Medical Cannabis Research:

What is its role in the opioid epidemic?

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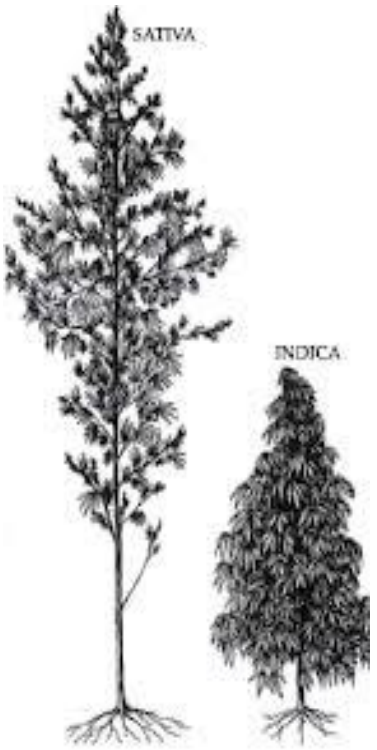
Outline

- What is cannabis?
- State and federal cannabis policies
- Cannabis and opioids

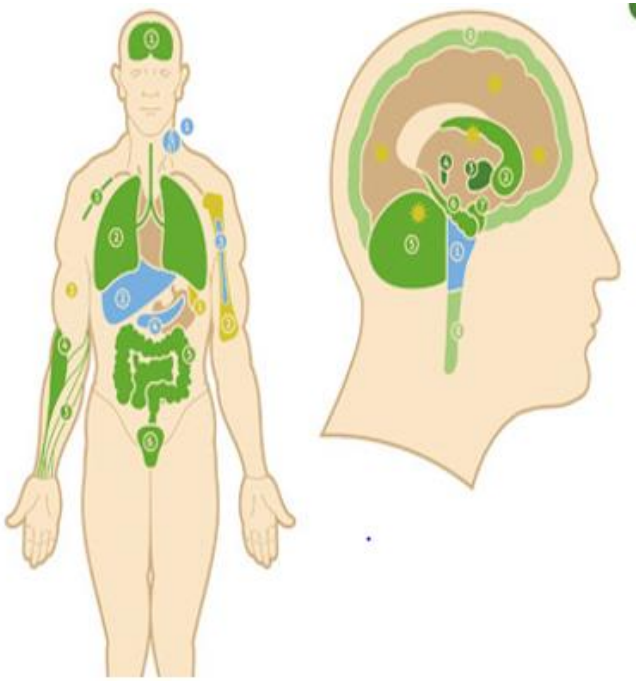
What is cannabis?

- Cannabis vs. marijuana
- **Cannabis is not one thing**
- Cannabis plant, main subspecies
  - Sativa (higher THC content)
  - Indica (higher CBD content)
  - Hybrids
- >100 cannabinoids in cannabis
  - THC = Δ-9-tetrahydrocannabinol
  - CBD = cannabidiol



Endocannabinoid system

- 2 cannabinoid receptors
  - CB_1 - brain, GI tract, lungs, fat, liver, skeletal muscles
  - CB_2 – brain, macrophages, microglia, bone, liver
- 2 endocannabinoids
  - 2-archidonoylglycerol (2-AG)
  - Anandamide



Matsuda 1990, Munro 1993, Mackie 2006

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THC vs. CBD

- THC
  - Main psychoactive component of cannabis
  - Effects on pain, muscle relaxation, nausea, appetite stimulation
- CBD
  - Non-psychoactive
  - Anti-oxidant, anti-inflammatory, anticonvulsant, anxiolytic
  - May decrease psychoactive effect of THC
- THC & CBD together
  - CBD may potentiate and block specific effects of THC
  - Together, may be more effective in treating pain

