Dr Justin Sinclair

AMCREC Lead Coordinator; Research Fellow

Medicinal Cannabis Expert and Pharmacognosist

Dr Graham Gulbransen

Cannabis Consultant

GP

Addiction Specialist

Associate Professor David Caldicott

Emergency Physician

ED, Calvary Hospital

Clinical Lead, Australian Drug Observatory

Dr Ben Jansen

Director of Cannabis Doctors Australia

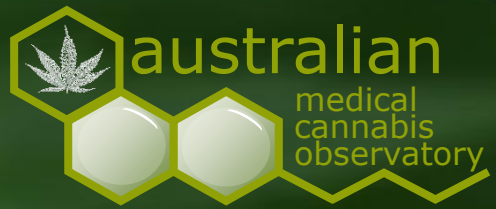
Saturday, August 10, 2019 (Room 4)

16:30 - 17:30 WS #135: Prescribing Medicinal Cannabis

17:35 - 18:30 WS #145: Prescribing Medicinal Cannabis (Repeated)

Medical Cannabis- Why Should GPs Care?

Associate Professor David Caldicott
B.Sc (Hons), MBBS(Lond.), FRCEM, Dip.Med.Tox

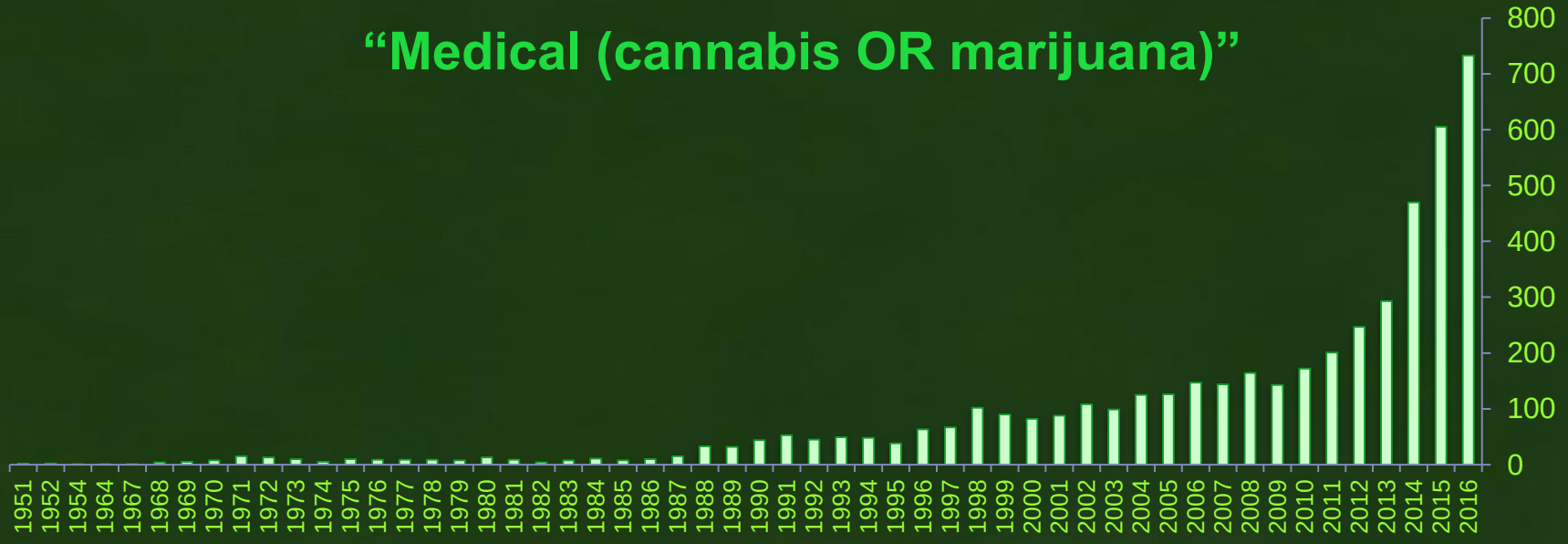


What do GPs need / want to know?

- Will it hurt my patients?

- Will it help my patients?

Cannabinoid Publications



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Need to acknowledge…

There is already an awful lot already known about using cannabis for medical purpose

(…just not by doctors.)

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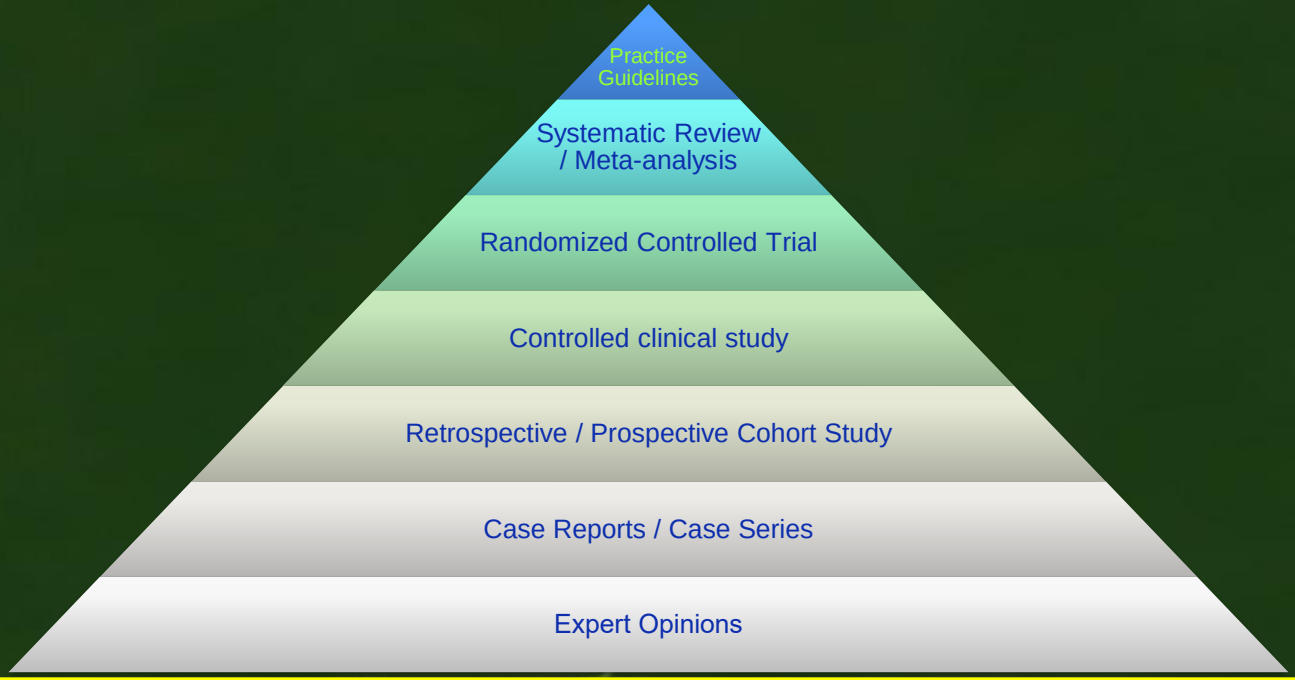
‘Where’s the evidence…?’



The Historical Human Experience

This is not an academic ‘Terra nullius’

