed laws decriminalizing the possession and use of marijuana.
DE FACTO DECRIMINALIZATION

Often prior to passing decriminalization legislation, many states go through a period of "de facto decriminalization," whereby no actual decriminalization law has been officially passed, but the existing criminal law prohibiting use is no longer enforced.

It is an implicit recognition that decriminalization might be a potentially useful policy position, even if sufficient social and political will to enact it is currently absent.
MARKET REGULATION

A medium for the exchange of goods or services over which a government body exerts a level of control. This control may require market participants to comply with environmental standards, product-safety specifications, information disclosure requirements and so on.

The market for both prescription and over-the-counter drugs is an example of a regulated market. The Food and Drug Administration (FDA), controls what drugs may be sold on the market, how they may be advertised, for what conditions they may be prescribed etc.
MEDICALIZATION

Medicalization is a policy position taken for some psychoactive drugs. Notably, in the case of marijuana, its use for medical purposes has now become law in the majority of US states.

Medicalization of marijuana is unusual in this regard because it is medically “recommended” rather than actually “prescribed,” due to limited availability of empirical evidence on health benefits. If properly regulated and supported by clinical science for specific medical conditions, medicalization of a drug can destigmatize use, decrease pain and suffering related to those specific conditions.

Because of safety concerns (e.g., in utero effects in pregnancy, drug-drug interactions, other medical contraindications), medicalization typically requires extensive testing to ensure users of the prescribed medication are not harmed by its use, and side-effects are minimized.
LEGALIZATION (IN ITS MANY FORMS)

While you might think legalization is simply a yes or no dichotomy, important to recognize are several forms that legalization can take, each accompanied by own set of pros/cons.
LEGALIZATION WITHOUT COMMERCIALIZATION

ALLOWS PRODUCTION, DISTRIBUTION, AND SALE, FORBIDS COMMERCIALIZATION. BANS BRANDING AND ADVERTISING DESIGNED TO INCREASE SALES.

ALTERNATIVE IS HAVE LOCAL, STATE, OR FEDERAL CONTROL OVER PRODUCTION, SALE; STILL MAKES DRUG LEGAL, AVAILABLE, AND ACCESSIBLE, AND RETAINS BETTER CONTROL OF QUALITY AND LABELING OF THE DRUG’S PSYCHOACTIVE POTENCY AND INGREDIENTS.

PLUS SIDE, PEOPLE WHO WANT TO USE IT RECREATIONALLY CAN WITHOUT FEAR OF RECRIMINATION; ERADICATES CRIMINALITY, INCARCERATION, BLACK MARKETS - LESSENS STIGMATIZATION OF ADDICTED USERS, LESSENING BARRIER TO TREATMENT.

DOWNSIDE, BECAUSE DRUGS CAUSE ACUTE IMPAIRMENTS, AS WELL AS ADDICTION (ABOUT 10% OF USERS MEET CRITERIA FOR ADDICTION), INCREASED ACCESSIBILITY, DE-STIGMATIZATION, AND DECREASED PRICES THAT COMES WITH LEGALIZATION, WOULD RESULT IN MORE USERS AND MORE POTENTIAL HAZARDS AND HARMs IN POPULATION (E.G., DRUGGED DRIVING) AS WELL AS ADDICTION CASES.
LEGALIZATION WITH LIMITS ON COMMERCIALIZATION

Legalization but allows at least some commercialization. E.g., restrictions placed on how much and to whom products are advertised. Drug could be made legal for recreational use, but commercial advertising in certain venues at certain times (e.g., when children/adolescents likely to be exposed to advertisements) is restricted.

Other restrictions could include minimum age (e.g. age 21), ensuring quality control, listing of ingredients including nature and potency of psychoactive content; limiting licensed outlets; still prohibiting use under certain conditions (e.g., driving); having minimum price per unit at which the drug sold (Many such restrictions are placed on the sale of alcohol, for example).

Note, just because laws in place to limit potential public health and safety harms from uptick in use, does not mean necessarily that such laws will be adequately enforced once drug legalized.
POLICY POSITIONS 101

LEGALIZATION WITH FULL COMMERCIALIZATION

OTHER END OF SPECTRUM FROM PROHIBITION, AND AT FAR END OF LEGALIZATION CONTINUUM, FREE MARKET COMMERCIALIZATION. ALLOWS FREE REIGN FOR INDUSTRY TO BRAND AND ADVERTISE AND SALES WITH FEW, IF ANY, RESTRICTIONS.

