



Michael G. DeGroot
CENTRE FOR MEDICINAL
CANNABIS RESEARCH

Innovations in the Science of Cannabis Conference

FEBRUARY 9-10, 2018

St. Joseph's Healthcare Hamilton | West 5th Campus | 100 West 5th Street | Hamilton, Ontario, Canada

Jason Busse, DC, PhD
Co-Director

James MacKillop, PhD
Co-Director

St. Joseph's
Healthcare  Hamilton



Peter Boris Centre
FOR ADDICTIONS RESEARCH



Michael G. DeGroot
CENTRE FOR MEDICINAL
CANNABIS RESEARCH

McMaster
University 
PSYCHIATRY AND
BEHAVIOURAL NEUROSCIENCES

Acknowledgments

- Michael G. DeGroote
- Dr. John Kelton and Sarrah Lal
- The Boris Foundation
- Drs. David Higgins & Kevin Smith
- Dr. Paul O'Byrne
- Centre staff, especially Allan Fein
- Invited speakers

Disclosures

■ Jason Busse, DC, PhD

- Research funding from CIHR and MGD IRPC
- No consultancies or ownership to commercial cannabis entities

■ James MacKillop, PhD

- Research funding from CIHR, NIH, RGCO, GREO, CSC
- No consultancies or ownership to commercial cannabis entities

■ No conference-level conflicts of interest to disclose.

- Funded by registration revenue and philanthropy

Overview

- Brief history and context
- Priorities for the Michael G. DeGroote Centre for Medicinal Cannabis Research
- *Innovations in the Science of Cannabis*

Brief Canadian Legislative History

**Geneva International
Convention on
Narcotics Control**

1925

**Marihuana for Medical
Purposes Regulations
(MMPR)**

2001

**Medical Marihuana
Access Regulations
(MMAR)**

2014

**Access to Cannabis for
Medical Purposes
Regulations (ACMPR)**

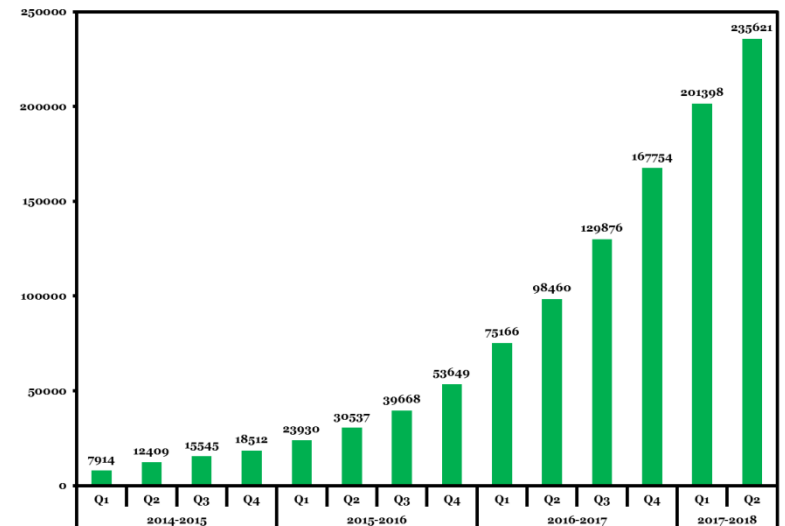
2017

**Federal
Legalization**

2018

Brief Canadian Legislative History

Registered Medical Cannabis Users, 2014-2017 (Health Canada)



Geneva International Convention on Narcotics Control

1925

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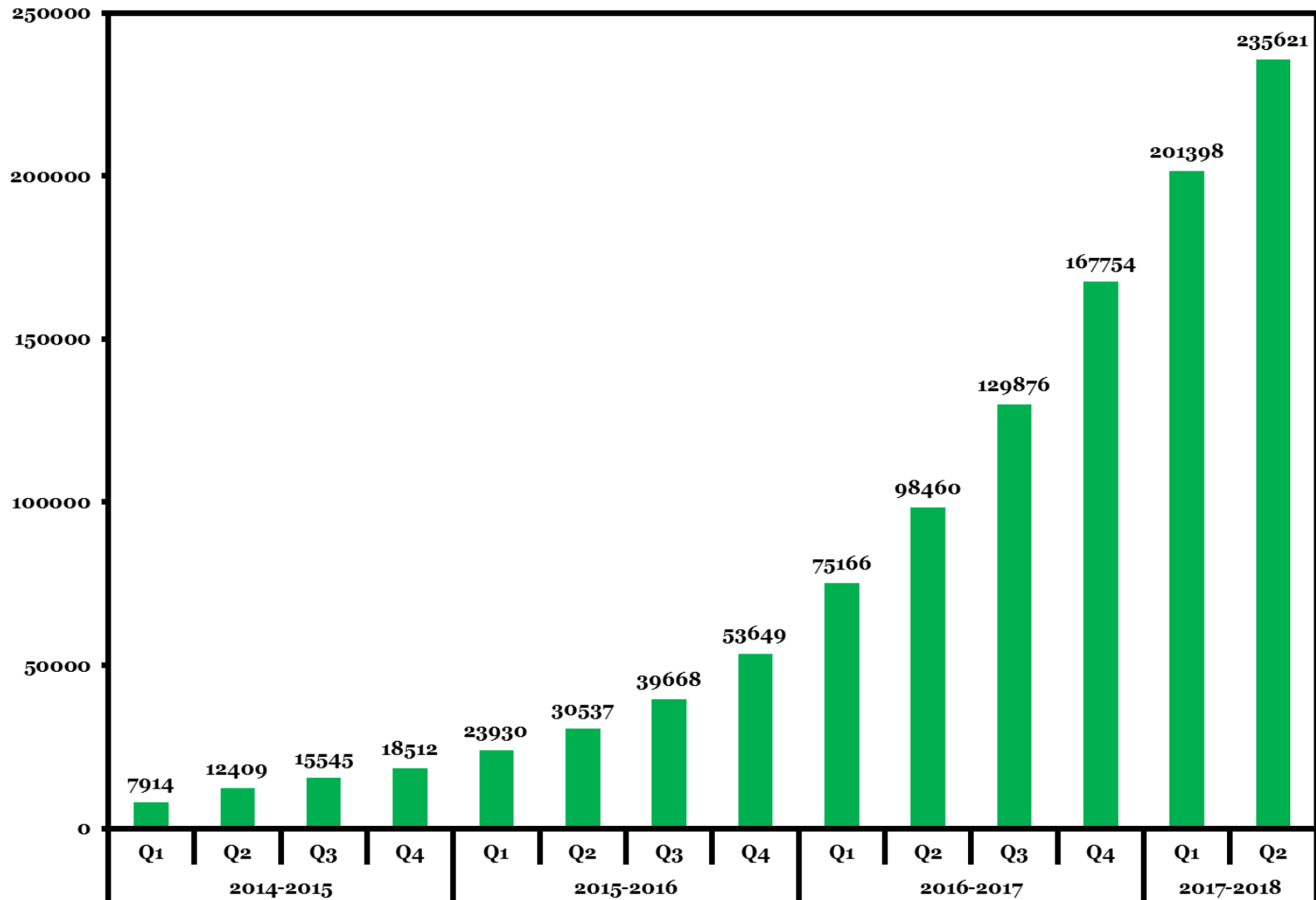
2014