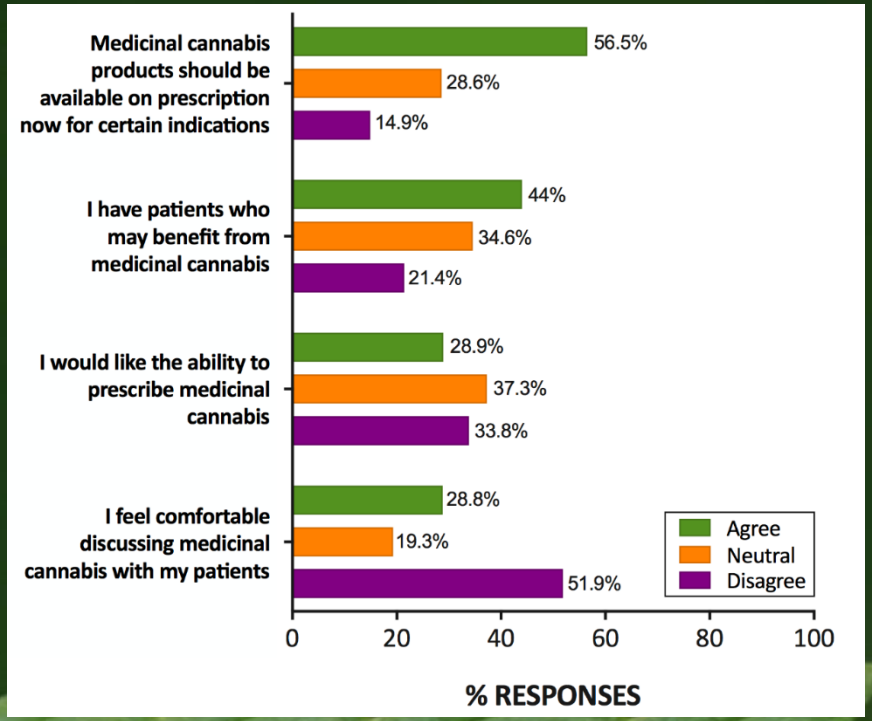
John Boyd Macdonald

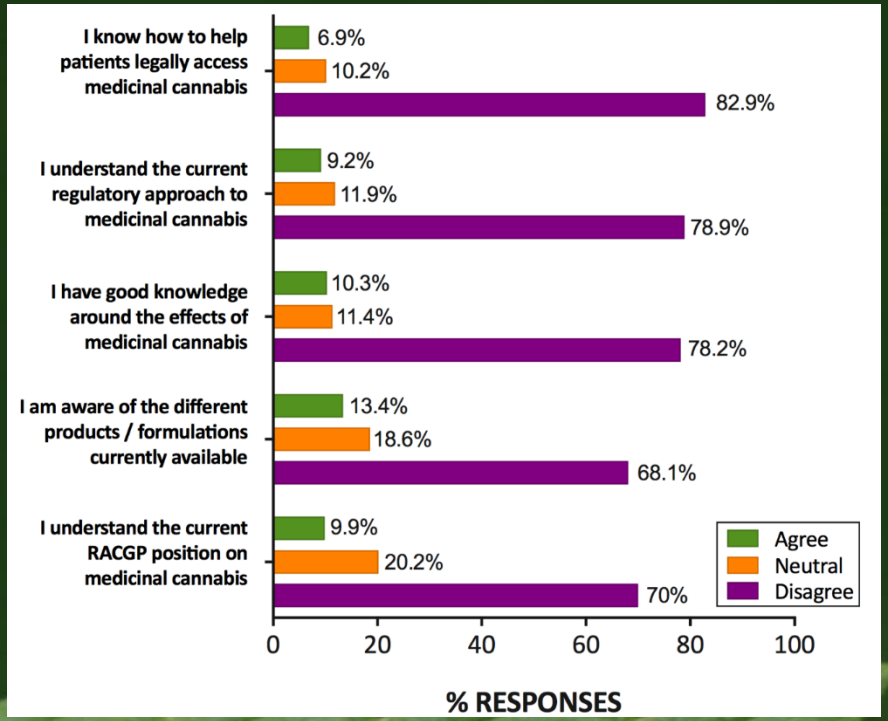
BMJ Open

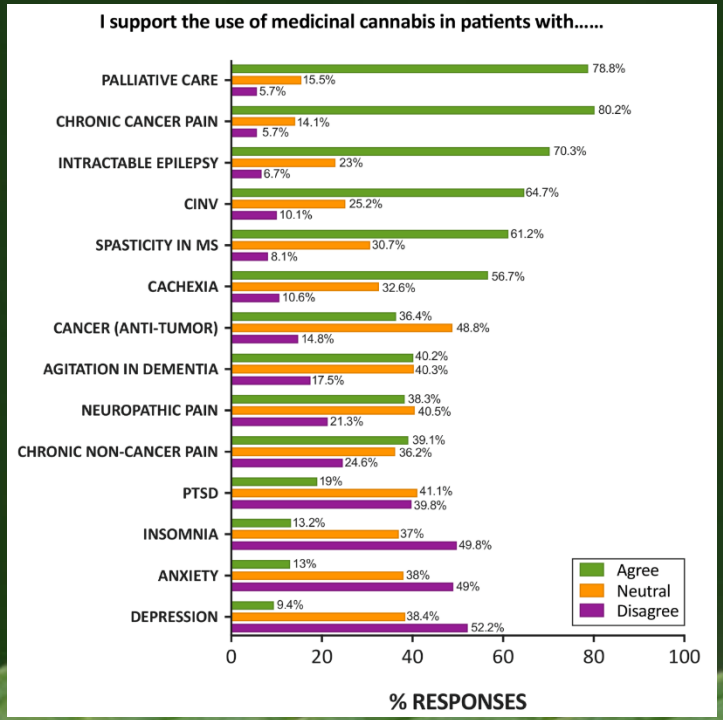
Knowledge and attitudes of Australian general practitioners towards medicinal cannabis: a cross-sectional survey

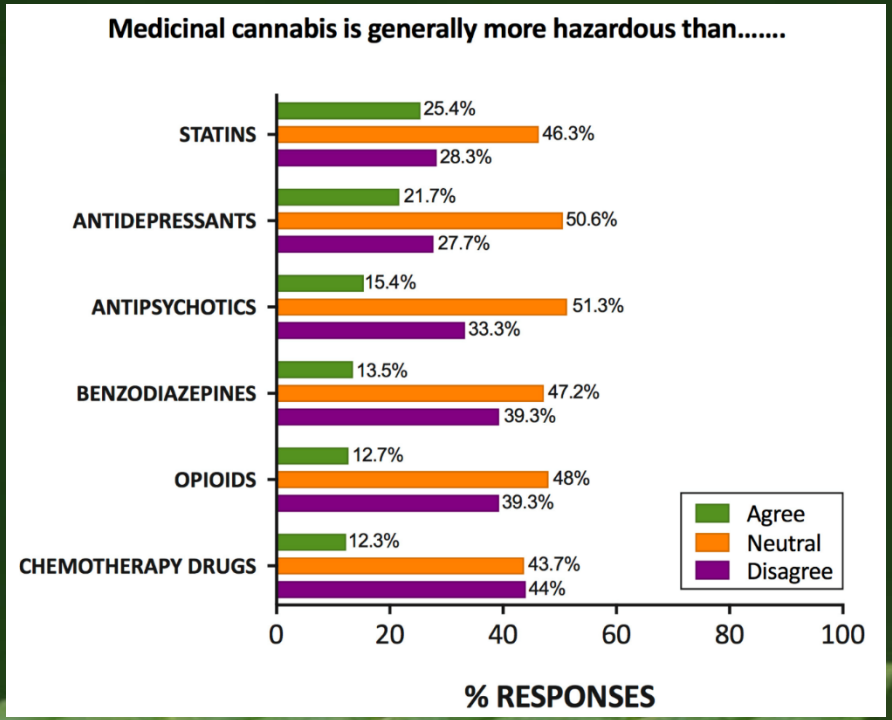
Emily A Karanges,[1,2] Anastasia Suraev,[1,2] Natalie Elias,[1,2] Ramesh Manocha,[3] Iain S McGregor[1,2]

Karanges EA, *et al*. *BMJ Open* 2018;**8**:e022101. doi:10.1136/bmjopen-2018-022101

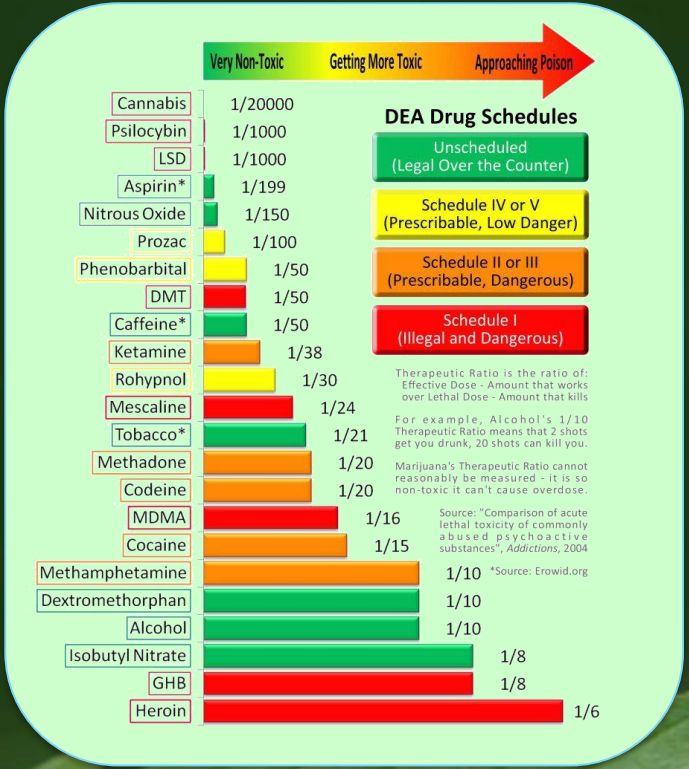

Medicinal cannabis products should be available on prescription now for certain indications
56.5%
28.6%
14.9%
I have patients who may benefit from medicinal cannabis
44%
34.6%
21.4%
I would like the ability to prescribe medicinal cannabis
28.9%
37.3%
33.8%
I feel comfortable discussing medicinal cannabis with my patients
28.8%
19.3%
51.9%
Agree
Neutral
Disagree
0
20
40
60
80
100
% RESPONSES