ADVERTISING AND BRANDING VALUABLE — IMAGINE CIGARETTES SOLD IN A PLAIN WHITE BOX WITH NOTHING ON THE OUTSIDE; OR WINE, BEER, LIQUOR, SOLD IN ORDINARY TRANSPARENT GLASS CONTAINERS WITH JUST A SIMPLE WHITE LABEL ON THE OUTSIDE STATING, “Wine” or “Vodka.”

INDUSTRY GOES TO GREAT EXPENSE TO ATTRACTIVELY SHAPE, TINT, COLOR, EMBOSSED GLASS, CREATE GILT-EDGED HIGH-COLOR LABELS, GOLD FOIL WRAPPINGS, AND LAUNCH MULTI-MILLION-DOLLAR PROFESSIONAL ADVERTISING CAMPAIGNS IN AN ATTEMPT TO CREATE AN IMAGE THAT ATTRACTIONS, SEDUCES, AND INCREASES SALES AND PROFITS.

INCREASING SALES INCREASES POPULATION EXPOSURE; MAY INCREASE HAZARDS/HAZARDS TO THE EXTENT THAT DRUG CAN CAUSE SUCH HAZARDS.
Degree of Problems Associated with Various Policy Approaches to Addressing the Drug Problem

Source: Canada Drug Policy Coalition, 2015
LEGALIZATION? HOW DID WE GET HERE?
“MEDICAL MARIJUANA”...
FOR WHICH CONDITIONS MIGHT MARIJUANA/THC HAVE A THERAPEUTIC BENEFIT?

Up to 259 conditions including:

- Alzheimer’s Disease
- Anorexia
- HIV/AIDS
- Arthritis
- Cachexia
- Cancer
- Crohn’s Disease
- Epilepsy
- Glaucoma
- Migraines
- Multiple Sclerosis
- Nausea
- Pain
- Spasticity
- Wasting Syndrome
**CANNABIDOIDS HAVE DOCUMENTED THERAPEUTIC POTENTIAL...**
**THC ADMINISTRATION & FDA APPROVED THC-BASED MEDICATIONS**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Administration</th>
<th>FDA Status</th>
<th>Approved Locations</th>
<th>Purposes</th>
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</thead>
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<tr>
<td>Dronabinol (Marinol)</td>
<td>Oral capsule</td>
<td>FDA-approved (1985)</td>
<td>USA, Germany</td>
<td>Nausea &amp; vomiting related to cancer chemotherapy and wasting associated with AIDS</td>
</tr>
<tr>
<td>Nabilone (Cesamet)</td>
<td>Oral capsule</td>
<td>FDA-approved (1985)</td>
<td>USA, Canada, UK, Mexico</td>
<td>Nausea &amp; vomiting related to cancer chemotherapy</td>
</tr>
<tr>
<td>Nabiximols (Sativex)</td>
<td>Oromucosal spray</td>
<td>Almost FDA-approved; late-stage clinical trials</td>
<td>Canada, UK, other European countries</td>
<td>Multiple sclerosis spasticity, cancer pain, neuropathic pain</td>
</tr>
</tbody>
</table>

Cannabinoids in medicine: A review of their therapeutic potential

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Abstract

In order to assess the current knowledge on the therapeutic potential of cannabinoids, a meta-analysis was performed through Medline and PubMed up to July 1, 2005. The key words used were cannabis, marijuana, marihuana, hashish, haschich, haschisch, cannabinoids, tetrahydrocannabinol, THC, dronabinol, nabilone, levonantradol, randomised, randomized, double-blind, simple blind, placebo-controlled, and human. The research also included the reports and reviews published in English, French and Spanish. For the final selection, only properly controlled clinical trials were retained, thus open-label studies were excluded.

Seventy-two controlled studies evaluating the therapeutic effects of cannabinoids were identified. For each clinical trial, the country where the project was held, the number of patients assessed, the type of study and comparisons done, the products and the dosages used, their efficacy and their adverse effects are described. Cannabinoids present an interesting therapeutic potential as antiemetics, appetite stimulants in debilitating diseases (cancer and AIDS), analgesics, and in the treatment of multiple sclerosis, spinal cord injuries, Tourette’s syndrome, epilepsy and glaucoma.

