Medical Marijuana: A Critical Look at Medicine, Politics, Public Health, and Profits

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- THC & CBD
- THC binds to CB1 receptors
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(Volkow et al., 2014)
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- Number of routes of administration
- High variability of concentration
- Addictive substance
  - Approximately 30% of active users have a SUD
  - 1:10 adults, 1:6 adolescents
- Well-studied detrimental impact on behavioral health and functioning

(CDC, 2017)

Is this medicine?

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

**Is this medicine?**
Therapeutic Uses for Marijuana

- What does quality research show it is good for?
  - Appetite stimulation
  - Nausea suppression
  - Some types of pain
  - MS spasticity (cannabinoids only)
  - Short-term sleep outcomes (cannabinoids only)
  - Good reference: National Academy of Sciences

- In Illinois, it is approved (by the legislature) for 51 conditions...starting at age 18 (Ohio 21)

Qualifying Conditions

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

- **Theory**
  - Endocannabinoid system impacts many different diseases
  - Manipulate the same receptors, get the desired effect

- **Reality**
  - Hit & Miss

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

Katherine A Belendiuk, Lisa L Baldini, and Marcel O Bonn-Miller

**Abstract**

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

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

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

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

- What about glaucoma?

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

- PTSD...

Is this medicine?

- Should lawmakers really be deciding what society calls “medicine?”
  - Public health implications? Perceived risk?
- Why are we doing an end-around the FDA?
  - And what are the consequences?
Healthcare before science: Why do clinical trials matter?

THE THALIDOMIDE TRAGEDY: LESSONS FOR DRUG SAFETY AND REGULATION
By: Bara Fintel, Athena T. Samaras, Edson Carlos
Jul 28, 2009

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

Opioid Substitute?

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

Lancet Public Health 2018; 3:e341-50

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

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

Theodore L. Caputi, BS and Keith Humphreys, PhD
J Addict Med • Volume 12, Number 4, July/August 2018
Association between medical cannabis laws and opioid overdose mortality has reversed over time

Chelsea L. Shover, Corey S. Davis, Sanford C. Gordon, and Keith Humphreys
PNAS June 25, 2019 116 (26) 12624-12626; first published June 10, 2019 https://doi.org/10.1073/pnas.1903434116

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

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

NESARC = National Epidemiological Survey on Alcohol and Related Conditions; wave 1 was conducted in 2001 and 2002, and wave 2 in 2004 and 2005.
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A little “dab” will do ya’ in: a case report of neuro-and cardiotoxicity following use of cannabis concentrates

Shannon S. Rickner, Dazhe Cao, Kurt Kleinschmidt, and Steven Fleming

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

Cannabis-induced psychosis associated with high potency “wax dabs”

Joseph M. Pierre, Michael Gandal, Maya Son

§ Department of Psychiatry and Behavioural Sciences, David Geffen School of Medicine at UCLA, Los Angeles, California

A multicentre case control study

Psychotic Disorders as Function of THC dose, Frequency of Use

11 Sites, 6 Nations in Europe, Brazil: 3 of the cities

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

Di Forti et al

www.thelancet.com/psychiatry

Published online March 10, 2019

12-13% of cases of first-episode psychosis could be prevented across 11 cities 30-35% prevented London 50-53% prevented Amsterdam

Chart prepared by BK Madras
ER visits linked to marijuana rose at Colorado hospital after legalization, study finds

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

March 25, 2019, 4:30 PM EDT
By Shamard Charles, M.D.

He loved weed. Then the vomiting began. Months later, he died

Shari Rudovsky, Indianapolis Star | Published 2:48 p.m. ET Sept. 20, 2019 | Updated 4:00 p.m. ET Sept. 20, 2019

What messages are customers receiving?

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

By Michael Niederman, CNN
Updated 6:05 AM ET, Thu May 10, 2018

Recommendations From Cannabis Dispensaries About First-Trimester Cannabis Use

Is cannabis safe to take during pregnancy?

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

Linden Oaks | Behavioral Health | Healthy Driven
Marijuana - Health and Safety Impact

- Negative health impact

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

<table>
<thead>
<tr>
<th>Effects of short-term use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired short-term memory, making it difficult to learn and to retain information</td>
</tr>
<tr>
<td>Impaired motor coordination, interfering with driving skills and increasing the risk of injuries</td>
</tr>
<tr>
<td>Altered judgment, increasing the risk of sexual behaviors that facilitate the transmission of sexually transmitted diseases</td>
</tr>
<tr>
<td>In high doses, paranoia and psychosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Effects of long-term or heavy use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction (in about 9% of users overall, 17% of those who begin use in adolescence, and 25 to 50% of those who are daily users)</td>
</tr>
<tr>
<td>Altered brain development*</td>
</tr>
<tr>
<td>Poor educational outcome, with increased likelihood of dropping out of school*</td>
</tr>
<tr>
<td>Cognitive impairment, with lower IQ among those who were frequent users during adolescence*</td>
</tr>
<tr>
<td>Diminished life satisfaction and achievement (determined on the basis of subjective and objective measures as compared with such ratings in the general population)*</td>
</tr>
<tr>
<td>Symptoms of chronic bronchitis</td>
</tr>
<tr>
<td>Increased risk of chronic psychosis disorders (including schizophrenia) in persons with a predisposition to such disorders</td>
</tr>
</tbody>
</table>

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

(Volkow et al., 2014)
The Role of Cannabinoids in Neuroanatomic Alterations in Cannabis Users

Figure 4. Percentage of studies reporting associations between regional neuroanatomy and cannabis use measures. Significant associations (red), nonsignificant associations (gray), and associations unexamined (blue).