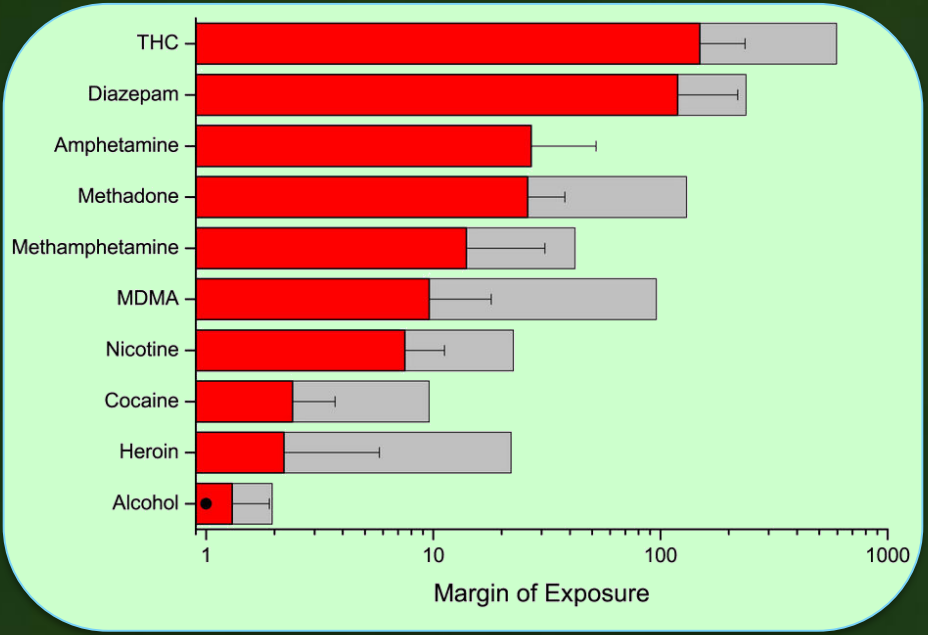

I know how to help patients legally access medicinal cannabis
6.9%
10.2%
82.9%
I understand the current regulatory approach to medicinal cannabis
9.2%
11.9%
78.9%
I have good knowledge around the effects of medicinal cannabis
10.3%
11.4%
78.2%
I am aware of the different products / formulations currently available
13.4%
18.6%
68.1%
I understand the current RACGP position on medicinal cannabis
9.9%
20.2%
70%
Agree
Neutral
Disagree
0
20
40
60
80
100
% RESPONSES


I support the use of medicinal cannabis in patients with.....
PALLIATIVE CARE
78.8%
15.5%
5.7%
CHRONIC CANCER PAIN
80.2%
14.1%
5.7%
INTRACTABLE EPILEPSY
70.3%
23%
6.7%
CINV
64.7%
25.2%
10.1%
SPASTICITY IN MS
61.2%
30.7%
8.1%
CACHEXIA
56.7%
32.6%
10.6%
CANCER (ANTI-TUMOR)
36.4%
48.8%
14.8%
AGITATION IN DEMENTIA
40.2%
40.3%
17.5%
NEUROPATHIC PAIN
38.3%
40.5%
21.3%
CHRONIC NON-CANCER PAIN
39.1%
36.2%
24.6%
PTSD
19%
41.1%
39.8%
INSOMNIA
13.2%
37%
49.8%
ANXIETY
13%
38%
49%
DEPRESSION
9.4%
38.4%
52.2%
Agree
Neutral
Disagree
0
20
40
60
80
100
% RESPONSES


Medicinal cannabis is generally more hazardous than.....
STATINS
25.4%
46.3%
28.3%
ANTIDEPRESSANTS
21.7%
50.6%
27.7%
ANTIPSYCHOTICS
15.4%
51.3%
33.3%
BENZODIAZEPINES
13.5%
47.2%
39.3%
OPIOIDS
12.7%
48%
39.3%
CHEMOTHERAPY DRUGS
12.3%
43.7%
44%
Agree
Neutral
Disagree
0
20
40
60
80
100
% RESPONSES

Will it hurt my patients?





Lachenmeier DW, Rehm J. Comparative risk assessment of alcohol, tobacco, cannabis and other illicit drugs using the margin of exposure approach. Sci Rep. 2015 Jan 30;5:8126.

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Recreational vs. Medicinal Cannabis Use

- ALL of the concerns expressed about medicinal cannabis are derived from experience of recreational use
- Hardly representative
- Deliberately focused upon by opponents

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Recreational vs. Therapeutic vs. Medicinal Cannabis Use

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Recreational vs. Therapeutic vs. Medicinal Cannabis Use

	Known Product	Known Dose	Known Patients	Medical supervision
Recreational	No	No	No	No
Therapeutic	Maybe	Maybe	Yes?	Generally Not
Medicinal	Yes	Yes	Yes	Yes

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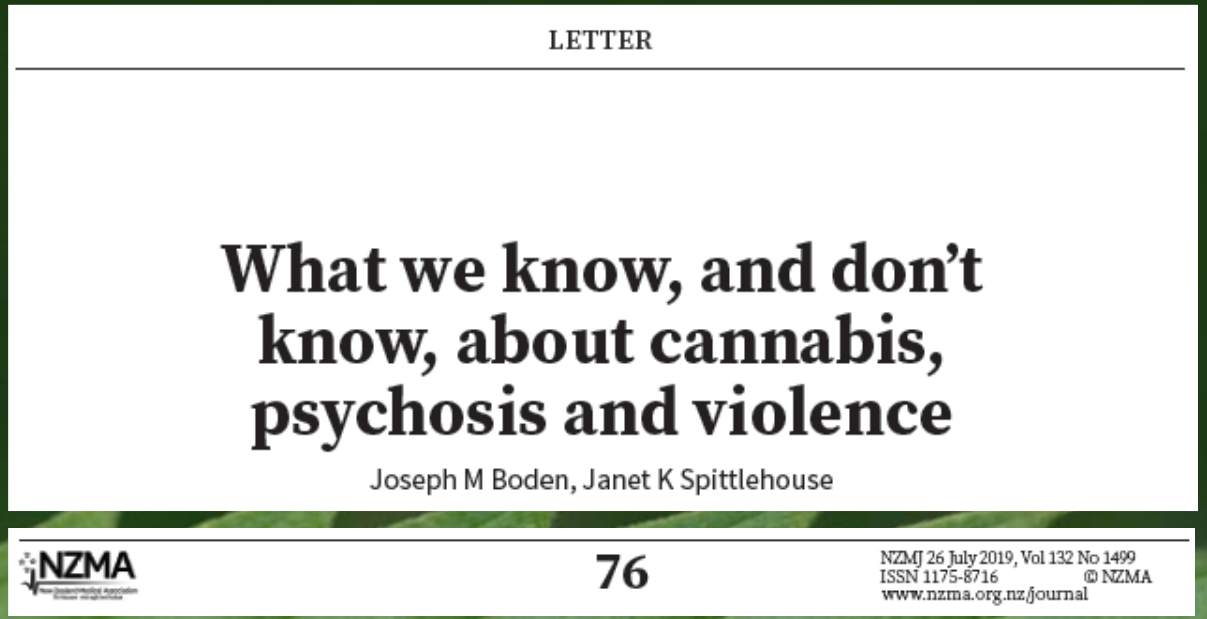
Will it hurt my patients?

- What about all of “the psychoses”?
  - Association with symptoms of psychosis

Will it hurt my patients?

- What about all of “the psychoses”?



LETTER

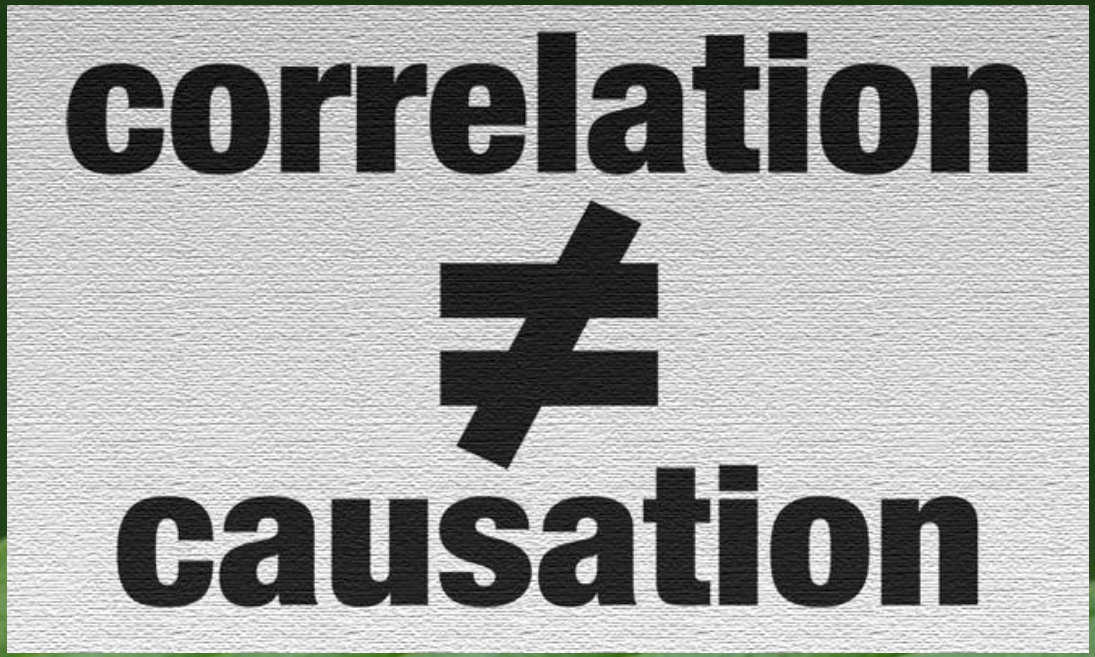
What we know, and don’t know, about cannabis, psychosis and violence