Access to Cannabis for Medical Purposes Regulations (ACMPR)

2017 2018

Federal Legalization

Registered Medical Cannabis Users, 2014-2017 (Health Canada)



Smoked cannabis for chronic neuropathic pain: a randomized controlled trial

Mark A. Ware MBBS, Tongtong Wang PhD, Stan Shapiro PhD, Ann Robinson RN, Thierry Ducruet MSc, Thao Huynh MD, Ann Gamsa PhD, Gary J. Bennett PhD, Jean-Paul Collet MD PhD

Table 2: Pairwise comparisons of the effects of four potencies of smoked cannabis on average daily pain

Potency, % of THC	Potency, % of THC, mean difference (95% CI)							
	0		2.5		6.0		9.4	
0	-	-	-	-	-	-	-	-
2.5	-0.13	(-0.83 to 0.56)	-	-	-	-	-	-
6.0	-0.09	(-0.78-0.60)	0.04	(-0.64 to 0.73)	-	-	-	-
9.4	-0.71	(-1.40 to -0.02)	-0.58	(-1.27 to 0.11)	-0.63	(-1.30 to 0.06)	-	-

Note: CI = confidence interval, THC = tetrahydrocannabinol.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 25, 2017

VOL. 376 NO. 21

Trial of Cannabidiol for Drug-Resistant Seizures in the Dravet Syndrome

Orrin Devinsky, M.D., J. Helen Cross, Ph.D., F.R.C.P.C.H., Linda Laux, M.D., Eric Marsh, M.D., Ian Miller, M.D., Rima Nabbout, M.D., Ingrid E. Scheffer, M.B., B.S., Ph.D., Elizabeth A. Thiele, M.D., Ph.D., and Stephen Wright, M.D., for the Cannabidiol in Dravet Syndrome Study Group*

Table 2. Primary Efficacy End Point of Percentage Change in Convulsive-Seizure Frequency in Each Trial Group.*

Variable	Cannabidiol	Placebo	Adjusted Median Difference (95% CI) <i>percentage points</i>	P Value†
No. of convulsive seizures per mo — median (range)				
Baseline	12.4 (3.9 to 1717)	14.9 (3.7 to 718)		
Treatment period	5.9 (0.0 to 2159)	14.1 (0.9 to 709)		
Percentage change in seizure frequency — median (range)	-38.9 (-100 to 337)	-13.3 (-91.5 to 230)	-22.8 (-41.1 to -5.4)	0.01

Low Quality Evidence of Overall Efficacy

Research

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 Schmidtkofer, MSc; Marie Westwood, PhD; Jos Kleijnen, MD, PhD

IMPORTANCE Cannabis and cannabinoid drugs are widely used to treat disease or alleviate symptoms, but their efficacy for specific indications is not clear.

OBJECTIVE To conduct a systematic review of the benefits and adverse events (AEs) of cannabinoids.

DATA SOURCES Twenty-eight databases from inception to April 2015.

**Of 79 trials,
4 judged to have
low risk of bias**

**Increased risk of
short-term AEs**

**Low quality evidence
in general**

**Moderate quality
evidence for pain
and spasticity**

Known Adverse Effects

Table 2. Level of Confidence in the Evidence for Adverse Effects of Marijuana on Health and Well-Being.

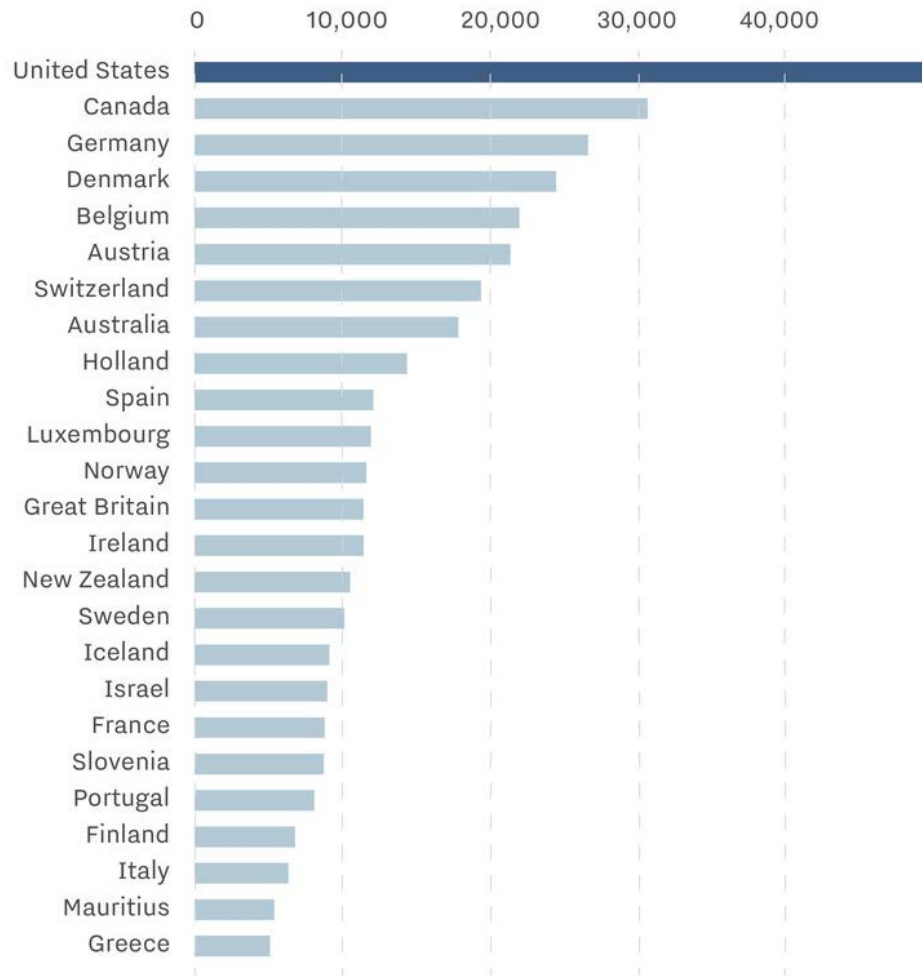
Effect	Overall Level of Confidence*
Addiction to marijuana and other substances	High
Abnormal brain development	Medium
Progression to use of other drugs	Medium
Schizophrenia	Medium
Depression or anxiety	Medium
Diminished lifetime achievement	High
Motor vehicle accidents	High
Symptoms of chronic bronchitis	High
Lung cancer	Low

