Cannabis & Mental Health Primer Webinar
Zach Walsh

1

Disclosure

- My research has received financial support from Tilray and Doja in the form of funding to sponsor a clinical trial for which I am principal investigator.
- Director of clinical research for Indigenous Bloom as an advisory board member.
- Potential for conflict(s) of interest:
  - Zach Walsh has received research support from Tilray & Doja.
  - Tilray & Doja are licensed producers of cannabis for medical purposes.
  - I hold shares in Indigenous Bloom.
  - Indigenous Bloom is an Indigenous operated cannabis company.
- Other funders of this research:

CIHR IRSC SSHRC CRSH Institute for Healthy Living and Chronic Disease Prevention MITACS

2

Overview - Me

- Clinical psychologists (#2011)
- Trained in addictions treatment
  - University of Chicago
  - Brown University – Center for Alcohol and Addiction Treatment
- Professor – UBC
- Lead - Therapeutic Recreational & Problematic Substance Use lab
- Published and presented widely on cannabis use and mental health
  - HOC
  - Senate
  - BC Supreme Court
  - Uruguay and Costa Rica
- PI – Canada's 1st clinical trial of cannabis to treat mental health d/o
- Advisory boards of MAPS Canada & Clinical team for MDMA for PTSD trials
- CIHR & SSHRC funded studies of cannabis use in young adults

3

Overview - Today

PART 1

- History
  - 3000 BCE to C-45
- The plant
  - Cannabinoids
    - THC-CBD…
  - Terpenes
    - Entourage effect
  - Strains/Chemovars
    - Indica / Sativa
  - Modes of Administration

4

Overview - Today

PART 2

- Cannabinoids in humans
  - The Endocannabinoid System
    - Endocannabinoid deficits
    - Endocannabinoid care
  - Cannabinoid pharmacology
- Medical Cannabis use
  - Patient reports
  - Cannabis for pain and anxiety
  - Substitution
    - Benzodiazapines
    - Opioids
    - Alcohol

5

Overview - Today

PART 3

- Cannabinoids and Mental Health
  - Anxiety
  - Depression
  - Psychosis
  - Cognition
  - Risk
  - PTSD
    - Trial
    - Case study

6

Overview - Today

PART 4

- Problems
  - Withdrawal
  - Disorder
  - Assessment
  - Treatment
  - Safe use
  - Driving
- Special populations
  - Youth
  - Older adults

7

Cannabinoids

- Endocannabinoids
  - Naturally occurring in animals
  - Anandamide
  - 2-AG
- Phytocannabinoids
  - From plants
  - THC, CBD and many others
- Synthetic
  - K9, Spice

8

9

History - China

Shen-Nung (c.2700 B.C.)

10

History - India

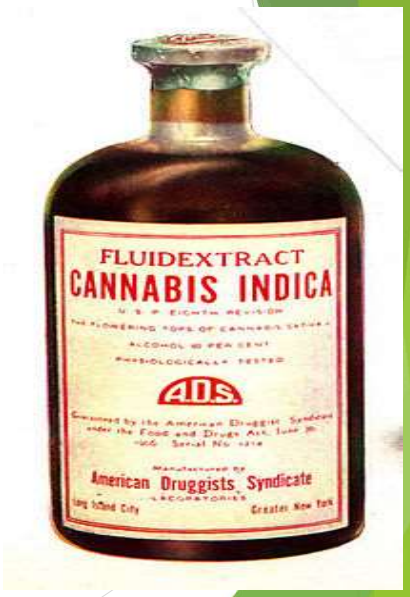
- Ganja
- Bhang
- Holi
- The Vedas call cannabis a source of happiness, joy-giver, liberator that was compassionately given to humans to help us attain delight and lose fear (Abel, 1980).

11

History - Europe

- **William Brooke O'Shaughnessy**
  - **Introduced medical use of cannabis to Europe**
  - **From India - 1841**

12



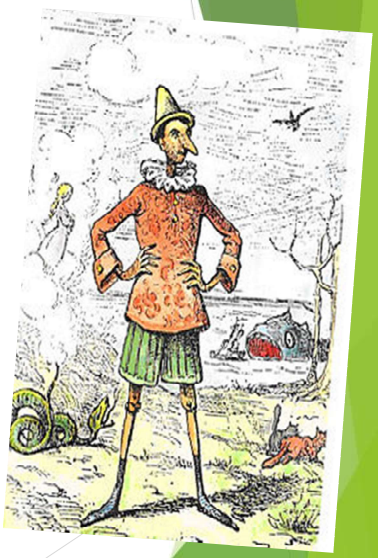
13

History - Prohibition

"Marihuana is a short cut to the insane asylum. Smoke marihuana cigarettes for a month and what was once your brain will be nothing but a storehouse of horrid specters. Hasheesh makes a murderer who kills for the love of killing out of the mildest mannered man who ever laughed at the idea that any habit could ever get him…"

Harry Aslinger, 1937

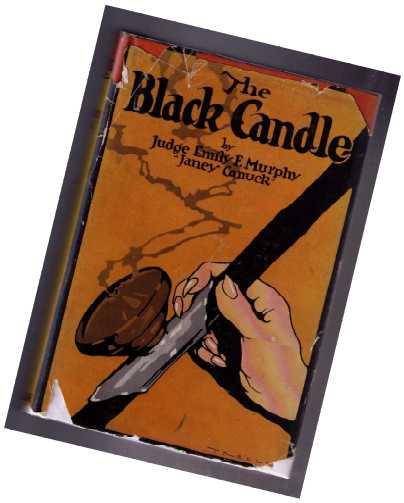
1st Commissioner of the Federal Bureau of Narcotics



14

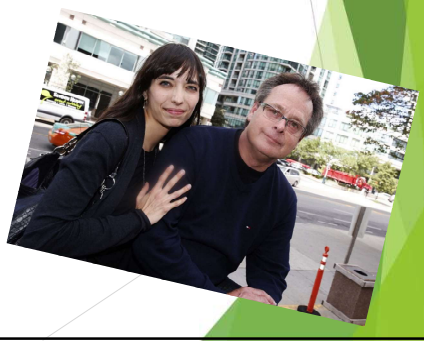
History - Canada

- Canada – Janey Canuck – The Black Candle (1922)



15

Canada - Recent



16

Background – Medical Cannabis in Canada

- *Parker* (2000) - constitutional right to choose cannabis as medicine without fear of criminal sanction
- In 2001, the *Marihuana Medical Access Regulations* (MMAR)
  - Access
    - Health Canada - Prairie PPS
    - Private production license
    - Designated grower (1:1…2:1)

17

CANADIAN MEDICAL MARIHUANA SYSTEM

18

MMPR

MARIHUANA FOR MEDICAL PURPOSES REGULATIONS

- Simplified/decentralized application process
- Multiple Licensed Producers
  - Increased quality & strain choice
- Research funding & materials
- No self-production or storefronts

  - Allard
- 2016 ACCESS TO CANNABIS FOR MEDICINAL PURPOSES REGULATIONS (ACMPR)

19

C-45: THE CANNABIS ACT

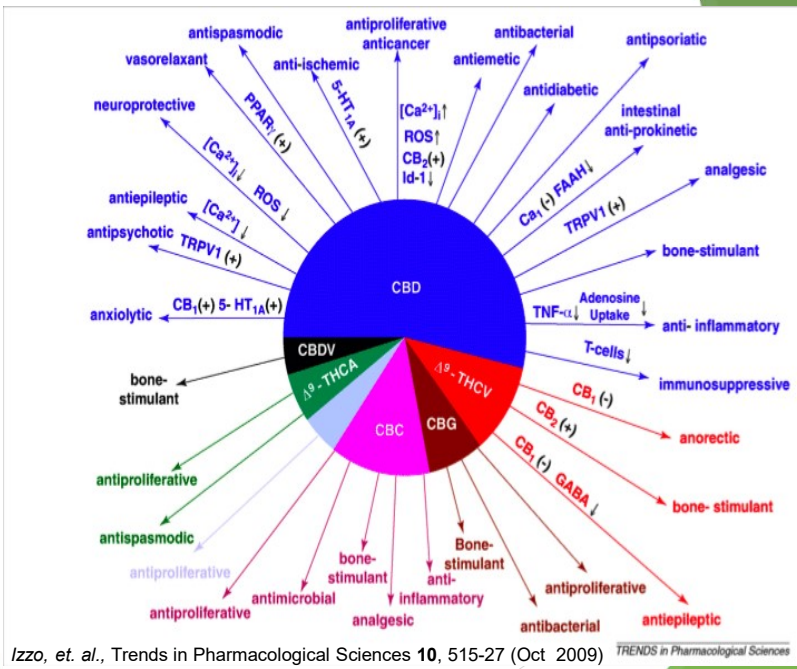
- Sale -provincial gov't
  - online (mail) and retail stores;
  - public/private models
- Minimum age of 18 (provinces can adjust)
- Adults –
  - up to 30 grams –
  - 4 plants per household
- Youth (12-17) –
  - decriminalized for 5 grams or less
  - Providing cannabis to minors – 14 year max
- Limits on advertising and branding
- Outside of regulated framework
  - 45+ new penalties

20

Cannabinoids

- The Cannabinoids
  - Delta-9-tetrahydrocannabinol (Δ^9-THC)
    - 5-25% "superweed?"
  - Cannabinoids
    - Over 100 Cannabinoids
      - Cannabinol and Cannabidiol (CBD)
    - THCA, THC, CBDA, CBD, CBGA, CBG, CBN
    - Some on plant ratios of 2:1, >20:1,
      - Terpenes
      - Entourage effect of herbal cannabis
      - Whole plant – coevolution with humans?
  - Synthetic Cannabinoids
    - Sativex - extract
    - Dronabinol (Marinol)-Levonantradol (30x THC)
    - Spice / K2
  - Rimonabant – antagonist

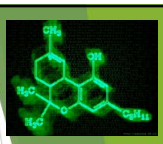
21



Izzo, et. al., Trends in Pharmacological Sciences **10**, 515-27 (Oct 2009)

22

Pharmacology of THC



- THC functions by binding to the Cannabinoid Receptor (CB_1).
  - The presence of this receptor indicates that there is a naturally occur (endogenous) ligand, Anandimide, as well as other related compounds.
- The response can affect the hippocampus and hypothalamus
  - Hippocampus –involved in ***motivation*** and ***emotion*** as part of the limbic system; has a central role in the ***formation of memories***.
  - Hypothalamus –regulating ***sleep cycles***, ***body temperature***, ***appetite***, etc., and that acts as an endocrine gland by ***producing hormones***, including the releasing factors that control the hormonal secretions of the pituitary gland.

23

CBD

- **Well Documented:**
  - Anti-epileptic
- **Potential**:
  - Analgesic (acute and chronic pain)
  - Antipsychotic
  - Anxiolytic
  - Anti-cancer
  - Anti-inflammatory

24

24

CBD

- CBD does not activate CB1 or CB2 receptors
- Does not mimic endocannabinoids.
- Interacts indirectly with the endocannabinoid system
- Agonist
  - **5 HT 1A** (anxiolytic; antidepressant)
  - **Adenosine** (anxiolytic)
  - **TRPV1** - (analgesic)
  - **Mu and delta opiate** – (analgesic)

25

Project CBD

CANNABIS OIL EXTRACTS
can be taken orally, sublingually or applied topically. Concentrated cannabis oil extracts can also be utilized as an ingredient to vaporize or cook with. Some cannabis oils come with an applicator for measured dosing. These oil extracts—CBD-rich and THC-dominant—are very potent. The time of onset and duration of effect vary depending on the method of administration.

Visit ProjectCBD.org for:

CBD Locator • Educational resources • Dispensary staff training • Updates on cannabis science & therapeutics • CBD-rich product list • Analysis of industry trends • Events • Announcements • Referrals

Advancing whole plant cannabis therapeutics

PROJECT CBD projectcbd.org

What to Look For

- ✓ **CBD-rich products.** Choose products that include both CBD, a non-intoxicating compound, and THC, the main psychoactive component of cannabis. CBD and THC work best together, enhancing each other's therapeutic benefits.
- ✓ **Clear labels.** Look for product labels showing the quantity and ratio of CBD and THC per dose, a manufacturing date and batch number (for quality control).
- ✓ **Lab testing.** Look for products that are tested for consistency, and verified as free of mold, bacteria, pesticides, solvent residues, and other contaminants.
- ✓ **Quality ingredients.** Select products with quality ingredients. (No corn syrup, GMOs, transfats, preservatives, and artificial additives.)
- ✓ **Safe extraction.** Avoid products extracted with toxic solvents like BHO, propane, hexane or other hydrocarbons. Solvent residues are especially dangerous for immune-compromised patients. Look for products that entail a safer method of extraction like supercritical CO_2.
- ✓ **Products made from organic cannabis not industrial hemp.** Compared to high resin cannabis, hemp is typically low in cannabinoid content. A huge amount of hemp is required to extract a small amount of CBD, raising the risk of contaminants because hemp, a bioaccumulator, draws toxins from the soil. The robust terpene profile of whole plant cannabis enhances the therapeutic benefits of CBD and THC.

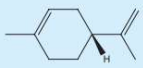
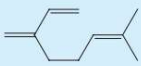
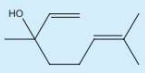
26

Terpenes

- Biologically active cannabis constituents with pharmacologic effects.
- > 200 in the cannabis plant.
- Most are “Generally Recognized as Safe” as food additives.
- To optimize terpene absorption cannabis must be inhaled

27

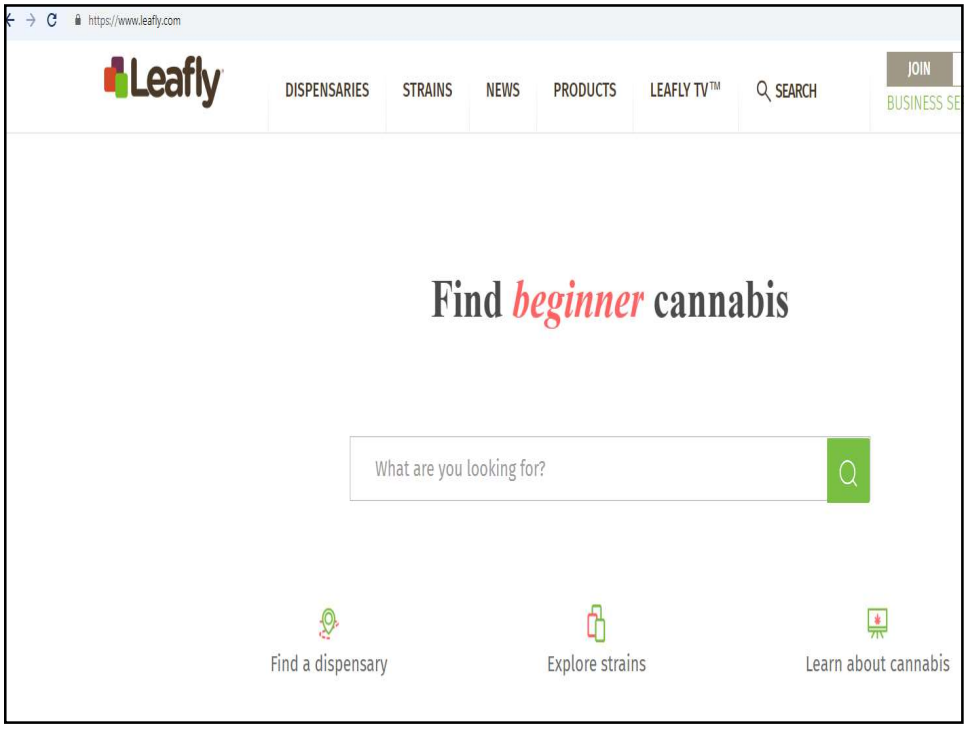
Cannabis Terpenoid Activity Table

Terpenoid	Structure	Commonly encountered in	Pharmacological activity (Reference)	Synergistic cannabinoid
Limonene		 Lemon	Potent AD/immunostimulant via inhalation (Komori *et al.*, 1995)	CBD
			Anxiolytic (Carvalho-Freitas and Costa, 2002; Pultrini Ade *et al.*, 2006) via 5-HT_{1A} (Komiya *et al.*, 2006)	CBD
			Apoptosis of breast cancer cells (Vigushin *et al.*, 1998)	CBD, CBG
			Active against acne bacteria (Kim *et al.*, 2008)	CBD
			Dermatophytes (Sanguinetti *et al.*, 2007; Singh *et al.*, 2010)	CBG
			Gastro-oesophageal reflux (Harris, 2010)	THC
α-Pinene		 Pine	Anti-inflammatory via PGE-1 (Gil *et al.*, 1989)	CBD
			Bronchodilatory in humans (Falk *et al.*, 1990)	THC
			Acetylcholinesterase inhibitor, aiding memory (Perry *et al.*, 2000)	THC?, CBD
β-Myrcene		 Hops	Blocks inflammation via PGE-2 (Lorenzetti *et al.*, 1991)	CBD
			Analgesic, antagonized by naloxone (Rao *et al.*, 1990)	CBD, THC
			Sedating, muscle relaxant, hypnotic (do Vale *et al.*, 2002)	THC
			Blocks hepatic carcinogenesis by aflatoxin (de Oliveira *et al.*, 1997)	CBD, CBG
Linalool		 Lavender	Anti-anxiety (Russo, 2001)	CBD, CBG?
			Sedative on inhalation in mice (Buchbauer *et al.*, 1993)	THC
			Local anesthetic (Re *et al.*, 2000)	THC
			Analgesic via adenosine A_{2A} (Peana *et al.*, 2006)	CBD
			Anticonvulsant/anti-glutamate (Elisabetsky *et al.*, 1995)	CBD, THCV, CBDV
			Potent anti-leishmanial (do Socorro *et al.*, 2003)	?
β-Caryophyllene		 Pepper	AI via PGE-1 comparable phenylbutazone (Basile *et al.*, 1988)	CBD
			Gastric cytoprotective (Tambe *et al.*, 1996)	THC
			Anti-malarial (Campbell *et al.*, 1997)	?
			Selective CB_2 agonist (100 nM) (Gertsch *et al.*, 2008)	THC
			Treatment of pruritus? (Karsak *et al.*, 2007)	THC
			Treatment of addiction? (Xi *et al.*, 2010)	CBD

28


Entourage?
BJP British Journal of Pharmacology
Themed Issue: Cannabinoids in Biology and Medicine, Part I
REVIEW
Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects
Ethan B Russo
Correspondence
Keywords
Received
Revised
Accepted
SCIENTIFIC AMERICAN
CHEMISTRY
Some of the Parts: Is Marijuana's "Entourage Effect" Scientifically Valid?
Industry players swear pot's many chemicals work in concert, but most scientists hear a THC solo

29


https://www.leafly.com
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Find a dispensary
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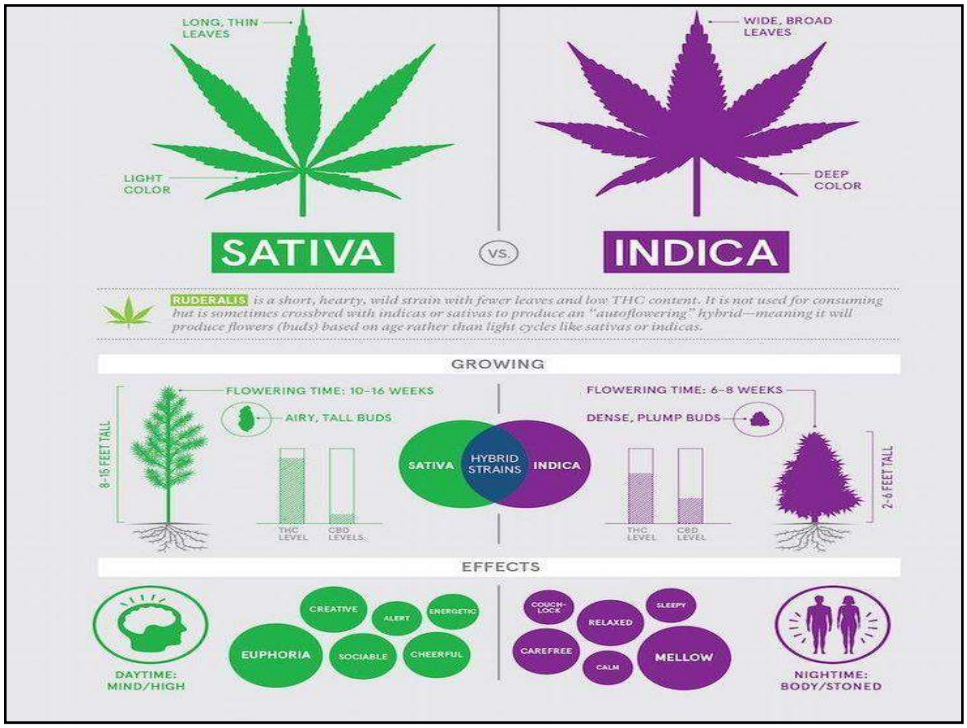
Learn about cannabis

30

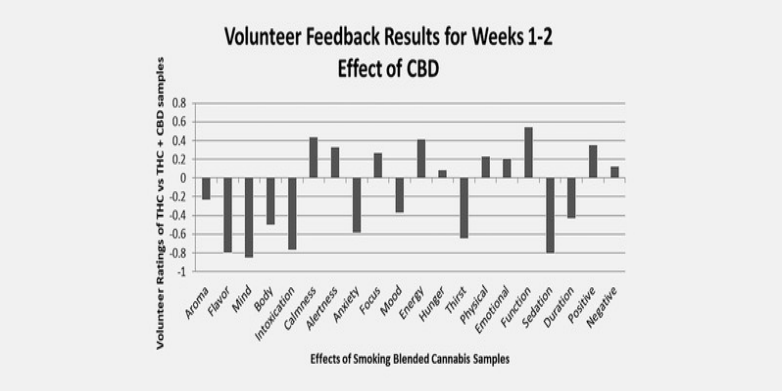

Hybrid
Gg4
Original Glue
Sativa
Jh
Jack Herer
Hybrid
Ww
White Widow
Indica
Bk
Bubba Kush
Hybrid
Pex
Pineapple Express
Sativa
Dp
Durban Poison
Indica
Nl
Northern Lights
Hybrid
Tw
Trainwreck
Hybrid
Ak
AK-47
Hybrid
Hb
Headband
Indica
Chz
Blue Cheese
Sativa
Lh
Lemon Haze
Indica
Pk
Purple Kush
Sativa
Sc
Strawberry Cough
Indica
Bry
Blueberry
Hybrid
Cd
Chemdawg
Sativa
Ss
Super Silver Haze
Indica
Ga
Grape Ape
Sativa
Atf
Alaskan Thunder Fuck
Indica
Bbk
Blackberry Kush
Sativa
Slh
Super Lemon Haze
Indica
Mks
Master Kush
Hybrid
Cp
Cherry Pie
Hybrid
Mzo
Mazar X Blueberry OG

31


LONG, THIN LEAVES
LIGHT COLOR
WIDE, BROAD LEAVES
DEEP COLOR
SATIVA
VS.
INDICA
RUDERALIS is a short, hearty, wild strain with fewer leaves and low THC content. It is not used for consuming but is sometimes crossbred with indicas or sativas to produce an "autoflowering" hybrid—meaning it will produce flowers (buds) based on age rather than light cycles like sativas or indicas.
GROWING
FLOWERING TIME: 10-16 WEEKS
AIRY, TALL BUDS
8-16 FEET TALL
THC LEVEL
CBD LEVELS
SATIVA
HYBRID STRAINS
INDICA
FLOWERING TIME: 6-8 WEEKS
DENSE, PLUMP BUDS
2-6 FEET TALL
THC LEVEL
CBD LEVEL
EFFECTS
DAYTIME: MIND/HIGH
CREATIVE
ALERT
ENERGETIC
EUPHORIA
SOCIABLE
CHEERFUL
COUCH-LOCK
SLEEPY
RELAXED
CAREFREE
CALM
MELLOW
NIGHTIME: BODY/STONED