Keywords: Cannabinoids; Cannabis; Therapeutic potential; Controlled clinical trials; Efficacy; Safety
CONTROOLED STUDIES EVALUATING THE THERAPEUTIC EFFECT OF THC
BY ADMINISTRATION TYPE

The use of cannabis and rapidly acting cannabinoids pose considerable challenges for blinding, as the psychoactive effects are expected to be quickly discernible to study participants, particularly those who have been previous users of such products.

Why should MJ be illegal?
Why should it be legalized?
20 drugs ranked by overall harm along 16 criteria

ARGUMENTS FOR CANNABIS LEGALIZATION

- "War on drugs" has failed
- 5% of world's population - 25% of world's prisoners
- 2.5 Million locked up; about 500,000 of whom are there for drugs
- Racial disparities in incarceration rates at same prevalence of use
- Legalization would reduce arrests/criminal justice costs (2013-41% of all illicit drug-related violations were MJ possession; 6% for MJ sale/manufacturing
- Demand is high- "gonna do it anyway" so why not regulate it and make it safe?
- It's not bad/as bad as alcohol/tobacco -Even good for you (medicinal)
- Tax it and bring in revenue for states
With 5% of the world’s pop, the US has 25% of its prisoners. Avg US cost per prison inmate = (2010) = $31K (range 14K-60K); about $16 Billion for the 500,000 drug-related prisoners (20% of all prisoners).
PRISONS OVERCROWDING: 20% (500,000) OF US PRISONERS ARE IN PRISON DUE TO DRUG OFFENCES; THE MAJORITY OF INMATES MEET CRITERIA FOR SUBSTANCE USE DISORDER/PSYCH ILLNESS
SO, LEGALIZE?

- Of the 2.5 million prisoners in US, about 500,000 are there due to drug law violations, but only about 40,000 of these are MJ.

- This would be justification for decriminalization, NOT legalization but even so, to “end the war on drugs” by legalization of MJ won’t do it.

- What will happen is the reduction on the arrests annually (FOR POSSESSION) in the US – about 700,000 reduction in arrests annually.

- How to legalize? Industry – majority of market is heavy users/ADDICTED—(80% of volume used is by 20%)

- If we make it more available and accessible, cheaper, remove social stigma and legal penalties and have industry aggressively advertising it, use will increase.

- Possible MJ could have subtractive effect on alc use? Don’t know. Could use both?
“Prohibition doesn’t work—everybody knows that!”
SO, LEGALIZE, REGULATE, TAX, EDUCATE (“JUST LIKE ALCOHOL”)
JUST LIKE ALCOHOL...

21ST AMENDMENT REPEALED ALCOHOL PROHIBITION... AND VIRTUALLY ENDED OUR ALCOHOL PROBLEMS (?)
3-3.5x more addiction cases for alcohol in the past year/lifetime than ALL illicit drugs combined.
...DID ALCOHOL RE-LEGALIZATION PUT AN END TO OUR ALCOHOL PROBLEMS?

- **Alcohol = addictive drug** - Majority of addicted individuals in US are addicted to alcohol
- **Alcohol = level I carcinogen** – known to cause cancer
- **40 million individuals drink at risky/harmful levels**
- **100,000 deaths due to alcohol annually** – 3rd leading cause preventable death
- **10,000 killed each year on roads in alcohol-related accidents** – Hundreds of thousands more injured
- **Alcohol-related crashes cost taxpayers $100 billion; overall economic burden $250 billion** (Fed/State/Local combined tax revenue from alcohol sales = $15 Billion)
- **3 million alcohol-related arrests annually** (e.g., liquor violations; underage sales; drunk and disorderly/violence/domestic violence); Nearly 1.4 million arrested for DUI
- If “prohibition doesn’t work” it’s hard to make the case that Legalization is the solution...
ALCOHOL AND HARM

• On alcohol containers, Why don’t we have:
  “alcohol can cause addiction” or
  “alcohol causes cancer”
1994 – Congressional Hearing

Each CEO of major tobacco companies state nicotine nor their products (cigarettes) are addictive.
HOW COULD INCREASED USE OF MJ CAUSE HARM TO PUBLIC HEALTH AND PUBLIC SAFETY?
Toxicity, Intoxication, and Addiction

Patterns of use

Average volume

Toxic Effects

Addiction

Chronic Disease

Accidents/injuries (acute disease)

Acute social problems

Chronic Social problems

Source: Babor et al, 2010
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

Hall, W.; and Degenhardt, L. Adverse health effects of non-medical cannabis use. Lancet 374:1383–1391, 2009;
2015 PAST MONTH USE OF SPECIFIC DRUGS IN THE UNITED STATES