Prevalence of Cannabis Use Disorder in Canada

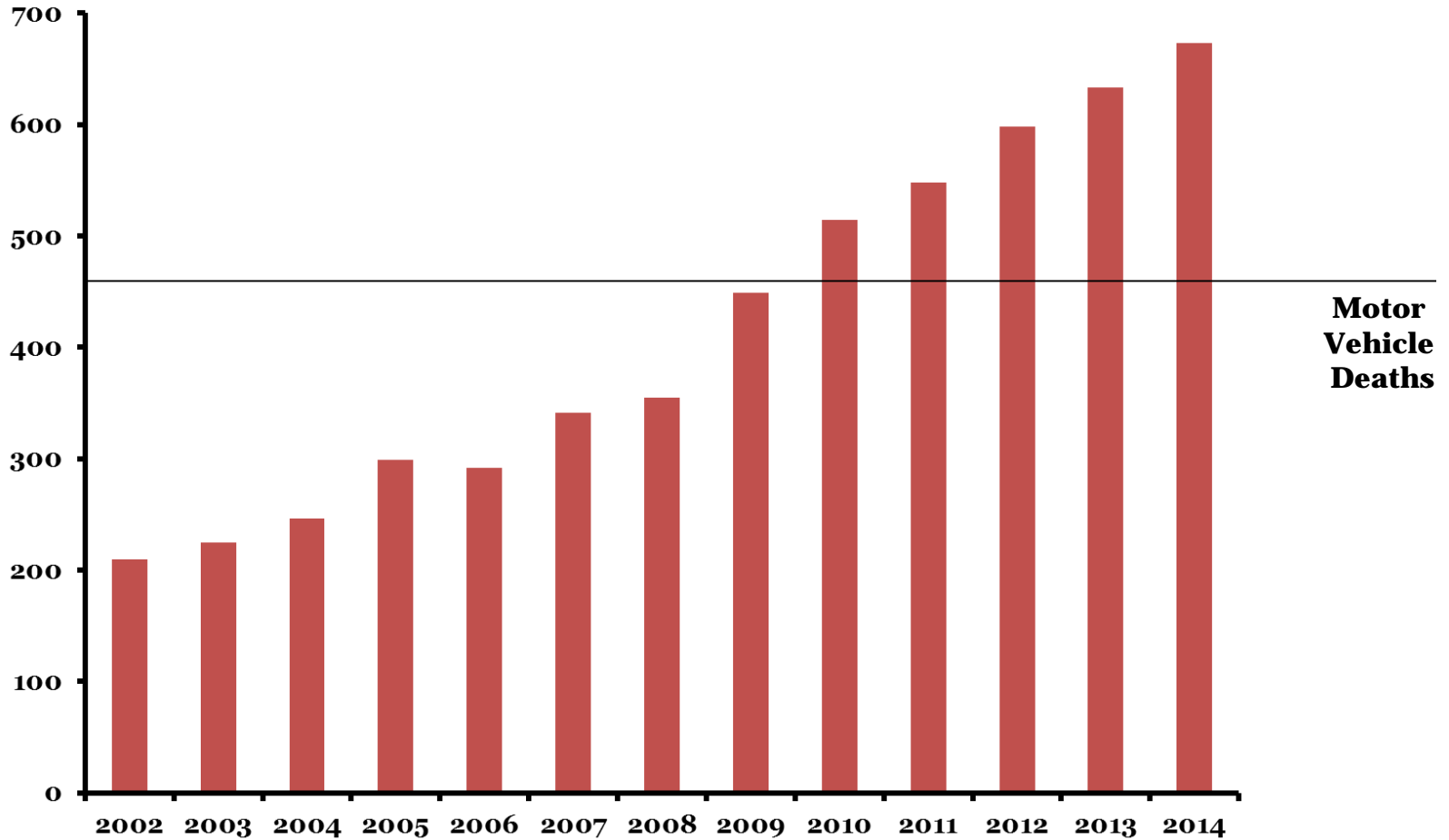
Lifetime	12-Month
6.8%	1.3%

Opioid Consumption by Country

Standard daily opioid dose for every 1 million people

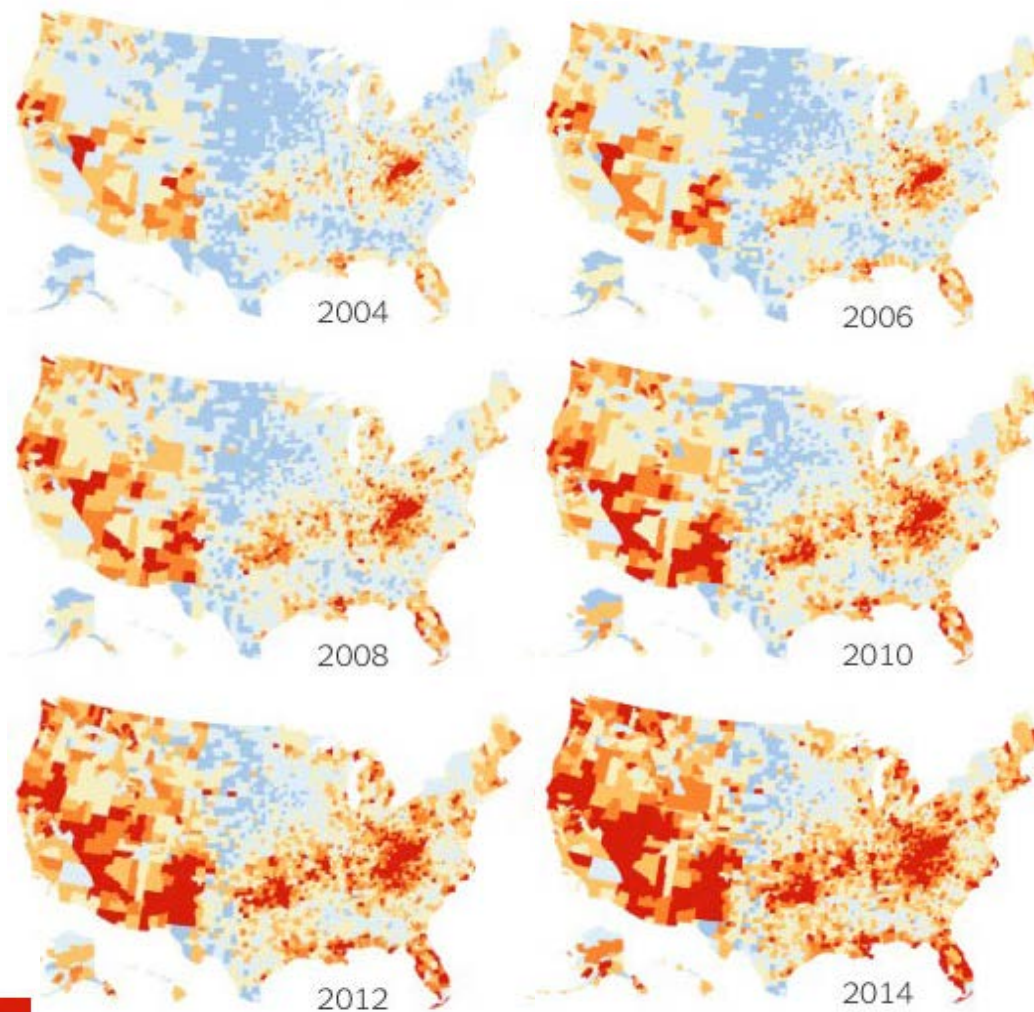


Opioid Overdose Deaths in Ontario, 2002-2014



Codeine	Fentanyl	Heroin	Hydromorphone	Methadone	Morphine	Oxycodone
+233%	+1660%	+334%	+600%	+84%	+124%	+370%

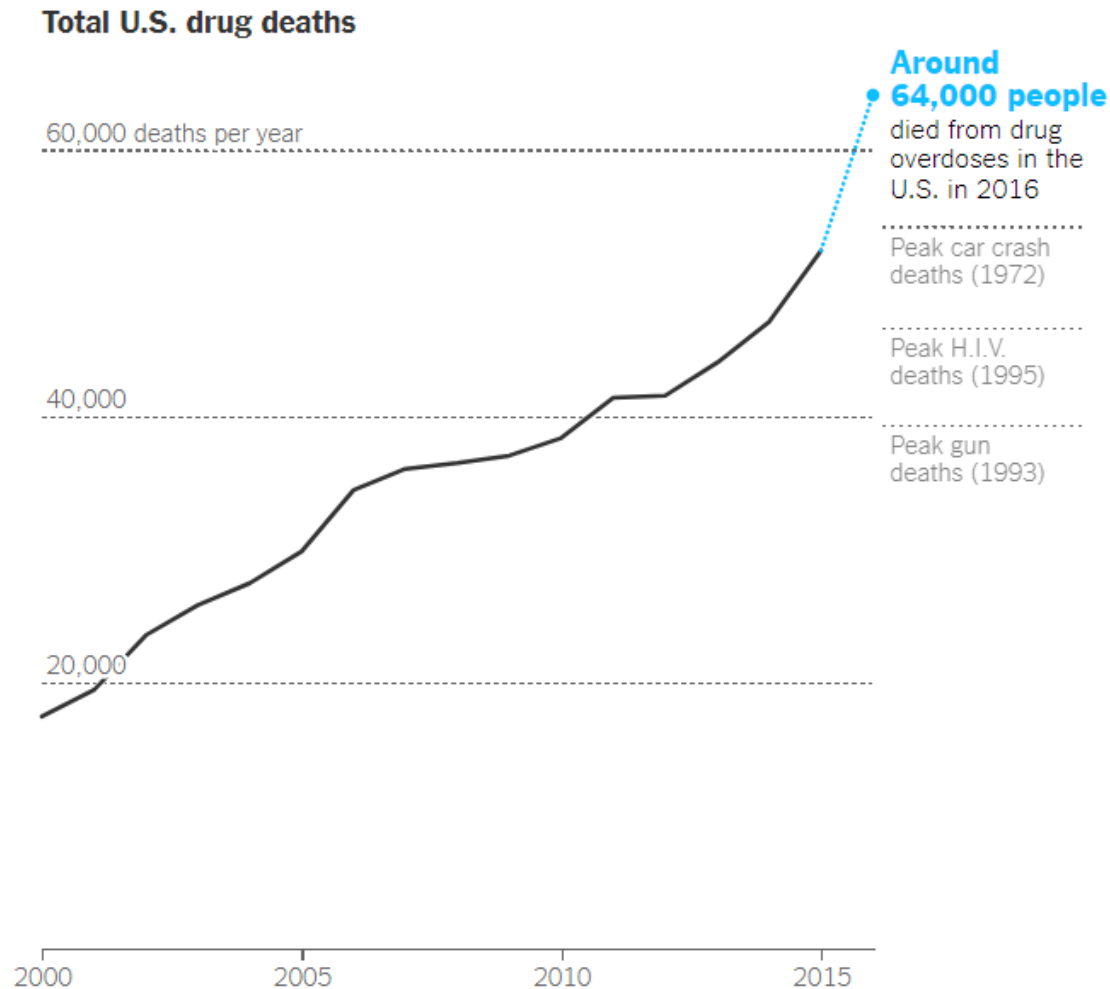
Opioid Overdose Deaths in the United States



Overdose deaths per 100,000

4 8 12 16 20

Opioid Overdose Deaths in the United States



2017 Opioid Therapy Guidelines

GUIDELINE 

Guideline for opioid therapy and chronic noncancer pain

Jason W. Busse DC PhD, Samantha Craigie MSc, David N. Juurlink MD PhD, D. Norman Buckley MD, Li Wang PhD, Rachel J. Couban MA MSt, Thomas Agoritsas MD PhD, Elie A. Akl MD PhD, Alonso Carrasco-Labra DDS MSc, Lynn Cooper BES, Chris Cull, Bruno R. da Costa PT PhD, Joseph W. Frank MD MPH, Gus Grant AB LLB MD, Alfonso Iorio MD PhD, Navindra Persaud MD MSc, Sol Stern MD, Peter Tugwell MD MSc, Per Olav Vandvik MD PhD, Gordon H. Guyatt MD MSc

■ Cite as: *CMAJ* 2017 May 8;189:E659-66. doi: 10.1503/cmaj.170363

CMAJ podcasts: author interview at <https://soundcloud.com/cmajpodcasts/170363-guide>

See related article www.cmaj.ca/lookup/doi/10.1503/cmaj.170431

Chronic noncancer pain includes any painful condition that persists for at least three months and is not associated with malignant disease.¹ According to seven national surveys conducted between 1994 and 2008, 15%–19% of Canadian

KEY POINTS

- We recommend optimization of nonopioid pharmacotherapy and nonpharmacologic therapy, rather than a trial of opioids.