32

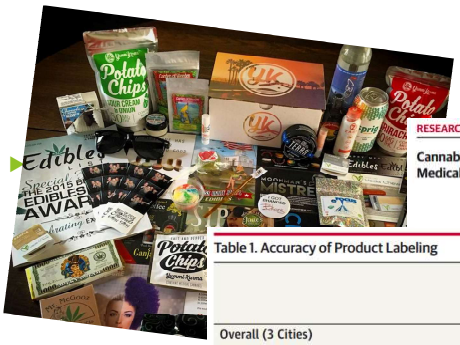
CBD vs



Lewis, Russo & Smith, 2018

33

Edibles



RESEARCH LETTER JAMA June 23/30, 2015 Volume 313, Number 24

Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products

Ryan Vandrey, PhD
Jeffrey C. Raber, PhD
Mark E. Raber
Brad Douglass, PhD
Cameron Miller, MS
Marcel O. Bonn-Miller. PhD

Table 1. Accuracy of Product Labeling

	Accuracy of Labeled Tetrahydrocannabinol (THC) Content		
	Accurately Labeled[a]	Underlabeled[b]	Overlabeled[c]
Overall (3 Cities)			
Products tested, No. (%) (N = 75)	13 (17)	17 (23)	45 (60)
Type of product, No.			
Baked goods	2	7	13
Beverages	3	2	8
Candy or chocolate	8	8	24
Amount of THC, mg			
Label range	15 to 200	20 to 1000	2 to 325
Actual range	15 to 183	34 to 1236	<1 to 267
Deviation in THC content amount, %[d]			
Mean (SD)	−3 (4)	28 (13)	−47 (29)
Maximum	9	55	−99

34

EDIBLES DOSING CHART

THC CONTENT PER DOSE	WHAT TO EXPECT	WHO'S IT FOR?
1 - 2.5 mg THC	• Mild relief of pain, stress, anxiety, and other symptoms • Improved focus and creativity	• First-time consumers • Microdosers
2.5 - 15 mg THC	• Stronger symptom relief • Euphoria • May impair coordination and alter perception	• Patients with persistent problems • Restless sleepers • Social butterflies
15 - 30 mg THC	• Strong euphoria or unwanted effects in unaccustomed consumers • May impair coordination and alter perception	• Well-seasoned consumers • Medical patients with developed tolerances • Experienced consumers seeking to sustain sleep
30 - 50 mg THC	• Very strong euphoria in unaccustomed consumers • Likely to impair coordination and alter perception	• Consumers who have poor GI absorption of cannabinoids • People with significant tolerance to THC
50 - 100 mg THC	• Can cause extreme side effects such as rapid heart rate, nausea, and pain • Highly likely to impair coordination and alter perception	• For experienced THC individuals only • Patients with cancer, inflammatory disorders, or conditions that necessitate high doses

Always begin at the lowest recommended dose. Gradually increase by 1 or 2mg per dose, if necessary, to find your optimal dose. For more information go to Healer programs: ***www.healer.com/programs***

HEALER Leafly

35

Concentrates

36

Concentrates

CRUMBLE
Dried oil with a honey-comb like consistency

BADDER/BUDDER
Concentrates whipped under heat to create a cake-batter like texture

SHATTER
A translucent, brittle, & often golden to amber colored concentrate made with a solvent

DISTILLATE
Refined cannabinoid oil that is typically free of taste, smell & flavor. It is the base of most edibles and vape cartridges

CRYSTALLINE
Isolated cannabinoids in their pure crystal structure

DRY SIFT
Ground cannabis filtered with screens leaving behind complete trichome glands. The end-product is also referred to as kief

ROSIN
End product of cannabis flower being squeezed under heat and pressure

BUBBLE HASH
Uses water, ice, and mesh screens to pull out whole trichomes into a paste-like consistency

37

Concentrates

38

Modes of use

- Absorption
  - Oral Administration
    - Highly Lipid Soluble
      - Will hardly dissolve in water
      - Bake in food
        - First pass metabolism
      - Oral dose must be doubled or tripled to have same effect as inhalation
        - Peak effects: 1 to 3 hrs after ingestion
  - Inhalation
    - Depth of Inhalation

      Vs duration

      10-25% cannabinoids

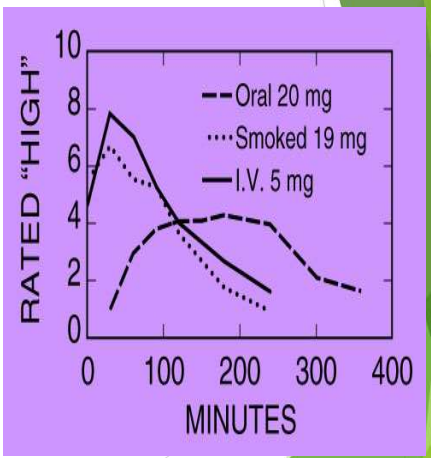
      Peak effects: 15 to 60 minutes

39

Modes

Distribution

- The time course for intensity of a subjective "high" after consuming various doses of THC via different routes of administration



40

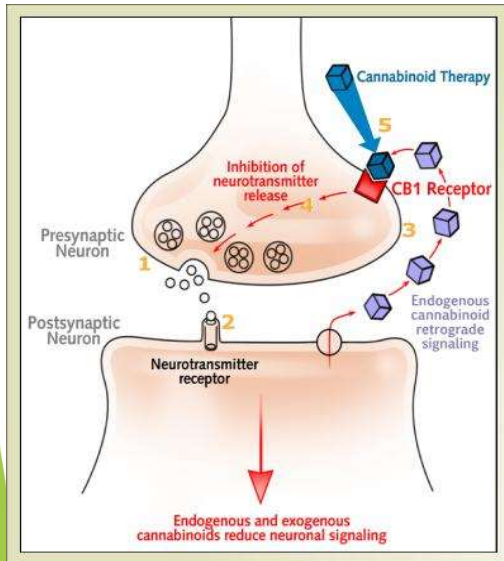
Part 2 - Cannabis, the Brain & Mental Health

41

Neurological Effects of THC

- Endocannabinoid Synaptic Transmission
  1. Transmission of neurotransmitter into the post-synaptic neuron.
  2. Production of endocannabinoids in the post-synaptic neuron.
  3. The endocannabinoid (e.g. anadamide, 2AG) is released into the synaptic cleft.
  4. In the synaptic cleft the endocannabinoid binds to the Cannabinoid Receptor of the pre-synaptic neuron.
     - This in turn modulates neurotransmission pre-synapticly
     - Post-Synaptic Neuron → Pre-Synaptic Neuron (Retrograde Transmission)
  - This mechanism is reverse of what is typically seen
    - Pre-Synaptic Neuron → Post-Synaptic Neuron (Normal Transmission)

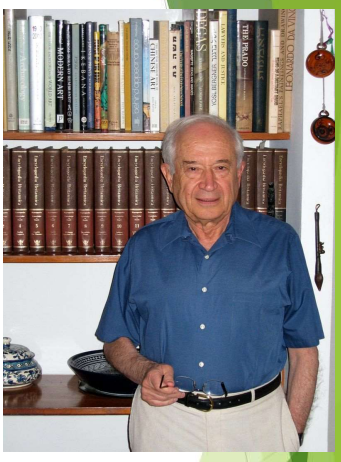
42



1. Neurotransmitter (NT) released from vesicles within the presynaptic neuron activates the postsynaptic neuron
2. Activation of the postsynaptic neuron leads to the biosynthesis and nonvesicular release of an endocannabinoid
3. The endogenous CB1 ligand diffuses back to and binds to the presynaptic CB1 receptor
4. The CB1 receptor activates a G-protein, which leads to presynaptic events that result in inhibition of NT release
5. Exogenous cannabinoids activate CB1 receptors directly to regulate NT release

43

Neuropharmacology

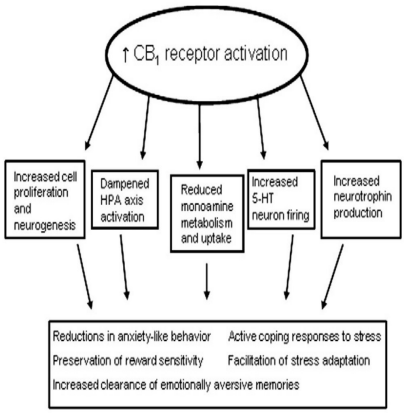


- Receptors – 2 discovered 1990
  - Likely many more
  - Second Messenger System
- Endocannabinoids
  - Anandamide
  - 2-arachidonylglycerol (2-AG)
  - THC > duration & effect
- Presynaptic Neuromodulators
  - From post to pre synaptic
  - Effects depend on nature of pre
    - Depolarization-induced **suppression of inhibition**
    - Depolarization-induced **suppression of excitation**

44

Neuropharmacology- ECS

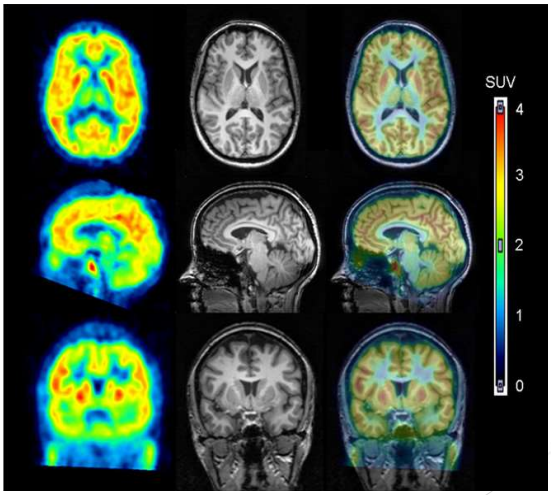
- Affects neurons for NE, DA, 5-ht, Ach, GABA
- Receptor Location
  - Nucleus Accumbens
    - Mesolimbic DA via endorphin
  - Cerebellum
  - Basal Ganglia
  - Hippocampus
    - Memory
  - Amygdala
    - Stress & fear
  - Stress Recovery
    - Relax, eat, sleep, forget & protect



Gorzalka & Hill, 2010

45

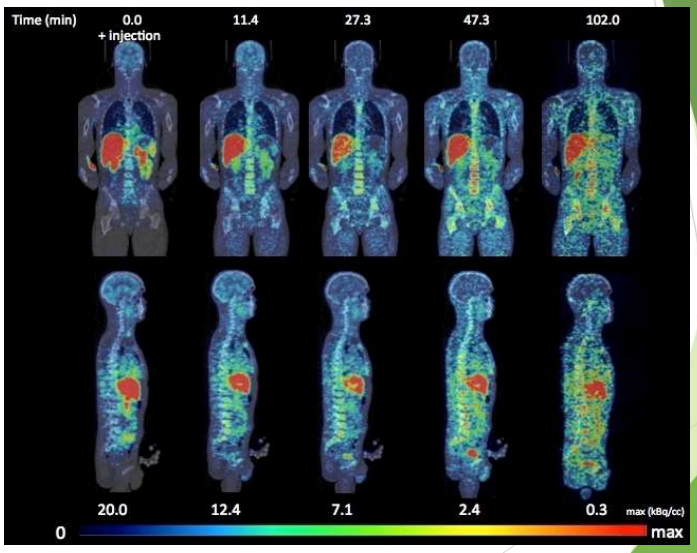
CB1 Receptor Distribution in Human CNS



(Terry, 2010)

46

CB2 Receptor Distribution



(Ahmad, 2013)

47

Effects on Behavior of Humans

- Subjective Effects
  - Bipolar / contradictory
- Mood Changes and Getting High
  - Mood swings
  - Social effects
- Perception
  - Loss of sensitivity to pain
  - Time distortion

McKim, 2017

48

Effects on Behavior of Humans

- Memory
  - No effect on the ability to recall material already well learned or on recognition memory
  - Does disrupt the ability to recall words or narrative material
    - Short term memory
    - Temporal disintegration
- Attention
  - Easily distracted
- Creativity
  - Appreciation
  - No evidence that creativity is enhanced

McKim, 2017

49

Effects on Behavior of Humans

- Performance
  - Varied results
    - Level of use
    - Features of task
    - Ability vs attention/ motivation
- Performance Screening Tests
  - Standardized Field Sobriety Tests
    - Gaze nystagmus, Walk and turn test, One-leg stand
    - 56% of high THC group identified vs 2.5% placebo

McKim, 2017

50

Cannabis for Therapeutic Purposes

- Risks and benefits
- Cannabis is:
  - **"…one of the safest therapeutically active substances known to man"**

    US Drug Enforcement Administration

    Judge Francis Young -1988

51

Conditions in Clinical Practice

Rank order - Hergenrather 2016

- Pain (acute pain, chronic inflammatory, neuropathic)
- Mental disorders (all kinds)
- Cancers
- Gastrointestinal disorders
- Insomnia
- Migraine headaches
- Harm reduction, alternative to opioids . . .
- Spastic disorders
- Autoimmune disorders
- Neurodegenerative disorders
- Glaucoma
- Skin diseases
- Epilepsy, Autism, Tourettes, ADD, Dystonia, Dementia
- AIDS and other infections

52

Cannabis for Therapeutic Purposes

International Journal of Drug Policy 24 (2013) 511–516

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Editors' choice

Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use

Zach Walsh[a,*], Robert Callaway[b], Lynne Belle-Isle[c,d], Rielle Capler[e], Robert Kay[f], Philippe Lucas[d], Susan Holtzman[a]

International Journal of Drug Policy 25 (2014) 691–699

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research paper

Barriers to access for Canadians who use cannabis for therapeutic purposes

Lynne Belle-Isle[a,b,*,1], Zach Walsh[c,1], Robert Callaway[d], Philippe Lucas[b], Rielle Capler[e], Robert Kay[f], Susan Holtzman[c]

Institute for Healthy Living and Chronic Disease Prevention

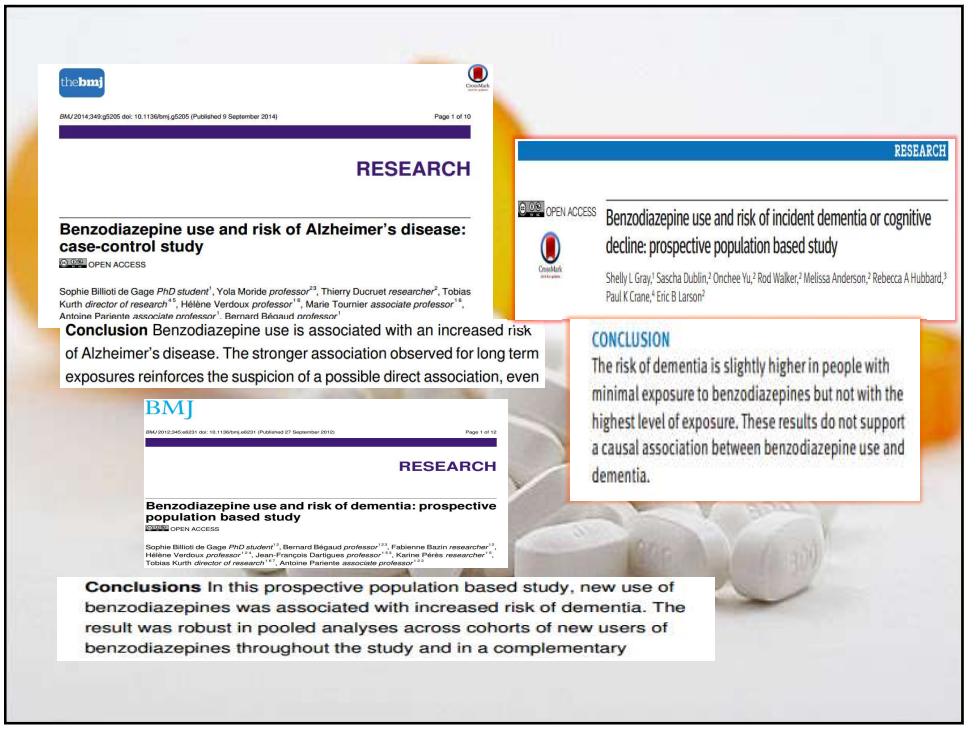
PARTNERS IN RESEARCH FOR BETTER HEALTH

53

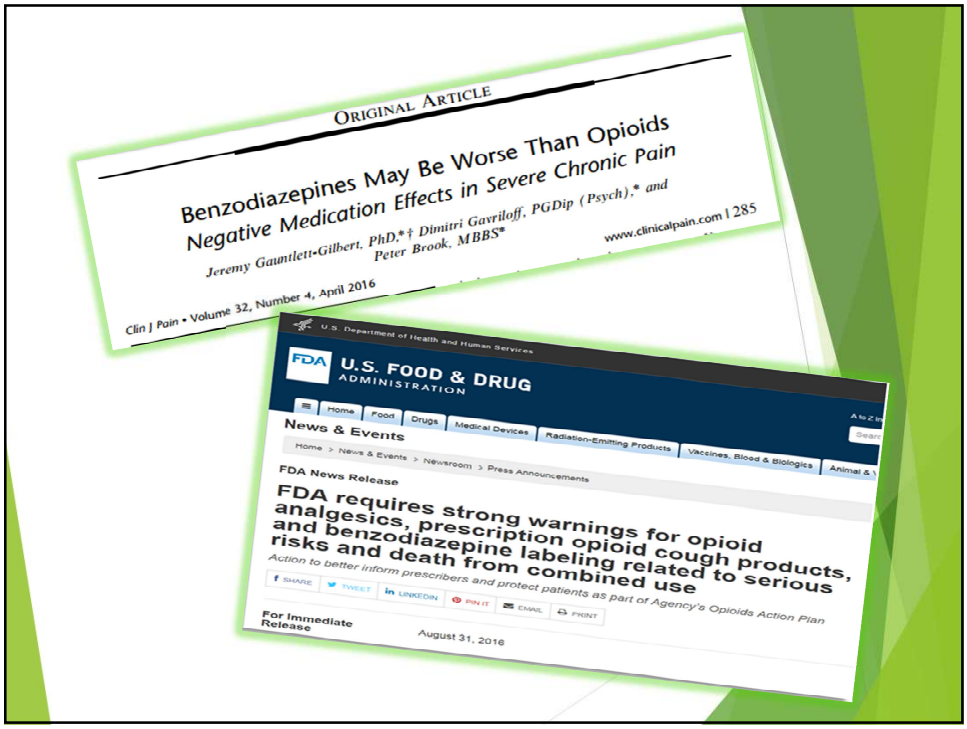
Cannabis & Mental Health

Cannabis Access for Medical Purposes Study (CAMPS)	N=628
Sleep	85%
Pain	82%
Anxiety	78%
Depression	66%
Appetite/ Weight	56%
Nausea	49%

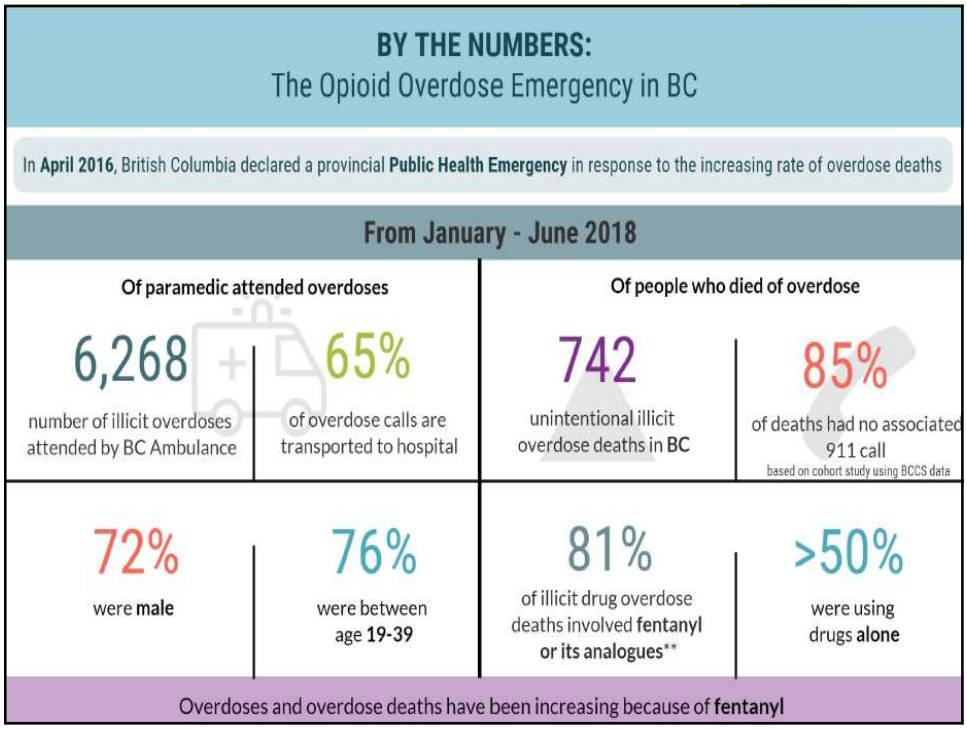
54


thebmj
BMJ 2014;349:g5205 doi: 10.1136/bmj.g5205 (Published 9 September 2014)
Page 1 of 10
RESEARCH
Benzodiazepine use and risk of Alzheimer's disease: case-control study
OPEN ACCESS
Sophie Billioti de Gage PhD student[1], Yola Moride professor[2,3], Thierry Ducruet researcher[3], Tobias Kurth director of research[1,5], Hélène Verdoux professor[1,6], Marie Tournier associate professor[1,6], Antoine Pariente associate professor[1], Bernard Bégaud professor[1]
Conclusion Benzodiazepine use is associated with an increased risk of Alzheimer's disease. The stronger association observed for long term exposures reinforces the suspicion of a possible direct association, even
RESEARCH
OPEN ACCESS
Benzodiazepine use and risk of incident dementia or cognitive decline: prospective population based study
Shelly L Gray,[1] Sascha Dublin,[2] Onchee Yu,[2] Rod Walker,[2] Melissa Anderson,[2] Rebecca A Hubbard,[3] Paul K Crane,[4] Eric B Larson[2]
CONCLUSION
The risk of dementia is slightly higher in people with minimal exposure to benzodiazepines but not with the highest level of exposure. These results do not support a causal association between benzodiazepine use and dementia.
BMJ
RESEARCH
Benzodiazepine use and risk of dementia: prospective population based study
OPEN ACCESS
Sophie Billioti de Gage PhD student[1], Bernard Bégaud professor[1,2], Fabienne Bazin researcher[1], Hélène Verdoux professor[1,2,3], Jean-François Dartigues professor[1,2,3], Karine Pérès researcher[1,3], Tobias Kurth director of research[1,4], Antoine Pariente associate professor[1,2,3]
Conclusions In this prospective population based study, new use of benzodiazepines was associated with increased risk of dementia. The result was robust in pooled analyses across cohorts of new users of benzodiazepines throughout the study and in a complementary