Figure 1. Numbers of Past Month Illicit Drug Users among People Aged 12 or Older: 2015

- No Past Month Illicit Drug Use: 240.6 Million People (89.9%)
- Past Month Illicit Drug Use: 27.1 Million People (10.1%)

Bar chart showing:
- Marijuana: 22.2 million people
- Misuse of Prescription Pain Relievers: 3.8 million people
- Cocaine: 1.9 million people
- Misuse of Prescription Tranquilizers: 1.9 million people
- Misuse of Prescription Stimulants: 1.7 million people
- Hallucinogens: 1.2 million people
- Methamphetamine: 0.9 million people
- Inhalants: 0.5 million people
- Misuse of Prescription Sedatives: 0.4 million people
- Heroin: 0.3 million people

Note: Estimated numbers of people refer to people aged 12 or older in the civilian, noninstitutionalized population in the United States. The numbers do not sum to the total population of the United States because the population for NSDUH does not include people aged 11 years old or younger, people with no fixed household address (e.g., homeless or transient people not in shelters), active-duty military personnel, and residents of institutional group quarters, such as correctional facilities, nursing homes, mental institutions, and long-term care hospitals.

Note: The estimated numbers of current users of different illicit drugs are not mutually exclusive because people could have used more than one type of illicit drug in the past month.
Figure 27. Numbers of People Aged 12 or Older with a Past Year Substance Use Disorder: 2015

Note: Estimated numbers of people refer to people aged 12 or older in the civilian, noninstitutionalized population in the United States. The numbers do not sum to the total population of the United States because the population for NSDUH does not include people aged 11 years old or younger, people with no fixed household address (e.g., homeless or transient people not in shelters), active-duty military personnel, and residents of institutional group quarters, such as correctional facilities, nursing homes, mental institutions, and long-term care hospitals.

Note: The estimated numbers of people with substance use disorders are not mutually exclusive because people could have use disorders for more than one substance.
SUBSTANCES FOR WHICH MOST RECENT TREATMENT WAS RECEIVED IN THE PAST YEAR AMONG PERSONS AGED 12 OR OLDER: 2013

- Alcohol: 2,513
- Marijuana: 845
- Pain Relievers: 746
- Cocaine: 584
- Heroin: 526
- Stimulants: 461
- Tranquilizers: 376
- Hallucinogens: 303

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

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**IMPORANCE** 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

Overall DSM-IV Marijuana Use Disorder

- 2001-2002 NESARC
- 2012-2013 NESARC - III
Toxic Effects
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
Marijuana Users Show Worse Performance on a Memory Test

- MJ users, particularly early-onset users (<16), show impaired learning compared to non-users.
- Could mean students using MJ regularly could have difficulty attending to and learning new information.
WHAT HAPPENS AFTER 30 DAYS OF ABSTINENCE?

- **Psychiatric**
  - Improvement in mood
- **Cognition**
  - ↑ Attention
  - ↑ Executive functions
Pre-frontal cortex associated with weighing pros/cons, impulse control, judgment, abstract reasoning, planning last to develop...

There are “critical” periods in brain development wherein substances can have more profound developmental effects...
Persistent cannabis users show neuropsychological decline from childhood to midlife

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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.
What will be the effects of higher potency MJ?

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

Sources: NSDUH, TEDS, National Seizure System
Cannabis and adolescent brain development

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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 brain development 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
IMPLICATIONS FOR LEGAL, COMMERCIALIZED RECREATIONAL USE

- Important implications because CO, which has a legal age of use set at 21 yrs or older, just released latest report on MJ impact and found that while MJ use nationally declined 4% in 2015 among youth, it went up 20% in CO during the past 2 yrs in which MJ use was legalized
Does MJ affect:

- Neuro-cognition?
- Motivation?
- Psychosis?
### What About Psychotic Symptoms and Schizophrenia?