Joseph M Boden, Janet K Spittlehouse

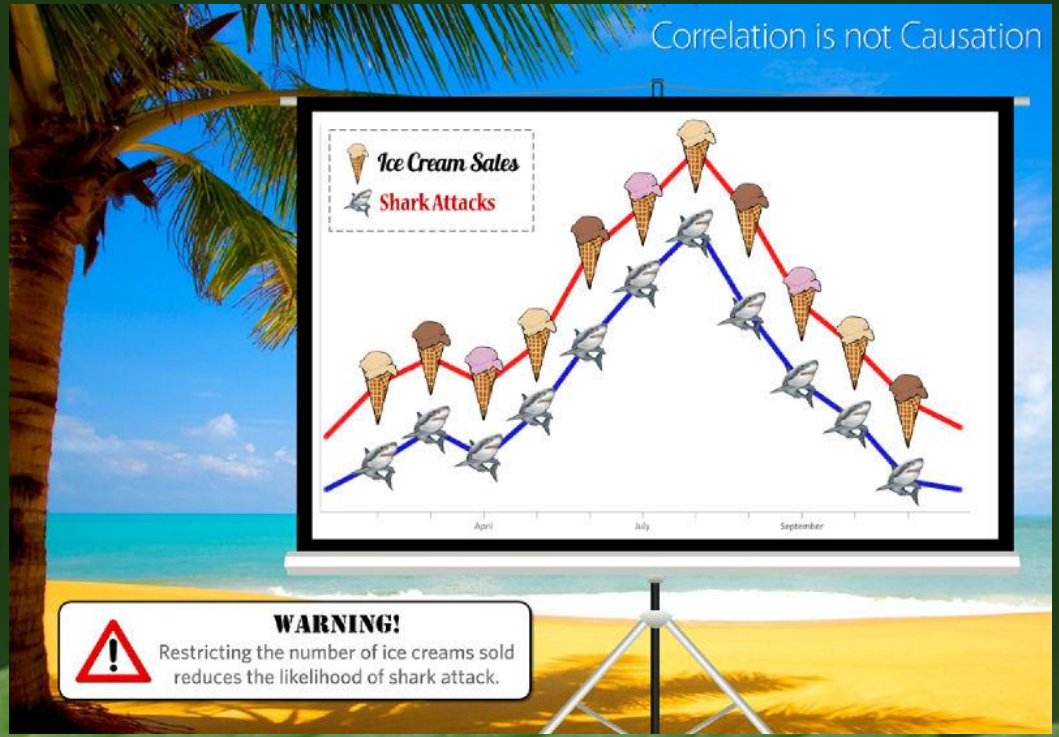
NZMJ 26 July 2019, Vol 132 No 1499
ISSN 1175-8716
www.nzma.org.nz/journal

Cannabis and Psychosis

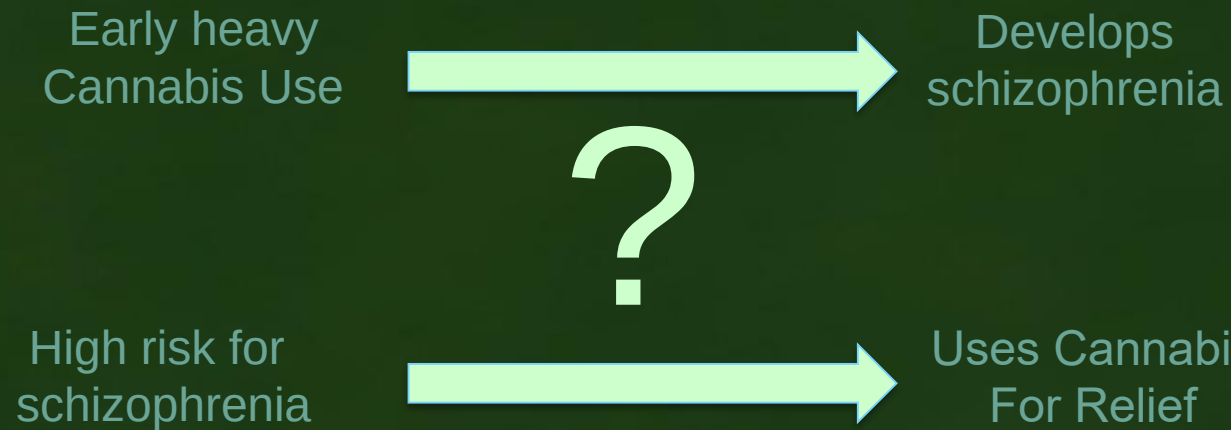
- Sorry, were you assuming ‘causation’?



Cannabis and Psychosis



Cannabis and Psychosis



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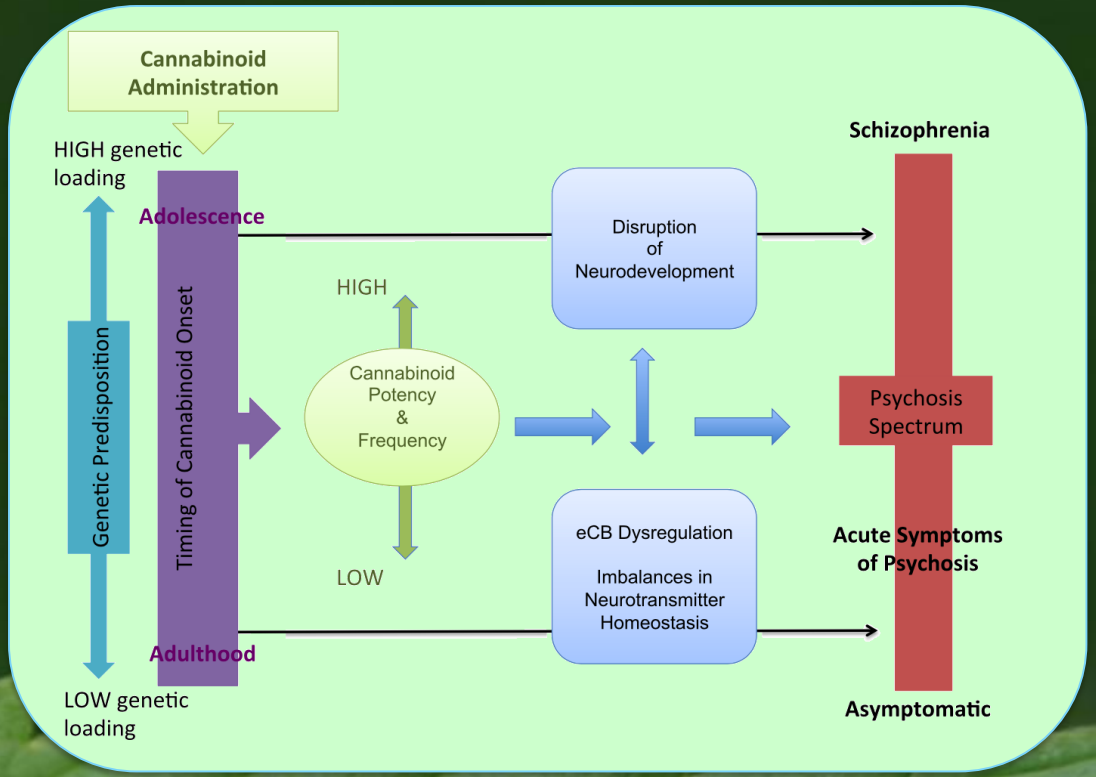
Complex association



What is Cannabis Actually Used For?

- Conditions in Clinical Practice Rank order - Hergenrather 2015
  - Pain (acute pain, chronic, inflammatory, neuropathic)
  - Mental disorders (all kinds)
  - Cancers
  - Gastrointestinal disorders
  - Insomnia
  - Migraine / headaches
  - Harm reduction, alternative to opioids…
  - Spasticity
  - Autoimmune disorders
  - Neurodegenerative disorders
  - Glaucoma
  - Skin diseases
  - Epilepsy, Autism, Tourettes, ADD, Dystonia, Dementia •
  - AIDS and other infections