Matsuda 1990, Munro 1993, Mackie 2006

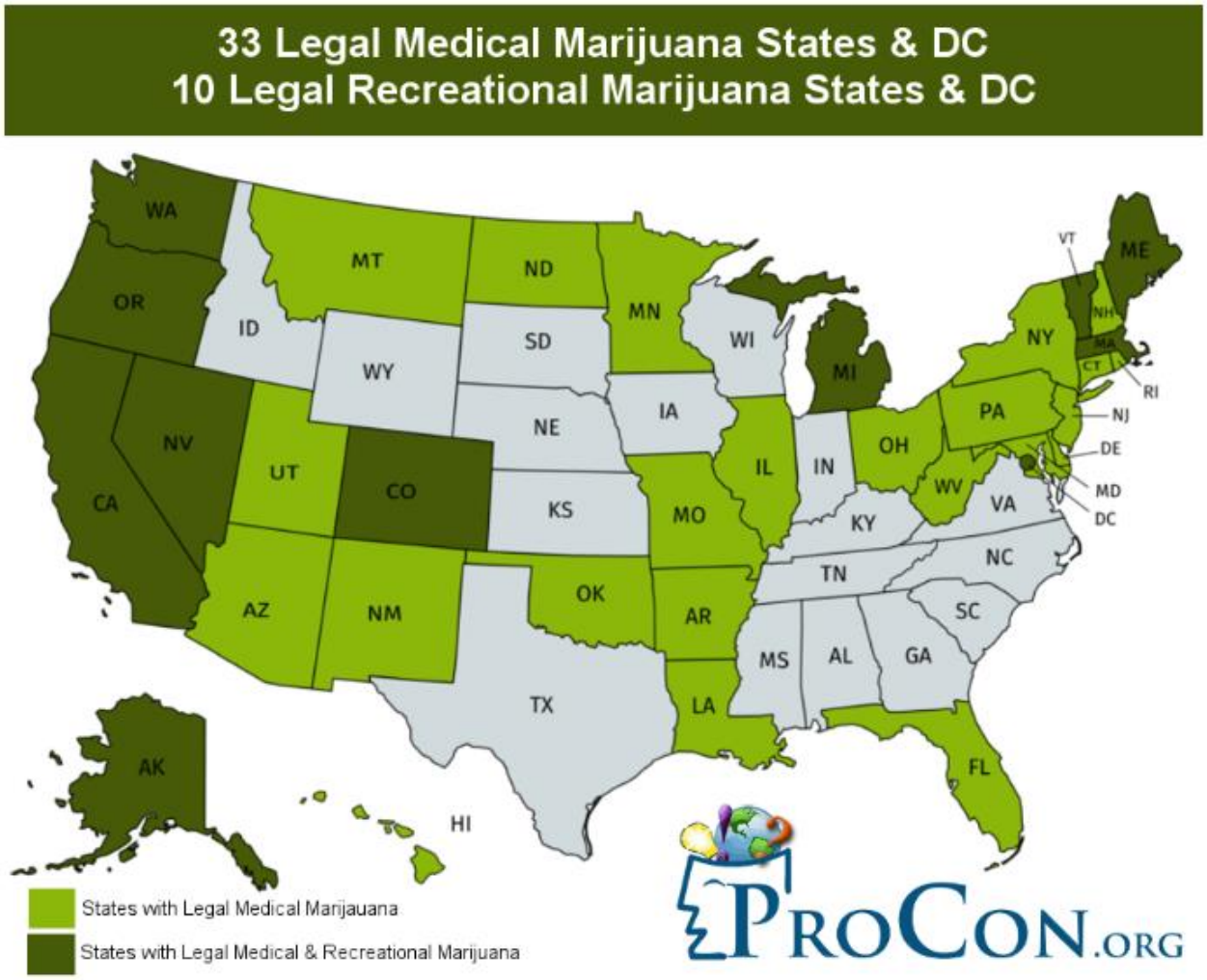
FDA-approved cannabinoid products

- Synthetic cannabinoid products
  - Dronabinol (Marinol) – THC
    - Nausea, weight loss
  - Nabilone (Cesamet, Canemes) – THC-like
    - Nausea, fibromyalgia
- Herbal-derived products
  - Epidiolex – CBD
    - Severe childhood epilepsy

Outline

- What is cannabis?
- State and federal cannabis policies
  - NY's Medical Marijuana Program
  - Qualifying conditions and complications
  - Dispensaries and products
  - Federal cannabis policies
- Cannabis and opioids

States with medical and adult use cannabis



Your State's Cannabis Policies?

- Which medical providers certify and how?
- How do patients qualify?
- What formulations exist?
- Measurement of cannabis content?

NY Medical Marijuana Program

- Implemented January 2016
- Medical providers
  - MD, DO, NP, PA
  - 4-hour on-line training
  - Register with NYS DOH
  - Certify patients, +/- dosing recommendations, NOT prescribe to patients
- Patients
  - Find medical provider who certifies
  - Meet qualifying conditions and complications
  - Register with NYS DOH

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NY Medical Marijuana Program

- Dispensaries
  - 5 →10 companies, 4 dispensaries/company
  - Pharmacists on-site, provide guidance
  - CASH ONLY – no insurance coverage, no credit cards
  - Maximum price set by NYS DOH

- Products
  - Must carry products with varying THC:CBD content
    - ↑THC:↓CBD, THC=CBD, ↓THC: ↑CBD
  - Tested by independent lab at NYS DOH
  - NO smoked or edible products
  - Available products:
    - Vaped oils
    - Oral capsules, tablets, lozenges, tincture, oil, sprays, powder
    - Sublingual tinctures/oils
    - Topical creams, patches
    - Suppositories

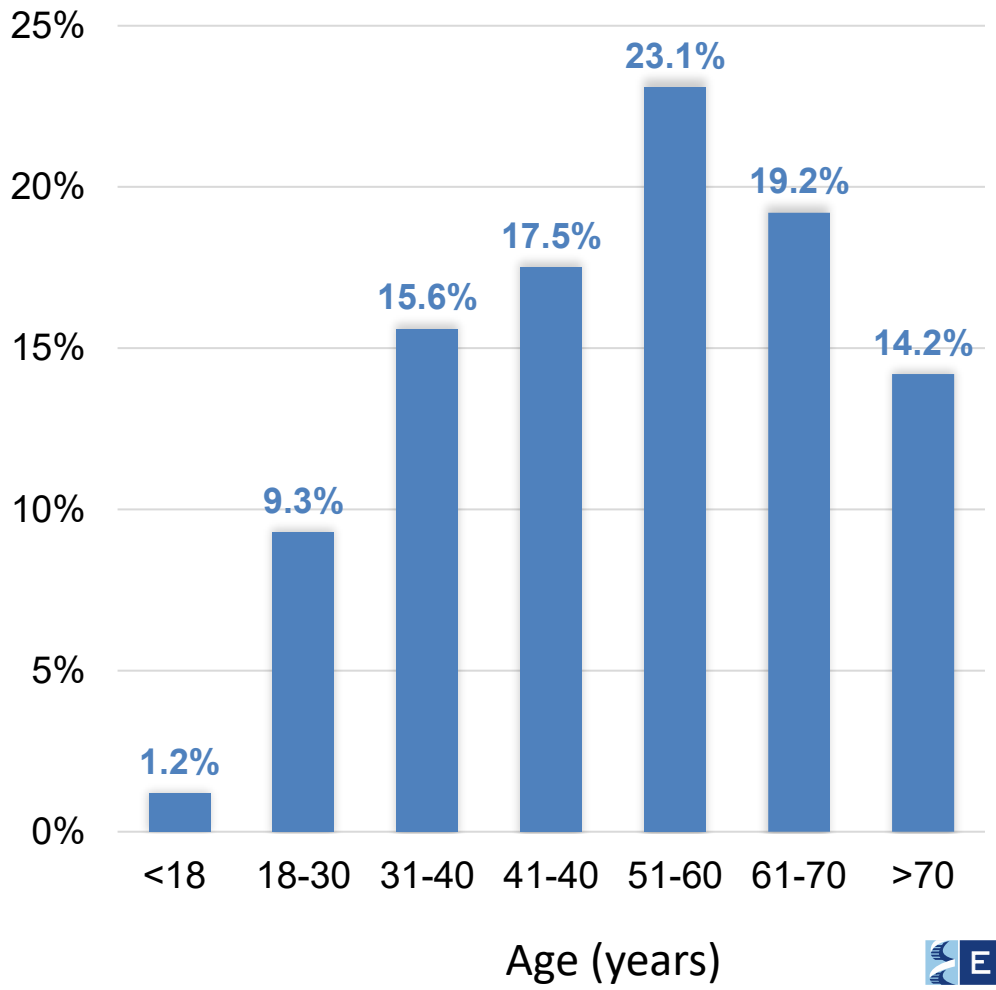
NY Medical Marijuana Program
Qualifying Conditions and Complications