Widespread Existing Use and Patient Interest

VIEWPOINT

Opioids Out, Cannabis In Negotiating the Unknowns in Patient Care for Chronic Pain

Esther K. Choo, MD, MPH
Center for Policy and Research in Emergency Medicine, Oregon Health & Science University, Portland.

Sarah W. Feldstein Ewing, PhD
Department of Psychiatry, Oregon Health & Science University, Portland.

Travis I. Lovejoy, PhD, MPH
Department of Psychiatry, Oregon Health & Science University, Portland; and Center to Improve Veteran Involvement in Care, VA Portland Health Care System, Portland, Oregon.



Viewpoint page 1765

With the current nationwide epidemic of opioid abuse, dependence, and fatalities, clinicians are being asked by federal agencies and professional societies to control their prescribing of narcotic medications for pain. Federal guidelines emphasize tapering, discontinuing, and limiting initiation of these drugs except in provision of end-of-life care.¹ Reducing reliance on opioids, however, is a massive task. According to one estimate, more than 650 000 opioid prescriptions are dispensed each day in the United States.² Unless the nation develops an increased tolerance to chronic pain, reduction in opioid prescribing leaves a vacuum that will be filled with other therapies.

Enter cannabis. As of August 2016, the District of Columbia and 25 states have legalized cannabis for medical use. Recreational use of cannabis has been legalized in 4 of these states and Washington, DC, and

The mandated transition to limit use of opioids, paired with the current climate around liberalizing cannabis, may lead to patients' formal and informal substitution of cannabis for opioids.

like initiatives are pending in other states.³ The mandated transition to limit use of opioids, paired with the

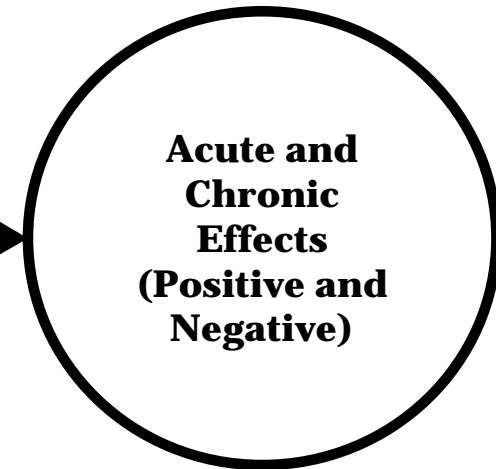
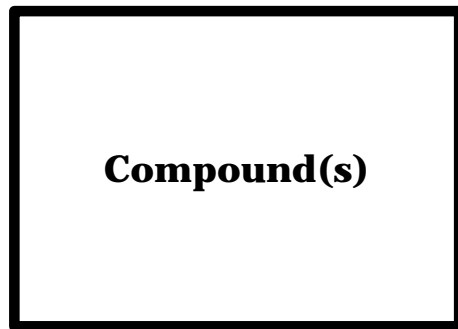
may lack awareness about the potential harms of cannabis, parameters for safe use, interactions with other medications, and initiation or escalation of THC (Δ^9 -tetrahydrocannabinol) dosing and thus report poor self-efficacy in prescribing and guiding cannabis use for pain and other therapeutic purposes.⁷ Although current evidence supports cannabis use for a limited number of conditions, (eg, chronic pain, muscle spasticity), medical cannabis has been approved by individual states for a wide variety of indications, including anorexia in HIV/AIDS, depression and anxiety disorders, psychosis, insomnia, glaucoma, Parkinson disease, seizures, Tourette syndrome, rheumatoid arthritis, traumatic brain injury, myasthenia gravis, and a host of autoimmune and neuromuscular conditions.⁸

Therefore, physicians may be placed in the uncomfortable position of explaining to patients why they might advise against treatment that appears to be endorsed by a governing body (eg, health departments of states in which medicinal use has been legalized) rather than supported by science. The ongoing federal ban on cannabis that recently was reinforced by the US Drug Enforcement Agency creates added complexity for physicians. Inconsistency across individual practitioners and health agencies regarding how to approach this substance

Complexities of Cannabis

PHARMACODYNAMICS

PHARMACOKINETICS

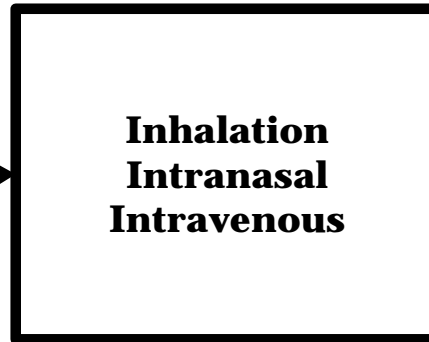


Complexities of Cannabis

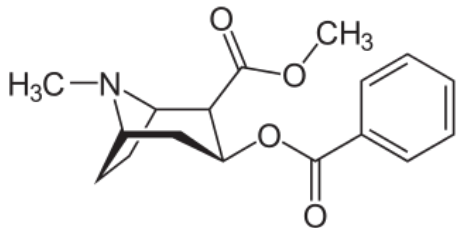
PHARMACODYNAMICS



PHARMACOKINETICS



**Acute and
Chronic
Effects
(Positive and
Negative)**

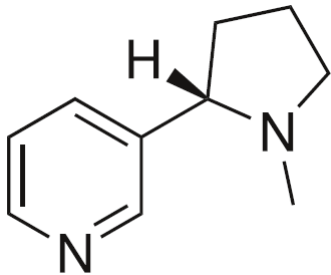
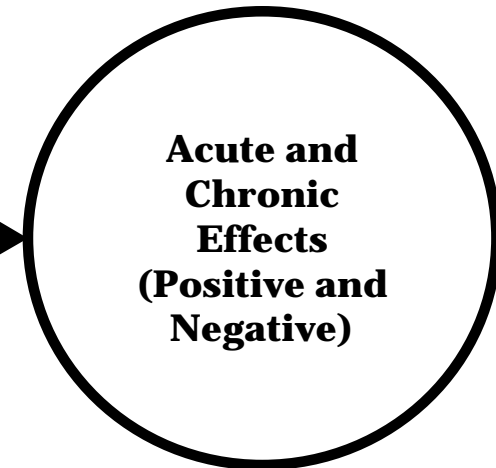
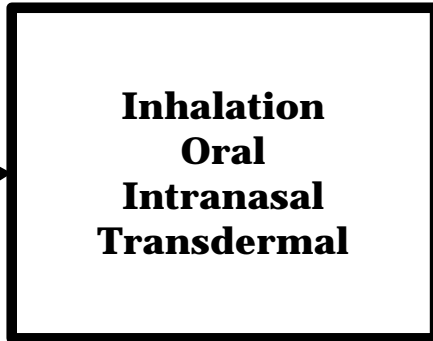


