Cannabis: Cure or Cause for Concern?

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@ZivaCooper
@UCLACannabis
# Cannabis as Medicine?

> 700 hypothesized indications!

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<tr>
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<tr>
<td>10. Amyotrophic lateral sclerosis (ALS)</td>
<td>27. Eczema</td>
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<th>No.</th>
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<td>Nonorganic Failure to Thrive</td>
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<td>Obsessive Compulsive Disorder</td>
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<td>Stress</td>
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<td>Stroke</td>
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What is Cannabis?
Cannabis (Plant)
Phytocannabinoids (Unique Constituents >140)

**Cannabidiol (CBD)**
Non-intoxicating, anti-seizure effects
↓ Opioid craving, ↓ Pain (?)

**Δ9-Tetrahydrocannabinol (THC)**
Intoxicant, cognitive effects, abuse
↓ PAIN, ↑ appetite, ↓ nausea
**Cannabis (Plant)**

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  - Intoxicant, cognitive effects, abuse
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- **Cannabidivarin (CBDV)**
  - Non-intoxicating, anti-nausea (?), anti-seizure (?)

- **Cannabinol (CBN)**
  - Drowsiness, some psychoactive effects

- **Cannabigerol (CBG)**
  - Non-intoxicating, antidepressant (?), ↑ appetite (?), pain (?)
Cannabis (Plant)  
Terpenes (Common Constituents)

- **B-Caryophyllene**  
  woody / spicy / pepper / cloves  
  ↓ pain, anti-inflammatory, antiseptic

- **Myrcene**  
  earthy / herbal / thyme  
  ↓ pain, anti-inflammatory, relaxing

- **Pinene**  
  pine / sage / trees  
  alertness, energy, anti-inflammatory

- **Limonene**  
  citrus / lemons  
  stress relief, elevated mood, antiseptic, anti-inflammatory

- **Linalool**  
  floral / citrus / lavender  
  sedation, anxiety, antidepressant
Emerging Trends Impacting Cannabis as Medicine & Public Health Concern

Elsohly et al., 2016
Emerging Trends
Cannabis as Medicine & Public Health Concern

Year

THC %

## Trends: Modes of Use

<table>
<thead>
<tr>
<th>Smoked</th>
<th>Vaporized</th>
<th>Oral</th>
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<tbody>
<tr>
<td>Joint, Prerolls, Blunts</td>
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<td>Tinctures</td>
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<tr>
<td>Topical</td>
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*Illustrations of methods of cannabis use.*
Trends: THC, CBD, CBG, CBXYZ

**Smoked**
- Joint, Prerolls, Blunts

**Vaporized**
- Vaporizer
- Vap-pen

**Oral**
- Beverages
- Baked Goods
- Tinctures

**Topical**
Trends: Terpenes

Smoked
Joint, Prerolls, Blunts

Vaporized
Vaporizer

Vap-pen

Oral
Beverages
Baked Goods
Tinctures
Shifting Demographics of Cannabis Users
Use is increasing

- Daily cannabis
- Vaping
- Medical use
- Past-month use
- Use during pregnancy
- Increase in monthly use

Volkow et al., 2019, SAMHSA, NIH, CDC
Cannabis use during COVID-19: Medical and Non-medical Use (N = 1886)

- **Medical use**: General increase in frequency
  - **Daily use** increased (16.9% to 21.4%)
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  - 40% used for **anxiety** before and during COVID
  - Daily use for **anxiety** increased (19% to 25%)
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Cannabis use during COVID-19: Medical and Non-medical Use (N = 1886)

- **Medical use**: General increase in frequency

- **Non-medical**: General increase in frequency
  - Daily use increased (21.3% to 24.3%)
  - 24% of nonusers prior now report weekly / daily use
Cannabis use during COVID-19: Medical and Non-medical Use (N = 1886)

- **Medical use**: General increase in frequency
- **Non-medical**: General increase in frequency
- **Mode of administration**: No sig change
- **Other substance use?**
Change in Cannabis Use