Condition
Chronic pain
Pain – alternative to opioid use or SUD
PTSD
Neuropathy
Cancer
HIV infection
Spinal cord injury w/ spasticity
ALS
Parkinson's Disease
Inflammatory Bowel Disease
Huntington's Disease
Epilepsy
Multiple Sclerosis

Complication
Severe or chronic pain
Opioid use disorder
PTSD
Cachexia or wasting syndrome
Severe nausea
Seizures
Severe/persistent muscle spasms

*Patients must have 1 condition and 1 complication

NY Medical Marijuana Program
Age of registered patients, June 2018



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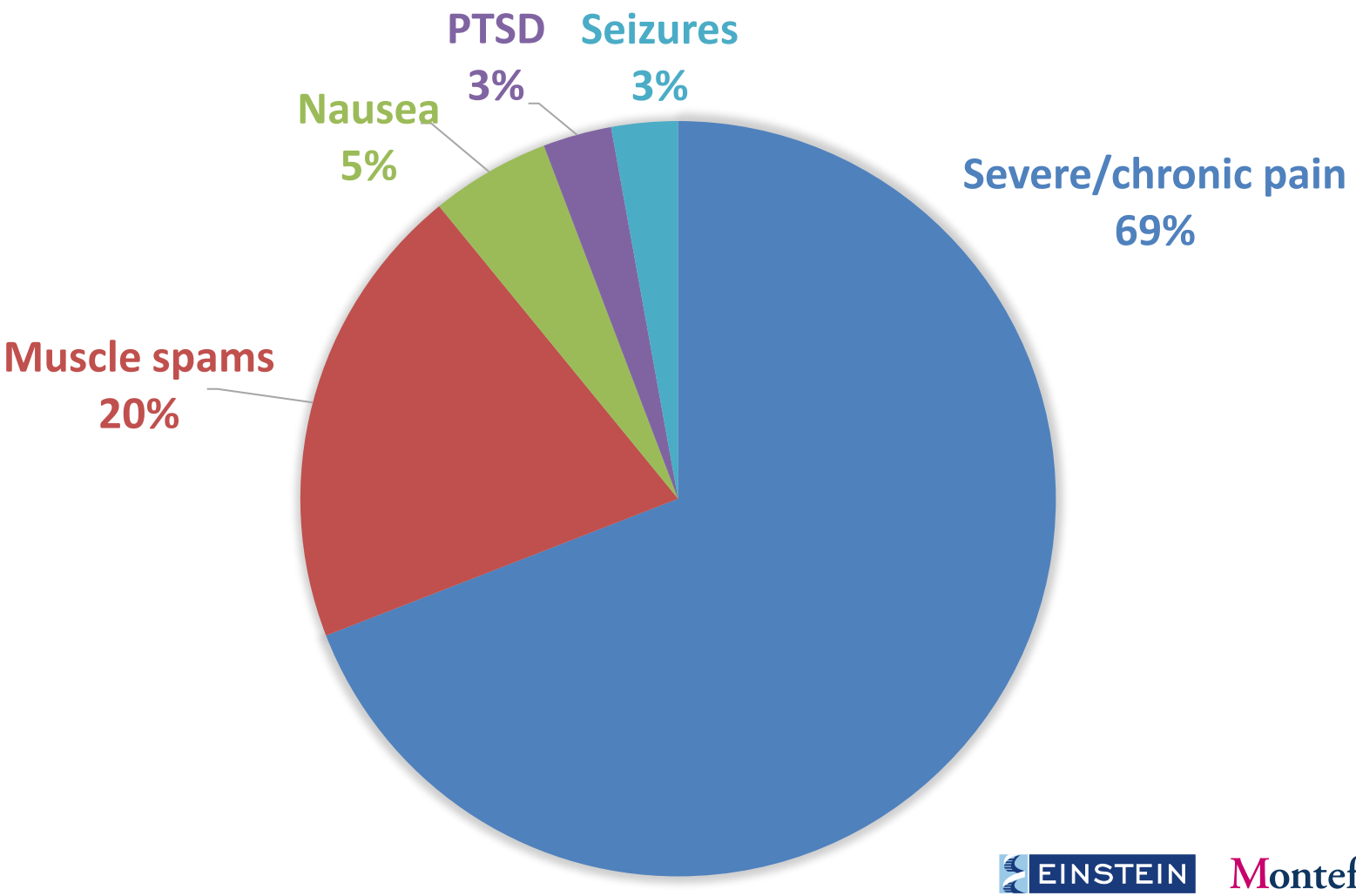
NY Medical Marijuana Program Qualifying Complications, June 2018