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<th>Design</th>
<th>Results</th>
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<td>Andréasson</td>
<td>15-year follow-up study of more than 45,000 Swedish conscripts</td>
<td>Cannabis use by age 18 led to a 6-fold increase in the risk of schizophrenia later in life</td>
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<td>Arsenault</td>
<td>Prospective longitudinal study of adolescent cannabis use and psychosis in Dunedin, New Zealand</td>
<td>Those with early-onset cannabis use experienced more psychotic symptoms than controls</td>
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<td>Caspi</td>
<td>Secondary analysis of the influence of the COMT gene Val158Met variant on the development of psychosis among cannabis users in Dunedin, New Zealand</td>
<td>The presence of the Val allele led to an increased risk of psychosis in adulthood when coupled with a history of adolescent cannabis use</td>
</tr>
<tr>
<td>Fergusson</td>
<td>21-year longitudinal study of the link between cannabis and psychosis in a birth cohort in Christchurch, New Zealand</td>
<td>Rates of psychotic symptoms were 3.7 and 2.3 times higher in cannabis-dependent individuals when measured at ages 18 and 21, respectively</td>
</tr>
<tr>
<td>Henquet</td>
<td>Prospective cohort study of psychotic symptoms as a function of cannabis use and baseline psychosis predisposition</td>
<td>Cannabis use at baseline increased the risk of psychosis (adjusted OR, 1.7); predisposition to psychosis significantly increased this effect</td>
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<tr>
<td>Tien</td>
<td>Multisite US epidemiological study of the relationship between self-reported psychotic experiences and cannabis use</td>
<td>Any cannabis use was associated with a 30% increased risk of psychotic experiences, while daily use was associated with a 2.4-fold greater risk</td>
</tr>
<tr>
<td>van Os</td>
<td>3-year population-based prospective study of the effects of baseline cannabis use on the development of psychosis in the Netherlands</td>
<td>Baseline cannabis use was associated with the presence of psychotic symptoms (adjusted OR, 2.8)</td>
</tr>
</tbody>
</table>

*COMT, catechol-O-methyltransferase; OR, odds ratio.*
Cannabis as a risk factor for psychosis: systematic review

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Abstract

Various lines of evidence suggest an association between cannabis and psychosis. Five years ago, the only significant case–control study addressing this question was the Swedish Conscript Cohort. Within the last few years, other studies have emerged, allowing the evidence for cannabis as a risk factor to be more systematically reviewed and psychosis. Seven were included in the meta-analysis, with a derived odds ratio (fixed effects) of 2.9 (95% confidence interval – 2.4–3.6). No evidence of publication bias or heterogeneity was found. Early use of cannabis did appear to increase the risk of psychosis. For psychotic symptoms, a dose–related effect of cannabis use was seen with
Dose–related effect of cannabis use with vulnerable groups including individuals who used cannabis during adolescence, those who had previously experienced psychotic symptoms, and those at high genetic risk of developing schizophrenia.

Available evidence supports the hypothesis that cannabis is an independent risk factor, both for psychosis and the development of psychotic symptoms.

Six case–control studies found psychotic symptoms in cannabis users vs. non–users in both ‘high risk’ and ‘general’ population samples.

Dunedin Birth Cohort Study (Arseneault et al., 2002) found that, even when psychotic symptoms at age 11 years were controlled for, cannabis users by age 15 years and by age 18 years had significantly more ‘schizophrenia symptoms’ compared to controls (although data did not permit calculation of ORs).
Influence of adolescent marijuana use on adult psychosis is affected by genetic variables
Influence of adolescent-onset cannabis use on adult psychosis is moderated by variations in the COMT gene

- Individuals with copies of the Val variant have a higher risk of developing schizophrenic-type disorders if they used cannabis during adolescence.

- Those with only the Met variant were unaffected by cannabis use.

Confirmation that the \textit{AKT1} (rs2494732) Genotype Influences the Risk of Psychosis in Cannabis Users

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\textbf{Background:} Cannabis use is associated with an increased risk of psychosis. One study has suggested that genetic variation in the \textit{AKT1} gene might influence this effect.

\textbf{Methods:} In a case-control study of 489 first-episode psychosis patients and 278 control subjects, we investigated the interaction between variation at the \textit{AKT1} rs2494732 single nucleotide polymorphism and cannabis use in increasing the risk of psychosis.

\textbf{Results:} The rs2494732 locus was not associated with an increased risk of a psychotic disorder, with lifetime cannabis use, or with frequency of use. We did, however, find that the effect of lifetime cannabis use on risk of psychosis was significantly influenced by the rs2494732 locus (likelihood ratio statistic for the interaction = 8.54; \(p = .014\)). Carriers of the C/C genotype with a history of cannabis use showed a greater than twofold increased likelihood of a psychotic disorder (odds ratio = 2.18 [95\% confidence interval: 1.12, 4.31]) when compared with users who were T/T carriers. Moreover, the interaction between the rs2494732 genotype and frequency of use was also significant at the 5\% level (likelihood ratio = 13.39; \(p = .010\)). Among daily users, C/C carriers demonstrated a sevenfold increase in the odds of psychosis compared with T/T carriers (odds ratio = 7.23 [95\% confidence interval: 1.37, 38.12]).