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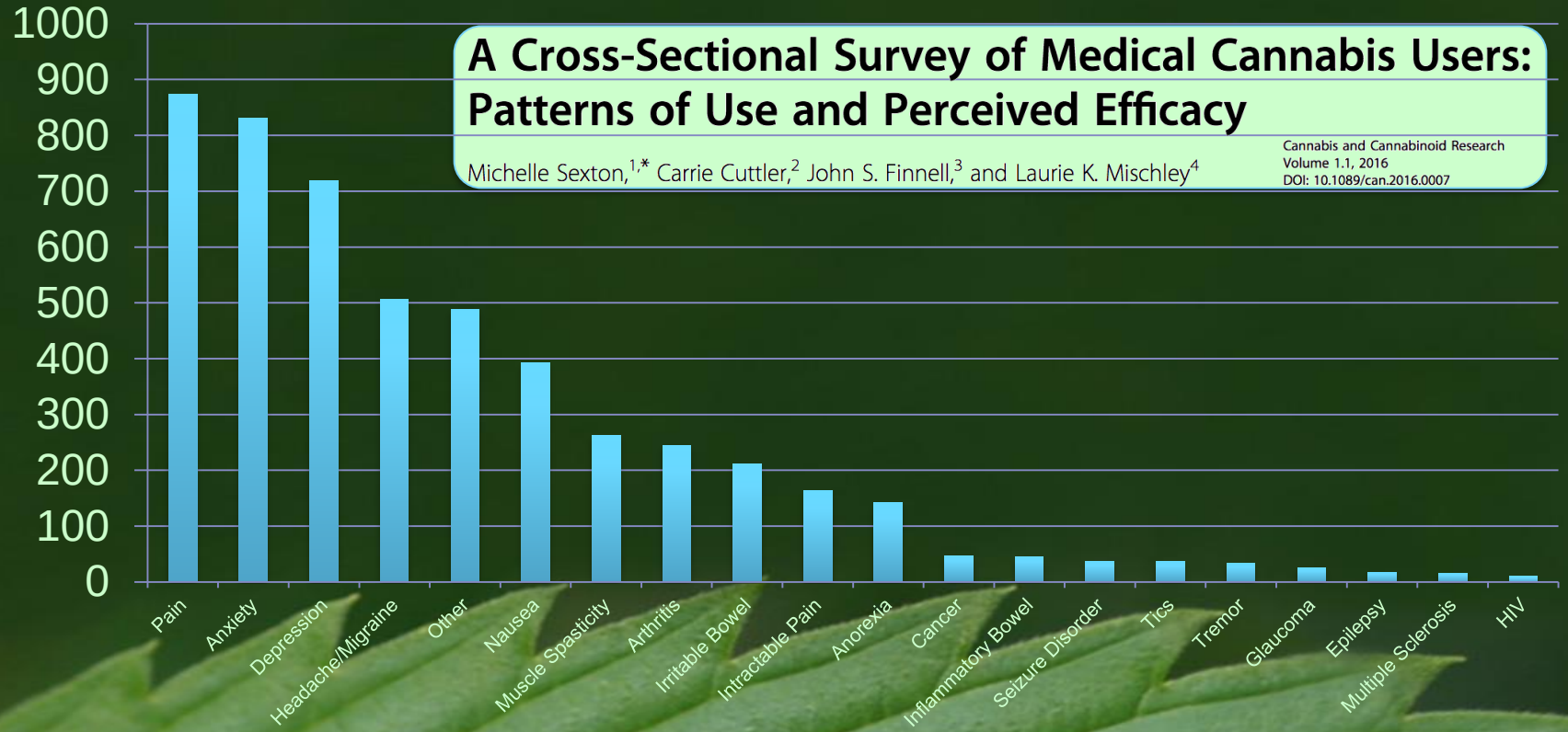
Pain

Pain is THE issue for Users of Medicinal Cannabis..

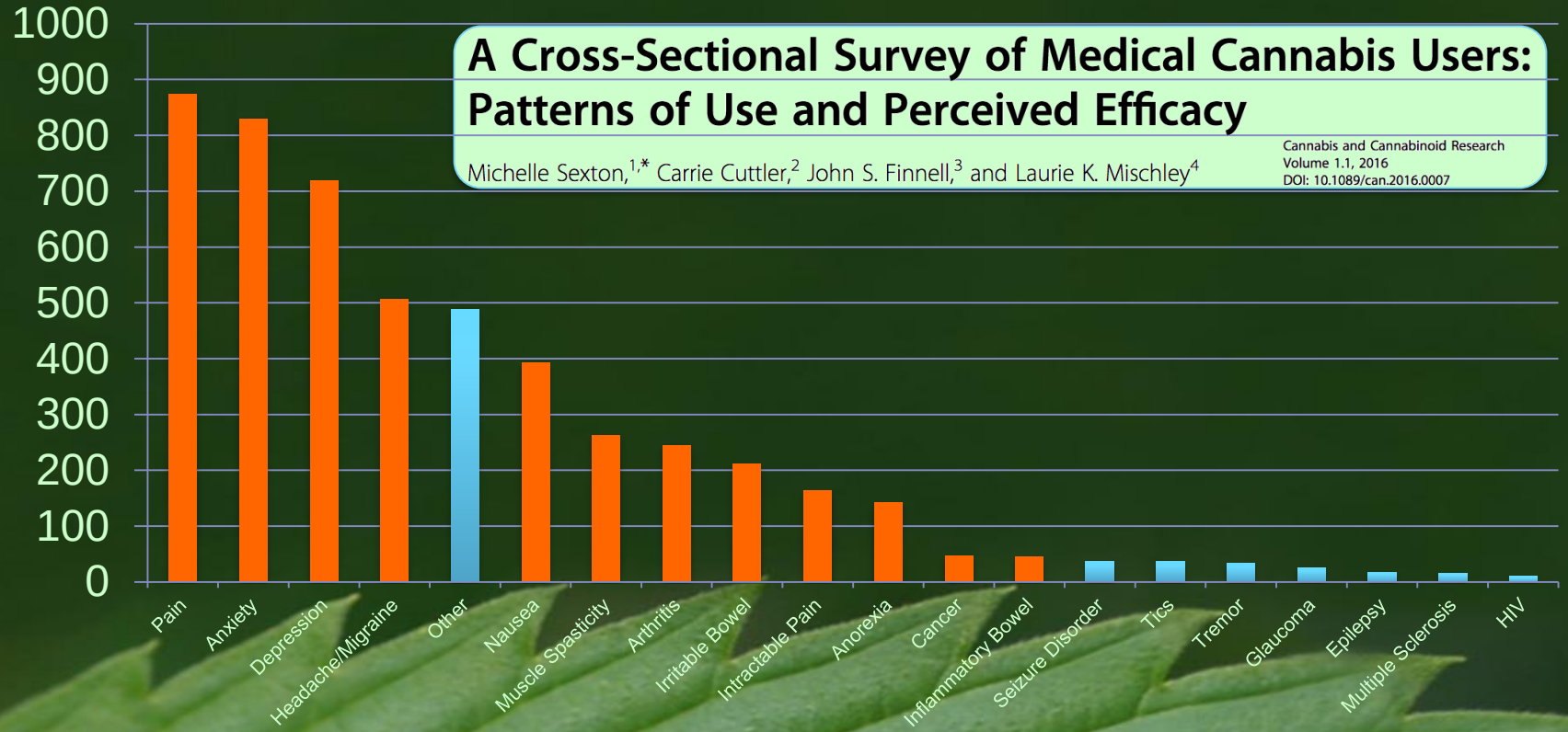


A Cross-Sectional Survey of Medical Cannabis Users: Patterns of Use and Perceived Efficacy

Michelle Sexton,[1,*] Carrie Cuttler,[2] John S. Finnell,[3] and Laurie K. Mischley[4]

Cannabis and Cannabinoid Research
Volume 1.1, 2016
DOI: 10.1089/can.2016.0007

Pain is THE issue for Users of Medicinal Cannabis..



A Cross-Sectional Survey of Medical Cannabis Users: Patterns of Use and Perceived Efficacy

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Cannabis and Cannabinoid Research
Volume 1.1, 2016
DOI: 10.1089/can.2016.0007

Patients are turning to Cannabis-based medication

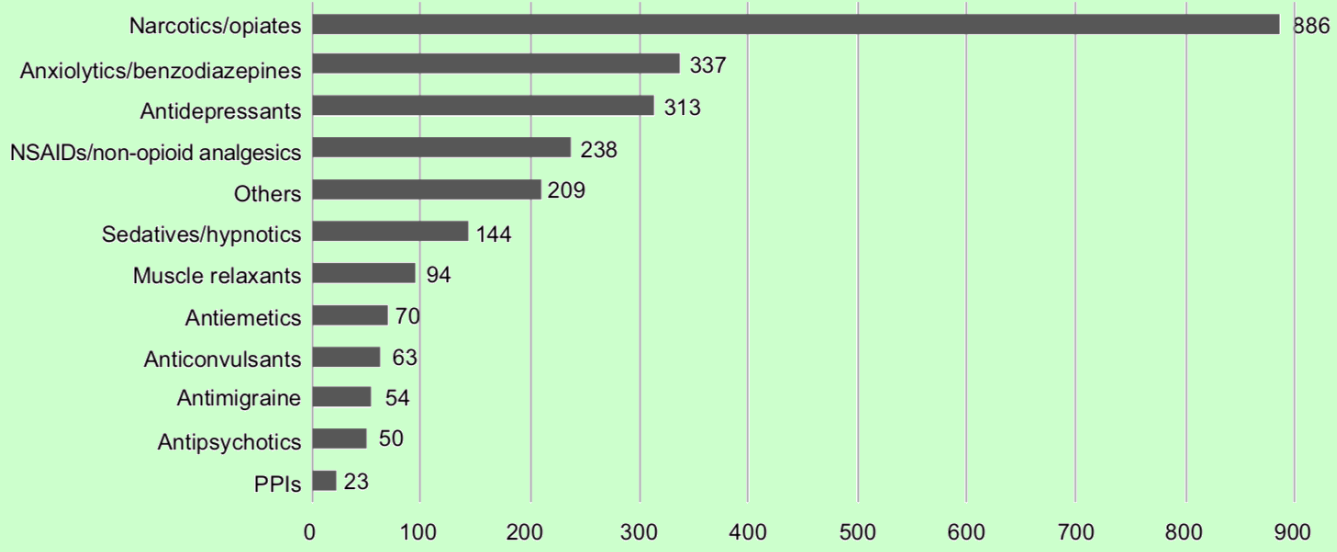

Figure 1 Number of reported prescription drug substitutions, by drug category, during 2016 (n=2,473).
Abbreviations: PPI, proton pump inhibitor; NSAIDs, nonsteroidal anti-inflammatory drugs.