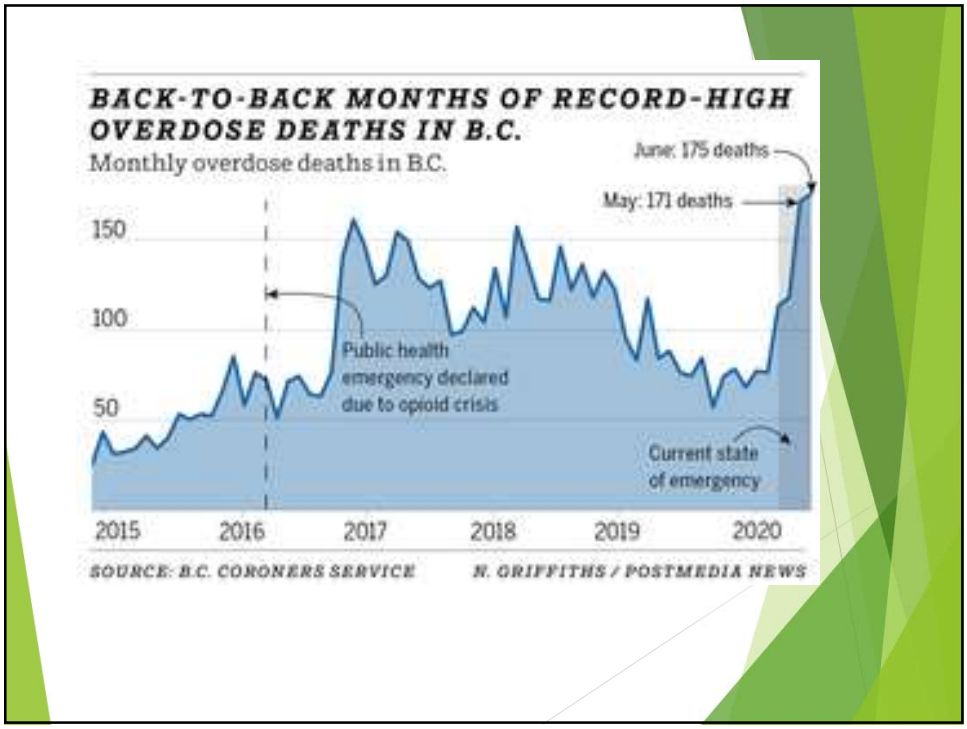
55


ORIGINAL ARTICLE
Benzodiazepines May Be Worse Than Opioids
Negative Medication Effects in Severe Chronic Pain
Jeremy Gauntlett-Gilbert, PhD,*† Dimitri Gavriloff, PGDip (Psych),* and Peter Brook, MBBS*
Clin J Pain • Volume 32, Number 4, April 2016
www.clinicalpain.com | 285
U.S. Department of Health and Human Services
FDA U.S. FOOD & DRUG ADMINISTRATION
Home Food Drugs Medical Devices Radiation-Emitting Products Vaccines, Blood & Biologics
News & Events
Home > News & Events > Newsroom > Press Announcements
FDA News Release
FDA requires strong warnings for opioid analgesics, prescription opioid cough products, and benzodiazepine labeling related to serious risks and death from combined use
Action to better inform prescribers and protect patients as part of Agency's Opioids Action Plan
For Immediate Release
August 31, 2016

56


BY THE NUMBERS:
The Opioid Overdose Emergency in BC
In April 2016, British Columbia declared a provincial Public Health Emergency in response to the increasing rate of overdose deaths
From January - June 2018
Of paramedic attended overdoses
6,268
number of illicit overdoses attended by BC Ambulance
65%
of overdose calls are transported to hospital
Of people who died of overdose
742
unintentional illicit overdose deaths in BC
85%
of deaths had no associated 911 call
based on cohort study using BCCS data
72%
were male
76%
were between age 19-39
81%
of illicit drug overdose deaths involved fentanyl or its analogues**
>50%
were using drugs alone
Overdoses and overdose deaths have been increasing because of fentanyl

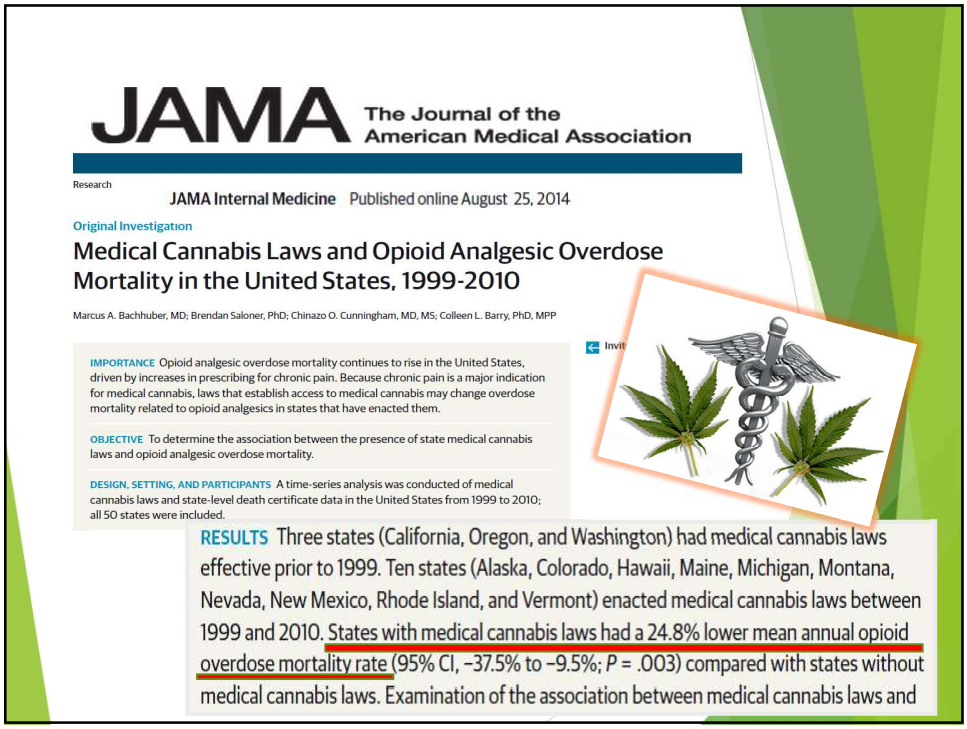
57


BACK-TO-BACK MONTHS OF RECORD-HIGH OVERDOSE DEATHS IN B.C.
Monthly overdose deaths in B.C.
June: 175 deaths
May: 171 deaths
150
100
50
Public health emergency declared due to opioid crisis
Current state of emergency
2015
2016
2017
2018
2019
2020
SOURCE: B.C. CORONERS SERVICE
N. GRIFFITHS / POSTMEDIA NEWS

58


Global NEWS
Okanagan
Change Location
TV News Programs
Newscasts & Videos
World Canada Local Politics Money Entertainment Health Lifestyle Tech Science Sports
HEALTH
More people using pot as substitute for pills and booze
By Kelly Hayes
Video Journalist Global News
Comments 14 Facebook 8.5k Twitter 99 Email
Drug and Alcohol REVIEW
Drug and Alcohol Review (2015)
DOI: 10.1111/dar.12323
Substituting cannabis for prescription drugs, alcohol and other substances among medical cannabis patients: The impact of contextual factors
PHILIPPE LUCAS[1], ZACH WALSH[2], KIM CROSBY[3], ROBERT CALLAWAY[4], LYNNE BELLE-ISLE[1,5], ROBERT KAY[6], RIELLE CAPLER[7] & SUSAN HOLTZMAN[8]

59


JAMA The Journal of the American Medical Association
Research
JAMA Internal Medicine Published online August 25, 2014
Original Investigation
Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010
Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD, MS; Colleen L. Barry, PhD, MPP
IMPORTANCE Opioid analgesic overdose mortality continues to rise in the United States, driven by increases in prescribing for chronic pain. Because chronic pain is a major indication for medical cannabis, laws that establish access to medical cannabis may change overdose mortality related to opioid analgesics in states that have enacted them.
OBJECTIVE To determine the association between the presence of state medical cannabis laws and opioid analgesic overdose mortality.
DESIGN, SETTING, AND PARTICIPANTS A time-series analysis was conducted of medical cannabis laws and state-level death certificate data in the United States from 1999 to 2010; all 50 states were included.
RESULTS Three states (California, Oregon, and Washington) had medical cannabis laws effective prior to 1999. Ten states (Alaska, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Mexico, Rhode Island, and Vermont) enacted medical cannabis laws between 1999 and 2010. States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate (95% CI, −37.5% to −9.5%; P = .003) compared with states without medical cannabis laws. Examination of the association between medical cannabis laws and

60

PRESCRIPTION DRUGS

By Ashley C. Bradford and W. David Bradford

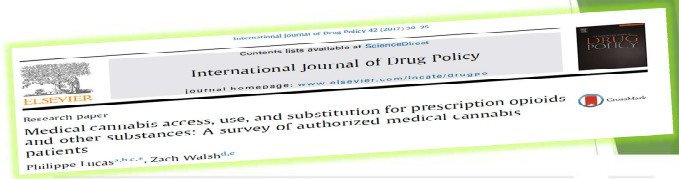
DOI: 10.1377/hlthaff.2015.1661
HEALTH AFFAIRS 35,
NO. 7 (2016): 1230–1236
©2016 Project HOPE—
The People-to-People Health
Foundation, Inc.

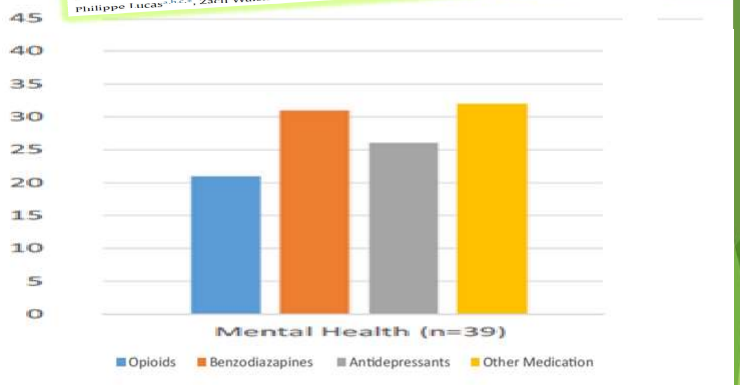
Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D

"…the use of prescription drugs … **fell significantly**, once a medical marijuana law was implemented. National **reductions** in Medicare program and enrollee spending when states implemented medical marijuana laws were estimated to be **$165.2 million per year**"

61

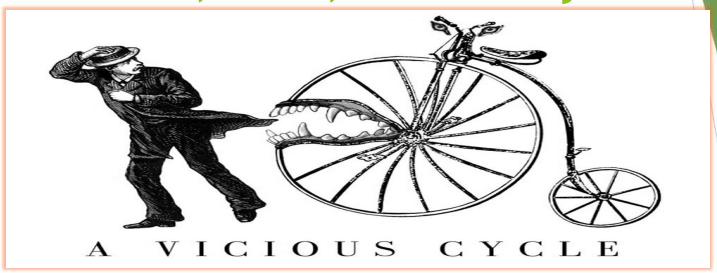
Substituting Cannabis





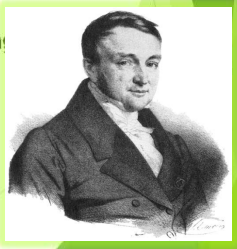
62

Cannabis, Pain, & Anxiety



"I saw in it (cannabis)a means of effectively combating the fixed ideas of depressives, disruptin the chain of their ideas, of unfocusing their attention …

Jacques-Joseph Moreau (1845)



63

Cannabis, mental health & pain

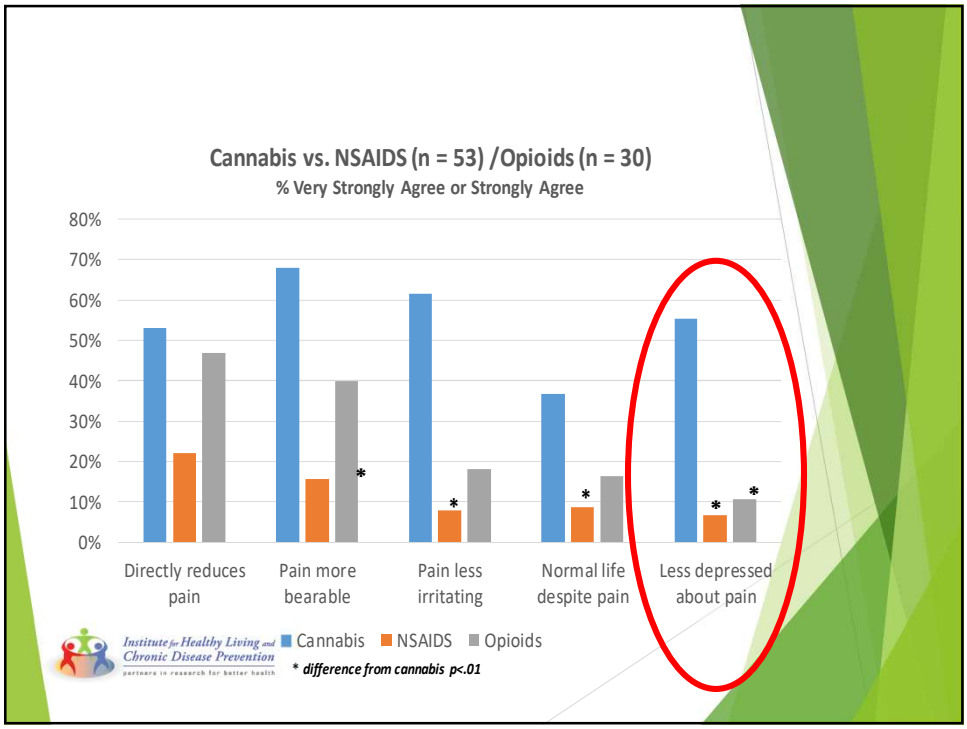
- Kam Shojania, MD - Arthritis Research Centre
- Cheryl Koehn - Arthritis Consumer Experts
- 264 individuals with arthritis
- Not required to have used medical cannabis
- Online and hard copies mailed out

Arthritis Consumer Experts™

Arthritis Research Centre of Canada
Arthrite-recherche Canada

Institute for Healthy Living and Chronic Disease Prevention

64



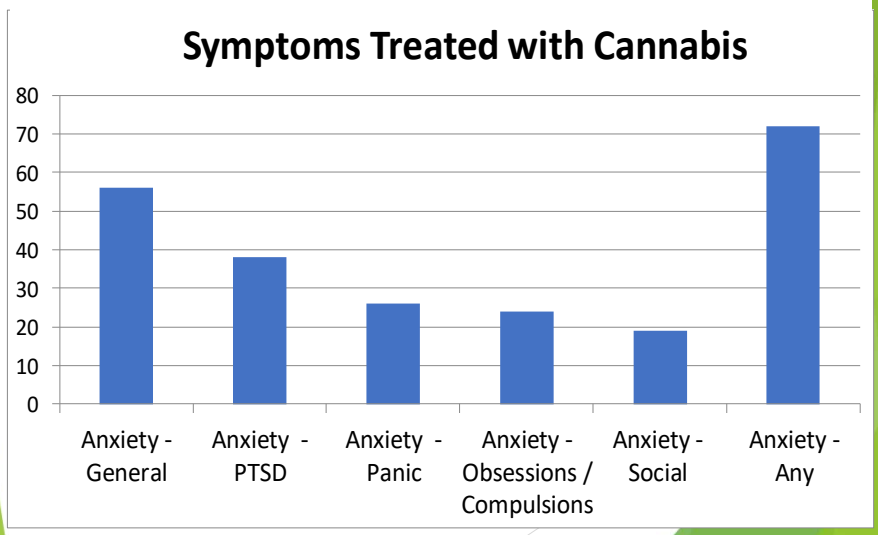
65

Cannabis, Anxiety, & Pain

- Cross-sectional, in person
- BeKind Medical Cannabis Dispensary – Kelowna, BC
- 68 self-selected current medical cannabis users who use cannabis to treat pain
- Collected Jan - Nov 2013
- Detailed examination of anxiety and related constructs

66

Cannabis, Anxiety, & Pain



67

Substituting cannabis for alcohol

- 67 university students
- Cannabis & alcohol use in past 6 months
- Aged 17-24 (median age 20), 57% female
- Preliminary results from

"Cannabis and alcohol substitution among young adults"
Walsh, Lucas, Lozenski & Crosby, *in prep*

68

Substituting cannabis for alcohol

- Top reasons for using cannabis over alcohol:
  1. Avoid hangovers - 27%
  2. Safer - 20%
  3. Prefer the feeling - 19%
- Top reasons for using alcohol over cannabis:
  1. Can use in public - 35%
  2. Legal - 24%
  3. Socially acceptable - 24%
  4. Effects are more predictable - 24%

69

Substituting cannabis for alcohol

UBC students (n=253)

When using cannabis	
Don't drink as quickly	71%
Don't drink as much	53%
Don't desire alcohol	34%
Crave alcohol	0%

Walsh, Crosby & Lucas, *in prep*

70

[*Journal of Law and Economics*, vol. 56 (May 2013)]

Medical Marijuana Laws, Traffic Fatalities, and Alcohol Consumption

D. Mark Anderson *Montana State University*
Benjamin Hansen *University of Oregon*
Daniel I. Rees *University of Colorado Denver*

Abstract

To date, 19 states have passed medical marijuana laws, yet very little is known about their effects. The current study examines the relationship between the legalization of medical marijuana and traffic fatalities, the leading cause of death among Americans ages 5–34. The first full year after coming into effect, legalization is associated with an 8–11 percent decrease in traffic fatalities. The impact of legalization on traffic fatalities involving alcohol is larger and estimated with more precision than its impact on traffic fatalities that do not involve alcohol. Legalization is also associated with sharp decreases in the price of marijuana and alcohol consumption, which suggests that marijuana and alcohol are substitutes. Because alternative mechanisms cannot be ruled out, the negative relationship between legalization and alcohol-related traffic fatalities does not necessarily imply that driving under the influence of marijuana is safer than driving under the influence of alcohol.

71

Addictive Behaviors 72 (2017) 138–143
Contents lists available at ScienceDirect
Addictive Behaviors
journal homepage: www.elsevier.com/locate/addictbeh

Intentional cannabis use to reduce crack cocaine use in a Canadian setting: A longitudinal analysis

M. Eugenia Socías[a,b], Thomas Kerr[a,b], Evan Wood[a,b], Huiru Dong[a], Stephanie Lake[a], Kanna Hayashi[a,b], Kora DeBeck[a,c], Didier Jutras-Aswad[d,e], Julio Montaner[a,b], M.-J. Milloy[a,b,c]

[a] British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada
[b] Department of Medicine, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada
[c] School of Public Policy, Simon Fraser University, 515 West Hastings Street – Suite 3271, Vancouver, BC V6B 5K3, Canada
[d] Research Center, Centre Hospitalier de l'Université de Montréal (CRCHUM), 900 Rue Saint-Denis, Montréal, QC, H2X 0A9, Canada
[e] Department of Psychiatry, Université de Montréal, C.P. 6128, Succursale Centre-ville, Montréal, QC H3C 3J7, Canada

Drug and Alcohol Review
Drug and Alcohol Review (March 2018), 37, 421–428
DOI: 10.1111/dar.12667

Cannabis use is associated with lower rates of initiation of injection drug use among street-involved youth: A longitudinal analysis

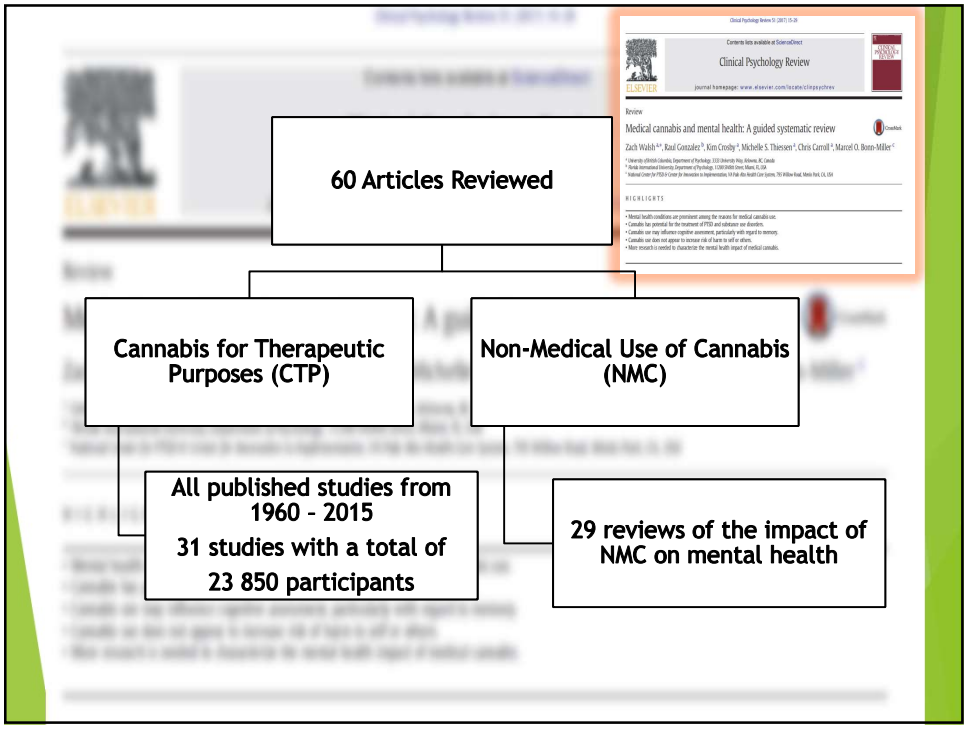
HUDSON REDDON[1,2], KORA DEBECK[1,3], MARIA EUGENIA SOCIAS[1,4], HUIRU DONG[1], EVAN WOOD[1,4], JULIO MONTANER[1,4], THOMAS KERR[1,4] & MICHAEL-JOHN MILLOY[1,4]

[1]*British Columbia Centre for Excellence in HIV/AIDS, Urban Health Research Initiative, St. Paul's Hospital, Vancouver, Canada,* [2]*Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Canada,* [3]*School of Public Policy, Simon Fraser University, Vancouver, Canada, and* [4]*Department of Medicine, University of British Columbia, St. Paul's Hospital, Vancouver, Canada*

72


Clinical Psychology Review 51 (2017) 15–29
Contents lists available at ScienceDirect
Clinical Psychology Review
journal homepage: www.elsevier.com/locate/clinpsychrev
Review
Medical cannabis and mental health: A guided systematic review
Zach Walsh [a,*], Raul Gonzalez [b], Kim Crosby [a], Michelle S. Thiessen [a], Chris Carroll [a], Marcel O. Bonn-Miller [c]
HIGHLIGHTS
• Mental health conditions are prominent among the reasons for medical cannabis use.
• Cannabis has potential for the treatment of PTSD and substance use disorders.
• Cannabis use may influence cognitive assessment, particularly with regard to memory
• Cannabis use does not appear to increase risk of harm to self or others.
• More research is needed to characterize the
LA WEEKLY
Marijuana Makes You Crazy, Says New Study (Yeah, Tell us Something we Don't Know)
TIME
Marijuana Appears to Benefit Mental Health: Study

73


60 Articles Reviewed
Cannabis for Therapeutic Purposes (CTP)
Non-Medical Use of Cannabis (NMC)
All published studies from 1960 - 2015
31 studies with a total of 23 850 participants
29 reviews of the impact of NMC on mental health

74

Overview - Anxiety

- Anxiety disorders - Overview
- Cannabis and general anxiety
- Cannabis and social anxiety disorder
- Cannabis substitution for benzodiazepines
- CBD
- Summary / conclusions

75

Generalized Anxiety Disorder

Associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months);

1. **Restlessness or feeling keyed up or on edge.**
2. Being easily fatigued.
3. Difficulty concentrating or mind going blank.
4. **Irritability.**
5. Muscle tension.
6. **Sleep disturbance.**

(American Psychiatric Association, 2013)