\textbf{Conclusions:} Our findings provide strong support for the initial report that genetic variation at rs2494732 of \textit{AKT1} influences the risk of developing a psychotic disorder in cannabis users.

\textbf{Whether adolescent marijuana use can contribute to developing psychosis later in adulthood may depend on existing genetically based vulnerability}
AKT1 Gene Variants and Psychosis

- Daily users with C/C variant have seven times higher risk of developing psychosis than infrequent marijuana users or nonusers
- Risk for users with T/T variant unaffected by marijuana use

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

Top 10 states for highest rate of current marijuana use were all medical marijuana states; bottom 10 were all non-medical-marijuana states.
IMPACT OF EDIBLES?
Kids and Marijuana Edibles: A Worrisome Trend Emerges

Experts say states should mandate child-resistant packaging.

EDs are seeing a surge in the number of young children having adverse reactions to marijuana. In three-quarters of the cases reported from 2000 through 2013, the children were younger than three years old, ages when children tend to explore their environment by mouth. Most children ate items found in their homes, such as brownies, cookies, candy, and other foods spiked with marijuana.

“A typical adult serving size for a marijuana edible often is a quarter of a brownie, but a small child eats an entire brownie and ends up in the [ED],” says Sarah Ramsey, nurse manager at the Rocky Mountain Poison and Drug Center in Denver.

Data from the National Poison Data System show that the rate of marijuana exposure among children younger than six in the United States rose 147.5% from 2006 to 2013, particularly in states where medical marijuana use is legal.

From 2000 to 2013, poison control centers received reports on 1,969 children younger than six who were exposed to marijuana. Boys and girls were affected equally. Almost half (48%) of exposures involved high concentrations of the drug’s active ingredient. Some parents give marijuana edibles to a child...
Pediatric Marijuana Exposures in a Medical Marijuana State

George Sam Wang, MD; Genie Roosevelt, MD, MPH; Kennon Heard, MD

**Importance** An increasing number of states are decriminalizing the use of medical marijuana, and the effect on the pediatric population has not been evaluated.

**Objective** To compare the proportion of marijuana ingestions by young children who sought care at a children's hospital in Colorado before and after modification of drug enforcement laws in October 2009 regarding medical marijuana possession.

**Design** Retrospective cohort study from January 1, 2005, through December 31, 2011.

**Setting** Tertiary-care children's hospital emergency department in Colorado.

**Participants** A total of 1378 patients younger than 12 years evaluated for unintentional ingestions: 790 patients before September 30, 2009, and 588 patients after October 1, 2009.

**Main Exposure** Marijuana ingestion.

**Main Outcomes and Measures** Marijuana exposure visits, marijuana source, symptoms, and patient disposition.

**Results** The proportion of ingestion visits in patients younger than 12 years (age range, 8 months to 12 years) that were related to marijuana exposure increased after September 30, 2009, from 0 of 790 (0%; 95% CI, 0%-0.6%) to 14 of 588 (2.4%; 95% CI, 1.4%-4.0%) (P < .001). Nine patients had lethargy, 1 had ataxia, and 1 had respiratory insufficiency. Eight patients were admitted, 2 to the intensive care unit. Eight of the 14 cases involved medical marijuana, and 7 of these exposures were from food products.

**Conclusions and Relevance** We found a new appearance of unintentional marijuana ingestions by young children after modification of drug enforcement laws for marijuana possession in Colorado. The consequences of unintentional marijuana exposure in children should be part of the ongoing debate on legalizing marijuana.