Complexities of Cannabis

PHARMACODYNAMICS



PHARMACOKINETICS

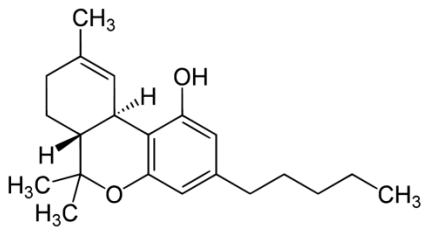


Complexities of Cannabis

PHARMACODYNAMICS

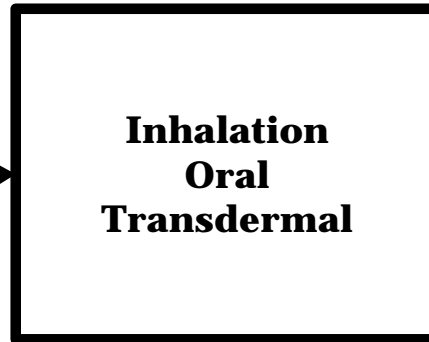


>500 active compounds (!)



THC

PHARMACOKINETICS



Cigarette
Pipe
Waterpipe
Vaporizer
Edible
Oil
Patch
Salve

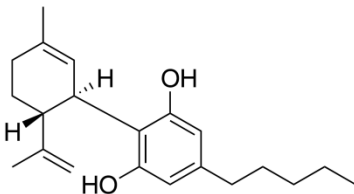
**Acute and
Chronic
Effects
(Positive and
Negative)**

Complexities of Cannabis

PHARMACODYNAMICS

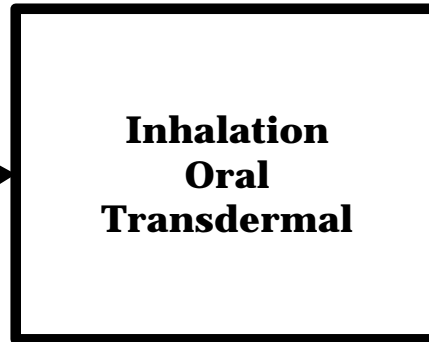


>500 active compounds (!)



CBD

PHARMACOKINETICS



Cigarette
Pipe
Waterpipe
Vaporizer
Edible
Oil
Patch
Salve

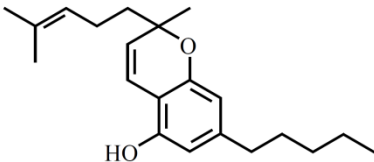
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Complexities of Cannabis

PHARMACODYNAMICS

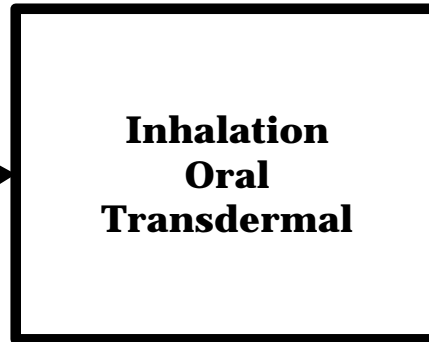


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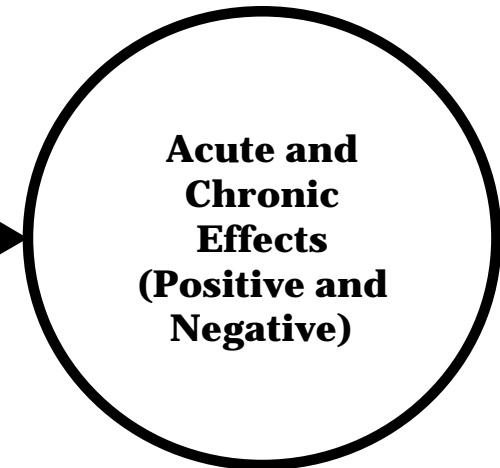


CBC

PHARMACOKINETICS



- Cigarette
- Pipe
- Waterpipe
- Vaporizer
- Edible
- Oil
- Patch
- Salve

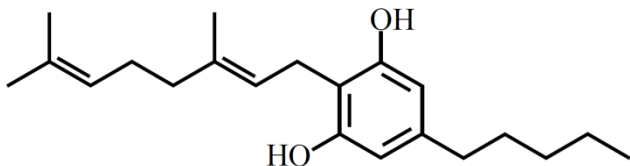


Complexities of Cannabis

PHARMACODYNAMICS

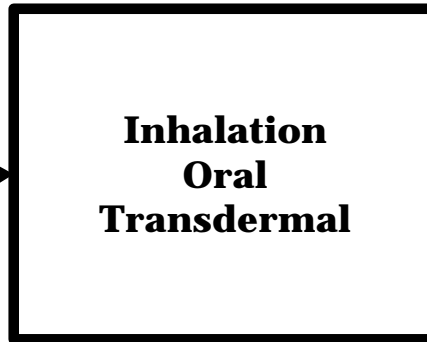


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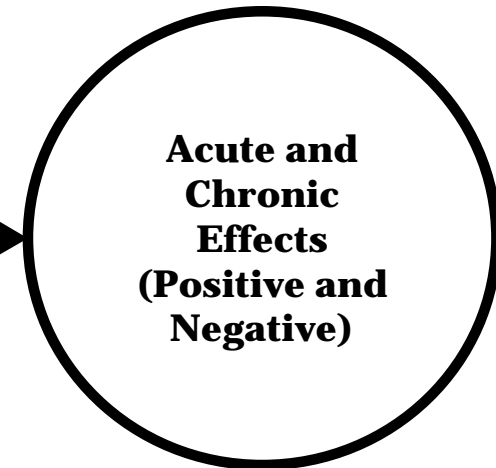


CBG

PHARMACOKINETICS



Cigarette
Pipe
Waterpipe
Vaporizer
Edible
Oil
Patch
Salve

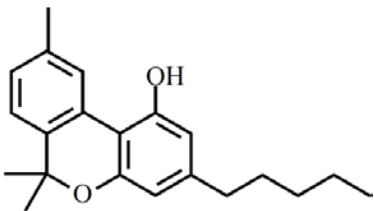


Complexities of Cannabis

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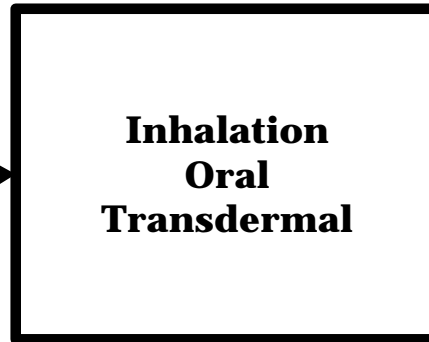


>500 active compounds (!)