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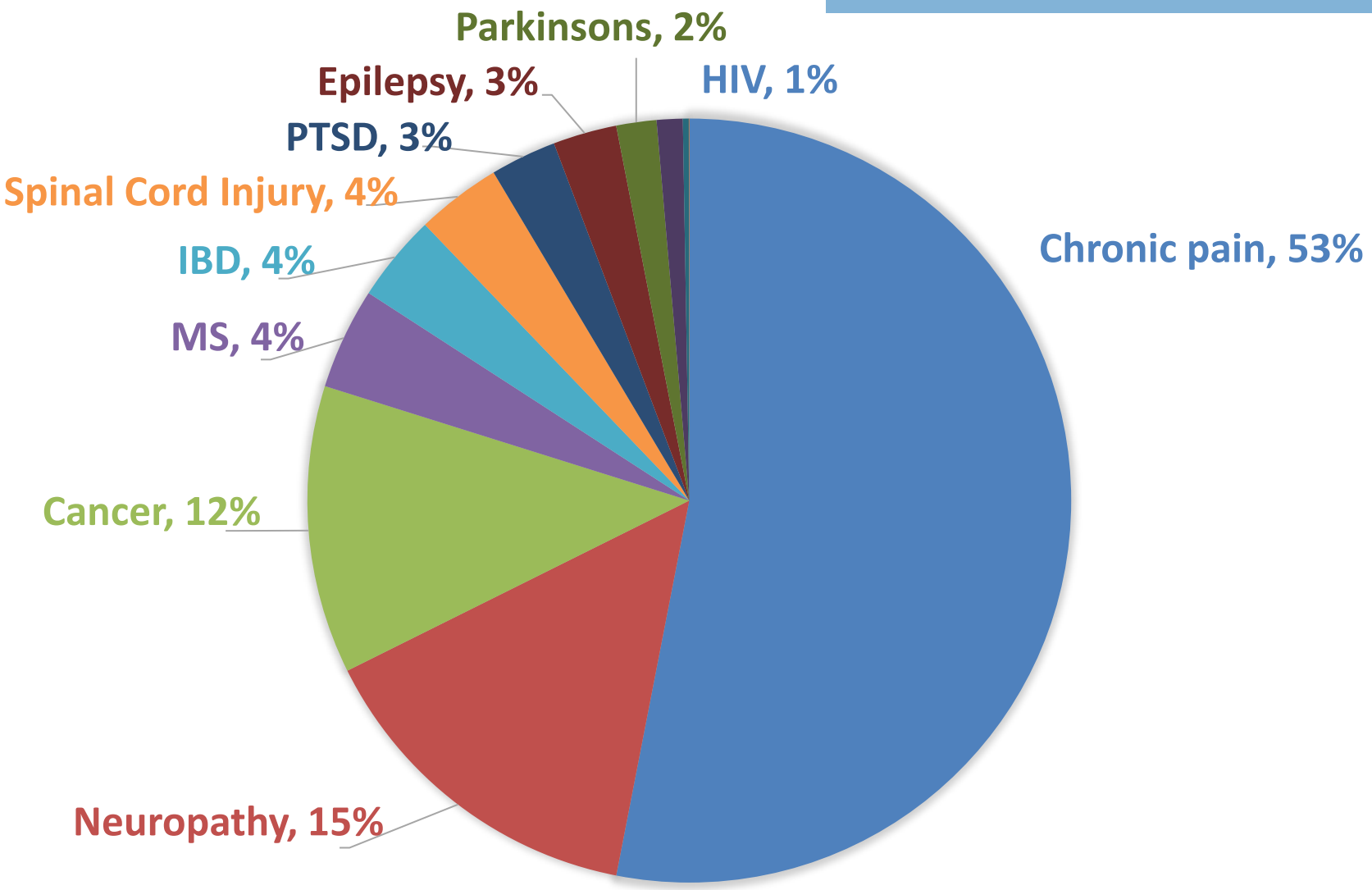
NY Medical Marijuana Program Qualifying Conditions, June 2018



Federal Cannabis Policies

- What are the federal cannabis policies?
- How do federal policies differ from state policies?
- What implications do federal policies have on research?

Federal Cannabis Policies

- **Cannabis = schedule 1 substance**
  - "No currently accepted medical use…high potential for abuse"
- Clinical implications
  - Cannot prescribe cannabis, only certify
  - Patients have autonomy with content, dose, amount, route
  - No insurance coverage
- Research implications
  - Schedule 1 license
  - Cannot purchase state-legal cannabis with federal funds
  - Only one site in US with approved research cannabis
  - Must administer cannabis (no take home products)
- Other implications
  - Banking/credit cards
  - Travel across states

Outline

- What is cannabis?
- State and federal cannabis policies
- Cannabis and opioids
  - Pain
  - Opioid overdose deaths
  - Opioid prescribing
  - Opioid use
  - Opioid use disorder

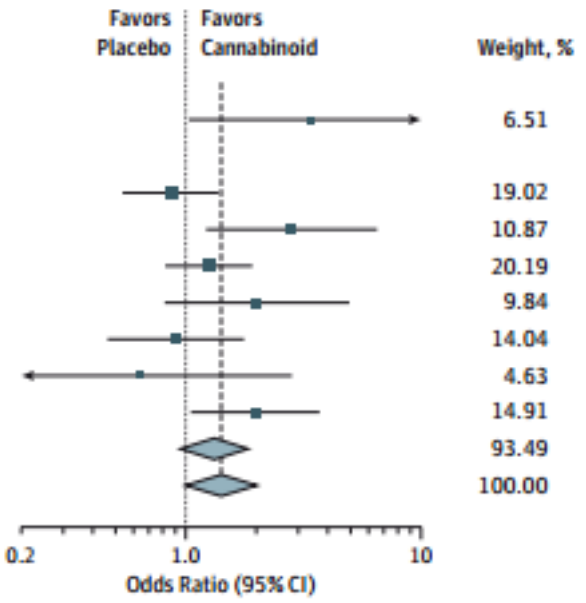
Original Investigation

Cannabinoids for Medical Use
A Systematic Review and Meta-analysis

Penny F. Whiting, PhD; Robert F. Wolff, MD; Sohan Deshpande, MSc; Marcello Di Nisio, PhD; Steven Duffy, PgD; Adrian V. Hernandez, MD, PhD; J. Christiaan Keurentjes, MD, PhD; Shona Lang, PhD; Kate Misso, MSc; Steve Ryder, MSc; Simone Schmidlkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

Figure 2. Improvement in Pain

Improvement in Pain With Cannabinoid vs Placebo by Study	Cannabinoid Events No.	Cannabinoid Events Total No.	Placebo Events No.	Placebo Events Total No.	Odds Ratio (95% CI)
Tetrahydrocannabinol (smoked)					
Abrams et al,[77] 2007	13	25	6	25	3.43 (1.03-11.48)
Nabiximols					
GW Pharmaceuticals,[22] 2005	54	149	59	148	0.86 (0.54-1.37)
Johnson et al,[69] 2010	23	53	12	56	2.81 (1.22-6.50)
Langford et al,[65] 2013	84	167	77	172	1.25 (0.81-1.91)
Nurmikko et al,[76] 2007	16	63	9	62	2.00 (0.81-4.96)
Portenoy et al,[67] 2012	22	90	24	91	0.90 (0.46-1.76)
Selvarajah et al,[70] 2010	8	15	9	14	0.63 (0.14-2.82)
Serpell et al,[88] 2014	34	123	19	117	1.97 (1.05-3.70)
Subtotal $I^2 = 44.5\%$, ($P = .0.94$)	241	660	209	660	1.32 (0.94-1.86)
Overall $I^2 = 47.6\%$, ($P = .0.64$)	254	685	215	685	1.41 (0.99-2.00)