76

Generalized Anxiety Disorder

- Prevalence - 3% adults
- Female 2:1
- Many report lifelong anxiety and nervousness
- Median age of diagnosis is 30 - broad range
- chronic fluctuation between syndromal and subsyndromal
  - low rates of full remission
- 1/3 risk is genetic - overlap with neuroticism/ personality
- Most moderately to seriously disabled

(American Psychiatric Association, 2013)

77

Social Anxiety/ Phobia

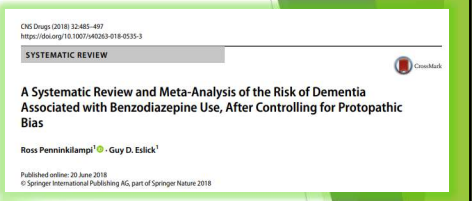
- The 12-month prevalence US & CND 7%. elsewhere .5-2.0%
- Females 1.5-2:1
- 75% onset between 8 and 15 years
- Approx 50% in North America seek treatment
  - after 15-20 years of experiencing symptoms.
- decreased well-being, employment, productivity, SES , QOL
- Comorbidity with depression

(American Psychiatric Association, 2013)

78

Treatment for anxiety

- Treated with both behavioral therapy, pharmacotherapy, or a combination.
- Cognitive behavioral therapy (CBT) tailored to specific d/o has strongest evidence
  - Barriers
- Pharmacotherapies- SSRI & SNRI
- Benzodiazepines are widely used in real-world clinical settings

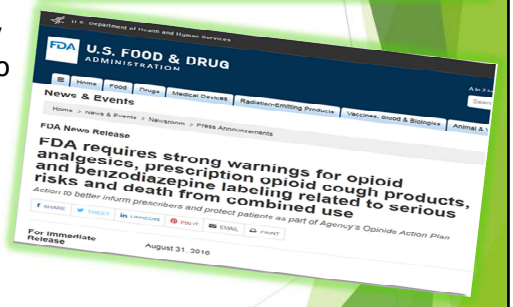

CNS Drugs (2018) 32:485–497
https://doi.org/10.1007/s40263-018-0535-3

SYSTEMATIC REVIEW

A Systematic Review and Meta-Analysis of the Risk of Dementia Associated with Benzodiazepine Use, After Controlling for Protopathic Bias

Ross Penninkilampi[1] · Guy D. Eslick[1]

Published online: 20 June 2018
© Springer International Publishing AG, part of Springer Nature 2018


U.S. FOOD & DRUG ADMINISTRATION

News & Events

FDA News Release

FDA requires strong warnings for opioid analgesics, prescription opioid cough products, and benzodiazepine labeling related to serious risks and death from combined use

Action to better inform prescribers and protect patients as part of Agency's Opioids Action Plan

For Immediate Release

August 31, 2016

79

Cannabis & Anxiety


International Journal of Drug Policy 24 (2013) 511–516

Contents lists available at ScienceDirect

International Journal of Drug Policy

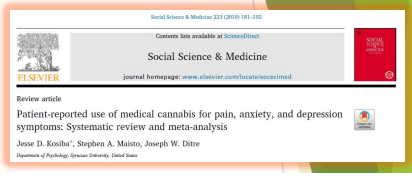
journal homepage: www.elsevier.com/locate/drugpo

Editors' choice

Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use

Zach Walsh[a,*], Robert Callaway[b], Lynne Belle-Isle[c,d], Rielle Capler[e], Robert Kay[f], Philippe Lucas[d], Susan Holtzman[g]

Cannabis Access for Medical Purposes Study (CAMPS)	N=628
Sleep	85%
Pain	82%
Anxiety	78%
Depression	66%
Appetite/ Weight	56%
Nausea	49%


Social Science & Medicine 233 (2019) 181–192

Contents lists available at ScienceDirect

Social Science & Medicine

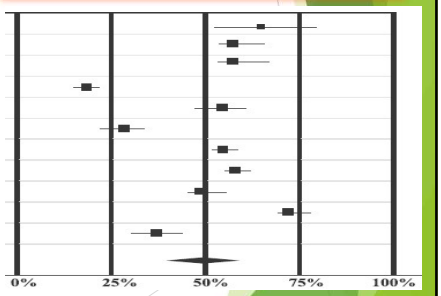
journal homepage: www.elsevier.com/locate/socscimed

Review article

Patient-reported use of medical cannabis for pain, anxiety, and depression symptoms: Systematic review and meta-analysis

Jesse D. Kosiba*, Stephen A. Maisto, Joseph W. Ditre

Department of Psychology, Syracuse University, United States



80

Human studies – Medical


Clinical Psychology Review

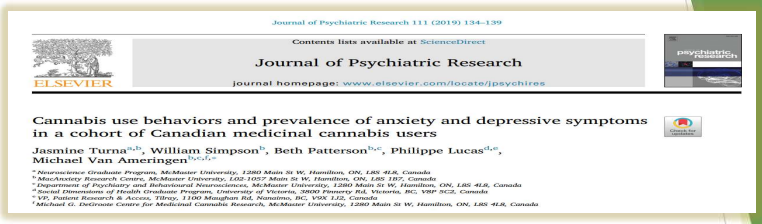
Review

Medical cannabis and mental health: A guided systematic review

Anxiety

- 8 Cross-sectional studies of medical
  - 8 reported relief of anxiety as a primary or secondary benefit
  - 1 reported anxiety returned after cessation of use
- 2 Reviews of non-medical
  - Small positive association between cannabis use and anxiety - no causation

81


Journal of Psychiatric Research 111 (2019) 134–139

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Cannabis use behaviors and prevalence of anxiety and depressive symptoms in a cohort of Canadian medicinal cannabis users

Jasmine Turna[a,b], William Simpson[b], Beth Patterson[b,c], Philippe Lucas[d,e], Michael Van Ameringen[b,c,f,*]

888/2032 (43.7%) reported authorization to treat anxiety symptoms

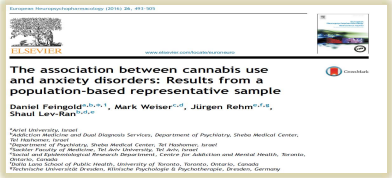
46% Generalized Anxiety Disorder
42% Social Anxiety Disorder
26% Panic Disorder/Agoraphobia
26% Major Depressive Disorder

63% met screening criteria for ≥1 disorder

92% - Cannabis improved symptoms	
1	Anxiety
2	Irritability
3	Sleep onset
4	Anxiety attack
5	Low mood
6	Muscle tension
7	Restlessness
8	Sleep interruption

82

Human studies – Harms?


The association between cannabis use and anxiety disorders: Results from a population-based representative sample

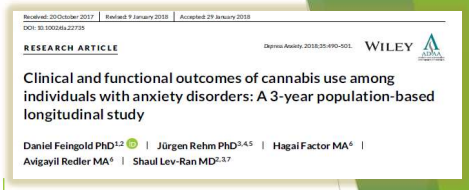
Daniel Feingold, Mark Weiser, Jürgen Rehm, Shaul Lev-Ran

Large longitudinal epidemiological study National Epidemiological Study of Alcohol and Related Conditions(NESARC)

3yrs & >30, 000 participants

Cannabis use was not associated with development of any anxiety disorder

Individuals with baseline panic disorder were more prone to initiate cannabis use at follow-up – medical?


RESEARCH ARTICLE

Clinical and functional outcomes of cannabis use among individuals with anxiety disorders: A 3-year population-based longitudinal study

Daniel Feingold PhD | Jürgen Rehm PhD | Hagai Factor MA | Avigayil Redler MA | Shaul Lev-Ran MD

NESARC focusing on social anxiety, panic disorder, generalized anxiety disorder, and specific phobias (N = 3,723).

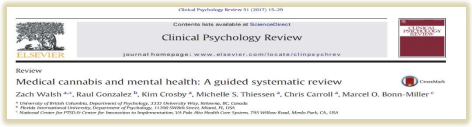
Compared cannabis users and non users in rates of remission, suicidality, general functioning, and quality of life

With control factors in analyses - no differences in outcome.

"poorer outcome of anxiety disorders among cannabis users may be attributed mainly to differences in baseline factors and not cannabis use."

83

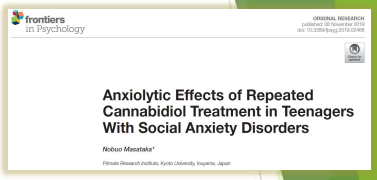
Human studies – SAD


Clinical Psychology Review

Medical cannabis and mental health: A guided systematic review

Zach Walsh, Raul Gonzalez, Kim Crosby, Michelle S. Thiessen, Chris Carroll, Marcel O. Bonn-Miller

- Socially anxious > cannabis use to relieve symptoms than individuals with other anxiety d/o
- Nonmedical cannabis use among the socially anxious may be associated with cannabis-related problems
  - SAD typically precedes the development of problematic cannabis use
- CBD use is associated with:
  - decreased subjective anxiety among SAD patients
  - decreased cognitive impairment and anxiety in a simulated public speaking task


frontiers in Psychology

Anxiolytic Effects of Repeated Cannabidiol Treatment in Teenagers With Social Anxiety Disorders

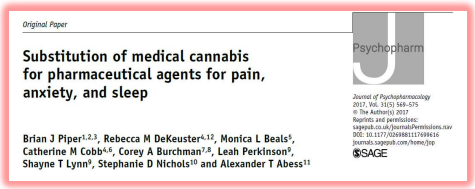
Nobuo Masataka

- 300mg CBD/ day – 4 weeks
- 18-19 y/o w/ SAD and Avoidant PD
  - (N= 17 CBD v 20 placebo)
- Significant reductions in anxiety in the CBD group

"many of the participants treated with CBD became positive in their attitude toward seeking treatment."

84

Cannabis – benzodiazepine substitution



Original Paper

Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep

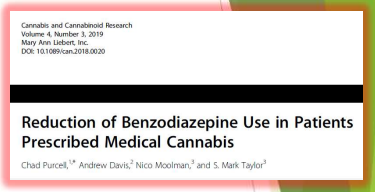
Psychopharm

Journal of Psychopharmacology 2017, Vol. 31(5) 569–575 © The Author(s) 2017 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/0269881117699616 journals.sagepub.com/home/jop

SAGE

Brian J Piper[1,2,3], Rebecca M DeKeuster[4,12], Monica L Beals[5], Catherine M Cobb[4,6], Corey A Burchman[7,8], Leah Perkinson[9], Shayne T Lynn[9], Stephanie D Nichols[10] and Alexander T Abess[11]

- Dispensary members (*n* = 1513) survey
- 72% decreased use of benzodiazepines
  - Over half decreased "a lot"
- 77% reduced opioids
- 38% antidepressants



Cannabis and Cannabinoid Research
Volume 4, Number 3, 2019
Mary Ann Liebert, Inc.
DOI: 10.1089/can.2018.0020

Reduction of Benzodiazepine Use in Patients Prescribed Medical Cannabis

Chad Purcell,[1,*] Andrew Davis,[2] Nico Moolman,[3] and S. Mark Taylor[3]

- Benzodiazepines using patients (n = 146) from a cannabis clinic
- 30% discontinued benzodiazepines after 2-month
- 45% after 4 & 6 months

85

Substituting Cannabis - Polypharmacy

International Journal of Drug Policy 42 (2017) 30–35

Contents lists available at ScienceDirect

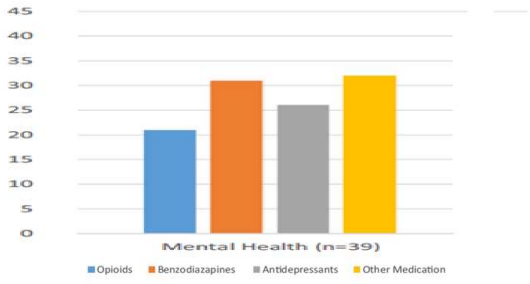
International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research paper

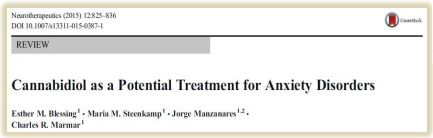
Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients

Philippe Lucas[a,b,c,*], Zach Walsh[d,e]

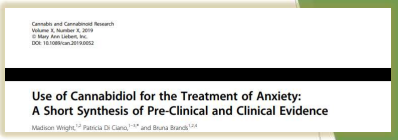


86

CBD & Anxiety


Neurotherapeutics (2015) 12:825–836
DOI 10.1007/s13311-015-0387-1
REVIEW
Cannabidiol as a Potential Treatment for Anxiety Disorders
Esther M. Blessing[1] · Maria M. Steenkamp[1] · Jorge Manzanares[1,2] · Charles R. Marmar[1]

- CBD's efficacy in reducing anxiety is relevant to multiple disorders (e.g. GAD, PD, SAD)
- Anxiolytic effects due to CB1Rs and 5-HT1ARs
- Human experimental findings:
  - anxiolytic
  - a lack of anxiogenic effects
  - minor sedation
  - excellent safety profile
- Further studies required
  - chronic dosing
  - clinical populations


Cannabis and Cannabinoid Research
Volume X, Number X, 2019
© Mary Ann Liebert, Inc.
DOI: 10.1089/can.2019.0052
Use of Cannabidiol for the Treatment of Anxiety: A Short Synthesis of Pre-Clinical and Clinical Evidence
Madison Wright,[1,2] Patricia Di Ciano,[1,3,4] and Bruna Brands[1,2,3]

- Pre-Clinical
  - CBD anxiolytic at low/intermediate doses
  - Effects similar to diazepam in rodents
- Clinical
  - A single dose reduces experimental anxiety
  - Impacted anxiety-related brain structures
- Retrospective studies
  - CBD reduced anxiety symptoms in patients with anxiety disorders.

87

Cannabis & Anxiety – Summary

- Anxiety is among the most frequently cited reasons for using medical cannabis
- Patients report relief of symptoms including irritability, agitation, sleep
- Cannabis use does not appear to lead to development of anxiety d/o
- Cannabis use does not appear to worsen outcomes among those with anxiety d/o
  - BUT anxiety can be a symptom of cannabis overdose and withdrawal
- Cannabis is being used as a substitute for benzodiazepines
  - Comparative efficacy trials required
- Preliminary evidence suggests that CBD isolate has anxiolytic effects independent of THC or herbal cannabis
- No RCT has examined the effectiveness of cannabis versus placebo

88

Overview - Depression

- Mood disorders - background
- Cannabis and mood
- Cannabis and motivation
- Preclinical studies
- Among medical users
- Bipolar
- Mechanisms
- Summary & conclusions

89

Major Depressive Disorder

- 7% - prevalence
- Negative Affect is a well-established risk factor –
  - Traits/ personality
  - Refractory?
- Among largest contributors to non-fatal health loss
- Annual cost >200B$ in US
- High comorbidity
  - Anxiety
  - Substance use – including cannabis
- Extant treatments – behavioral therapy and pharmacotherapy
- High proportion of US adults prescribed antidepressants
  - adverse effects
  - questionable effectiveness


Jakobsen et al. BMC Psychiatry (2017) 17:58
DOI 10.1186/s12888-016-1173-2

BMC Psychiatry

RESEARCH ARTICLE Open Access

Selective serotonin reuptake inhibitors versus placebo in patients with major depressive disorder. A systematic review with meta-analysis and Trial Sequential Analysis

Janus Christian Jakobsen[1,2*], Kiran Kumar Katakam[1], Anne Schou[1], Signe Gade Hellmuth[1], Sandra Ebjerg Stallknecht[1], Katja Leth-Møller[1], Maria Iversen[1], Marianne Bjerrum Bankel[1], Iggaannguaq Juhl Petersen[1], Sarah Louise Klingenberg[1], Jesper Krogh[3], Sebastian Elgaard Ebert[1], Anne Timm[1], Jane Lindschou[1] and Christian Gluud[1]

"Our results show that the harmful effects of SSRIs versus placebo for major depressive disorder seem to outweigh any potentially small beneficial effects."

90

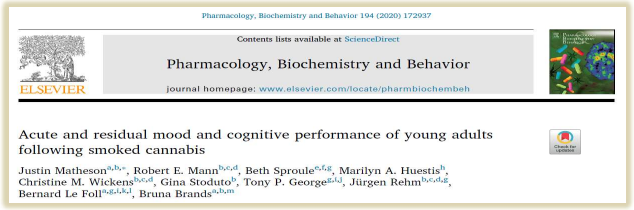
Major Depression

- 1. Depressed mood most of the day, nearly every day*
- 2. Diminished interest or pleasure in all, or almost all, activities*
- 3. Significant weight loss when not dieting or weight gain
- 4. Insomnia or hypersomnia nearly every day.
- 5. Psychomotor agitation or retardation
- 6. Fatigue or loss of energy
- 7. Feelings of worthlessness or excessive or inappropriate guilt
- 8. Diminished ability to think or concentrate, or indecisiveness
- 9. Recurrent thoughts of death / suicidal ideation

(American Psychiatric Association, 2013)

91

Cannabis & Depression - Mood


Pharmacology, Biochemistry and Behavior 194 (2020) 172937

Contents lists available at ScienceDirect

Pharmacology, Biochemistry and Behavior

journal homepage: www.elsevier.com/locate/pharmbiochembeh

ELSEVIER

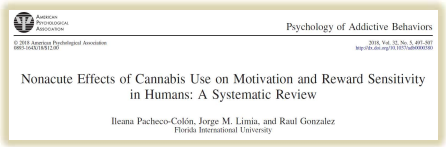
Acute and residual mood and cognitive performance of young adults following smoked cannabis

Justin Matheson[a,b,*], Robert E. Mann[b,c,d], Beth Sproule[e,f,g], Marilyn A. Huestis[h], Christine M. Wickens[b,c,d], Gina Stoduto[b], Tony P. George[g,i,j], Jürgen Rehm[b,c,d,g], Bernard Le Foll[a,g,i,k,l], Bruna Brands[a,b,m]

- Healthy adults (n=91) – pre, 1h, 24h, 48h
  - smoked 12.5% THC cannabis vs placebo
- 1h - Increased Arousal and Positive Mood, Friendliness, Elation, Confusion
- 24h - Increases in Friendliness and Elation for 24 h.
- No evidence of residual cognitive impairment.

92

Cannabis & Depression - Motivation


Psychology of Addictive Behaviors

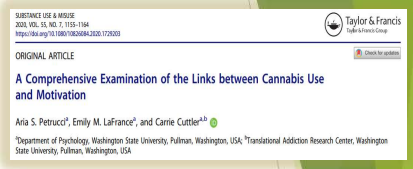
Nonacute Effects of Cannabis Use on Motivation and Reward Sensitivity in Humans: A Systematic Review

Ileana Pacheco-Colón, Jorge M. Limia, and Raul Gonzalez
Florida International University

(a) Decreased motivation among cannabis users?
- Partial support
  - Lack of control – depression, personality
  - Inconsistent definitions of motivation

(b) Is lack of motivation specific to use of cannabis?
- Equivocal – evidence supports general substance use

(c) Is it a causal relationship?
- 2 longitudinal studies
  - Long term CU associated with lower NA activity in reward anticipation
  - CU associated with later lower self efficacy
  - Neuroimaging mixed on striatal reward sensitivity


SUBSTANCE USE & MISUSE
2020, VOL. 55, NO. 7, 1155–1164

Taylor & Francis

ORIGINAL ARTICLE

A Comprehensive Examination of the Links between Cannabis Use and Motivation

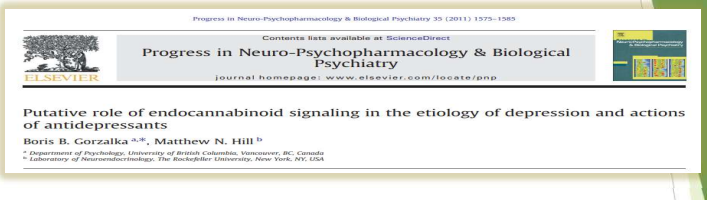
Aria S. Petrucci, Emily M. LaFrance, and Carrie Cuttler

Department of Psychology, Washington State University, Pullman, Washington, USA; Translational Addiction Research Center, Washington State University, Pullman, Washington, USA

- Small associations between various aspects of cannabis use and motivation
- Attributable to differences in depression, substance use, and personality
- Relationships between cannabis misuse and "apathy" remained after controls

93

Cannabis & Depression - Preclinical


Progress in Neuro-Psychopharmacology & Biological Psychiatry 35 (2011) 1575–1585

Contents lists available at ScienceDirect

Progress in Neuro-Psychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp

Putative role of endocannabinoid signaling in the etiology of depression and actions of antidepressants

Boris B. Gorzalka, Matthew N. Hill

- Endocannabinoid signaling deficiencies can:
  - produce a preclinical "depressive-like" phenotype
  - induce depression symptoms in humans
  - clinical depression populations have reduced levels of circulating endocannabinoids
  - could be involved in the generation or maintenance of a depressive episode
- Endocannabinoid signaling facilitation can:
  - reproduce behavioral and biochemical effects of conventional antidepressants
  - impact the neuroadaptive effects of antidepressant treatments

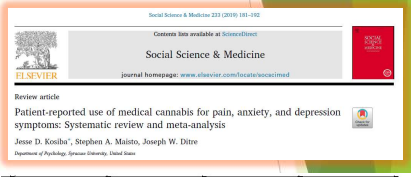
94

Cannabis & Depression


International Journal of Drug Policy

Editors' choice

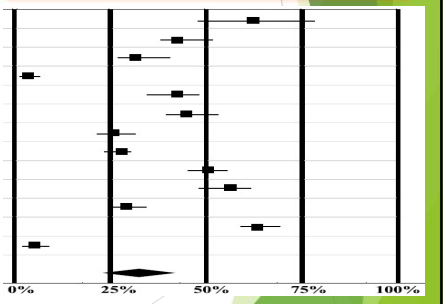
Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use


Social Science & Medicine

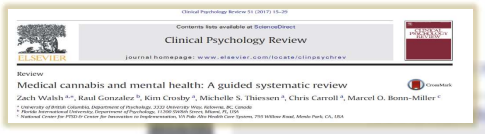
Review article

Patient-reported use of medical cannabis for pain, anxiety, and depression symptoms: Systematic review and meta-analysis

Cannabis Access for Medical Purposes Study (CAMPS)	N=628
Sleep	85%
Pain	82%
Anxiety	78%
Depression	66%
Appetite/ Weight	56%
Nausea	49%



95


Clinical Psychology Review

Review

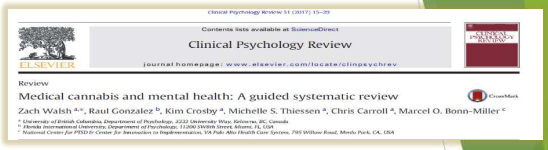
Medical cannabis and mental health: A guided systematic review

Depression

- 9 Cross-sectional studies of therapeutic
  - 7 noted mood improvement
  - 1 reported positive association between depression severity and problematic cannabis use
- 4 Reviews of nonmedical
  - Small positive association between cannabis and depression - no causation

96

Cannabis & Bipolar Disorder


Clinical Psychology Review

Review

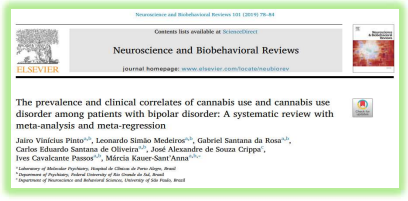
Medical cannabis and mental health: A guided systematic review

Zach Walsh, Raul Gonzalez, Kim Crosby, Michelle S. Thiessen, Chris Carroll, Marcel O. Bonn-Miller

