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GREATER INTERMOUNTAIN NODE

Cannabis and Opioid Use Disorder Treatment: the Science

Presentation to the Utah DoH Cannabinoid Product Board

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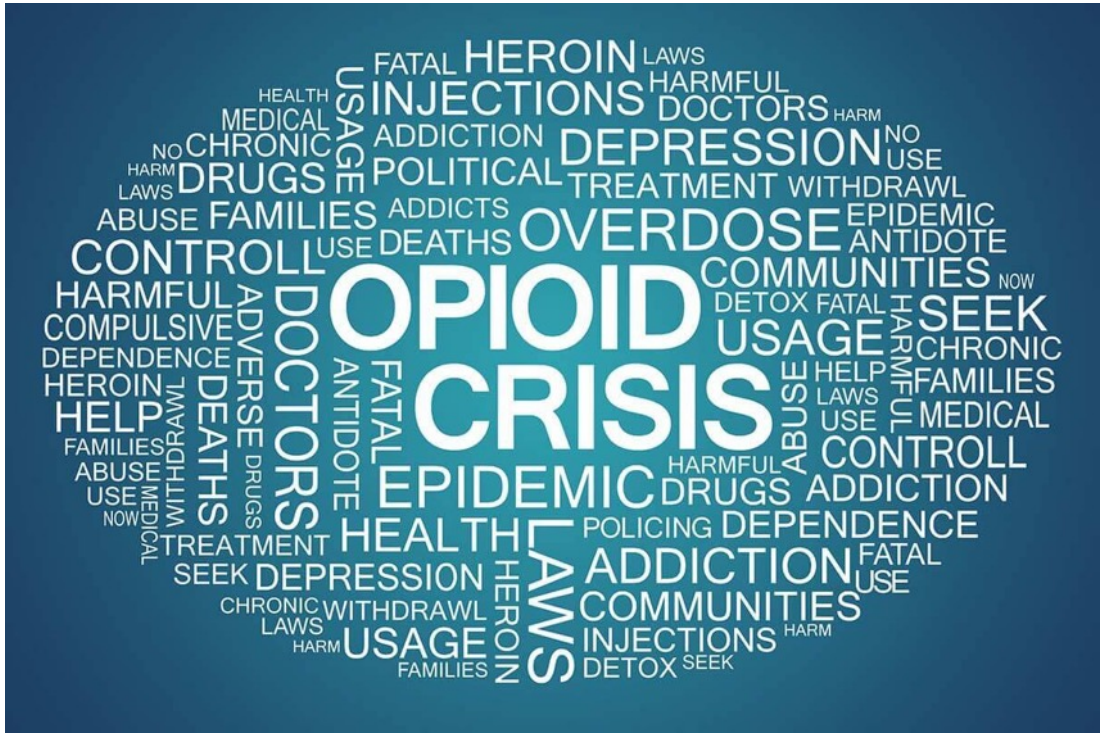
Disclosures

- Dr. Gordon has no fiduciary conflicts of interest
- Some of the material presented herein has been previously published from his work at the University of Pittsburgh, University of Utah, and the Veterans Health Administration
- I do serve (without payment or remuneration) on the American Society of Addiction Medicine (ASAM), International Society of Addiction Journal Editors (ISAJE), and the Association for Multidisciplinary Education and Research in Substance use and Addiction (AMERSA)
- The views expressed in this presentation are Dr. Gordon's and do not necessarily reflect the position or policy any institution, agency, organization, or government

Central Question

Is medical cannabis an effective and appropriate treatment for persons with an opioid use disorder (OUD)?

Caveats



- Definitions are important
  1. **Opioid use**
     - Short term or Long term
     - Use is not inherently bad
     - Long term use is not encouraged
  2. **Opioid misuse**
     - Characterized by prescription use
     - Adherent behaviors
     - Vexes providers
     - Opioid Risk Assessment and Risk Mitigation (e.g., reduction in dose, monitoring)
  3. **Opioid Use Disorder (OUD)**
     - Characterized by illicit or prescription use
     - Addiction (2+ of 11 criteria)
     - A maladaptive pattern of use that causes harm
     - GOLD STANDARD TREATMENT: medications (methadone, buprenorphine, naltrexone)
- Opioid overdoses occur within opioid use, opioid misuse, and OUD