+ Changing policy and public perception
+ Emerging cannabis product trends
+ Shifting use patterns

URGENT NEED TO KNOW
+- HEALTH EFFECTS
Cannabis / Cannabinoids as Effective Therapeutics?
Evidence for Therapeutic Effects

20 most common qualifying conditions

- Addiction
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Anxiety
- Cancer
- Chemo-associated nausea vomiting, anorexia
- Chronic Pain
- Depression
- Seizure Disorder
- Glaucoma
- HIV associated anorexia, cachexia
- Huntington’s disease
- IBS
- Multiple Sclerosis
- Parkinson’s disease
- PTSD
- Schizophrenia and other psychoses
- Sleep Disorders
- TBI
- Tourette syndrome
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*Slides reflect updates since NAS report published*
20 most common qualifying conditions

- Addiction
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Anxiety
- Cancer
- Chemo-associated nausea vomiting, anorexia
- **Chronic Pain** (Substantial Evidence)
- Depression
- Seizure Disorder
- Glaucoma
- HIV associated anorexia, cachexia
- Huntington’s disease
- IBS
- Multiple Sclerosis
- Parkinson’s disease
- PTSD
- Schizophrenia and other psychoses
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*Slides reflect updates since NAS report published*
20 most common qualifying conditions

- **Addiction** (Promise)
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- **Anxiety** (Promise)
- Cancer
- Chemo-associated nausea and vomiting, anorexia
- Chronic Pain
- Depression
- Epilepsy
- Glaucoma

- HIV associated anorexia, cachexia
- Huntington’s disease
- IBS
- Multiple Sclerosis
- Parkinson’s disease
- **PTSD** (Promise)
- **Schizophrenia and other psychoses** (Promise)
- Sleep Disorders
- TBI
- Tourette syndrome

*Slides reflect updates since NAS report published*
20 most common qualifying conditions

- Addiction
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Anxiety
- Cancer
- Chemotherapy-associated nausea and vomiting
- Chronic pain
- Depression
- Epilepsy
- Glaucoma
- HIV associated anorexia, cachexia
- Huntington’s disease
- Irritable bowel syndrome
- Multiple sclerosis
- Parkinson’s disease
- PTSD
- Schizophrenia and other psychoses
- Sleep disorders
- TBI
- Tourette syndrome

Overwhelming # Studies **NOT** with Cannabis
20 most common qualifying conditions

- Addiction
- Alzheimer’s disease
- Amyotrophic lateral sclerosis
- Anxiety
- Cancer
- Chemo-associated nausea, vomiting, anorexia
- Chronic Pain
- Depression
- Epilepsy
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- HIV associated anorexia, cachexia
- Huntington’s disease
- IBS
- Multiple Sclerosis
- Parkinson’s disease
- PTSD
- Schizophrenia and other psychoses
- Sleep Disorders
- TBI
- Tourette syndrome

None with dispensary product
Is Cannabis an effective medicine?

• Data overwhelmingly from not from the whole cannabis plant

• Legislation and popular belief are outpacing science
Is Cannabis a Cause for Concern?
Adverse Effects

• Frequent bronchitis (smoking)
Adverse Effects

• Frequent bronchitis (smoking)

• Risk of vehicle crashes
Adverse Effects

- Frequent bronchitis (smoking)
- Risk of vehicle crashes
- Low birth weight, preterm birth, NICU
Adverse Effects

• Frequent bronchitis (smoking)
• Risk of vehicle crashes
• Low birth weight, preterm birth, NICU
• **Mental health**
  schizophrenia, depression, anxiety, suicidal ideation, cannabis use disorder
Adverse Effects

• Frequent bronchitis (smoking)
• Risk of vehicle crashes
• Low birth weight, preterm birth, NICU
• Mental health
  schizophrenia, depression, anxiety,
  suicidal ideation, cannabis use disorder
• Impaired learning, memory, attention
Adverse Effects