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Corresponding Author: George Sam Wang, MD, Rocky Mountain Poison and Drug Center, 777 Bannock St, Office Box 0180, Denver, CO 80204 (george.wang@childrenscolorado.org).
New increase in unintentional marijuana ingestions by young children

Opposite trend to all other toxic ingestions

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>790</td>
<td>588</td>
</tr>
<tr>
<td>Age, median (IQR), y</td>
<td>2.6 (1.6-3.0)</td>
<td>2.3 (1.5-3.6)</td>
</tr>
<tr>
<td>Male sex</td>
<td>449 (56.8)</td>
<td>334 (56.8)</td>
</tr>
<tr>
<td>Types of ingestions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>90 (11.3)</td>
<td>48 (8.2)</td>
</tr>
<tr>
<td>Antihistamine</td>
<td>43 (5.4)</td>
<td>32 (5.4)</td>
</tr>
<tr>
<td>Antidepressant</td>
<td>23 (2.9)</td>
<td>14 (2.3)</td>
</tr>
<tr>
<td>Antitussive</td>
<td>18 (2.2)</td>
<td>14 (2.3)</td>
</tr>
<tr>
<td>Marijuana exposures</td>
<td>0</td>
<td>14 (2.3)</td>
</tr>
</tbody>
</table>

*All data are presented as n (%) unless otherwise noted.*

Changes in Marijuana Use Patterns, Systematic Literature Review, and Possible Marijuana-Related Health Effects

colorado.gov/cdphe/marijuana-health-report
Figure 1. Children under 9 years of age; Rates of hospitalizations (HD) and emergency department (ED) visits with poisoning possibly due to marijuana in Colorado

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Emergency Department Visits</th>
<th>Hospitalizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000 (Prior to Legalized Medical Marijuana)</td>
<td>NA</td>
<td>1</td>
</tr>
<tr>
<td>2001-2009 (Medical Marijuana Legalized)</td>
<td>N&lt;5†</td>
<td>NA</td>
</tr>
<tr>
<td>2010-2013 (Medical Marijuana Commercialized)</td>
<td>N=9.0</td>
<td>N=6*</td>
</tr>
<tr>
<td>2014-Sept 2015 (Retail Marijuana Legalized)</td>
<td>N=42</td>
<td>N=19</td>
</tr>
</tbody>
</table>

Rates Per 100,000
After retail marijuana was legalized, increasing trend in the amount of hospitalizations and ED visits...

Figure 2. Rates of hospitalizations (HD) and emergency department (ED) visits with marijuana-related billing codes in Colorado.
intoxication
Risk of motor vehicle accident increase about 2x after smoking MJ. Critical tracking tasks, reaction times. Divided-attention tasks, lane-position variability all show MJ-induced impairments. Dose dependent. Even among more tolerant regular users, impairments persist.
Method: Online survey of past month MJ users in WA and CO states (N=865)

Results: Prevalence of past-yr driving under influence of MJ was 44%  
Prevalence of driving within 1 hour of using MJ 5+ times in past month = 24%  
69% lower odds of driving if perceived risky  
37% lower odds of driving if had knowledge of MJ DUI laws
Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado

Stacy Salomonsen-Sautel¹, Sung-Joon Min¹, Joseph T. Sakai¹, Christian Thurstone¹,², and Christian Hopfer¹
¹Department of Psychiatry, University of Colorado Anschutz Medical Campus, Aurora, CO, 80045
²Denver Health and Hospital Authority, Denver, CO, 80204

Abstract

Background—Legal medical marijuana has been commercially available on a widespread basis in Colorado since mid-2009; however, there is a dearth of information about the impact of marijuana commercialization on impaired driving. This study examined if the proportions of drivers in a fatal motor vehicle crash who were marijuana-positive and alcohol-impaired, respectively, have changed in Colorado before and after mid-2009 and then compared changes in Colorado with 34 non-medical marijuana states (NMMS).

Methods—Thirty-six 6-month intervals (1994–2011) from the Fatality Analysis Reporting System were used to examine temporal changes in the proportions of drivers in a fatal motor vehicle crash who were alcohol-impaired (≥ 0.08 g/dl) and marijuana-positive, respectively. The pre-commercial marijuana time period in Colorado was defined as 1994–June 2009 while July 2009–2011 represented the post-commercialization period.

Results—In Colorado, since mid-2009 when medical marijuana became commercially available and prevalent, the trend became positive in the proportion of drivers in a fatal motor vehicle crash who were marijuana-positive (change in trend, 2.16 (0.45), p < 0.0001); in contrast, no significant changes were seen in NMMS. For both Colorado and NMMS, no significant changes were seen in the proportion of drivers in a fatal motor vehicle crash who were alcohol-impaired.
Figure 2.
Proportion of drivers in a fatal motor vehicle crash who were marijuana-positive in Colorado and 34 states without medical marijuana laws from 1994–2011

Commercialization of medical MJ in CO
Percent of All Traffic Deaths That Were Marijuana-Related*

*Percent of All Fatalities Where the Operators Tested Positive for Marijuana

Number of Drivers Involved in Fatal Crashes Who Tested Positive for Marijuana

![Bar chart showing the number of drivers involved in fatal crashes who tested positive for marijuana from 2013 to 2015.]