- 8 RCTs examining chronic pain with outcome of 30% reduction in pain
- Variety of pain etiologies
- Variety of cannabinoids
- Cannabinoid group 40% higher odds of reduction in pain

Cannabis & Pain: 5 Meta-analyses

Author	Year	# of Studies	Pain	Results: Cannabinoid vs. control
Iskedjian	2007	7	MS neuropathic pain	↓ 0.8 on 11-point pain scale
Martin-Sanchez	2009	7/18*	Multiple etiologies	↓ 0.6 on 11-point pain intensity scale
Whiting	2015	8/28*	Multiple etiologies	OR=1.4 of 30% reduction of pain
Andreae	2015	5	Neuropathic pain	OR=3.2 of 30% reduction of pain
Aviram	2017	24/43*	Multiple etiologies	Hedge's g = -0.35 (reduction in standard mean differences)

*Subgroup of studies included in meta-analyses
Study follow-up ranged from hours to several weeks

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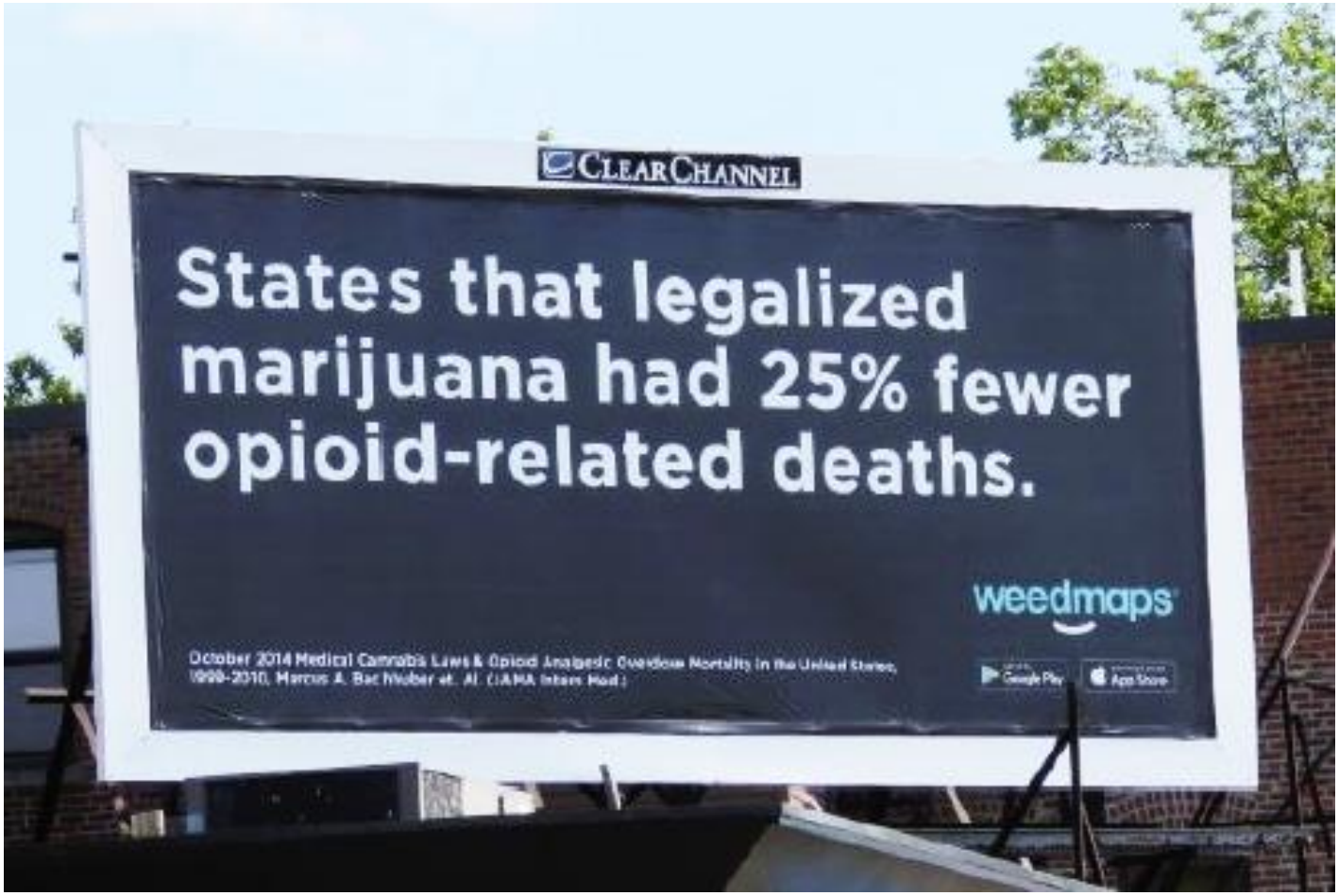
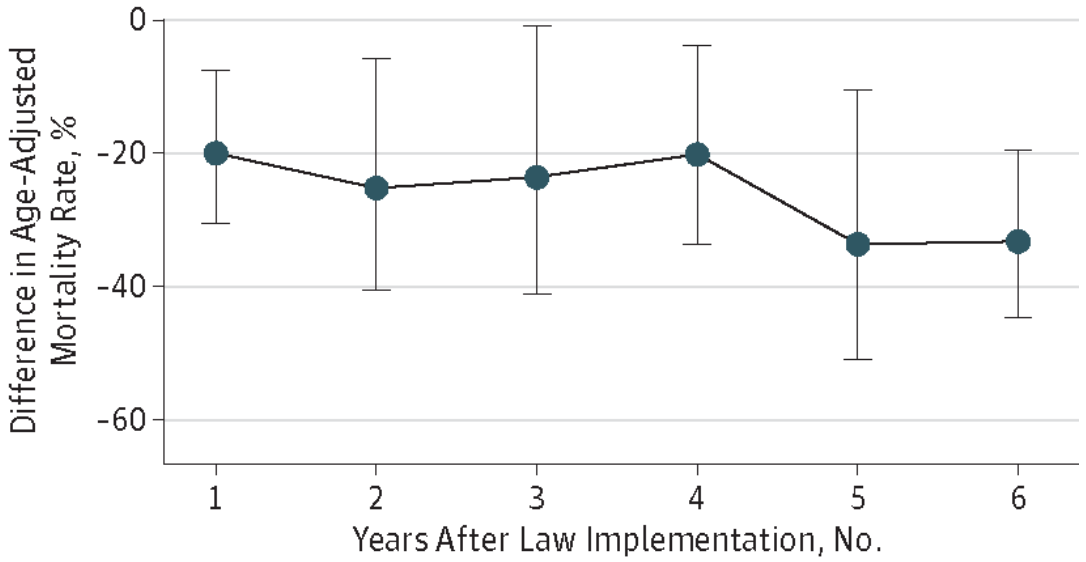
Cannabis & Opioid Overdose Deaths