CBN

PHARMACOKINETICS



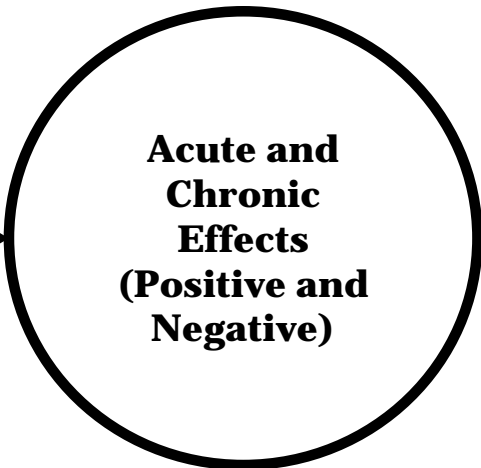
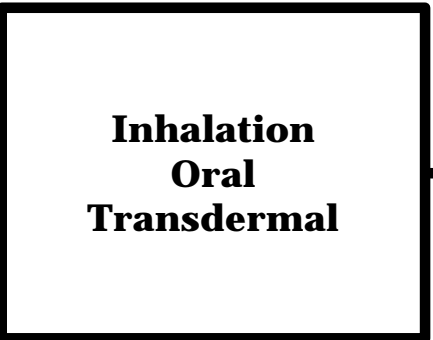
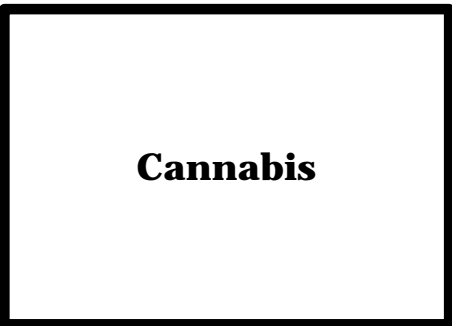
Cigarette
Pipe
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**Acute and
Chronic
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Complexities of Cannabis

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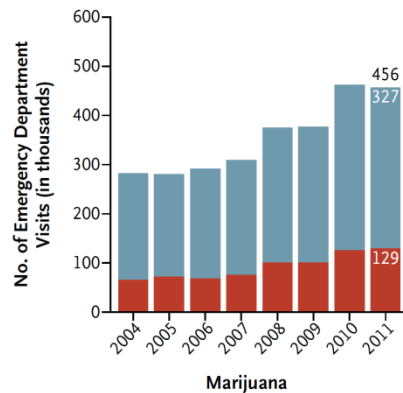
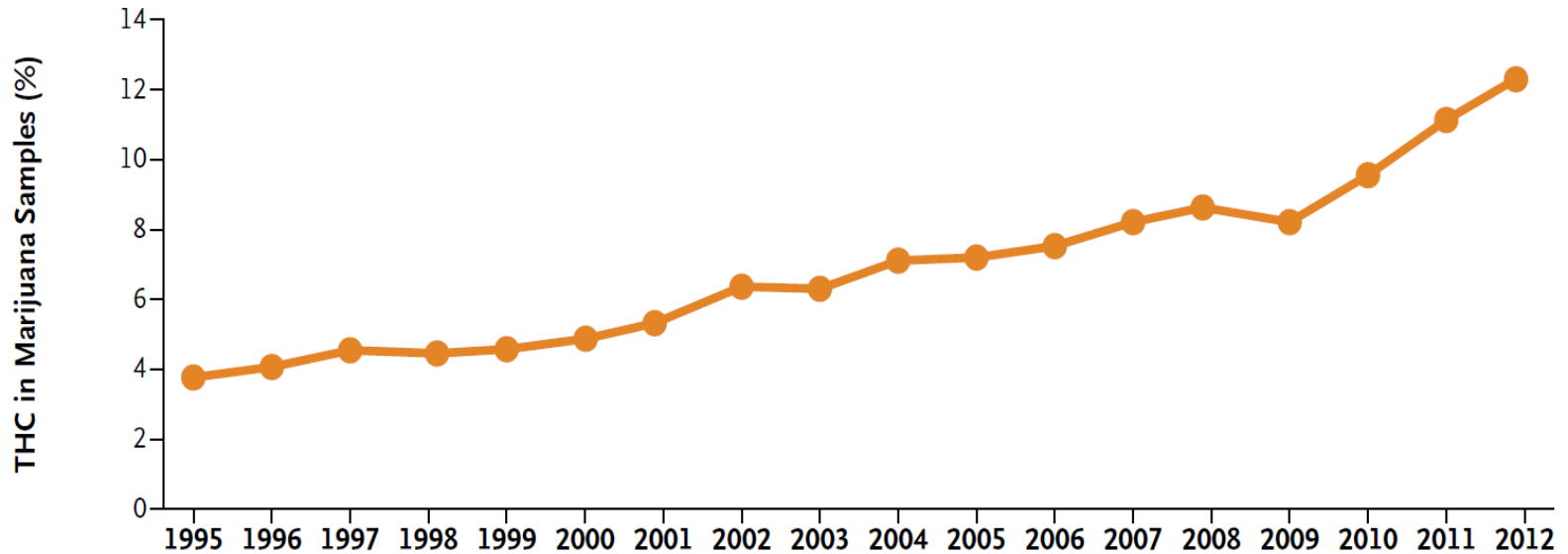


**>500 active
compounds (!)**

- | | |
|----------------------|-----------------------|
| Myrcene | Camphene |
| Linalool | Terpineol |
| α Bisalol | Δ-3-carene |
| Borneol | Limonene |
| Caryophyllene | Eucalyptol |
| α Pinene | Humulene |
| β Pinene | Trans-neroliol |

- Cigarette**
- Pipe**
- Waterpipe**
- Vaporizer**
- Edible**
- Oil**
- Patch**
- Salve**

Escalation in THC Over Time



New Formulations



“Wax”



“Shatter”



“Budder”

Extractions (40-90% THC)



Michael G. DeGroot
CENTRE FOR MEDICINAL
CANNABIS RESEARCH

Vision and Mission

Vision

An evidence-based understanding of medicinal cannabis, encompassing both its potential therapeutic effects and associated risks.

Mission

To leverage the highest standards of research methodology to collectively advance the understanding of medicinal cannabis.

To do this via:

- ❑ Curating the collective body of knowledge on medicinal cannabis
- ❑ Conducting innovative research projects to advance scientific discovery
- ❑ Creating a network of researchers, clinicians, and patients dedicated to evidence-based increasing the clinical understanding of cannabis

Curating the Evidence Base



Research Summaries

Synopses of high impact research publications from clinical and research experts studying cannabis.



Evidence Briefs

Consolidated overviews of the state of medicinal cannabis across various clinical and research areas.