Corroon, J.M., LK; Sexton,M, *Cannabis as a Substitute for Prescription Drugs- a Cross Sectional Study.* Journal of Pain Research, 2017. **10**: p. 989-998.

“So where’s the evidence?”

- Trials have been terribly difficult (legality)
- What are we measuring?

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

Gabrielle Campbell, Wayne D Hall, Amy Peacock, Nicholas Lintzeris, Raimondo Bruno, Briony Larance, Suzanne Nielsen, Milton Cohen, Gary Chan, Richard P Mattick, Fiona Blyth, Marian Shanahan, Timothy Dobbins, Michael Farrell, Louisa Degenhardt

NATIONAL SCIENCE

In major study, cannabis shows no benefit for chronic pain

By Liam Mannix

July 3, 2018 — 7.59am

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(Yeah, not so much…)

- Study of data that preceded introduction medical cannabis in Australia
- Nil analytical elements

"Cannabis use was common in our cohort, patients reported that it reduced their pain, and the proportion interested in using cannabis for pain doubled over the 4-year follow-up."

"…participants who used cannabis reported that the mean effectiveness of cannabis on pain was 7 out of a possible score of 10…"

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American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY
PUBLISHED BY
ELSEVIER

The Journal of Pain, Vol 20, No 7 (July), 2019: pp 830–841
Available online at www.jpain.org and www.sciencedirect.com

Pills to Pot: Observational Analyses of Cannabis Substitution Among Medical Cannabis Users With Chronic Pain

Kevin F. Boehnke,* J. Ryan Scott,* Evangelos Litinas,† Suzanne Sisley,‡ David A. Williams,* and Daniel J. Clauw*

*Anesthesiology Department, University of Michigan Medical School, Ann Arbor, Michigan., †Om of Medicine, Ann Arbor, Michigan., ‡Scottsdale Research Institute, Phoenix, Arizona.

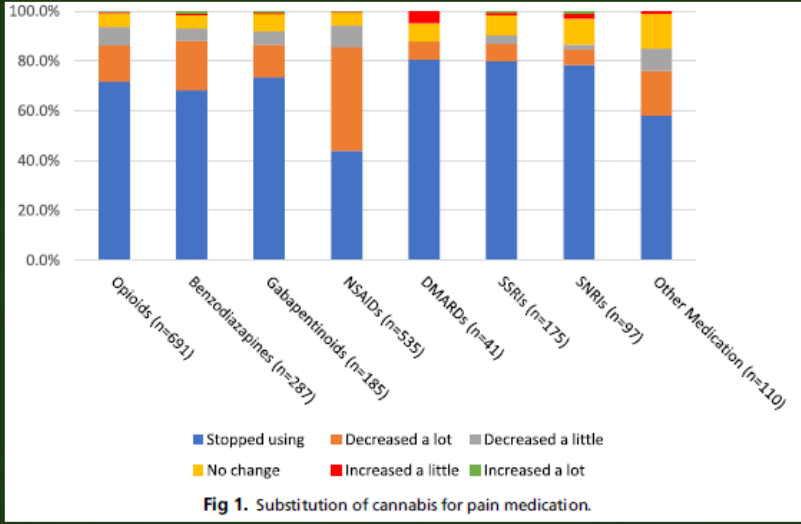

Fig 1. Substitution of cannabis for pain medication.

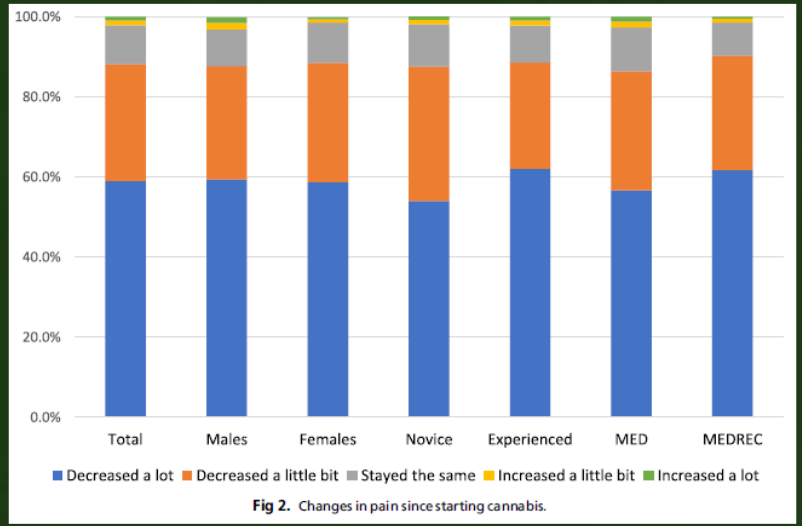

Fig 2. Changes in pain since starting cannabis.

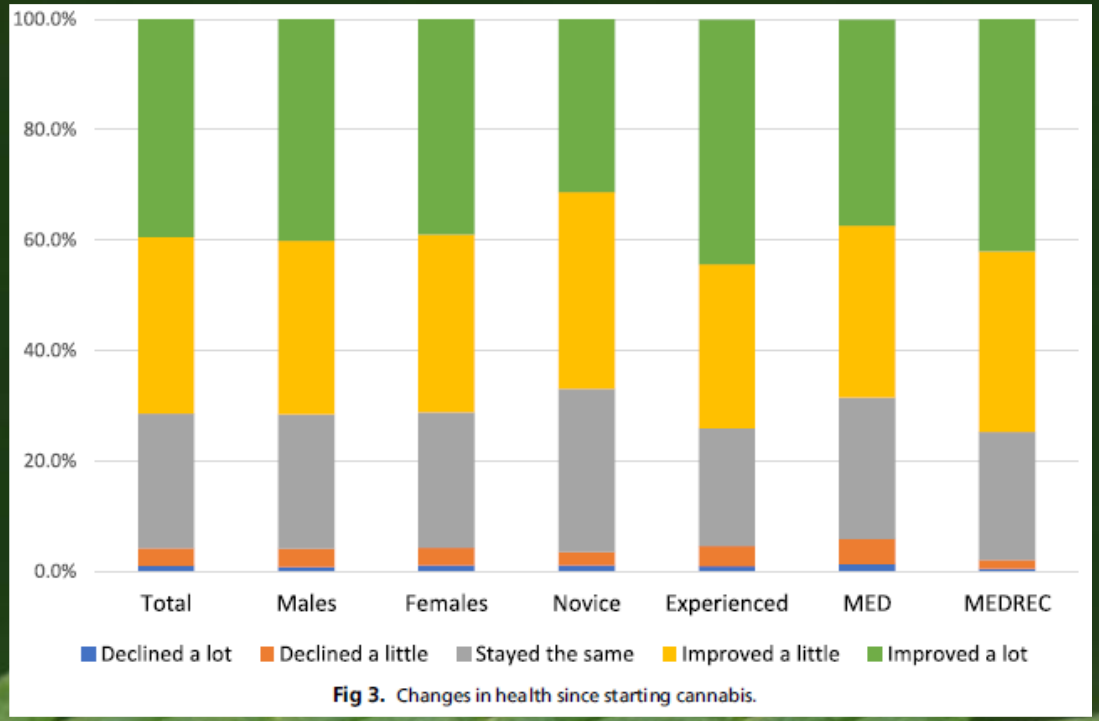

Fig 3. Changes in health since starting cannabis.

“So where’s the evidence?”

- Trials have been terribly difficult (legality)
- What are we measuring?
- Material very variable

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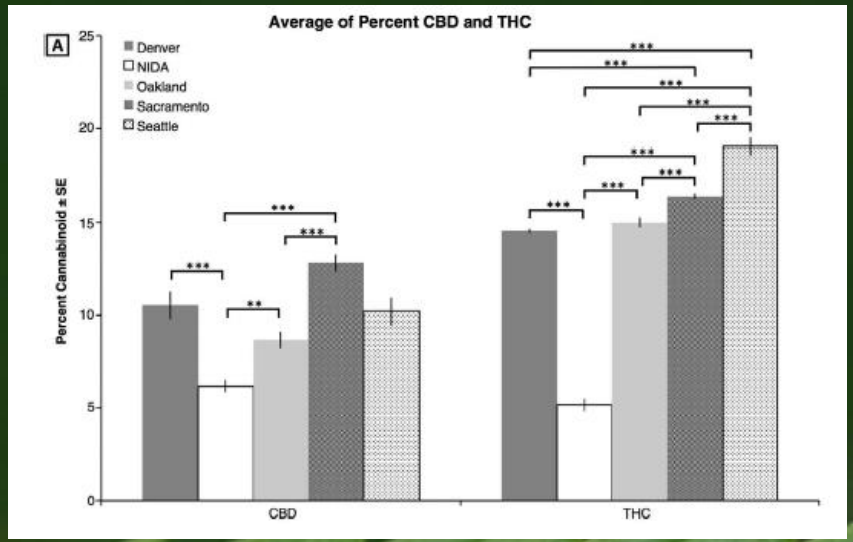
Compromised External Validity: Federally Produced *Cannabis* Does Not Reflect Legal Markets

Daniela Vergara[1], L. Cinnamon Bidwell[2], Reggie Gaudino[3], Anthony Torres[3], Gary Du[3], Travis C. Ruthenburg[3,†], Kymron deCesare[3], Donald P. Land[3], Kent E. Hutchison[4] & Nolan C. Kane[1]



What people are using for relief…

≠

What people have used for trials.