- Frequent bronchitis (smoking)
- Risk of vehicle crashes
- Low birth weight, preterm birth, NICU
- Mental health
  schizophrenia, depression, anxiety, suicidal ideation, cannabis use disorder
- Impaired learning, memory, attention
- **Drug-drug interaction** (*CBD liver tox*)
Adverse Effects

What’s in the bottle?
Emerging Trends Impacting Cannabis as Medicine & Public Health Concern

- **Rapid** industry growth
- **Novel** products, new ways to use
Emerging Trends Impacting 
Cannabis as Medicine & Public Health Concern

• **Rapid** industry growth
• **Novel** products, new ways to use
• Many **people** using
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- **Therapeutic** benefit (cannabinoids)
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• **Rapid** industry growth
• **Novel** products, new ways to use
• Many **people** using
• **Therapeutic** benefit (cannabinoids)
• **Adverse** effects
• **Unknowns:** Safety, Effectiveness
Summary

These are significant times for cannabis & cannabinoid research, policy, health
These are significant times for cannabis & cannabinoid research, policy, health

- Cannabis and cannabinoids hold therapeutic promise; risks / unknowns must be considered

- Work towards establishing and sharing evidence
LEARN MORE HERE

1) EMAIL cannabis@mednet.ucla.edu

2) www.uclahealth.org/cannabis/

3) @UCLACannabis

4) @zivacoooper
Funding Source and Disclosures

Research support by CMCR, NIH, CHP, BCC

Semel Charitable Foundation  Shirley & Stefan Hatos Foundation

Independent of these studies, in the past year Cooper served on the scientific advisory board of FSD Pharma
Adverse Effects of Acute Cannabis Intoxication and Long-term Cannabis Use

MADELINE H. MEIER, PHD
What We Know
Cannabis intoxication (THC) causes...

- Cognitive impairment (memory, attention, working memory)
- Motor impairment
- Psychotic-like experiences
- Anxiety at higher doses

CBD might attenuate the psychological effects of THC
Long-Term, Heavy Cannabis Users Show...

◦ IQ decline
◦ Learning, memory, attention problems
◦ Smaller regional brain volume (in some studies)
◦ Mental health problems: depression, suicide, psychosis

....But generally NOT physical health problems
Duration of Cannabis Use is Not Associated With Laboratory Measures of Physical Health Problems

What We Don’t Know
Are Adolescents More Vulnerable than Adults?

- Some evidence of this from animal studies
- Harder to study in humans
  - Some human studies suggest earlier-onset use is associated with worse outcomes
  - Few studies have compared adolescent-onset users with adult-onset users
Are Adolescents More Vulnerable than Adults?

Does Quitting Cannabis Help?

Some evidence suggests yes

- Some cognitive functions might improve after quitting
- Reductions in cannabis use are associated with decreases in depression symptoms
- Overall, too few studies to make strong conclusions
Are Associations Causal?

In lab studies, yes

In naturalistic studies,
  ◦ Cannot conclusively demonstrate causality
  ◦ Rule out alternative explanations
  ◦ Test for dose-response
What About?

Effects on fetal development?

Differences for medical vs. non-medical cannabis users?
Thank you!

Funding:
US National Institute on Aging (R01AG032282, R01AG048895)
US National Institute of Mental Health (MH077874)
  US National Institute on Drug Abuse Grant (P30 DA023026)
United Kingdom Medical Research Council (MR/K00381X)
Economic and Social Research Council (ES/M010309/1)
Jacobs Foundation

Role of the Funder/Sponsor: The funding agencies were not involved in the design or conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.
Questions

What do you think is lacking in the media about this topic?
- When comparing studies, must take into account differences between studies in terms of cannabis frequency, duration of use, and dependence

Take home message?
- Poorer outcomes are concentrated among long-term, heavy cannabis users, which comprise a small minority of cannabis users


Scott JC, Slomiak ST, Jones JD, Rosen AF, Moore TM, Gur RC. Association of cannabis with cognitive functioning in adolescents and young adults: a systematic review and meta-analysis. JAMA Psychiatry. 2018 Jun 1;75(6):585-95.