- Anecdotal reports suggest that some individuals use cannabis to effectively treat symptoms of bipolar disorder (BD)
- Narrative review suggested potential for managing manic and depressive symptoms
- Evidence of improved neurocognitive functioning in BD patients who use cannabis
- Reviews concluded that non-medical cannabis use among those with BD may:
  - prolong or worsen manic states
  - increased odds of suicide attempts
  - earlier age of BD onset
  - psychosis
  - more severe course of illness

97

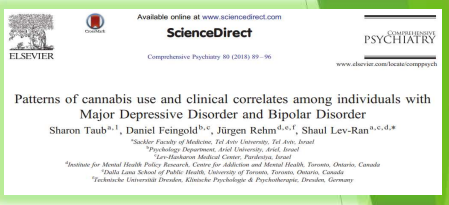
Cannabis & Bipolar Disorder


Neuroscience and Biobehavioral Reviews

The prevalence and clinical correlates of cannabis use and cannabis use disorder among patients with bipolar disorder: A systematic review with meta-analysis and meta-regression

Jairo Vinícius Pinto, Leonardo Simão Medeiros, Gabriel Santana da Rosa, Carlos Eduardo Santana de Oliveira, José Alexandre de Souza Crippa, Ives Cavalcante Passos, Márcia Kauer-Sant'Anna

- 35 studies (n=51,756; female: 60%),
- 24% cannabis use among Bipolar D/O
- Cannabis users were younger at first episode
- More lifetime suicide attempts
- More lifetime psychotic symptoms
- No differences in:
  - rapid cycling
  - comorbid anxiety disorders


Available online at www.sciencedirect.com

ScienceDirect

Comprehensive Psychiatry 80 (2018) 89–96

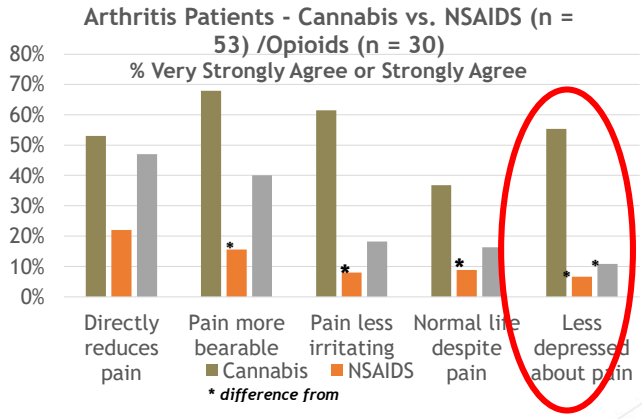
Patterns of cannabis use and clinical correlates among individuals with Major Depressive Disorder and Bipolar Disorder

Sharon Taub, Daniel Feingold, Jürgen Rehm, Shaul Lev-Ran

- Compared Bipolar to Major Depression
- BPD > frequency and quantity cannabis
- BPD> criteria for CUDs
- No differences in associations:
  - rates of other co-morbid psychiatric d/o
  - treatment utilization
  - suicidality

98

Substituting Cannabis - Pain



Walsh, Crosby et al,. *In prep*

99

Cannabis and Depression - Summary

- Endocannabinoid system implicated in depression
- Mood improvement is a frequently cited motive among medical cannabis users
- Cannabis produces short term improvements in mood
- Evidence is mixed with regard to reduction in motivation
- Cannabis use is prevalent among those with bipolar depression
  - Similar outcomes to major depression
  - Some additional cautions regarding psychosis risk
- Cannabis may be particularly helpful for relieving negative mood in the context of chronic pain

100

Withdrawal

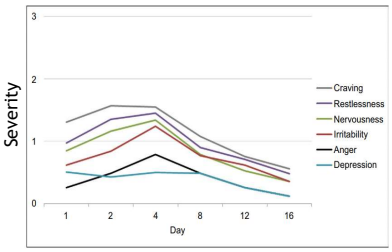
Substance Abuse and Rehabilitation
Dovepress
REVIEW

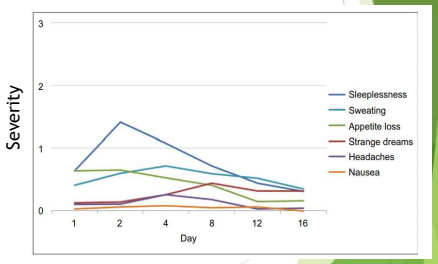
The cannabis withdrawal syndrome: current insights

Udo Bonnet[1,2]
Ulrich W Preuss[3,4]

[1]Department of Psychiatry, Psychotherapy and Psychosomatic Medicine, Evangelisches Krankenhaus Castrop-Rauxel, Academic Teaching Hospital of the University of Duisburg-Essen, Castrop-Rauxel,

This article was published in the following Dove Press journal:
Substance Abuse and Rehabilitation
27 April 2017
Number of times this article has been viewed





101

Cannabis Anxiolytics & Antidepressants

Received: 6 March 2017 | Revised: 30 May 2017 | Accepted: 1 June 2017
DOI: 10.1002/da.22664
REVIEW
WILEY

Is cannabis treatment for anxiety, mood, and related disorders ready for prime time?

Jasmine Turna BSc, PhD(c)[1,2] | Beth Patterson BScN, MSc[1,3] | Michael Van Ameringen MD, FRCPC[1,3,4]

- Extant treatment evidence is a few small, primarily single-dose studies.
- Not whole plant

"...it may be difficult to objectively place cannabis in the armamentarium of psychopharmacological treatments until further research is conducted and treatment guidelines developed"

102

Overview - Sleep

- Sleep disorders - background
- THC, CBD and sedation
- Cultivars and terpenes
- Preclinical research
- Clinical research
- Summary / conclusions

103

Cannabis and Insomnia

- Insomnia:
  - clinical feature
  - risk factor
  - residual symptom
- Difficult to determine the precise nature of relationship
- Initial insomnia - sleep onset
- Middle insomnia - sleep maintenance
- Late insomnia - early-morning awakening
- Sleep maintenance is the most common single symptom
- Combination is the most common overall.

(American Psychiatric Association, 2013)

104

Insomnia Disorder

- Most prevalent of all sleep disorders
- One-third of adults report insomnia symptoms
- Primary care -10%-20% complain of significant insomnia symptoms
- Females 1.4:1
- Situational / acute lasts a few days or a few weeks
  - often with life events or changes in schedules /environment
  - may persist possibly because of conditioning factors and arousal
  - Precipitating factors may differ from perpetuating
- Decreased attention and concentration - related to higher rates of accidents

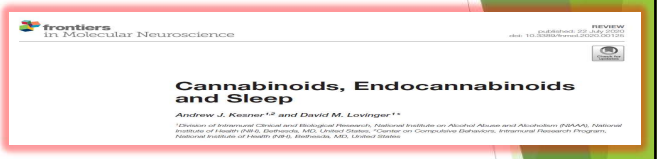
105

Extant treatment

- Behavioral interventions
- Sleep hygiene
- Benzodiazepines
- Non-benzo benzo agonists
  - Z-drugs
- Antihistamines
- Valerian
- Melatonin
- Magnesium
- Kava

106

Cannabis and sleep - preclinical


frontiers in Molecular Neuroscience

REVIEW

Cannabinoids, Endocannabinoids and Sleep

Andrew J. Kesner[1,2] and David M. Lovinger[1]*

- Endocannabinoids are important in sleep and sleep neurophysiology
- Sleep patterns clearly altered by cannabinoid drugs
- Cannabis /THC
  - decreased sleep onset latency,
  - decreased waking after sleep onset
  - increased slow-wave sleep and decreased REM sleep

107

Cannabis and sleep


Contents lists available at ScienceDirect

International Journal of Drug Policy

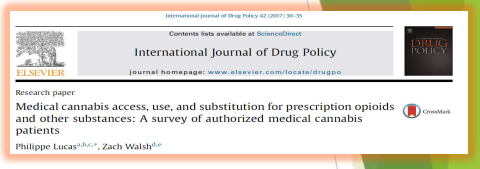
journal homepage: www.elsevier.com/locate/drugpo

Editors' choice

Cannabis for therapeutic purposes: Patient characteristics, access, and reasons for use

Zach Walsh, Robert Callaway, Lynne Belle-Isle, Rielle Capler, Robert Kay, Philippe Lucas, Susan Holtzman

Cannabis Access for Medical Purposes Study (CAMPS)	N=628
Sleep	85%
Pain	82%
Anxiety	78%
Depression	66%
Appetite/ Weight	56%
Nausea	49%


Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research paper

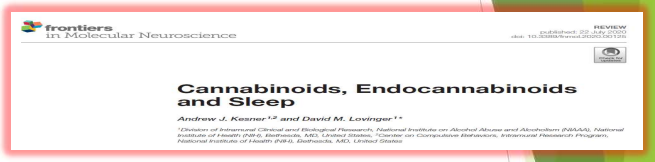
Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients

Philippe Lucas, Zach Walsh

Licensed producer survey	N=271
Pain	73%
Stress	60%
Insomnia	57%
Depression	46%
Headache	32%

108

Cannabis and sleep


frontiers in Molecular Neuroscience

REVIEW

Cannabinoids, Endocannabinoids and Sleep

Andrew J. Kesner[1,2] and David M. Lovinger[1]*

- Patients may decrease their use of pharmaceutical sleep medication
- Relatively rapid tolerance with regular use
- Withdrawal/ cessation associated with:
  - Decreases in total sleep time
  - Decreased sleep efficiency
  - Increased Latency to sleep onset
  - Increased wake after sleep

109

Cannabis and sleep


Sleep Medicine Reviews 18 (2014) 477–487

Contents lists available at ScienceDirect

Sleep Medicine Reviews

journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

The effects of cannabinoid administration on sleep: a systematic review of human studies

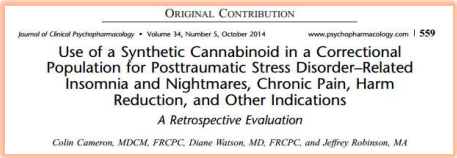
Peter J. Gates*, Lucy Albertella, Jan Copeland

National Cannabis Prevention and Information Centre, UNSW Medicine, Australia

- Studies are flawed
- Cannabis use associated with decrease in slow wave sleep & increase in stage 2
- No effect on total sleep time.
- Reduced disturbance & better sleep quality with a medical condition (e.g. pain, spasticity, PTSD)
  - Secondary effects of cannabinoids
- More research needed on dose

110

Cannabis & nightmares


ORIGINAL CONTRIBUTION

Journal of Clinical Psychopharmacology • Volume 34, Number 5, October 2014 www.psychopharmacology.com | 559

Use of a Synthetic Cannabinoid in a Correctional Population for Posttraumatic Stress Disorder–Related Insomnia and Nightmares, Chronic Pain, Harm Reduction, and Other Indications

A Retrospective Evaluation

Colin Cameron, MDCM, FRCPC, Diane Watson, MD, FRCPC, and Jeffrey Robinson, MA

Cross sectional / retrospective

Reduced PTSD symptoms

Improved sleep & nightmares

Discontinuation of meds (e.g. opioids, benzos)


Addictive Behaviors 50 (2015) 176–181

Contents lists available at ScienceDirect

Addictive Behaviors

Short Communication

Cannabis species and cannabinoid concentration preference among sleep-disturbed medicinal cannabis users

Katherine A. Belendiuk [a], Kimberly A. Babson [b], Ryan Vandrey [c], Marcel O. Bonn-Miller [b,d,e,f,*]

Dispensary sample

n = 163 – 81 insomnia & 14 nightmare

Reported "sativa" preference for reduced nightmares

Higher CBD preference for insomnia

Small trial from PTSD clinic (n=10)

Reduced nightmares

General clinical improvement


Psychoneuroendocrinology (2015) 51, 585–588

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/psyneuen

The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: A preliminary randomized, double-blind, placebo-controlled cross-over design study

Rakesh Jetly [a,*], Alexandra Heber [a], George Fraser [b], Denis Boisvert [c]

111

Cannabis and sleep – Summary

- Clear role for endocannabinoid system in sleep
- Use for sleep disturbance is common among medical users
- May be most effective for sleep in the context of other symptoms
  - Pain, PTSD
- Cannabis withdrawal involves sleep disturbance
- Nabilone reduces nightmares
- Preliminary evidence of high-CBD cannabis preference for insomnia
- More research needed

112

Overview -Schizophrenia

- Prevalence & consequences
- Psychosis and cannabis – History
  - recent revival
- Preclinical
- Human studies – reviewed
- CBD and psychosis
- Latest findings
- Causal or co-occurring –
  - A detailed looks at competing hypotheses
- Summary & conclusions

113

Schizophrenia - Prevalence

- Prevalence (w/psychotic disorders) in the U.S. 0.25 - 0.64%; international (non-institutionalized) 0.33 - 0.75%

- A major causes of disability despite relatively low prevalence.

- Approximately half of individuals with schizophrenia have co-occurring mental and/or behavioral health disorders.

- Co-occurring medical conditions contribute to excess early mortality.

(American Psychiatric Association, 2013)

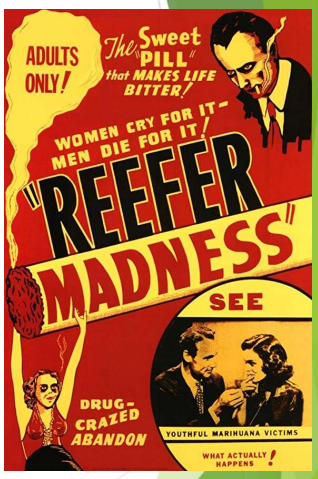
114

Cannabis and madness

"The deleterious, even vicious, qualities of the drug render it highly dangerous to the mind and body upon which it operates to destroy the will, cause one to lose the power of connected thought, producing imaginary delectable situations and gradually weakening the physical powers.

Its use frequently leads to insanity."

Harry Anslinger, 1937
1st Commissioner of the Federal Bureau of Narcotics



115

Cannabis and madness

FEBRUARY 14, 2019

RESOURCE

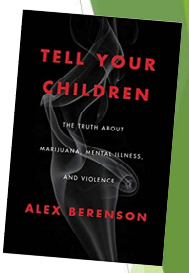
We are the Drug Policy Alliance.

Letter from Scholars and Clinicians who Oppose Junk Science about Marijuana

When research is misrepresented to uphold and perpetuate the worst myths about people of color and people with mental illness, we are required to speak up.

We urge policymakers and the public to rely on scientific evidence, not flawed pop science and ideological polemics, in formulating their opinions about marijuana legalization.

https://www.drugpolicy.org/resource/letter-scholars-and-clinicians-who-oppose-junk-science-about-marijuana



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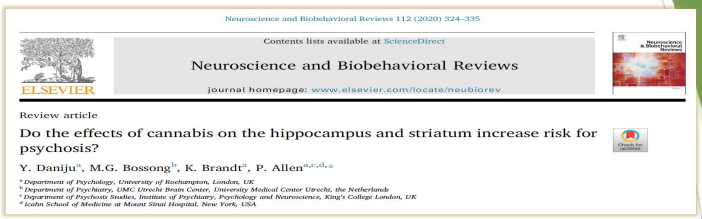
Preclinical



Neuroscience and Biobehavioral Reviews 112 (2020) 324–335

Contents lists available at ScienceDirect

Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

Review article

Do the effects of cannabis on the hippocampus and striatum increase risk for psychosis?

Y. Daniju[a], M.G. Bossong[b], K. Brandt[a], P. Allen[a,c,d,*]

[a] Department of Psychology, University of Roehampton, London, UK
[b] Department of Psychiatry, UMC Utrecht Brain Center, University Medical Center Utrecht, the Netherlands
[c] Department of Psychosis Studies, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK
[d] Icahn School of Medicine at Mount Sinai Hospital, New York, USA

Review of animal studies examining leading animal model of psychosis

<u>Proposal:</u>

Psychosis develops due to of hippocampal hyperactivity ->leading to elevated striatal dopamine

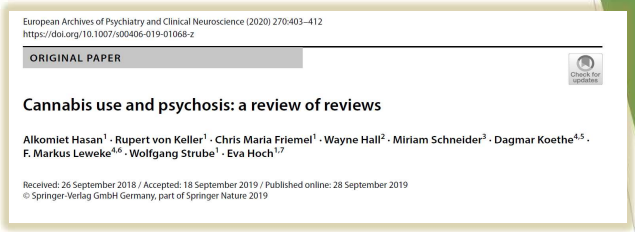
<u>Conclusions:</u>

Cannabis impacts hippocampal function

Can't conclude that this drives psychosis via striatal dopamine

117

Clinical



European Archives of Psychiatry and Clinical Neuroscience (2020) 270:403–412
https://doi.org/10.1007/s00406-019-01068-z

ORIGINAL PAPER

Cannabis use and psychosis: a review of reviews

Alkomiet Hasan[1] · Rupert von Keller[1] · Chris Maria Friemel[1] · Wayne Hall[2] · Miriam Schneider[3] · Dagmar Koethe[4,5] · F. Markus Leweke[4,6] · Wolfgang Strube[1] · Eva Hoch[1,7]

Received: 26 September 2018 / Accepted: 18 September 2019 / Published online: 28 September 2019
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

1 - Does the prevalence of psychotic disorders differ according to cannabis use?

2- Do cannabis users have earlier onsets of psychotic illnesses?

3- Differences between cannabis users and non-users with psychotic illnesses?

4- Biological link between cannabis use of and the development of psychosis?

Largest meta-analyses n = 66,816 participants & and the largest systematic review 113,802 participants

(American Psychiatric Association, 2013)

118

Clinical

European Archives of Psychiatry and Clinical Neuroscience (2020) 270:403–412
https://doi.org/10.1007/s00406-019-01068-z

ORIGINAL PAPER

Cannabis use and psychosis: a review of reviews

Alkomiet Hasan[1] · Rupert von Keller[1] · Chris Maria Friemel[1] · Wayne Hall[2] · Miriam Schneider[3] · Dagmar Koethe[4,5] · F. Markus Leweke[4,6] · Wolfgang Strube[1] · Eva Hoch[1,7]

Received: 26 September 2018 / Accepted: 18 September 2019 / Published online: 28 September 2019

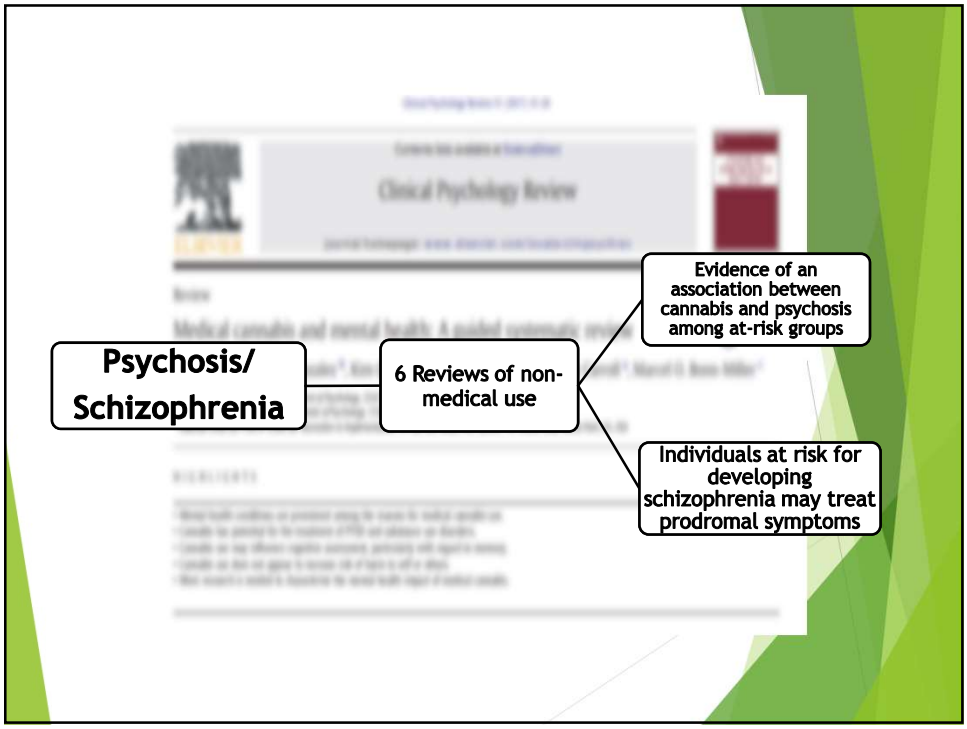
1 - Does the prevalence of psychotic disorders differ according to cannabis use?
YES - Dose-dependent

2- Do cannabis users have earlier onsets of psychotic illnesses?
YES - 2-3 years earlier

3- Differences between cannabis users and non-users with psychotic illnesses?
MIXED – may worsen positive symptoms, relapse, hospitalizations – NOT duration, suicidality

4- Biological link between cannabis use of and the development of psychosis?
NO clear relationship

119



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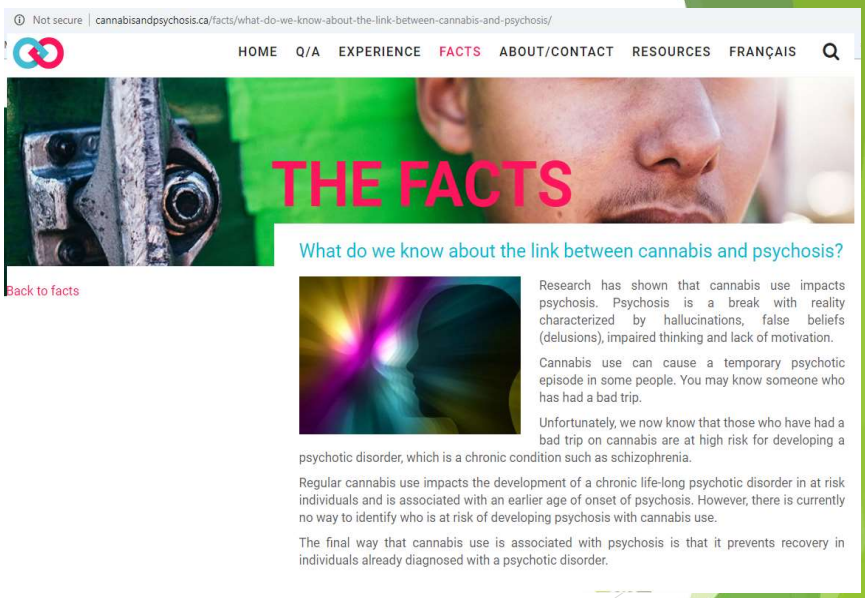

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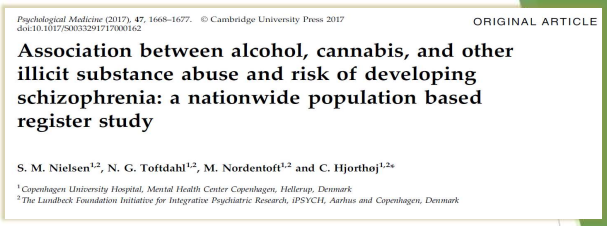
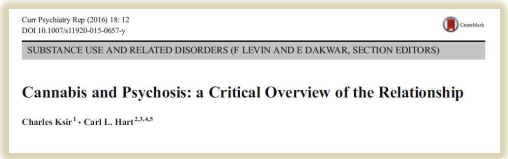
Clinical



- Danish survey >3m ; 200k SUD, 20k Schz
- Any SUD increased risk of developing schizophrenia [hazard ratio (HR) 6.04 (CI) 5.84–6.26].
  - Cannabis (HR 5.20, 95% CI 4.86–5.57)
  - Alcohol (HR 3.38, 95% CI 3.24–3.53)
  - Hallucinogens (HR 1.86, 95% CI 1.43–2.41),
  - Sedatives (HR 1.68, 95% CI 1.49–1.90)
  - Other substances (HR 2.85, 95% CI 2.58–3.15)
- Associations between “almost any type” of SUD and schizophrenia

122

Clinical – Causal versus co-occuring


Curr Psychiatry Rep (2016) 18: 12
DOI 10.1007/s11920-015-0657-y

SUBSTANCE USE AND RELATED DISORDERS (F LEVIN AND E DAKWAR, SECTION EDITORS)

Cannabis and Psychosis: a Critical Overview of the Relationship

Charles Ksir[1] · Carl L. Hart[2,3,4,5]

- > 100 papers/ year 2012-2015 versus < 10/yr 1990s

- Current /prior cannabis associated with 1st episode psychosis/ schizophrenia
- Cannabis use is part of a cluster of "general deviant behavior"
- Schizophrenia is linked to diverse array of variables

"Future research studies that focus exclusively on the cannabis-psychosis association will therefore be of little value in our quest to better understand psychosis and how and why it occurs."