Medical Cannabis Laws & Opioid Overdose Deaths

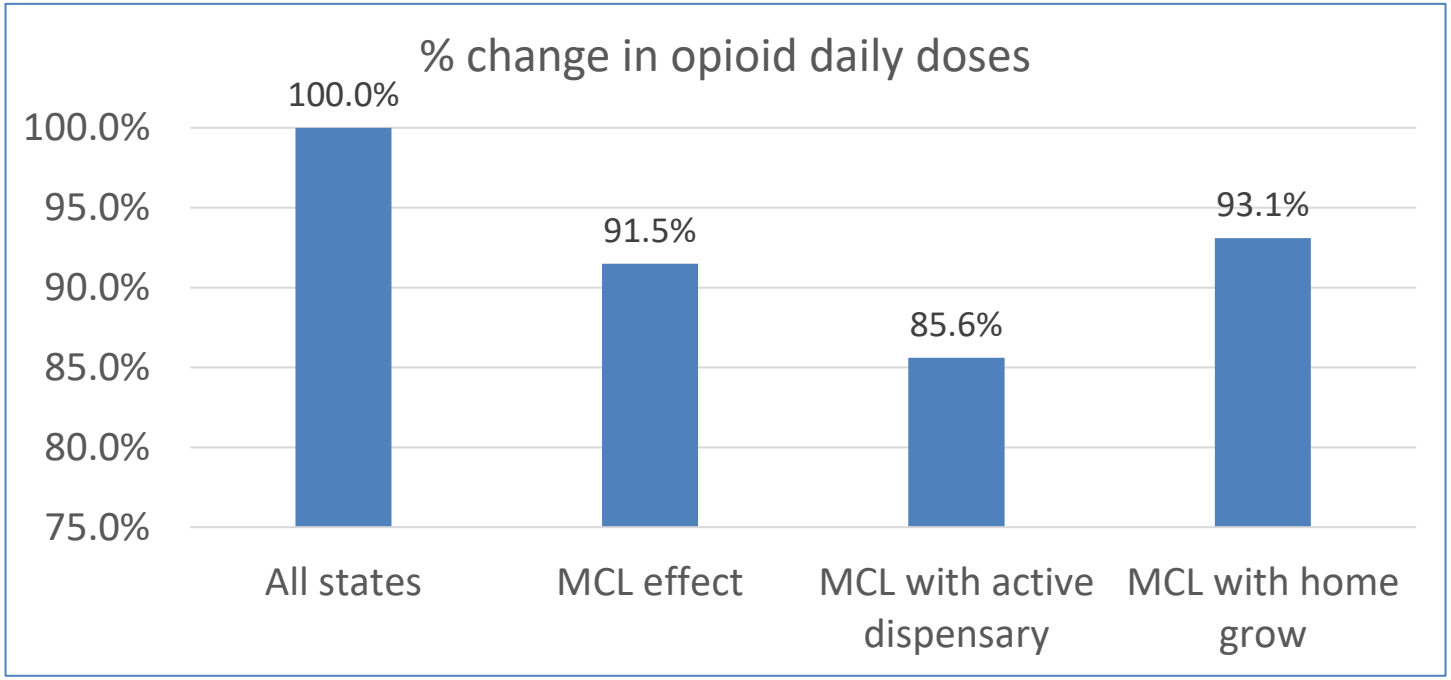
- Compared opioid overdose death rates in states with vs. without medical cannabis laws from 1999-2010
- States with laws had 25% ↓ in opioid overdose death rate
- Findings stronger with time after law implemented
- Findings replicated in 2018, strongest in states with active dispensaries



Bachhuber M, et al. JAMA Int Med, 2014; Powell D, et al. J Health Econ, 2018

Medical Cannabis Laws & Opioid Prescribing

- Compared prescribed opioid daily doses in Medicare Part D in states with vs. without medical cannabis laws (MCL), 2010-2015
- Significant reduction in prescribed opioid daily doses in states with MCL and active dispensaries or home grow
- Similar findings in patients with Medicaid