Science

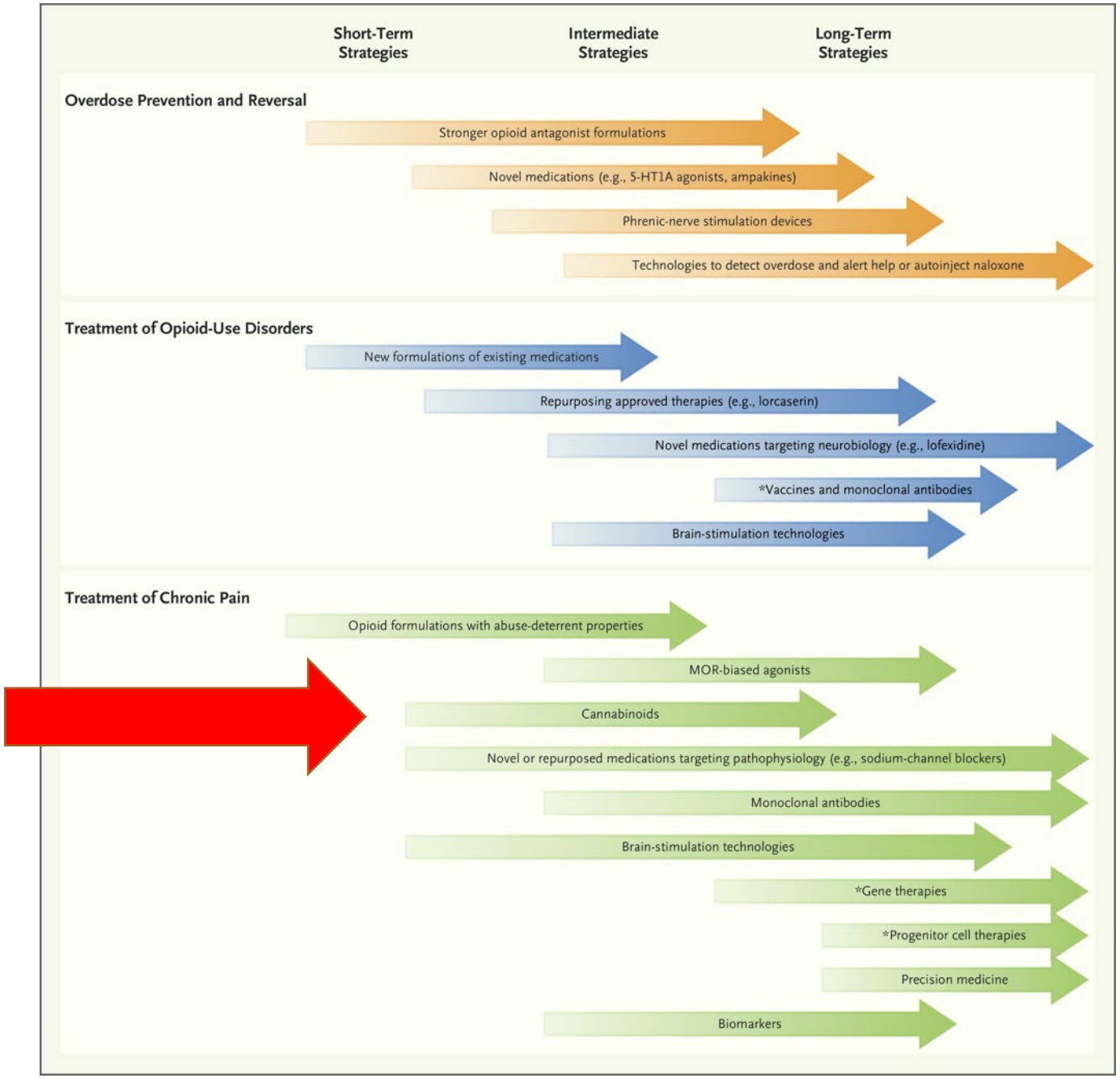
The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL REPORT

The Role of Science in Addressing the Opioid Crisis

Nora D. Volkow, M.D., and Francis S. Collins, M.D., Ph.D.