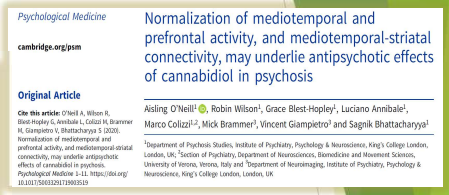
123

CBD & Psychosis


Am J Psychiatry 2018; 175:225–231; doi: 10.1176/appi.ajp.2017.17030325

Cannabidiol (CBD) as an Adjunctive Therapy in Schizophrenia: A Multicenter Randomized Controlled Trial

Philip McGuire, F.R.C.Psych., F.Med.Sci., Philip Robson, M.R.C.P., F.R.C.Psych., Wieslaw Jerzy Cubala, M.D., Ph.D., Daniel Vasile, M.D., Ph.D., Paul Dugald Morrison, Ph.D., M.R.C.Psych., Rachel Barron, B.Vet.Med., M.R.C.V.S., Adam Taylor, Ph.D., Stephen Wright, F.R.C.P.(Edin), F.F.P.M.


Psychological Medicine

cambridge.org/psm

Original Article

Cite this article: O'Neill A, Wilson R, Blest-Hopley G, Annibale L, Colizzi M, Brammer M, Giampietro V, Bhattacharyya S (2020). Normalization of mediotemporal and prefrontal activity, and mediotemporal-striatal connectivity, may underlie antipsychotic effects of cannabidiol in psychosis. *Psychological Medicine* 1–11. https://doi.org/10.1017/S0033291719003519

Normalization of mediotemporal and prefrontal activity, and mediotemporal-striatal connectivity, may underlie antipsychotic effects of cannabidiol in psychosis

Aisling O'Neill[1], Robin Wilson[1], Grace Blest-Hopley[1], Luciano Annibale[1], Marco Colizzi[1,2], Mick Brammer[3], Vincent Giampietro[3] and Sagnik Bhattacharyya[1]

[1]Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK; [2]Section of Psychiatry, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy and [3]Department of Neuroimaging, Institute of Psychiatry, Psychology & Neuroscience, King's College London, London, UK

- Large dose of single molecule isolate
  - CBD 1000 mg/day (N=43) /placebo (N=45)
- At 6 weeks the CBD group had:
  - Lower positive symptoms
  - Higher rate of improvement
- Well tolerated / no difference in adverse events

- One time/ single dose of CBD (600 mg)
- FMRI indicated CBD attenuated acute dysfunction in mediotemporal and prefrontal activation & mediotemporal-striatal function during experimental task
- Psychosis patients w/ CBD (13) were intermediate between controls (19) and placebo
- Trend-level symptom reduction in psychosis patients at 5.5hrs.

124

CBD & Psychosis

Lancet Psychiatry 2020; 7: 344-53
Published Online March 17, 2020
https://doi.org/10.1016/S2215-0366(20)30074-2

Psychiatric symptoms caused by cannabis constituents: a systematic review and meta-analysis

Guy Hindley, Katherine Beck, Faith Borgan, Cedric E Ginestet, Robert McCutcheon, Daniel Kleinloog, Suhas Ganesh, Rajiv Radhakrishnan, Deepak Cyril D'Souza, Oliver D Howes

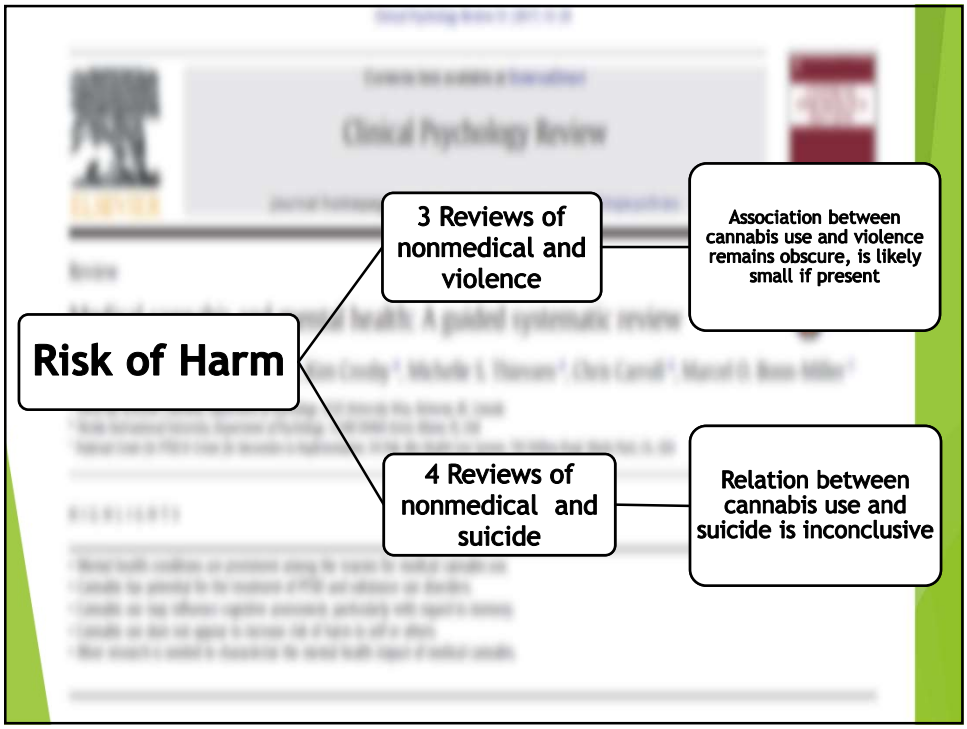
- THC acutely increases psychotic-like symptoms among healthy non-psychotic adults
- 4 studies examined impact of CBD
  - 1 of these found an attenuating effect/ 3 no difference
- CBD administration did not increase symptoms

125

Schizophrenia – Summary

- Exaggerated and lurid depictions of the association between cannabis and psychosis are an enduring aspect of cannabis related-stigma from the early days of prohibition to the current backlash against progressive cannabis policy
- The etiology of both psychotic disorders and substance use is complex and multidetermined
  - The ECS likely has a role
- Individuals with psychotic disorders are more likely to use cannabis
  - This use often precedes formal diagnosis of psychosis
- Individuals with psychotic disorders who use cannabis demonstrate earlier onset and worse course of treatment
- The preponderance of evidence suggests shared vulnerabilities rather than a casual relationship
- CBD may have anti-psychotic effects

126



127

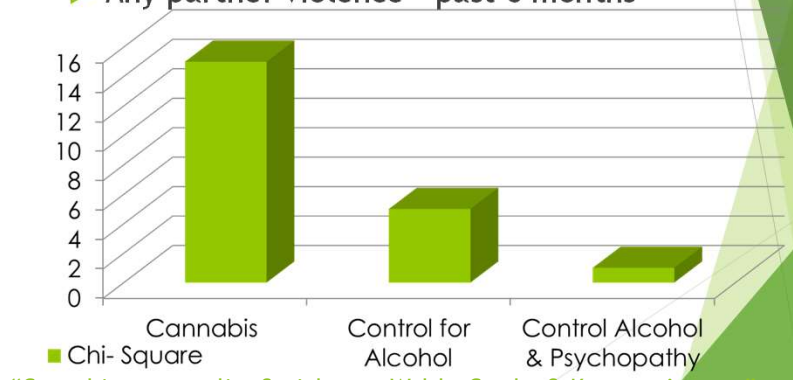
Cannabis & violence – General deviance/ spurious model

- Observed relationship with violence is due to confounding factors NOT related to direct effects of cannabis
  - Polysubstance use
  - Sensation seeking
  - Rule breaking
  - General antisociality

128

Cannabis & partner violence - I

- 924 Canadian university students
- Cannabis Use Disorder scores
- Any partner violence - past 6 months



"Cannabis, personality & violence, Walsh, Crosby & Kosson, *in prep*"

129

Psychology of Addictive Behaviors

0893-164X/14/$12.00 http://dx.doi.org/10.1037/a0037302

Couples' Marijuana Use Is Inversely Related to Their Intimate Partner Violence Over the First 9 Years of Marriage

Philip H. Smith
University at Buffalo, SUNY and Yale University

Gregory G. Homish, R. Lorraine Collins, and Gary A. Giovino
University at Buffalo, SUNY

Helene R. White
Rutgers University

Kenneth E. Leonard
University at Buffalo, SUNY

more frequent marijuana use by husbands and wives predicted less frequent IPV perpetration by husbands. Husbands' marijuana use also predicted less frequent IPV perpetration by wives. Moderation analyses demonstrated that couples in which both spouses used marijuana frequently reported the least frequent IPV perpetration. There was a significant positive association between wives' marijuana use and

130

Overview -PTSD

- Prevalence & consequences
- Extant treatments
- PTSD and cannabis
- Preclinical Human studies – cross sectional
- Synthetic cannabinoids in inmates
- Potential targets of cannabinoids within PTSD symptomology
- Overview of ongoing RCT
- Case study
- Summary & conclusions

131

PTSD prevalence & consequences - I

- Added to DSM-III in 1980
- Validity was controversial – no longer the case
- People with PTSD have very high healthcare service use
- Nearly 50% of outpatient mental health patients have PTSD
- Extant treatments leave a substantial proportion of patients with unresolved symptoms
- Comorbidity and polypharmacy are common

(American Psychiatric Association, 2013)

132

PTSD prevalence & consequences - II

- Approximately 60% of men and 50% of women experience at least one traumatic event.
  - Women more likely to develop PTSD subsequent to trauma
- 7-8% of the US population will have PTSD at some point in their lives.
- About 8 million US adults have PTSD during a given year. This is only a small portion of those who have gone through a trauma.

www.ptsd.va.gov

133

Extant treatment

- Prolonged Exposure (PE)
- Cognitive Processing Therapy (CPT)
- Eye Movement Desensitization and Reprocessing (EMDR)
- Stress Inoculation Training (SIT)
- Present-Centered Therapy (PCT)
- Interpersonal Psychotherapy (IPT)

134

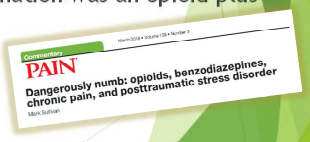
Extant treatment II

- Antidepressants – selective serotonin reuptake inhibitor (SSRI):
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)
  - Fluoxetine (Prozac)
  - Venlafaxine (Effexor)
- Others
  - Nefazodone (Serzone) - serotonin reuptake inhibitor (SRI)
  - Imipramine (Tofranil) - tricyclic antidepressant (TCA)
  - Phenelzine (Nardil) - monoamine oxidase inhibitor (MAOI)

135

Extant treatment III

- Behavioral therapies may be difficult to access and are ineffective for many.
- Pharmacotherapies are ineffective for up to 50% of patients & may have negative side effects and generally require long-term use.
- PTSD is associated with opioid- benzodiazepine co-prescribing
- The most commonly prescribed polysedative combination was an opioid plus a benzodiazepine
  - taken concurrently by 16% of veterans with PTSD

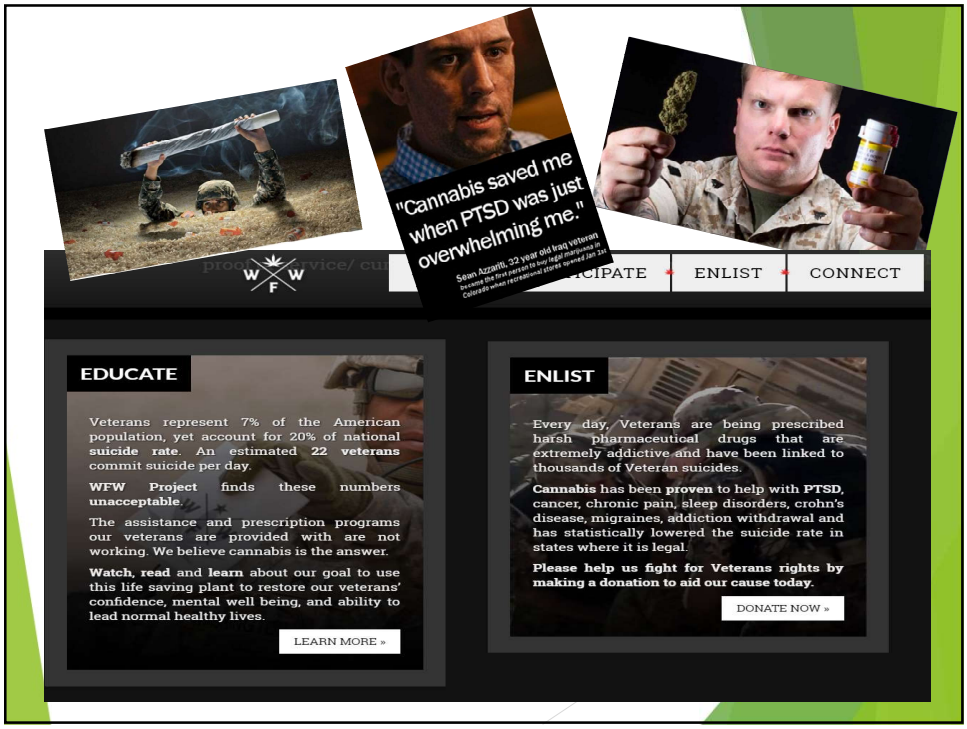

Commentary
PAIN
Dangerously numb: opioids, benzodiazepines, chronic pain, and posttraumatic stress disorder

136

History – PTSD & Cannabis

- Patient/combat veterans have taken a leading role in advocacy
- CNN WEEDS 3 Documentary – 2015
- US VA – will not recommend
- Canada – Vets only group to get federal coverage for cannabis
- Advocacy continues – several groups e.g Veterans for Medical Cannabis Access

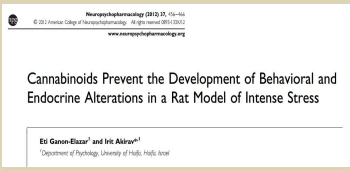
137



138

139

Preclinical - I



Cannabinoids Prevent the Development of Behavioral and Endocrine Alterations in a Rat Model of Intense Stress

Eti Ganon-Elazar[1] and Irit Akirav*[,1]

[1]Department of Psychology, University of Haifa, Haifa, Israel

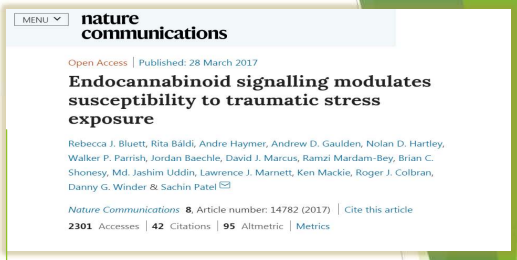
Administration of cannabinoid receptor agonists normalized stress-related behavioral and neuroendocrine abnormalities resulting from prior stress exposure in rats.

Administration at 2 or 24 h (but not 48) prevented trauma-induced alterations in:

avoidance conditioning and extinction

startle potentiation

HPA axis inhibition



MENU nature communications

Open Access | Published: 28 March 2017

Endocannabinoid signalling modulates susceptibility to traumatic stress exposure

Rebecca J. Bluett, Rita Báldi, Andre Haymer, Andrew D. Gaulden, Nolan D. Hartley, Walker P. Parrish, Jordan Baechle, David J. Marcus, Ramzi Mardam-Bey, Brian C. Shonesy, Md. Jashim Uddin, Lawrence J. Marnett, Ken Mackie, Roger J. Colbran, Danny G. Winder & Sachin Patel

Nature Communications 8, Article number: 14782 (2017) | Cite this article

2301 Accesses | 42 Citations | 95 Altmetric | Metrics

Augmenting CB1 agonists increased stress-resilience in mice

Depleting CB1 receptors increased stress susceptibility in previously resilient mice

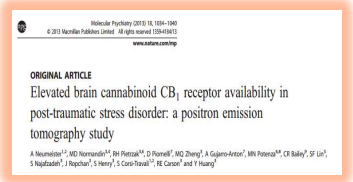
Stress-resilience is associated with cannabinoid activity in ventral hippocampus & amygdala

Amygdala-specific cannabinoid depletion impairs adaptation to repeated stress.

ECS mechanisms promote resilience to adverse effects of acute stress and facilitate adaptation to repeated exposure.

140

Preclinical - II



Molecular Psychiatry (2013) 18, 1034–1040
© 2013 Macmillan Publishers Limited All rights reserved 1359-4184/13
www.nature.com/mp

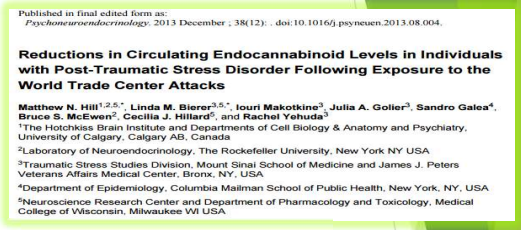
ORIGINAL ARTICLE

Elevated brain cannabinoid CB_1 receptor availability in post-traumatic stress disorder: a positron emission tomography study

A Neumeister[1,2], MD Normandin[3,4], RH Pietrzak[3,4], D Piomelli[5], MQ Zheng[3], A Gujarro-Anton[3], MN Potenza[3,4], CR Bailey[6], SF Lin[3], S Najafzadeh[3], J Ropchan[3], S Henry[3], S Cosi-Travali[1,2], RE Carson[3] and Y Huang[3]

Anandamide was > 50% lower in PTSD versus healthy non-trauma controls and trauma positive controls without PTSD.

Abnormal CB_1 signaling is implicated in the etiology of PTSD.



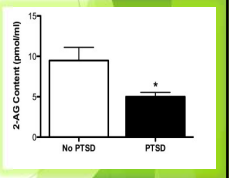
Published in final edited form as:
Psychoneuroendocrinology. 2013 December ; 38(12): . doi:10.1016/j.psyneuen.2013.08.004.

Reductions in Circulating Endocannabinoid Levels in Individuals with Post-Traumatic Stress Disorder Following Exposure to the World Trade Center Attacks

Matthew N. Hill[1,2,5,*], Linda M. Bierer[3,5,*], Iouri Makotkine[3], Julia A. Golier[3], Sandro Galea[4], Bruce S. McEwen[2], Cecilia J. Hillard[5], and Rachel Yehuda[3]
[1]The Hotchkiss Brain Institute and Departments of Cell Biology & Anatomy and Psychiatry, University of Calgary, Calgary AB, Canada
[2]Laboratory of Neuroendocrinology, The Rockefeller University, New York NY USA
[3]Traumatic Stress Studies Division, Mount Sinai School of Medicine and James J. Peters Veterans Affairs Medical Center, Bronx, NY, USA
[4]Department of Epidemiology, Columbia Mailman School of Public Health, New York, NY, USA
[5]Neuroscience Research Center and Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee WI USA

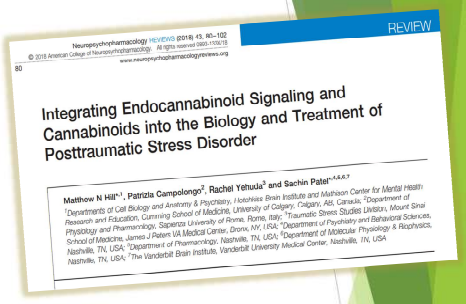
Deficient eCB signaling may be a component of the dysregulation associated with PTSD.

Negative association between anandamide levels and intrusive symptoms suggest anandamide reductions promote retention of aversive emotional memories.



141

Preclinical - summary



Neuropsychopharmacology REVIEWS (2018) 43, 80–102
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www.neuropsychopharmacologyreviews.org

REVIEW

Integrating Endocannabinoid Signaling and Cannabinoids into the Biology and Treatment of Posttraumatic Stress Disorder

Matthew N Hill[*,1], Patrizia Campolongo[2], Rachel Yehuda[3] and Sachin Patel[*,4,5,6,7]
[1]Departments of Cell Biology and Anatomy & Psychiatry, Hotchkiss Brain Institute and Mathison Center for Mental Health Research and Education, Cumming School of Medicine, University of Calgary, Calgary, Alb, Canada; [2]Department of Physiology and Pharmacology, Sapienza University of Rome, Rome, Italy; [3]Traumatic Stress Studies Division, Mount Sinai School of Medicine, James J Peters VA Medical Center, Bronx, NY, USA; [4]Department of Psychiatry and Behavioral Sciences, Nashville, TN, USA; [5]Department of Pharmacology, Nashville, TN, USA; [6]Department of Molecular Physiology & Biophysics, Nashville, TN, USA; [7]The Vanderbilt Brain Institute, Vanderbilt University Medical Center, Nashville, TN, USA

"…deficiencies in eCB signaling can result in:

- hyperactivity of the amygdala
- hypoactivity of the mPFC
- impaired regulation of the stress response
- elevated levels of basal and stress-induced anxiety
- increased retrieval and impaired extinction of emotionally aversive memories
- increased propensity to develop a state of inflammation."

142

PTSD Symptoms I

CRITERION A – Experience traumatic event

CRITERION B - Intrusion

Presence of one (or more) of the following intrusion symptoms associated with the traumatic event(s), beginning after the event(s) occurred:

1. Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s)
2. **Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event.**
3. Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the event(s) were recurring.
4. Intense or prolonged psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event(s).
5. **Marked physiological reaction to external or internal cues that symbolize or resemble an aspect of the traumatic event(s).**

CRITERION C - Avoidance

Persistent avoidance of stimuli associated with the traumatic event(s), beginning after the traumatic event(s) occurred, as evidenced by one or both of the following:

1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic event(s).
2. Avoidance of or efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing, memories, thoughts, or feelings about or closely associated with the traumatic event(s).