Veraga, D.e.a., *Compromised External Validity: Federaly Produced Cannabis Does Not Reflect Legal Markets.* Nature Scientific Reports, 2017. **7**: p. 1-8.

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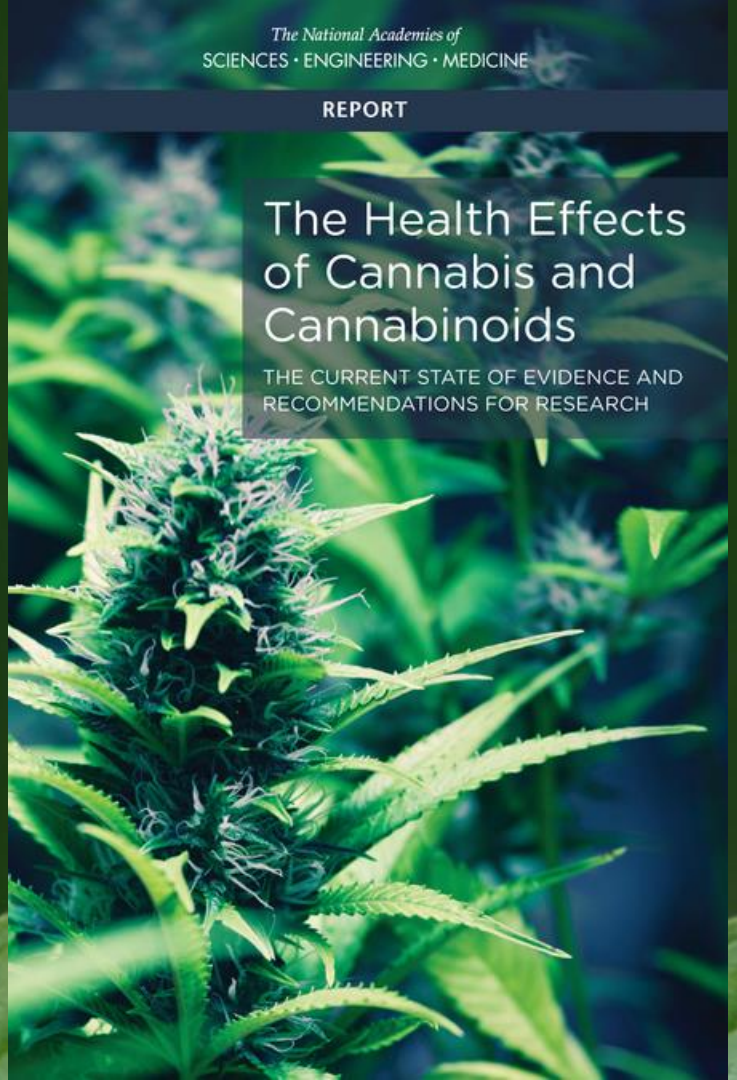

Bunch of Nobodies…

- **MARIE C. McCORMICK** (*Chair*), Sumner and Esther Feldberg Professor, Harvard T.H. Chan School of Public Health, Harvard University, Boston, MA
- **DONALD I. ABRAMS,** Professor of Clinical Medicine, University of California, San Francisco, and Chief of Hematology–Oncology Division, Zuckerberg San Francisco General Hospital, San Francisco
- **MARGARITA ALEGRÍA,** Professor, Departments of Medicine and Psychiatry, Harvard Medical School, and Chief, Disparities Research Unit, Massachusetts General Hospital, Boston
- **WILLIAM CHECKLEY,** Associate Professor of Medicine, International Health, and Biostatistics, Division of Pulmonary and Critical Care, Johns Hopkins University, Baltimore, MD
- **R. LORRAINE COLLINS,** Associate Dean for Research, School of Public Health and Health Professions and Professor, Department of Community Health and Health Behavior, State University of New York at Buffalo–South Campus
- **ZIVA D. COOPER,** Associate Professor of Clinical Neurobiology, Department of Psychiatry, Columbia University Medical Center, New York
- **ADRE J. dU PLESSIS,** Director, Fetal Medicine Institute; Division Chief of Fetal and Transitional Medicine; and Director, Fetal Brain Program, Children's National Health System, Washington, DC
- **SARAH FELDSTEIN EWING,** Professor, Department of Child and Adolescent Psychiatry, Oregon Health & Science University, Portland
- **SEAN HENNESSY,** Professor of Epidemiology and Professor of Systems Pharmacology and Translational Therapeutics, University of Pennsylvania Perelman School of Medicine, Philadelphia
- **KENT HUTCHISON,** Professor, Department of Psychology and Neuroscience and Director of Clinical Training, University of Colorado Boulder
- **NORBERT E. KAMINSKI,** Professor, Pharmacology and Toxicology, and Director, Institute for Integrative Toxicology, Michigan State University, East Lansing
- **SACHIN PATEL,** Associate Professor of Psychiatry and Behavioral Sciences, and of Molecular Physiology and Biophysics, and Director of the Division of Addiction Psychiatry, Vanderbilt University Medical Center, Nashville, TN
- **DANIELE PIOMELLI,** Professor, Anatomy and Neurobiology, School of Medicine and Louise Turner Arnold Chair in Neurosciences, Department of Anatomy and Neurobiology, University of California, Irvine
- **STEPHEN SIDNEY,** Director of Research Clinics, Division of Research, Kaiser Permanente Northern California, Oakland
- **ROBERT B. WALLACE,** Irene Ensminger Stecher Professor of Epidemiology and Internal Medicine, Department of Epidemiology, University of Iowa Colleges of Public Health and Medicine, Iowa City
- **JOHN WILEY WILLIAMS,** Professor of Medicine, Duke University Medical Center, Durham, NC

There is conclusive or substantial evidence that cannabis or cannabinoids are effective:

- For the treatment of chronic pain in adults (cannabis) (4-1)
- As antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) (4-3)
- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)

conclusive or substantial evidence

“So where’s the evidence?”

- Trials have been terribly difficult (legality)
- Material very variable
- Emerging surrogate evidence

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“So where’s the evidence?”

- Trials have been terribly difficult (legality)
- Material very variable
- Emerging surrogate evidence
  - Demographic data
  - Prescribing data

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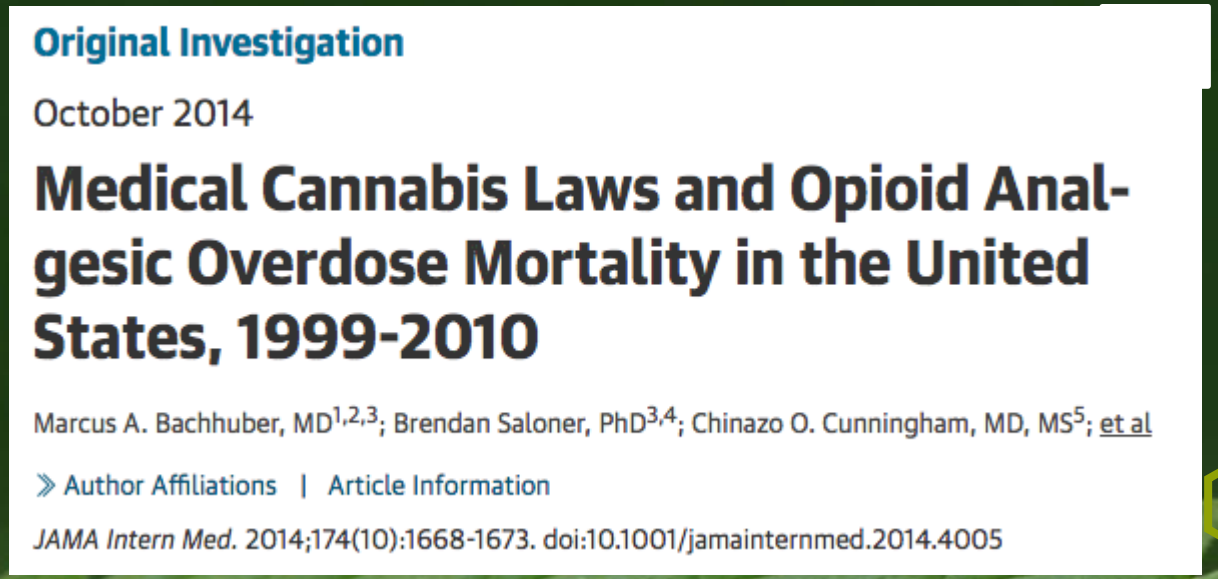
Where's the evidence?