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

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

- A. Cannabis Use Frequency and Working Memory
- B. Cannabis Use Frequency and Perceptual Reasoning
- C. Cannabis Use Frequency and Delayed Memory Recall
- D. Cannabis Use Frequency and Inhibitory Control
Drivers of Brain Aging

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

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

Accelerated Aging Prediction

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

Aging SPECT scans

Age 20
Age 50
Age 80

"We can now link clinical diagnoses and addictions to premature aging of the brain. Better treatment of these disorders can slow or even halt brain aging. The cannabis abuse result was especially important, as our culture is starting to view marijuana as a harmless substance. These findings invite us to rethink its effects on the brain."

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

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

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

Vox

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

By Julia Belluz | @juliall bellus | vox.com | Sep 3, 2018, 2:20pm EDT

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

First death linked to vaping reported in Illinois

24 August 2019

The New York Times

Bronx Teenager's Death Is the Youngest Vaping Fatality in U.S.

The 17-year-old who died last week is the youngest of 23 people to die nationwide of a vaping-related lung illness.

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BBC

The Washington Post

Vaping lung injuries top 1,000 cases as deaths rise to 18

Health officials are amplifying their recommendation that people refrain from using e-cigarettes or vaping, particularly products containing THC.
Marijuana - Health and Safety Impact

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

Figure 4

Time Course of Standardized THC Concentration in Plasma, Performance Deficit and Subjective High after Smoking Marijuana
(Adapted from Berghaus et al., 1996; Sticht and Kafterstein, 1998 and Rothe, 1994)
Walk And Turn Clues & Observations

Number of WAT Clues ≥2 considered “Impaired”

Median = 0

Median = 3

Cases
Controls

p<0.001

p>0.05, THC ≥5 vs. <5 μg/L
Medical Cannabis Patients Driving While High

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

Erin E. Bonar\(^a\)\(^b\)\(^c\), James A. Cranford\(^a\), Brooke J. Arterberry\(^a\)\(^c\), Maureen A. Walton\(^a\)\(^b\), Kipling M. Bohnert\(^d\), Mark A. Ilgen\(^d\)

In the past 6 months…

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

To Recap: Delivery System

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

- **Local Example** / **Another Local Example**

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**Gateway Drug?**

Age, sex, and race/ethnicity adjusted past-month prevalence of cigarette, alcohol, and illicit drug other than marijuana use among youth aged 12-17 years, by marijuana use status (n = 17,000)

- Cigarette use: 2.7%
- Illicit drug other than marijuana use: 2.2%
- Alcohol use: 8.0%
- Binge alcohol use: 3.5%
- Heavy alcohol use: 0.4%
- Past-month marijuana use = No
- Past-month marijuana use = Yes

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

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Percentage of heroin/prescription painkiller users who first used another addictive drug in previous years

Source: National Survey on Drug Use and Health (NSDUH, 2013 & 2014)
Gateway Drug?

Full length article

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

Katherine M. Keyes\textsuperscript{a,b}, Caroline Rutherford\textsuperscript{a}, Richard Miech\textsuperscript{a}
\textsuperscript{a} Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA
\textsuperscript{b} Center for Research on Society and Health, Universidad Mayor, Santiago, Chile
\textsuperscript{c} Institute for Social Research, University of Michigan, Ann Arbor, MI, USA

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

So what’s this all about then?

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

- Do these ads look familiar?
Every doctor in private practice was asked:
—family physician, surgeon, specialist—
doctors in every branch of medicine—
“What cigarette do you smoke?”

According to a recent Nationwide survey:

More Doctors Smoke Camels
than any other cigarette!

Not a game, not just a trend—but an award to
those who select the brand that
the doctors themselves recommend:
Camel.

Your doctor has asked...along with thousands of
other doctors...to help you select the
brand that doctors recommend:
Camel.

Your doctor knows, as you do, that
Camel is the cigarette that
your doctor selects.

Camel:
more than just a name, it’s a
taste you can’t help but select.

20,679* Physicians
say “LUCKIES are
less irritating”

“It’s toasted”
Your Throat Protection
against irritation against cough.
Marijuana: Bottom Line

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

Cocaine Toothache Drops

Instantaneous Cure!

Price 15 Cents.

Prepared by the Lloyd Manufacturing Co.

For sale by all druggists.

(Registered March 186.)
Actual science-based therapeutic applications for cannabinoids are present, but limited
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The delivery system is not consistent with current models for healthcare, promoting speculative treatment, poor product choices, self-medication, and potential resale to youth
There are numerous health & safety concerns related to marijuana use, particularly for youth and young adults
- Addiction, brain development, achievement, psychosis, drug sequencing, & road safety
- Our perspective has shifted on drugs before…
...let's go in with eyes open this time.
Thank You!