(American Psychiatric Association, 2013)

143

PTSD Symptoms - II

D -Negative Alterations in Cognition & Mood

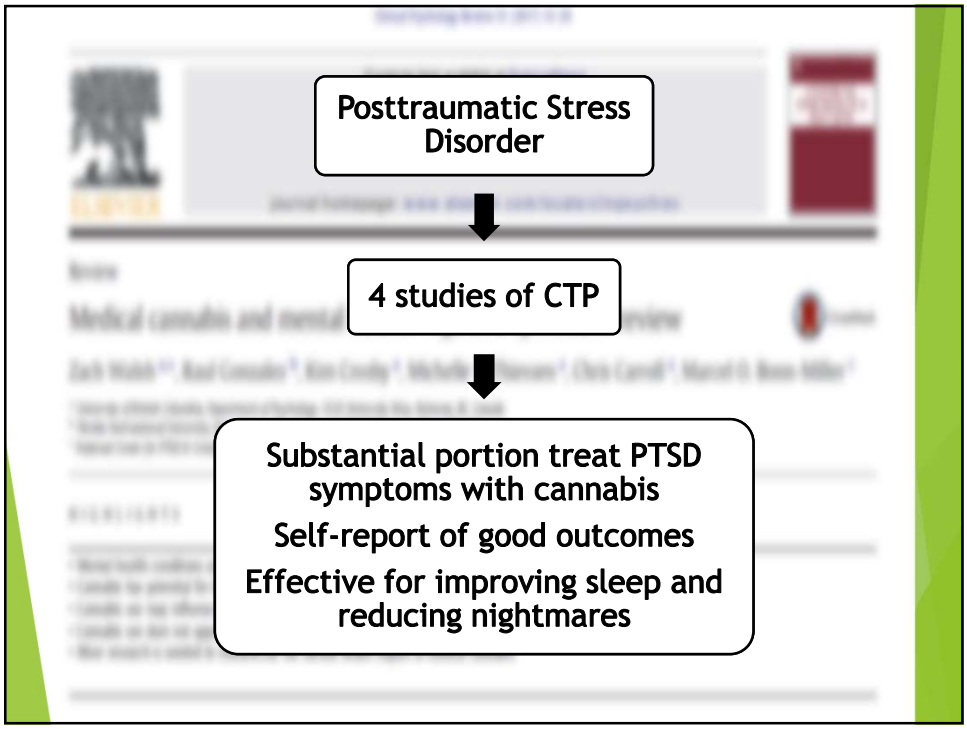
1. Inability to remember an important aspect of the traumatic event
2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world
3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that leads the individual to blame self or others.
4. **Persistent negative emotional state .**
5. **Marked diminished interest or participation in significant activities.**
6. **Feelings of detachment or estrangement from others.**
7. **Persistent inability to experience positive emotions (e.g., happiness, satisfaction, or loving feelings).**

E - Arousal & Reactivity

1. **Irritable behavior and angry outbursts (with little or no provocation) typically expressed as verbal or physical aggression toward people or objects.**
2. Reckless or self-destructive behavior.
3. Hypervigilance.
4. **Exaggerated startle response.**
5. Problems with concentration.
6. **Sleep disturbance (e.g. problems falling or staying asleep or restless sleep).**

(American Psychiatric Association, 2013)

144



145

Human studies -II

Clin Drug Investig (2014) 34:587–591
DOI 10.1007/s40261-014-0212-3

SHORT COMMUNICATION

Preliminary, Open-Label, Pilot Study of Add-On Oral Δ^9-Tetrahydrocannabinol in Chronic Post-Traumatic Stress Disorder

Pablo Roitman · Raphael Mechoulam · Rena Cooper-Kazaz · Arieh Shalev

- Small open label trial from PTSD clinic (n=10)
- Reduced symptom severity
- Improved sleep & nightmares
- Reduced hyperarousal

Journal of Psychoactive Drugs, 46 (1), 73–77, 2014
Copyright © Taylor & Francis Group, LLC
ISSN: 0279-1072 print/2159-9777 online
DOI: 10.1080/02791072.2013.873843

Routledge Taylor & Francis Group

PTSD Symptom Reports of Patients Evaluated for the New Mexico Medical Cannabis Program

George R. Greer, M.D.[a]; Charles S. Grob, M.D.[b] & Adam L. Halberstadt, Ph.D.[c]

- Cross sectional / retrospective
- Recruited from cannabis clinic
- Notable reductions in:
  - re-experiencing
  - avoidance
  - hyperarousal

146

Journal of Psychoactive Drugs, 46 (1), 73–77, 2014
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ISSN: 0279-1072 print / 2159-9777 online
DOI: 10.1080/02791072.2013.873843

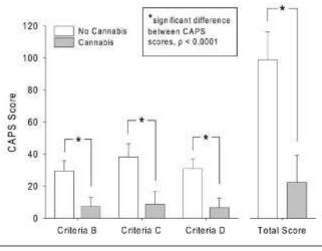
Routledge
Taylor & Francis Group

PTSD Symptom Reports of Patients Evaluated for the New Mexico Medical Cannabis Program

George R. Greer, M.D.[a]; Charles S. Grob, M.D.[b] & Adam L. Halberstadt, Ph.D.[c]

Greer et al., 2014	80 (20)	New Mexico, US	Medical evaluations of patients seeking CTP	PTSD	Cross-sectional (5)	Patients who used CTP reported reductions of 75% in symptoms of trauma related re-experiencing, avoidance, and hyperarousal.

FIGURE 1
CAPS Scores for the No-Cannabis and Cannabis Conditions. Data Are Expressed as Group Means ± S.D.
***Significant Difference Between CAPS Scores, $p < 0.0001$.**



147

ORIGINAL CONTRIBUTION

Journal of Clinical Psychopharmacology • Volume 34, Number 5, October 2014 www.psychopharmacology.com | 559

Use of a Synthetic Cannabinoid in a Correctional Population for Posttraumatic Stress Disorder–Related Insomnia and Nightmares, Chronic Pain, Harm Reduction, and Other Indications

A Retrospective Evaluation

Colin Cameron, MDCM, FRCPC, Diane Watson, MD, FRCPC, and Jeffrey Robinson, MA

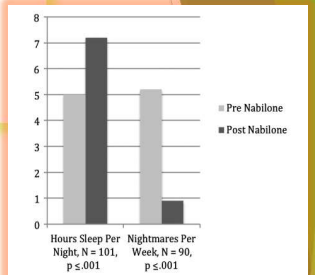


FIGURE 3. Sleep effects. Hours sleep per night = mean number of hours/night, nightmares per week = nights with nightmares/week. Pre nabilone = week prior to starting. Post nabilone = week after final dose was achieved.

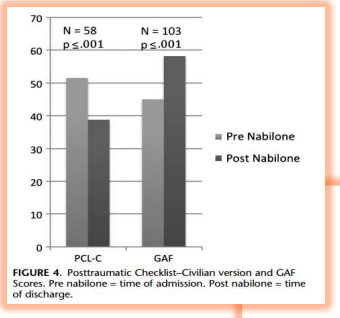


FIGURE 4. Posttraumatic Checklist–Civilian version and GAF Scores. Pre nabilone = time of admission. Post nabilone = time of discharge.

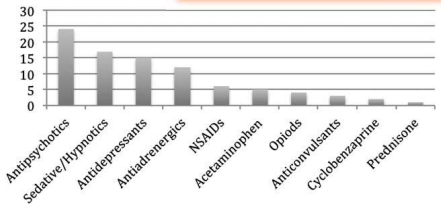


FIGURE 5. Number of medications discontinued.

148

149

Medical Cannabis & PTSD - Protocol Design

Randomized clinical trial
Placebo-controlled with 2 active treatments
Crossover design from Stage 1 to 2
Triple-blinded
42 participants
2 treatment phases and 3 periods of cannabis abstinence

Primary Objective:
To compare the independent effects of two active concentrations of vaporized cannabis to placebo on PTSD symptom severity measured by changes in CAPS-5 total scores during three weeks of ad-libitum self-administration during Stage 1 of the study protocol.

150

151

Case Study - Background

- 52 y/o Caucasian Female
- Multiple MVA
  - 10 years ago, coma, TBI
  - Re-triggered by MVA 2 yrs-ago
- History of moderate cannabis use
- BDI II: 28
- BAI: 24

152

Case Study – FU 1

- Reports from daily phone calls
- **Day 2 of vaporizing**
  - Reports sleeping longer between nightmares
- **Day 4 of vaporizing**
  - Reports relief from chronic pain in neck and shoulders, felt them release
  - Reports dreams occurring much later in sleep
- **Day 5 of vaporizing**
  - Reports nightmares have ceased, was startled awake but for no apparent reason
- **Day 7 of vaporizing**
  - Reported that he can "de-escalate" much faster when anxious or "triggered" by something (TV show etc.)

153

Case Study – FU 1a

- **Stage 1 follow-up CAPS 5**
  - **Total severity: 30**
  - **Total # Sx: 12**
- Criterion B - Intrusion Symptoms: 11 (+1)
- Criterion C - Avoidance: 2 (-1)
- Criterion D - Negative Cognitions/Mood: 7 (-6)
- Criterion E - Alterations in Arousal: 10 (0)

154

Case Study – FU 2

- **Cessation - 2-weeks follow-up**
  - **Total severity:** 40
  - **Total # Sx:** 14
- Criterion B – Intrusion Symptoms: 11
- Criterion C – Avoidance: 6
- Criterion D - Negative Cognitions/Mood: 11
- Criterion E - Alterations in Arousal: 12
- Self-report chronic pain, sleep, and general mood worse

155

CAPS 5 - Overview

	Intrusion	Avoidance	Cognition / mood	Arousal	Total Severity
Baseline	**10**	**3**	**13**	**10**	**36**
Follow-up 1	**11**	**2**	**7**	**10**	**30**
Cessation 1	**11**	**6**	**11**	**12**	**40**

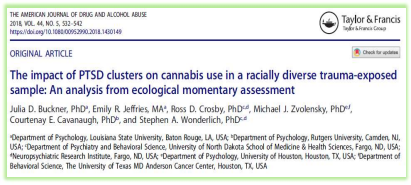
156

Case Study – Conclusions

- Consider mode of administration
- Prepare for withdrawal
- Consider symptoms profiles
- Cessation period difficult
- Cannabis addressed issues secondary to the PTSD (i.e., chronic pain)

157

Recent updates I



THE AMERICAN JOURNAL OF DRUG AND ALCOHOL ABUSE
2018, VOL. 44, NO. 5, 532–542
https://doi.org/10.1080/00952990.2018.1450149

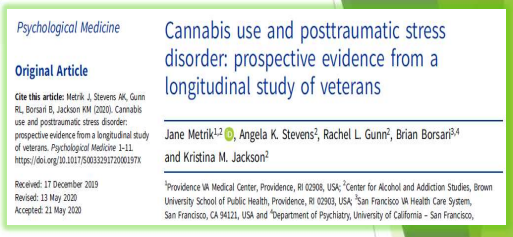
Taylor & Francis

ORIGINAL ARTICLE

The impact of PTSD clusters on cannabis use in a racially diverse trauma-exposed sample: An analysis from ecological momentary assessment

Julia D. Buckner, PhD[a], Emily R. Jeffries, MA[a], Ross D. Crosby, PhD[b,c], Michael J. Zvolensky, PhD[a,d], Courtenay E. Cavanaugh, PhD[b], and Stephen A. Wonderlich, PhD[b,c]

[a]Department of Psychology, Louisiana State University, Baton Rouge, LA, USA; [b]Department of Psychology, Rutgers University, Camden, NJ, USA; [c]Department of Psychiatry and Behavioral Science, University of North Dakota School of Medicine & Health Sciences, Fargo, ND, USA; [d]Neuropsychiatric Research Institute, Fargo, ND, USA; [e]Department of Psychology, University of Houston, Houston, TX, USA; [f]Department of Behavioral Science, The University of Texas MD Anderson Cancer Center, Houston, TX, USA



Psychological Medicine

Original Article

Cite this article: Metrik J, Stevens AK, Gunn RL, Borsari B, Jackson KM (2020). Cannabis use and posttraumatic stress disorder: prospective evidence from a longitudinal study of veterans. *Psychological Medicine* 1–11. https://doi.org/10.1017/S003329172000197X

Received: 17 December 2019
Revised: 13 May 2020
Accepted: 21 May 2020

Cannabis use and posttraumatic stress disorder: prospective evidence from a longitudinal study of veterans

Jane Metrik[1,2], Angela K. Stevens[2], Rachel L. Gunn[2], Brian Borsari[3,4] and Kristina M. Jackson[2]

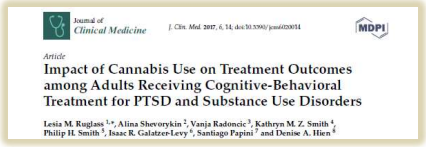
[1]Providence VA Medical Center, Providence, RI 02908, USA; [2]Center for Alcohol and Addiction Studies, Brown University School of Public Health, Providence, RI 02903, USA; [3]San Francisco VA Health Care System, San Francisco, CA 94121, USA and [4]Department of Psychiatry, University of California – San Francisco,

- Elevated hyperarousal symptoms are associated with anxiety-related cannabis use
- Higher hyperarousal patients reported greater anxiolytic effects relative to those with more avoidance and reexperiencing symptoms
- Consistent with a negative reinforcements model of PTSD and cannabis use

- Large prospective study in VA
- PTSD associated with later development of problematic cannabis use
- Cannabis use associated with greater intrusion symptoms at 6 months
- "Coping-oriented pattern of heightened avoidance of negative emotional states via cannabis use"
- Limitations –
  - No query of medical use
  - No reporting of other symptom groups

158

Recent updates II

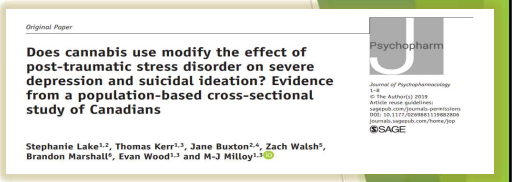

Journal of Clinical Medicine J. Clin. Med. 2017, 6, 14; doi:10.3390/jcm6020014 MDPI

Article

Impact of Cannabis Use on Treatment Outcomes among Adults Receiving Cognitive-Behavioral Treatment for PTSD and Substance Use Disorders

Lesia M. Ruglass [1,*], Alina Shevorykin [2], Vanja Radoncic [3], Kathryn M. Z. Smith [4], Philip H. Smith [5], Isaac R. Galatzer-Levy [6], Santiago Papini [7] and Denise A. Hien [8]

- Baseline cannabis use was unrelated to endpoint (12-wk) PTSD or SUD.
- Higher cannabis use was associated with higher PTSD symptom severity early in treatment, but lower PTSD symptom severity later in treatment.
  - Cannabis use may be synergistic with CBT to reduce PTSD symptoms.
- As cannabis use increased primary substance use decreased and vice versa.
  - Substitution?


Original Paper

Does cannabis use modify the effect of post-traumatic stress disorder on severe depression and suicidal ideation? Evidence from a population-based cross-sectional study of Canadians

Stephanie Lake[1,2], Thomas Kerr[1,3], Jane Buxton[2,4], Zach Walsh[5], Brandon Marshall[6], Evan Wood[1,3] and M-J Milloy[1,3]

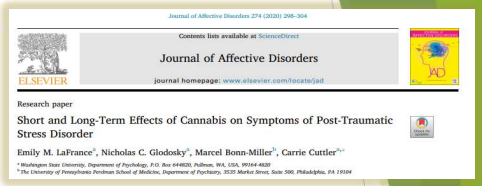
Psychopharm

SAGE

- Higher levels of cannabis use among those with PTSD.
- PTSD was associated with depression and suicidality among non-cannabis users
- PTSD was not associated with these outcomes among cannabis users

159

Recent updates III


Journal of Affective Disorders 274 (2020) 298–304

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

Short and Long-Term Effects of Cannabis on Symptoms of Post-Traumatic Stress Disorder

Emily M. LaFrance[a], Nicholas C. Glodosky[a], Marcel Bonn-Miller[b], Carrie Cuttler[a,*]

- 404 medical cannabis self-identified with PTSD were tracked with app
- >90% session resulted in acute reductions of over 50% in:
  - Intrusive thoughts
  - Flashbacks
  - Irritability
  - Anxiety
- PTSD symptoms did not change over time
- Doses increased over time
  - Tolerance?

160

PTSD SUMMARY

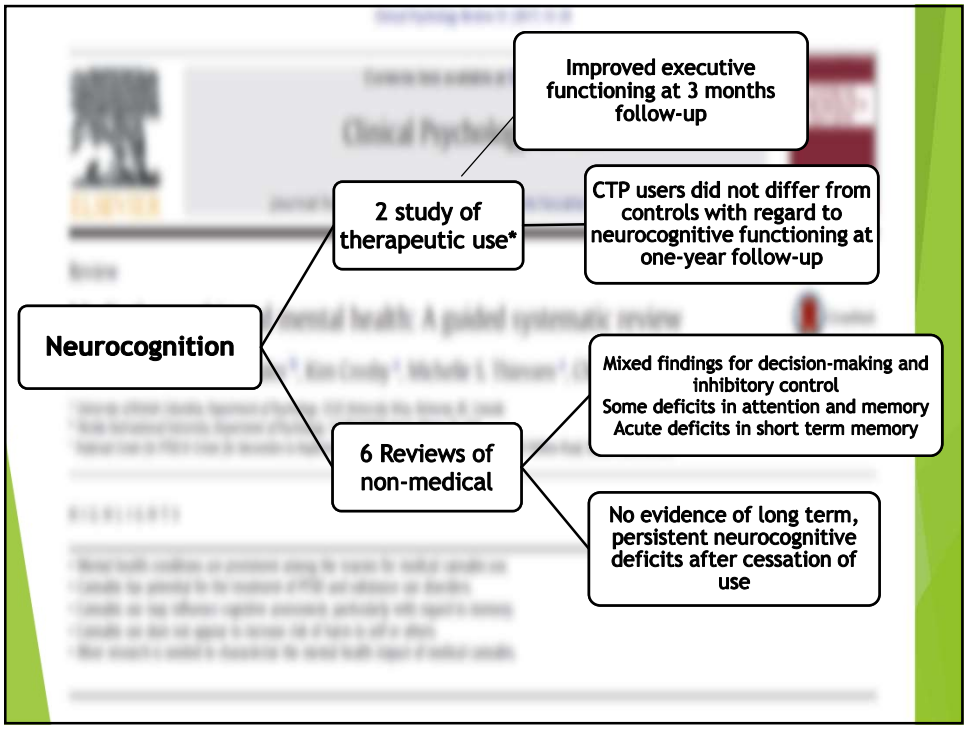
- Extant treatments are inadequate for many and consequences are severe
- Preclinical research has identified an etiological role for the ECS
- Substantial anecdote, advocacy and cross-sectional evidence in favour
- Nabilone reduced nightmares and improves sleep
- Longitudinal evidence is mixed – and methodologically limited
  - Some evidence for negative reinforcement/ exacerbation of avoidance
  - Some evidence for reduced anxiety, depression and suicidal ideation
- Evidence for acute symptom improvement with no long term gains

161

PROBLEMS

- Consider mode of administration
- Prepare for withdrawal
- Consider symptoms profiles

162

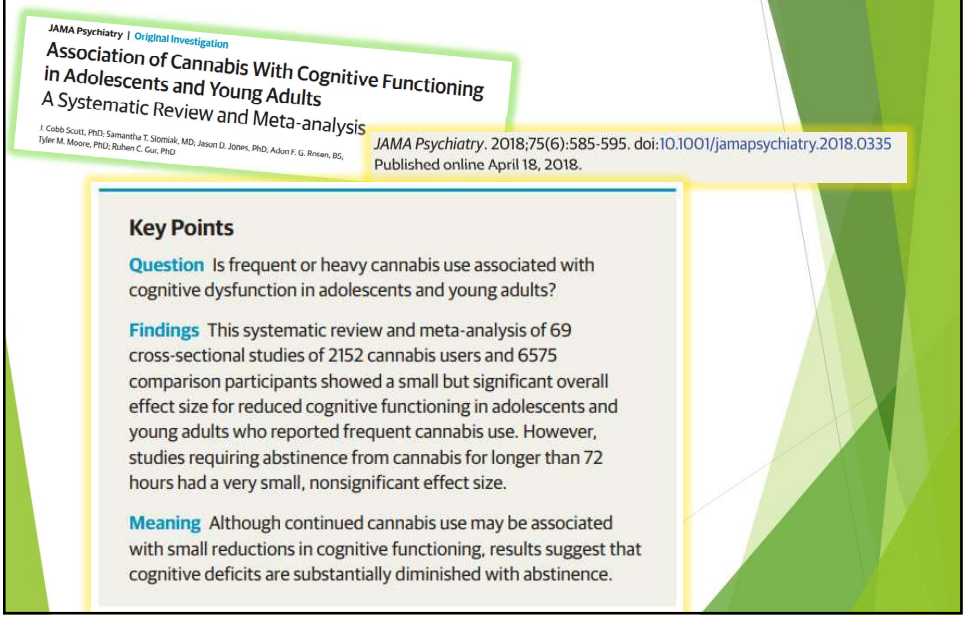

Neurocognition
2 study of therapeutic use*
Improved executive functioning at 3 months follow-up
CTP users did not differ from controls with regard to neurocognitive functioning at one-year follow-up
6 Reviews of non-medical
Mixed findings for decision-making and inhibitory control
Some deficits in attention and memory
Acute deficits in short term memory
No evidence of long term, persistent neurocognitive deficits after cessation of use

163


frontiers in Pharmacology
Splendor in the Grass? A Pilot Study Assessing the Impact of Medical Marijuana on Executive Function
Results suggest that in general, MMJ patients experienced some improvement on measures of executive functioning, including the Stroop Color Word Test and Trail Making Test, mostly reflected as increased speed in completing tasks without a loss of accuracy. On self-report questionnaires, patients also indicated moderate improvements in clinical state, including reduced sleep disturbance, decreased symptoms of depression, attenuated impulsivity, and positive changes in some aspects of quality of life. Additionally, patients reported a notable decrease in their use of conventional pharmaceutical agents from baseline, with opiate use declining more than 42%. While intriguing, these findings are preliminary and warrant further investigation
ADDICTION
RESEARCH REPORT
Structural neuroimaging correlates of alcohol and cannabis use in adolescents and adults
Drug and Alcohol Dependence
A longitudinal examination of the relationship between cannabis use and cognitive function in mid-life adults
Findings
Conclusions: Mid-life cannabis users had poorer verbal recall than non-users, but this was not related to their current level of cannabis use, and cannabis use was not associated with accelerated cognitive decline.

164

Cannabis - Young adults



JAMA Psychiatry | Original Investigation

Association of Cannabis With Cognitive Functioning in Adolescents and Young Adults
A Systematic Review and Meta-analysis

J. Cobb Scott, PhD; Samantha T. Slomiak, MD; Jason D. Jones, PhD; Adon F. G. Rosen, BS; Tyler M. Moore, PhD; Ruben C. Gur, PhD

JAMA Psychiatry. 2018;75(6):585-595. doi:10.1001/jamapsychiatry.2018.0335
Published online April 18, 2018.

Key Points

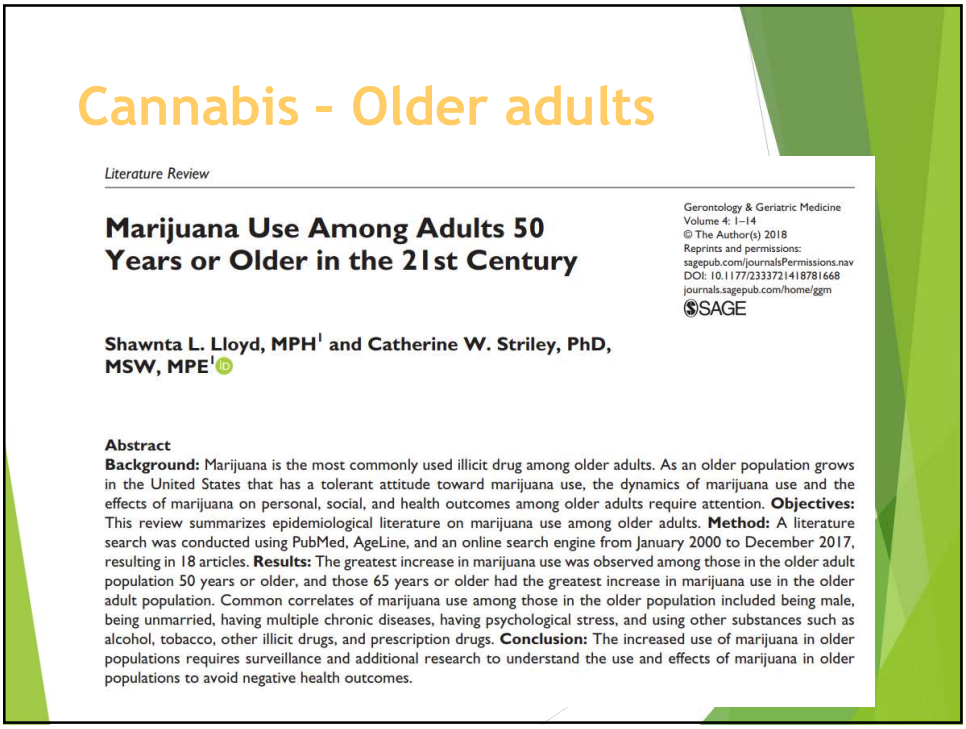
Question Is frequent or heavy cannabis use associated with cognitive dysfunction in adolescents and young adults?