Evidence Syntheses

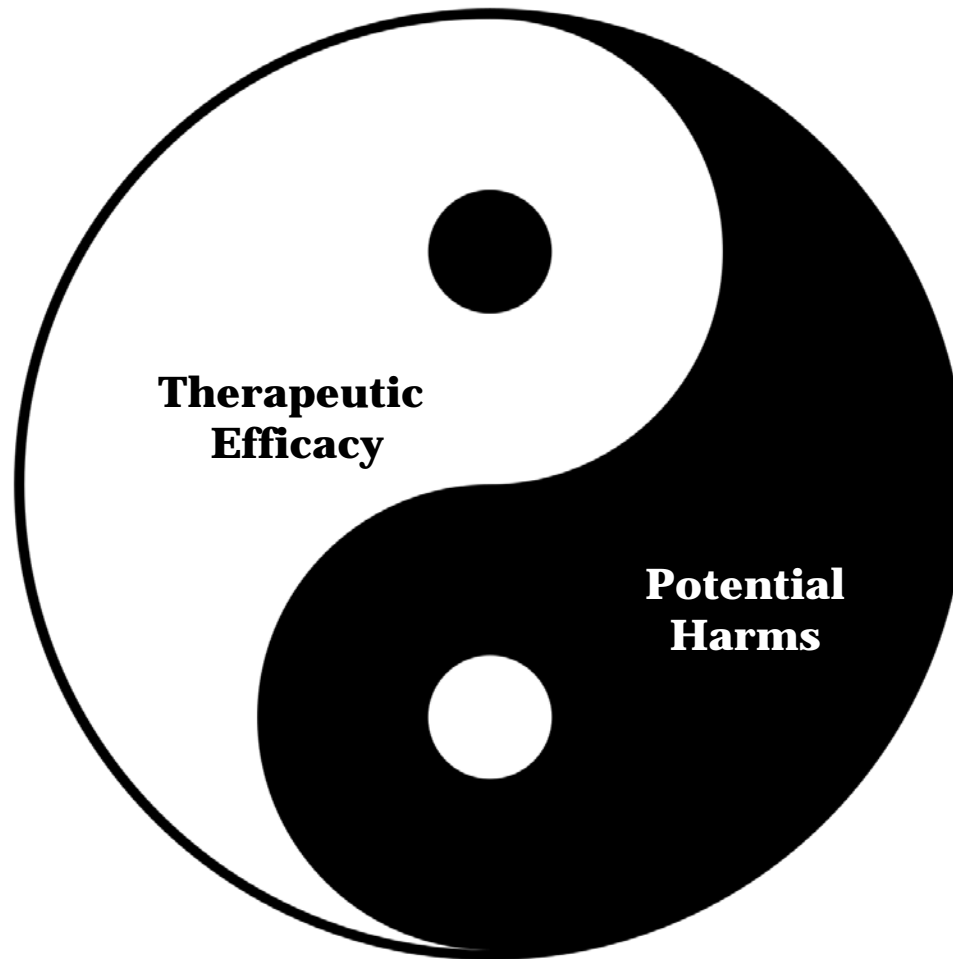
'Deep dive' explorations of topics related to medicinal cannabis via the McMaster Health Forum

**MEDICINAL
CANNABIS+**

**PREMIUM
LITERATURE
SERVICES**

**McMaster
PLUS**

Conducting Innovative Research



Priority Areas

Therapeutic Benefits

- Knowledge syntheses
- Systematic reviews
- Clinical guidelines
- Preclinical models
- Pilot randomized controlled trials

Adverse Consequences

- Cannabis use disorder (addiction)
- Neurocognitive sequelae
- Psychomotor impairment
- Psychosis and other psychiatric disorders

Surveillance Over the Course of Legalization

Priority Areas

Therapeutic Benefits

- Knowledge syntheses
- Systematic reviews
- Clinical guidelines
- Preclinical models
- Pilot randomized controlled trials

***Archival Data
Reviews***

***Constituent Analysis
Translational Screening***

***Cancer Pain
Post-surgical Pain
Anxiety Disorder
Bipolar Disorder
Sleep
Lupus***

Priority Areas

***Genetic Determinants
Novel CUD Treatments***

***Cognition
Motivation
Development***

***Alcohol
Criminal Behavior
Gambling
Psychosis***

Adverse Consequences

- Cannabis use disorder (addiction)
- Neurocognitive sequelae
- Other psychiatric disorders and adverse consequences
- Psychomotor impairment

Priority Areas

PATH Registry

Population Assessment for Tomorrow's Health

Middle-aged community adults

N=1435, M age = 58% female, 29% cannabis+

Assessment: pre-legalization/+6/+12/+18 mos.



Project Beta

Emerging adult binge drinkers

N=453 [ip], M age = 21.5, 68% female, 52% cannabis+

Assessment: 11 assessments, every 4 mos.,



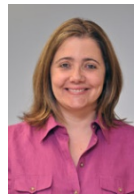
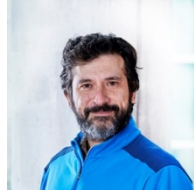
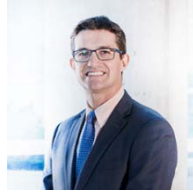
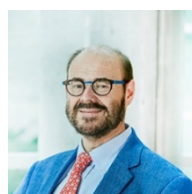
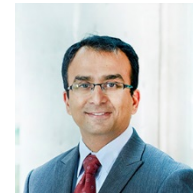
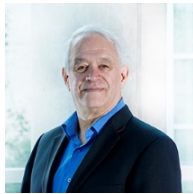
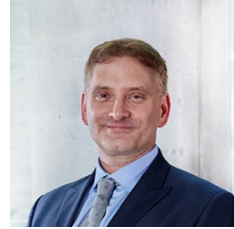
Authorized cannabis for pain patients

Five clinics in ON, MB, and BC

Assessment: BL, 4/8/12 mos., +6 mos. for 5 years

Surveillance Over the Course of Legalization

Creating a Network





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■ Federal Perspectives and Public Policy



Ms. Rebecca Jesseman



Dr. Wilson Compton



Mr. Michael Devillaer



Dr. Michael Amlung

■ Preclinical Animal Models



Dr. Andrea Hohmann



Dr. Linda Parker



Dr. Gurmit Singh

■ Human Brain Imaging



Dr. Sarah Feldstein Ewing



Dr. Bernard LeFoll



Dr. Iris Balodis

■ Human Psychopharmacology



Dr. Jane Metrik



Dr. Margaret Haney



Dr. Alan Budney



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■ Clinical Applications



Dr. Mark Ware



Dr. Jason Busse



Dr. Jason McDougall



Dr. Suzanne Archie



Dr. Marissa Slaven

Welcome!