"Third, we need safe, effective, non-addictive treatments **to manage chronic pain**.…Non-opioid-based approaches **like cannabinoids**, sodium channel blockers, gene therapies, and brain-stimulation technologies (such as transcranial magnetic stimulation [TMS], transcranial direct current stimulation, and electrical deep brain stimulation) also **may lead to new therapeutics.**



Volkow N, Collins FS, NEJM 2017

Searching for a treatment for OUD

- Society and health care providers have not embraced the best science to treat opioid use disorder (OUD)
- Providers simply don't provide medication treatments
- It's an indictment of our health care system that we are searching for "alternative treatments" when existing treatments WORK
  - Misunderstanding
  - Misinformation
  - Preconceived notions
  - Stigma of the disease and the treatment

Proposed Strategy 6A | Reform Legal Requirements for Buprenorphine

Once there is an assurance of appropriate training for all prescribing clinicians, Congress should repeal the requirement to obtain a waiver to prescribe buprenorphine.

Proposed Strategy 6B | Reduce Restrictions on Nurse Practitioners

States should consider expanding the training and scope of practice for nurse practitioners in order to facilitate greater access to medications for OUD.

Proposed Strategy 6C | Support Innovation in Methadone Delivery

DEA and SAMHSA should encourage innovation on methadone delivery.

Proposed Strategy 6D | Eliminate Unnecessary Barriers

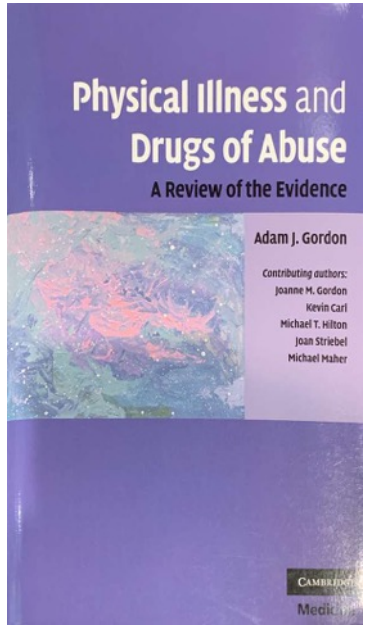
Congress should preempt state laws that add unnecessary additional barriers to the provision of medications for OUD.

Proposed Strategy 6E | Reduce Utilization Management Policies for Medications

Public and private payers should eliminate utilization policies that limit access to treatment.

Madras, et.al. Improving Access to Evidence –Based Treatment for Opioid Use Disorder… National Academy of Sciences. April 27, 2020

Cannabis: Brief Epidemiology



- Cannabis is the **most frequently** used illicit drug worldwide
- Marijuana is the **most commonly used "illicit" drug** in the US
  - About 12% of people 12+ years old report use in the past year
- With any use, the **LIFETIME** probability of developing Cannabis Use Disorder (CaUD or *addiction*) is approximately 9%
  - The risk of developing CaUD increases significantly during adolescence
  - Any cannabis use consistently associated with other substance use (opioids)
- In US, approximately 4 million people have CaUD
  - 1.5% of the US population has CaUD
  - Increase USE and CaUD in states with medical marijuana laws

Levesque A and Le Foll B. Med Clin N Am. 2018;102:667-681
http://www.unodc.org/wdr2016/
Lev-Ran S. et.al. Am J Addict 2013;22(1):7-13
Lopez-Quintero C. et.al. Drug Alcohol Depend 2011;115(1-2):120-130
Le Strat Y. et.al. Acid Anal Prev. 2015;76:1-5
SAMHSA. https://www.samhsa.gov/data/sites/default/files/NSDUH-FFR1-2015/NSDUHFFR1-2015/NSDUH-FFR1-2015.htm#sudyr04
Hasin DS, et.al. JAMA Psych. 2017;74(6):579-588

Some benefits in pain … maybe

- According to a Cochrane review, the effectiveness of cannabis-based medicines for neuropathic pain was small and may be outweighed by potential harms
- A systematic review of 43 randomized controlled trials found that cannabis-based medicine might be effective for chronic pain based on limited evidence, primarily for neuropathic pain, and that, due to small effect sizes, the clinical significance is uncertain
  - Chocolate analogy
- A huge boon to the industry to link cannabis to the treatment

  of pain – pain is the most common patient complaint

ASAM 2020 Public Policy Statement on Cannabis
Mücke M, et.al. Cochrane Database of Systematic Reviews 2018, Issue 3
Aviram J, Samuelly-Leichtag G. Pain Physician. 2017;20(6):E755-E796

How about OUD?