Regulation of legal cannabis in the U.S.: The implications of allowing the industry to drive regulation of the market

Rosalie Liccardo Pacula, PhD

Professor and Elizabeth Garrett Chair in Health Policy, Economics, and Law, USC Sol Price School of Public Policy
Senior Fellow, Leonard Schaeffer Center for Health Policy & Economics
President, International Society for the Study of Drug Policy
Cannabis is being regulated as a commercial enterprise, rather than a public health commodity

• Focus of regulations is on:
  – Licensing
  – Location of stores
  – On-site / off-site consumption
  – Testing for mold, pesticides and contaminants
  – Taxation based on sales or volume amount sold

• Public health minded regulations pertain only to edibles:
  – Testing and scoring of edibles in terms of single THC dosing
  – Production
  – Packaging, with limits on total amount in 1 package
  – In some states, product stamping
Key public health regulations are missing

1. Restrictions on ingredients and extractions allowed from cannabis plant
2. Restrictions on amount sold
3. Taxing potency instead of amounts sold
4. Compliance checks
5. Regulating advertising and promotions
1. Restrictions on ingredients and extractions allowed from cannabis plant

• Caps on potency of the plant (and its derivate products) sold
  ‒ Average potency of flower material sold = 21% THC (largest share of the market, but falling)
  ‒ Average potency of concentrate material sold = 70% THC (fastest growing segment of the market)

• Extracts allowed from the plant
  ‒ Delta-9 THC from “cannabis”
  ‒ Delta-8 THC from “hemp”

• Additives
2. Restrictions on amount sold

Most state restrictions on sales of products are based on amount in terms of weight, not potency

- Sales limits for states with recreational markets as of Jan 2020 ranged from 1-2.5 ounces of flower / bud and 5-15 grams of concentrates.
- Average potency across these different products varies (ranges from 8-34% for flower; 40-97% for concentrates in WA state)
- Implication is that very large amounts of 10-mg doses of THC can be purchased from all states
  - All states allow single purchases exceeding 500 10-mg THC doses
  - 6 states allow single purchases exceeding 1,000 10-mg THC doses

3. Few states tax THC, but instead tax based on volume weight sold

- Illinois is the only state that currently imposes a tax based on THC

- The price per gram is decreasing, and so is the price per THC dose
4. State regulations need to include (and finance) random compliance checks

Why?

- Ensure unlicensed stores do not crop up
- Ensure stores comply with rules regarding:
  - Sales to minors
  - Free giveaways / samples
  - Restrictions with on-premise consumption
  - Restrictions on product promotions & warning signs
- Ensure only legal and allowable products are sold in stores
5. Regulating advertising and promotions

Cannabis industry will promote itself in ways alcohol and tobacco have not or could not.
Industry tracking new product types and flower is not the biggest market
Implications of industry capture on regulation

• Positive scientific results for the industry are used immediately, before the results can be robustly replicated and deemed reliable

• Ways in which people are exposed to positive messaging and normalization of use is diverse and subtle

• Impacts of this normalization are national, not local (go beyond states with policies)

• It will be difficult to establish clinically appropriate standards for things like intoxication or impairment without some industry interference
Thank you!

Rosalie Liccardo Pacula, PhD

Professor and Elizabeth Garrett Chair in Health Policy, Economics and Law, USC Price School

President, International Society for the Study of Drug Policy
Testing needs to be done independently, with public health in mind

- No universal scientific standards for laboratory testing protocols of cannabis currently exist

- Most labs in the U.S. are not established quality control labs with a track record of testing food and pharmaceutical products

- Jikomes & Zoorob (2018) examine data from WA state seed-to-sale and find:
  - There is a systematic tendency for certain labs to report higher levels of cannabinoids across all products, something called “cannabis inflation”
  - Observed differences in lab testing cannot be explained by differences in the source of the cannabis (producer), product type, or strain name