- Epidemiology



Original Investigation

October 2014

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Marcus A. Bachhuber, MD[1,2,3]; Brendan Saloner, PhD[3,4]; Chinazo O. Cunningham, MD, MS[5]; et al

» Author Affiliations | Article Information

JAMA Intern Med. 2014;174(10):1668-1673. doi:10.1001/jamainternmed.2014.4005

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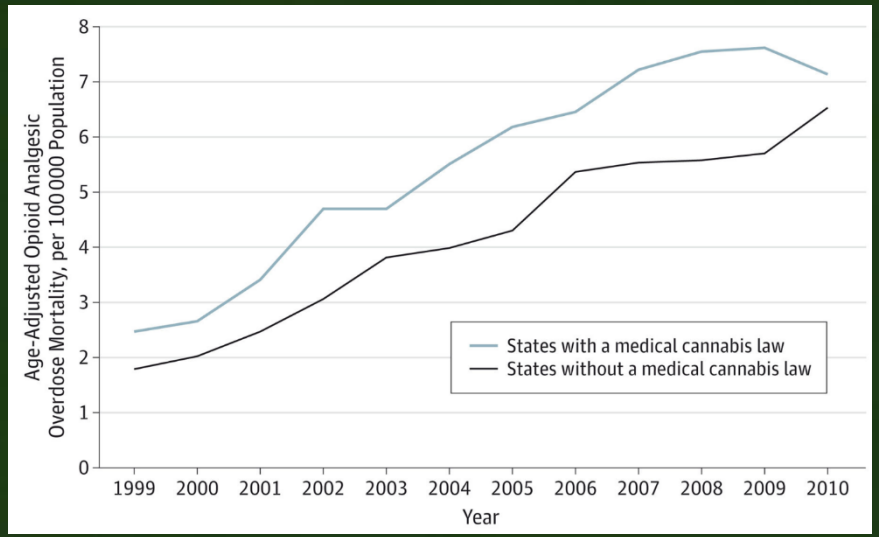
Public Health Implications



Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999–2010. JAMA internal medicine. 2014;174(10):1668-1673.

States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate without medical cannabis laws.

(95% CI, −37.5% to −9.5%; P = .003) compared with states

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Where's the evidence?

- Why?
  - patients choosing to initiate medical cannabis over opioid analgesics
  - patients already on opioid analgesics finding decreased requirements when using medical cannabis
  - medical cannabis laws lead to decreases in polypharmacy—particularly with benzodiazepines—in people taking opioid analgesics, overdose risk would be decreased

Public Health Implications

ommended. If the relationship between medical cannabis laws and opioid analgesic overdose mortality is substantiated in further work, enactment of laws to allow for use of medical cannabis may be advocated as part of a comprehensive package of policies to reduce the population risk of opioid analgesics.

Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999–2010. J AMA internal medicine. 2014;174(10):1668-1673.

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Where's the evidence?

- Prescribing Practice

Daily doses filled per physician per year in states with and without a medical marijuana law

Condition category	Annual number of daily doses prescribed per physician in states: Without a medical marijuana law	With a medical marijuana law	Difference
Anxiety	11,220.29	10,113.77	1,106.51***
Depression	9,576.73	8,296.25	1,280.47***
Glaucoma	2,551.40	2,616.04	−64.64***
Nausea	10,067.92	9,040.22	1,027.70***
Pain	31,810.07	28,165.54	3,644.53***
Psychosis	11,421.46	10,298.60	1,122.86***
Seizures	9,398.60	8,028.74	1,369.85***
Sleep disorders	7,557.97	6,942.94	615.03***
Spasticity	2,067.82	1,645.43	422.38***

Bradford AC, Bradford WD. Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D. Health Aff (Millwood). 2016 Jul 1;35(7):1230-6.

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Where's the evidence?

- Total estimated Medicaid savings $260.8 million in 2007, to $475.8 million in 2014
- If ***all*** states had legalized medical marijuana in 2014, "The national savings for fee-for-service Medicaid would have been approximately $1.01 billion"
-
- This works out to an average per state savings of $19.825 million a year

Bradford AC, Bradford WD. Medical Marijuana Laws May Be Associated With A Decline In The Number Of Prescriptions For Medicaid Enrollees. Health Aff (Millwood). 2017 May 1;36(5):945-951.

Evidentiary issues not without precedent

- Development of Penicillin…

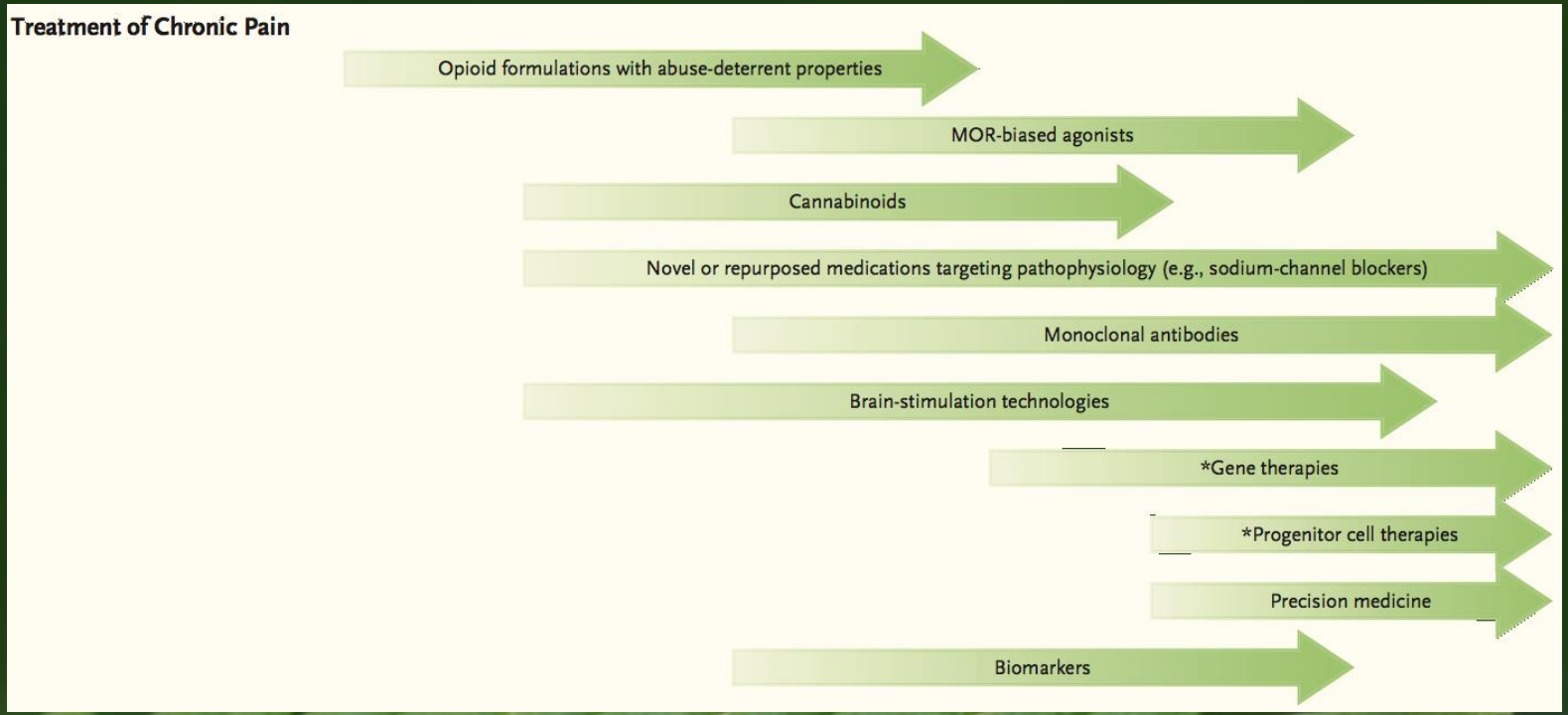
- Ongoing use of paracetamol…

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.


Treatment of Chronic Pain
Opioid formulations with abuse-deterrent properties
MOR-biased agonists
Cannabinoids
Novel or repurposed medications targeting pathophysiology (e.g., sodium-channel blockers)
Monoclonal antibodies
Brain-stimulation technologies
*Gene therapies
*Progenitor cell therapies
Precision medicine
Biomarkers

Compounds that target nonopioid pain pathways, such as the endocannabinoid system, are also being evaluated for chronic pain management. There is strong evidence of the efficacy of cannabinoids, including tetrahydrocannabinol (THC), in treating pain. Medications that target the endocannabinoid system without producing the cognitive impairment and rewarding effects of marijuana could provide a powerful new tool.

Can Medicinal Cannabis Meet 2 Criteria?

- Make your patient feel better?

- Benefits exceed the risks (by a wide margin)?

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So, what should we do?

- Israelis are producing research *in parallel* to compassionate access
- Good trials are in the pipeline…
- Important to maintain differentiation between recreational and medicinal markets

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In Summary…

- “There is no evidence”
- “It’s dangerous”
- “You can’t dose botanical products”
- “Opposition is purely scientific / medical”

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In Summary…

- There is actually quite a lot of evidence, and growing
- Far less dangerous than many alternatives
- Of course you can dose botanical products
- Opposition is mostly economic, political

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HAVE COURAGE AND BE KIND

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