- A widely publicized study found lower opioid overdose rates in states that legalized cannabis use for medical purposes compared with other states through 2010
  - This study is NOT about OUD, but overdose
- This led some states to include opioid use disorder (OUD) as a possible indication for cannabis used for medical purposes.
  - However, a subsequent analysis extended through 2017 and using similar methods with additional controls found the opposite association
- Studies of individuals show an association between cannabis use and increased rates of non-medical opioid use and OUD
- There is no current evidence that cannabis is effective OUD treatment
  - Further, due to its mechanism of action, cannabis would not be expected to reduce opioid overdose rates, unlike the existing (effective) FDA-approved OUD medications
- There has been a preliminary finding of an effect of CBD in reducing opioid cue-induced craving… (withdrawal treatment?)

ASAM 2020 Public Policy Statement on Cannabis, October 2020
Bachhuber MA et.al. JAMA Intern Med. 2014;174(10):1668-1673
Shover CL, et.al. Association between medical cannabis laws and opioid overdose mortality has reversed over time. Proc Natl Acad Sci U S A. 2019 Jun 25;116(26):12624-12626
Olfson M,et.al. Am Jour Psychiatry. 2018; 175(1):47-53
Humphreys K and Saitz R. Should Physicians Recommend Replacing Opioids With Cannabis? JAMA. 2019; 19;321(7):639-640
Hurd YL, et.al. Am Psychiatry. 2019;176(11):911-922

Shover Study, 2019

- Medical cannabis has been touted as a solution to the US opioid overdose crisis since Bachhuber et al. found that from 1999 to 2010 states with medical cannabis laws experienced slower increases in opioid analgesic overdose mortality
- That research received substantial attention in the scientific literature and popular press and served as a talking point for the cannabis industry and its advocates, **despite caveats from the authors and others to exercise caution when using ecological correlations to draw causal, individual-level conclusions**
- In this study, we used the same methods to extend Bachhuber et 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 accounting for recreational cannabis laws
- We also uncovered 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 cannabis—used by about 2.5% of the US population—has exerted large conflicting effects on opioid overdose mortality
- Research into therapeutic potential of cannabis should continue, but **the claim that enacting medical cannabis laws will reduce opioid overdose death should be met with skepticism**

ASAM 2020 Public Policy Statement on Cannabis, October 2020

Shover CL, et.al. Association between medical cannabis laws and opioid overdose mortality has reversed over time. Proc Natl Acad Sci U S A. 2019 Jun 25;116(26):12624-12626

American Society of Addiction Medicine

"6. Healthcare professionals should not recommend cannabis use for the treatment of OUD."

"9. A substantial proportion of cannabis tax revenue should be earmarked to fund prevention and mitigation of cannabis-related harm, and substance use disorder prevention and treatment programs, including public awareness campaigns about the risks of cannabis use, including cannabis use disorder…."

Recent review

Cannabinoids for the Treatment of Opioid Use Disorder: Where is the Evidence?

Joji Suzuki, MD and Roger D. Weiss, MD

- The evidence cited for the potential benefits of cannabis to treat OUD generally come from population-level research showing an inverse association between enactment of medical marijuana laws and opioid-related adverse outcomes
  - **there are other population-level studies that indicate cannabis use is associated with a higher risk of developing an OUD**
- A recent meta-analysis of 23 studies of patients in methadone maintenance treatment [patients in OUD treatment] compared outcomes (retention and nonprescribed opioid use) among those who did and did not use cannabis
  - Low evidence quality
  - The results suggested that **cannabis use did not affect patient outcomes overall**

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Suzuki J, Weiss RD. J Addict Med. 2020; Sep 8 epub ahead of print
McBrien, et.al . CMAJ Open. 2019;7(4):E665–E673

Recent review

Cannabinoids for the Treatment of Opioid Use Disorder: Where is the Evidence?

Joji Suzuki, MD and Roger D. Weiss, MD

- There have been **no prospective clinical trials** of cannabis or cannabinoids for the treatment of OUD, nor trials that compare such compounds to existing medication treatment for OUD such as buprenorphine
- As clinicians and researchers, we need to follow the science:
  - there are no data at present to support the listing by some states of cannabis or cannabinoids as a treatment for OUD
  - Evidence suggest arguing against recommending cannabis or cannabinoids as a substitute to existing medication treatment OUD options
  - Until we have more research to show their efficacy, policy makers and clinicians should refrain from portraying cannabis and cannabinoids as evidence-based treatments for OUD

Suzuki J, Weiss RD. J Addict Med. 2020; Sep 8 epub ahead of print
Humphreys K, Saitz R. Should physicians recommend replacing opioids with cannabis? JAMA. 2019;321(7):639–640.

DISCUSSION

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