*2015 data obtained from CDOT


- There was an 87 percent increase in drivers testing positive for marijuana who were involved in fatal crashes from 2013 to 2015.
Percentage of Total Driving Cases Positive for Carboxy-THC and Delta-9-THC 2009-2015*

<table>
<thead>
<tr>
<th>Year</th>
<th>Carboxy-THC</th>
<th>Delta-9-THC</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>26%</td>
<td>18%</td>
</tr>
<tr>
<td>2010</td>
<td>28%</td>
<td>19%</td>
</tr>
<tr>
<td>2011</td>
<td>28%</td>
<td>20%</td>
</tr>
<tr>
<td>2012</td>
<td>29%</td>
<td>19%</td>
</tr>
<tr>
<td>2013</td>
<td>40%</td>
<td>25%</td>
</tr>
<tr>
<td>2014</td>
<td>36%</td>
<td>28%</td>
</tr>
<tr>
<td>2015*</td>
<td>39%</td>
<td>33%</td>
</tr>
</tbody>
</table>

SOURCE: Washington State Patrol Toxicology Laboratory and NWHIDTA
2015*: January through April 2015
Drivers Positive for Any Cannabinoid

<table>
<thead>
<tr>
<th></th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboxy-THC</td>
<td>56%</td>
<td>43%</td>
<td>43%</td>
<td>36%</td>
<td>16%</td>
</tr>
<tr>
<td>Active THC</td>
<td>44%</td>
<td>57%</td>
<td>57%</td>
<td>64%</td>
<td>84%</td>
</tr>
<tr>
<td>Active THC Below 5 ng/ml</td>
<td>67%</td>
<td>59%</td>
<td>64%</td>
<td>50%</td>
<td>51%</td>
</tr>
<tr>
<td>Active THC At or Above 5 ng/ml</td>
<td>33%</td>
<td>41%</td>
<td>33%</td>
<td>47%</td>
<td>49%</td>
</tr>
</tbody>
</table>

Drivers by Age

SUMMARY

• POTENTIAL PROS
  • Legalization means improvements in product quality control
  • Eradication of arrests to due to possession (if 21 yrs +; decriminalization already does this)
  • Minimization/eradication of black market
  • Tax revenue/jobs

• POTENTIAL CONS
  • Public health and safety harms
  • Consumption will increase
  • Addiction cases will increase and harms related to acute intoxication (e.g., driving accidents) will increase
  • Toxicity-related poisoning and neurocognitive effects among children and teenagers are likely to increase
  • Enforcement of legalization regulations will be needed – arrests for violations (and related costs) could be high even if substantially less than alcohol
  • Productivity could go down in the population as more people could miss work days/underperform at work contributing to economic increased burden
Degree of Problems Associated with Various Policy Approaches to Addressing the Drug Problem

Source: Canada Drug Policy Coalition, 2015
SUMMARY

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

- **Decriminalization/controlled non-commercialized Market regulated legalization** – best middle ground options

- **If legalized - It matters how you do it** – full commercialization “like alcohol” or state regulated (quality) controlled, ban on advertising, plain packaging

- **Tax revenue, depending on how much is levied, may only be a fraction of societal costs; Industry lobbying down the road may gradually move taxes lower**
SUMMARY

• There are many vested interests and pressures on policy makers.

• Ultimately in a civilized society, good policy preserves individual freedoms, while respecting the rights and liberties of others likely to be affected.

• In the case of drugs (e.g., marijuana), added layer because while people make a free choice to use a drug initially, a proportion suffer from radically impaired ability to continue to make that rational choice— they become addicted (may also suffer from illnesses related to toxicity or intoxication).

• So, with regard to complexities of the ‘drug problem,’ if you hear someone proffer, “listen, all you gotta do is...,” you know they may be suffering from a case of the ‘clear-and-simple,’ but ultimately ‘wrong’ solution, described by Henry Mencken.

• “War on drugs” vs “the war on the war drugs” may each produce different types of casualties (lesser or greater degrees of criminalization, public health/safety).

• The “drug problem” is complex and obstinate; may never eradicate it completely only change its nature.

• As different experiments with different policy positions naturally occur, time will tell if there are “sweet” spots in reducing overall societal harms.
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