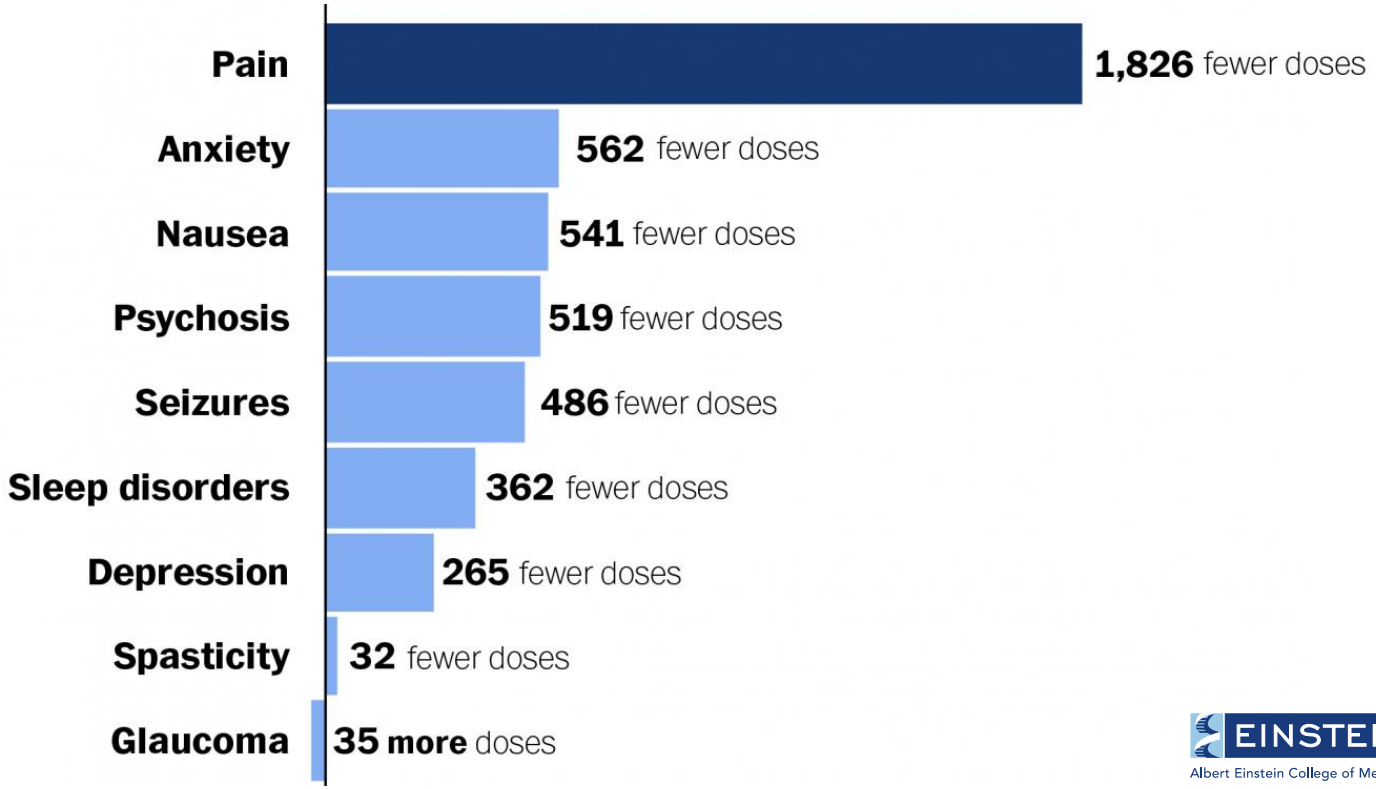
Bradford et al, JAMA Int Med. 2018; Wen & Hockenberry, JAMA Int Med. 2018

Medical Cannabis Laws & Opioid and Other Prescribing

PRESCRIPTION DRUGS

By Ashley C. Bradford and W. David Bradford

Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D



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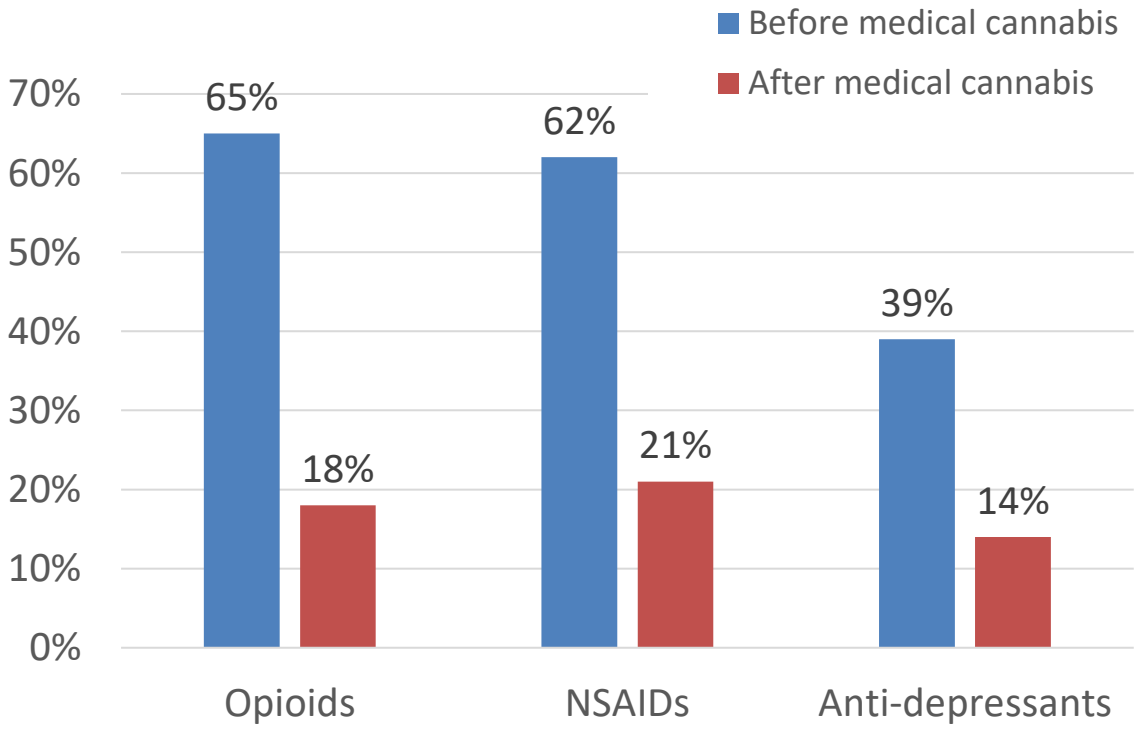
Medical Cannabis & Opioid Use

- Examine if medical cannabis use for pain changes opioid use (2013-2015)
- 185 patients with chronic pain at medical cannabis dispensary in Michigan
- Self-reported survey about medical cannabis use and medication use



Boehnke et al, Journal of Pain, 2016

Cannabis & Opioid Use

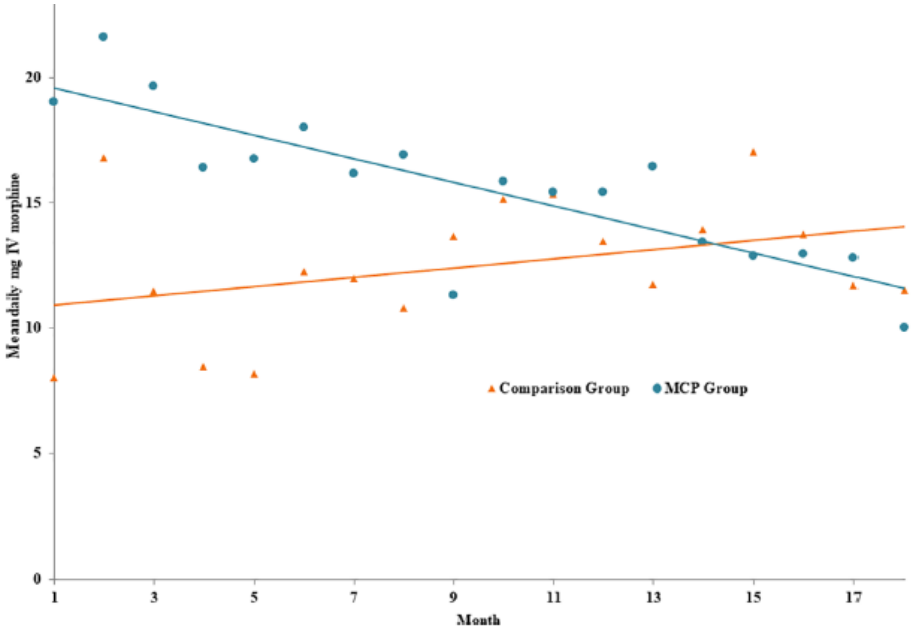
- Examine characteristics associated with prescription opioid use in HIV+ people with chronic pain in NYC
- N=459 patients, 47% with prescription opioid use
- Self-reported survey data

Characteristics	aOR of prescription opioid use (95% CI)
Age	1.01 (0.98-1.03)
100% Adherence to ARVs	1.00 (1.00-1.01)
Alcohol use	0.79 (0.53-1.20)
Marijuana use	**0.57 (0.38-0.87)**
Heroin use	0.68 (0.40-1.16)

Sohler N, et al. Subst Use Misuse, 2017

Medical Cannabis & Opioid Use

- Compare prescription opioid use in patients enrolled (vs not) in medical cannabis program in NM
- Sample:
  - patients from rehab clinic
  - Back or neck pain
  - 2 opioid prescriptions in prior 3 months
  - <200 MME/day
- Outcomes
  - cessation of opioids
  - reduction in daily MME
- N=37 in medical cannabis program
- N=29 with no medical cannabis use



Vigial, et al. PLOS One, 2017

Does Medical Cannabis Use Increase Opioid Use?

- Simulations from 2015 NSDUH data to examine association between medical cannabis use and medical/non-medical prescription drug use

- Medical cannabis use (vs. non-use) with:
  - RR=1.7 prescription pain relievers
  - RR=2.7 non-medical prescription pain relievers
- Similar findings for sedatives, stimulants, tranquilizers

- Conclusions conflict with several prior studies

Caputi & Humphreys, J Addict Med, 2018

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Medical Cannabis & Opioid Use

Does Medical Cannabis Use Increase or Decrease the Use of Opioid Analgesics and Other Prescription Drugs?

Marcus A. Bachhuber, MD, MSHP, Julia H. Arnsten, MD, MPH
Chinazo O. Cunningham, MD, MS, and Nancy Sohler, PhD, MPH

- It's complicated
- No published studies can determine causality
- Comparison group
  - Severe chronic pain vs. general population
- Need more rigorous studies

Bachhuber, et al. J Addict Med, 2018.

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Cannabis & Opioid Use Disorder

- What data exist to support/refute cannabis as treatment for OUD?

Cannabis & Opioid Use Disorder

- States' policies on OUD
  - Nearly all states have pain as qualifying condition
  - Only 3 of 33 states have OUD as qualifying condition
- Issues regarding cannabis as OUD treatment
  - Little/no data
  - We have good treatment for OUD
  - Problem
    - Need to get people the treatment that exists and works
    - Do need to search for another medication

Cannabis & Other Conditions

- States have several qualifying conditions for medical cannabis, yet data to support policies are minimal.
- What conditions other than pain/opioids needs to be examined?

Montefiore's Medical Marijuana Program

- Established in April 2017
- 16 physicians certified >400 patients
- 4 clinics throughout the Bronx
- Integrated within primary care
- Medicaid accepted

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Montefiore's Medical Marijuana Program

Characteristics of first 280 patients	N (%)
Age (mean years)	50
Female	163 (58)
Hispanic	116 (41)
Publicly insured	228 (81)
Clinical characteristic	
Chronic pain as qualifying condition	263 (94)
Current illicit marijuana	149 (53)
Taking opioid analgesics	115 (41)
HIV-infected	56 (20)
Medical cannabis use	
Ever purchased medical cannabis	**136 (49)**
Purchased medical cannabis >1 time	**28 (21)**

Montefiore's Cannabis Research

THE MEMO STUDY

- **ME**dical **M**arijuana & **O**pioids Study
- Does medical cannabis reduce opioid use in adults with chronic pain?
- Longitudinal cohort study:
  - 250 adults with chronic pain, opioid use, newly certified for medical cannabis in NY
  - 18-month follow-up
    - Quarterly visits
    - Web-based surveys every 2 weeks
  - Data: surveys, medical records, urine, functional tests, blood
- Status:
  - 40 participants enrolled (started Nov 2018)

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Summary

- Basic understanding of cannabis
- NY Medical Marijuana Program
- Cannabis and Opioids
  - Reduction in pain
  - Reduction in opioid overdose deaths
  - Reduction in opioid prescribing
  - Reduction in opioid use – some studies with conflicting findings
- Local clinical and research focused on cannabis
- The relationship between cannabis and opioids remains an important question – Need more rigorous studies.

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