Findings This systematic review and meta-analysis of 69 cross-sectional studies of 2152 cannabis users and 6575 comparison participants showed a small but significant overall effect size for reduced cognitive functioning in adolescents and young adults who reported frequent cannabis use. However, studies requiring abstinence from cannabis for longer than 72 hours had a very small, nonsignificant effect size.

Meaning Although continued cannabis use may be associated with small reductions in cognitive functioning, results suggest that cognitive deficits are substantially diminished with abstinence.

165

Cannabis - Older adults



Literature Review

Marijuana Use Among Adults 50 Years or Older in the 21st Century

Gerontology & Geriatric Medicine
Volume 4: 1–14

DOI: 10.1177/2333721418781668
journals.sagepub.com/home/ggm
SAGE

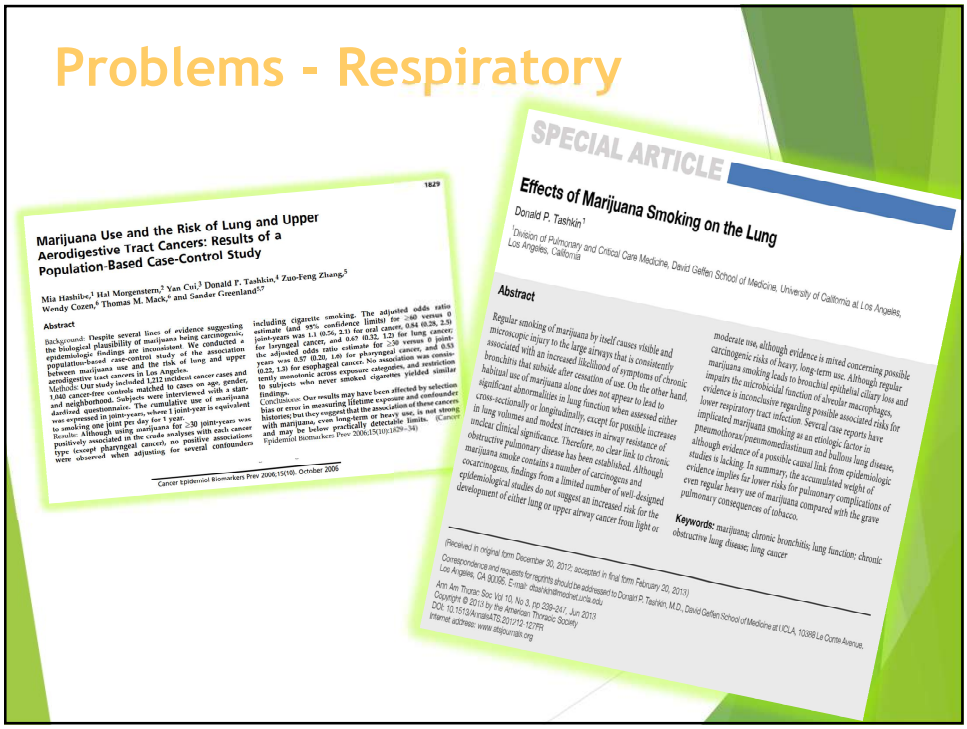
Shawnta L. Lloyd, MPH[1] and Catherine W. Striley, PhD, MSW, MPE[1]

Abstract

Background: Marijuana is the most commonly used illicit drug among older adults. As an older population grows in the United States that has a tolerant attitude toward marijuana use, the dynamics of marijuana use and the effects of marijuana on personal, social, and health outcomes among older adults require attention. **Objectives:** This review summarizes epidemiological literature on marijuana use among older adults. **Method:** A literature search was conducted using PubMed, AgeLine, and an online search engine from January 2000 to December 2017, resulting in 18 articles. **Results:** The greatest increase in marijuana use was observed among those in the older adult population 50 years or older, and those 65 years or older had the greatest increase in marijuana use in the older adult population. Common correlates of marijuana use among those in the older population included being male, being unmarried, having multiple chronic diseases, having psychological stress, and using other substances such as alcohol, tobacco, other illicit drugs, and prescription drugs. **Conclusion:** The increased use of marijuana in older populations requires surveillance and additional research to understand the use and effects of marijuana in older populations to avoid negative health outcomes.

166

Problems - Respiratory



Marijuana Use and the Risk of Lung and Upper Aerodigestive Tract Cancers: Results of a Population-Based Case-Control Study

Mia Hashibe,[1] Hal Morgenstern,[2] Yan Cui,[3] Donald P. Tashkin,[4] Zuo-Feng Zhang,[5] Wendy Cozen,[6] Thomas M. Mack,[7] and Sander Greenland[5,7]

Abstract

Background: Despite several lines of evidence suggesting the biological plausibility of marijuana being carcinogenic, epidemiologic findings are inconsistent. We conducted a population-based case-control study of the association between marijuana use and the risk of lung and upper aerodigestive tract cancers in Los Angeles.

Methods: Our study included 1,212 incident cancer cases and 1,040 cancer-free controls matched to cases on age, gender, and neighborhood. Subjects were interviewed with a standardized questionnaire. The cumulative use of marijuana was expressed in joint-years, where 1 joint-year is equivalent to smoking one joint per day for 1 year.

Results: Although using marijuana for ≥30 joint-years was positively associated in the crude analyses with each cancer type (except pharyngeal cancer), no positive associations were observed when adjusting for several confounders including cigarette smoking. The adjusted odds ratio estimate (and 95% confidence limits) for ≥60 versus 0 joint-years was 1.1 (0.56, 2.1) for oral cancer, 0.84 (0.28, 2.5) for laryngeal cancer, and 0.67 (0.32, 1.2) for lung cancer; the adjusted odds ratio estimate for ≥30 versus 0 joint-years was 0.57 (0.20, 1.6) for pharyngeal cancer, and 0.53 (0.22, 1.3) for esophageal cancer. No association was consistently monotonic across exposure categories, and restriction to subjects who never smoked cigarettes yielded similar findings.

Conclusion: Our results may have been affected by selection bias or error in measuring lifetime exposure and confounder histories; but they suggest that the association of these cancers with marijuana, even long-term or heavy use, is not strong and may be below practically detectable limits. (Cancer Epidemiol Biomarkers Prev 2006;15(10):1829–34)

Cancer Epidemiol Biomarkers Prev 2006;15(10). October 2006

SPECIAL ARTICLE

Effects of Marijuana Smoking on the Lung

Donald P. Tashkin[1]

[1]Division of Pulmonary and Critical Care Medicine, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, California

Abstract

Regular smoking of marijuana by itself causes visible and microscopic injury to the large airways that is consistently associated with an increased likelihood of symptoms of chronic bronchitis that subside after cessation of use. On the other hand, habitual use of marijuana alone does not appear to lead to significant abnormalities in lung function when assessed either cross-sectionally or longitudinally, except for possible increases in lung volumes and modest increases in airway resistance of uncertain clinical significance. Therefore, no clear link to chronic obstructive pulmonary disease has been established. Although marijuana smoke contains a number of carcinogens and cocarcinogens, findings from a limited number of well-designed epidemiological studies do not suggest an increased risk for the development of either lung or upper airway cancer from light or moderate use, although evidence is mixed concerning possible carcinogenic risks of heavy, long-term use. Although regular marijuana smoking leads to bronchial epithelial ciliary loss and impairs the microbicidal function of alveolar macrophages, evidence is inconclusive regarding possible associated risks for lower respiratory tract infection. Several case reports have implicated marijuana smoking as an etiologic factor in pneumothorax/pneumomediastinum and bullous lung disease, although evidence of a possible causal link from epidemiologic studies is lacking. In summary, the accumulated weight of evidence implies for lower risks for pulmonary complications of even regular heavy use of marijuana compared with the grave pulmonary consequences of tobacco.

Keywords: marijuana; chronic bronchitis; lung function; chronic obstructive lung disease; lung cancer

(Received in original form December 30, 2012; accepted in final form February 20, 2013)

Correspondence and requests for reprints should be addressed to Donald P. Tashkin, M.D., David Geffen School of Medicine at UCLA, 10398 Le Conte Avenue, Los Angeles, CA 90095. E-mail: dtashkin@mednet.ucla.edu

Am Am Thorac Soc Vol 10, No 3, pp 239–247, Jun 2013

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DOI: 10.1513/AnnalsATS.201212-127FR

Internet address: www.atsjournals.org

167

Problems- Withdrawal

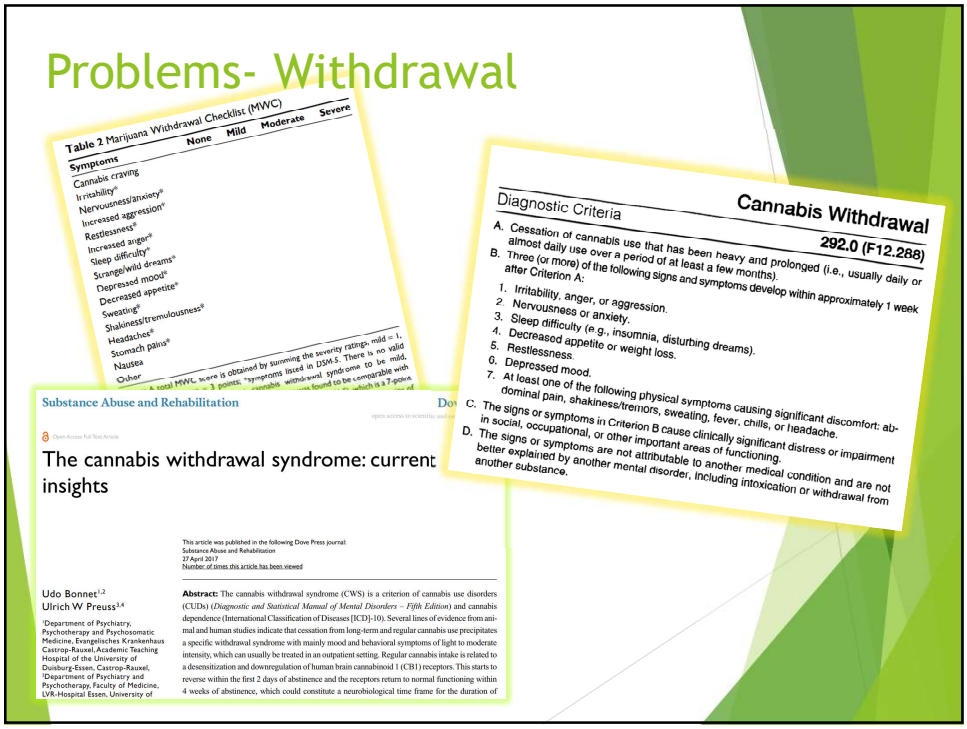


Table 2 Marijuana Withdrawal Checklist (MWC)

Symptoms	None	Mild	Moderate	Severe
Cannabis craving				
Irritability*				
Nervousness/anxiety*				
Increased aggression*				
Restlessness*				
Increased anger*				
Sleep difficulty*				
Strange/wild dreams*				
Depressed mood*				
Decreased appetite*				
Sweating*				
Shakiness/tremulousness*				
Headaches*				
Stomach pains*				
Nausea				
Other				

A total MWC score is obtained by summing the severity ratings, mild = 1, ... 3 points; "symptoms [as] in DSM-5 ... There is no valid ... withdrawal syndrome to be mild, ... found to be comparable with ... which is a 7-point,

Diagnostic Criteria

Cannabis Withdrawal

292.0 (F12.288)

A. Cessation of cannabis use that has been heavy and prolonged (i.e., usually daily or almost daily use over a period of at least a few months).
B. Three (or more) of the following signs and symptoms develop within approximately 1 week after Criterion A:
   1. Irritability, anger, or aggression.
   2. Nervousness or anxiety.
   3. Sleep difficulty (e.g., insomnia, disturbing dreams).
   4. Decreased appetite or weight loss.
   5. Restlessness.
   6. Depressed mood.
   7. At least one of the following physical symptoms causing significant discomfort: abdominal pain, shakiness/tremors, sweating, fever, chills, or headache.
C. The signs or symptoms in Criterion B cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The signs or symptoms are not attributable to another medical condition and are not better explained by another mental disorder, including intoxication or withdrawal from another substance.

Substance Abuse and Rehabilitation

Dov

open access to scientific and

Open Access Full Text Article

The cannabis withdrawal syndrome: current insights

This article was published in the following Dove Press journal:
Substance Abuse and Rehabilitation
27 April 2017
Number of times this article has been viewed

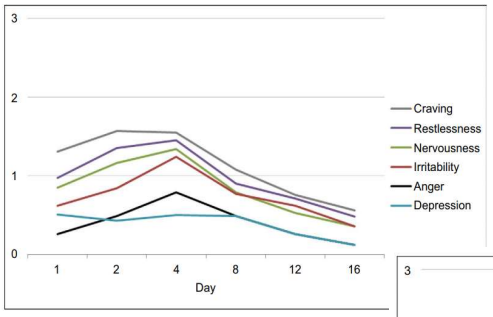
Udo Bonnet[1,2]
Ulrich W Preuss[3,4]

[1]Department of Psychiatry, Psychotherapy and Psychosomatic Medicine, Evangelisches Krankenhaus Castrop-Rauxel, Academic Teaching Hospital of the University of Duisburg-Essen, Castrop-Rauxel, [2]Department of Psychiatry and Psychotherapy, Faculty of Medicine, LVR-Hospital Essen, University of

Abstract: The cannabis withdrawal syndrome (CWS) is a criterion of cannabis use disorders (CUDs) (*Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition*) and cannabis dependence (International Classification of Diseases [ICD]-10). Several lines of evidence from animal and human studies indicate that cessation from long-term and regular cannabis use precipitates a specific withdrawal syndrome with mainly mood and behavioral symptoms of light to moderate intensity, which can usually be treated in an outpatient setting. Regular cannabis intake is related to a desensitization and downregulation of human brain cannabinoid 1 (CB1) receptors. This starts to reverse within the first 2 days of abstinence and the receptors return to normal functioning within 4 weeks of abstinence, which could constitute a neurobiological time frame for the duration of

168

Problems- Withdrawal



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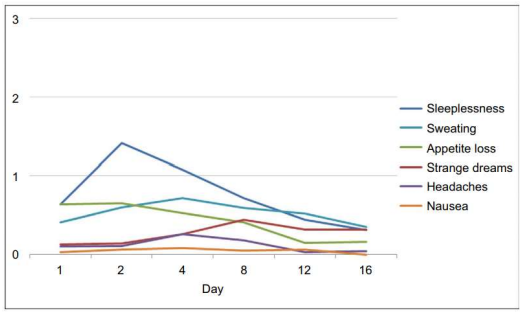


169

CUD

Cannabis Use Disorder

Diagnostic Criteria

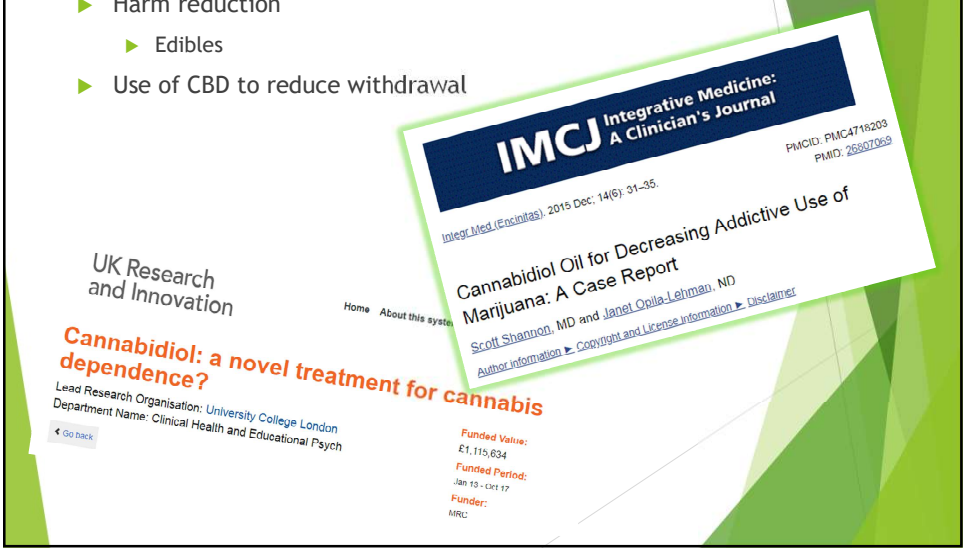
A. A problematic pattern of cannabis use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12-month period:

1. Cannabis is often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control cannabis use.
3. A great deal of time is spent in activities necessary to obtain cannabis, use cannabis, or recover from its effects.
4. Craving, or a strong desire or urge to use cannabis.
5. Recurrent cannabis use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued cannabis use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of cannabis.
7. Important social, occupational, or recreational activities are given up or reduced because of cannabis use.
8. Recurrent cannabis use in situations in which it is physically hazardous.
9. Cannabis use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by cannabis.
10. Tolerance, as defined by either of the following:
    a. A need for markedly increased amounts of cannabis to achieve intoxication or desired effect.
    b. Markedly diminished effect with continued use of the same amount of cannabis.
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for cannabis (refer to Criteria A and B of the criteria set for cannabis withdrawal, pp. 517–518).
    b. Cannabis (or a closely related substance) is taken to relieve or avoid withdrawal symptoms.

170

Treatment considerations

- Harm reduction
  - Edibles
- Use of CBD to reduce withdrawal



171

CUDIT

Appendix I. The Cannabis Use Disorders Identification Test (CUDIT)

Have you used any cannabis over the past 6 months — Yes / No

If YES, please answer the following questions about your cannabis use.

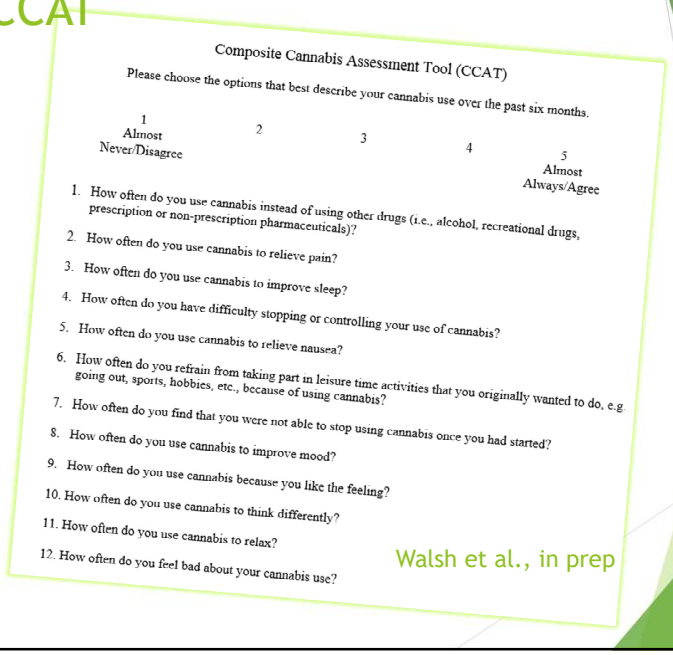
Please tick the box that is most correct for you in relation to your cannabis use *over the past 6 months*

1. How often do you used cannabis?
   never (Y) | monthly or less (Y) | 2–4 times a month (Y) | 2–3 times a week (Y) | 4 or more times a week (Y)
2. How many hours were you "stoned" on a typical day when you had been using cannabis?
   1 or 2 (Y) | 3 or 4 (Y) | 5 or 6 (Y) | 7 to 9 (Y) | 10 or more (Y)
3. How often were you "stoned" for 6 or more hours?
   never (Y) | less than monthly (Y) | monthly (Y) | weekly (Y) | daily or almost daily (Y)
4. How often during the past 6 months did you find that you were not able to stop using cannabis once you had started?
   never (Y) | less than monthly (Y) | monthly (Y) | weekly (Y) | daily or almost daily (Y)
5. How often during the past 6 months did you fail to do what was normally expected from you because of using cannabis?
   never (Y) | less than monthly (Y) | monthly (Y) | weekly (Y) | daily or almost daily (Y)
6. How often during the past 6 months did you needed to use cannabis in the morning to get yourself going after a heavy session of using cannabis?
   never (Y) | less than monthly (Y) | monthly (Y) | weekly (Y) | daily or almost daily (Y)
7. How often during the past 6 months did you have a feeling of guilt or remorse after using cannabis?
   never (Y) | less than monthly (Y) | monthly (Y) | weekly (Y) | daily or almost daily (Y)
8. How often in the past 6 months have you had a problem with your memory or concentration after using cannabis?
   never (Y) | less than monthly (Y) | monthly (Y) | weekly (Y) | daily or almost daily (Y)
9. Have you or someone else been injured as a result of your use of cannabis over the past 6 months?
   no (Y) | yes (Y)
10. Has a relative, friend or a doctor or other health worker been concerned about your use of cannabis or suggested you cut down over the past 6 months?
    no (Y) | yes (Y)

(Adamson & Sellman, 2003)

172

CCAT



Composite Cannabis Assessment Tool (CCAT)

Please choose the options that best describe your cannabis use over the past six months.

1	2	3	4	5
Almost Never/Disagree				Almost Always/Agree

1. How often do you use cannabis instead of using other drugs (i.e., alcohol, recreational drugs, prescription or non-prescription pharmaceuticals)?
2. How often do you use cannabis to relieve pain?
3. How often do you use cannabis to improve sleep?
4. How often do you have difficulty stopping or controlling your use of cannabis?
5. How often do you use cannabis to relieve nausea?
6. How often do you refrain from taking part in leisure time activities that you originally wanted to do, e.g. going out, sports, hobbies, etc., because of using cannabis?
7. How often do you find that you were not able to stop using cannabis once you had started?
8. How often do you use cannabis to improve mood?
9. How often do you use cannabis because you like the feeling?
10. How often do you use cannabis to think differently?
11. How often do you use cannabis to relax?
12. How often do you feel bad about your cannabis use?

Walsh et al., in prep

173

Overdose

Green out

- *Canadian Institute of Health Information*
- 2017-2018 -2,266 ER visits (>25, 000 for other substances)
- Mostly from edibles
  - Dabbing
- Symptoms:
  - Paranoia
  - Anxiety
  - Lethargy
  - Extreme dry mouth
  - Burning eyes
  - Shortness of breath
  - Increased heart rate
  - Shaking / trembling
  - Chills / sweats
  - Disorientation / lack of focus
  - Nausea

https://www.theleafnews.com/news/leaflet-Cannabis-overdoses-in-emergency-rooms-492201931.html

174

Cannabis & Driving

- Influence upon performance is short-lived
  - **Peak acute effects … obtained within 10 to 30 minutes** (NHTSA. 2004. *Drugs and Human Performance Facts Sheets*)
  - "impairment from cannabis **typically clears 3-4 hours after use**. …a minimum wait period before driving." (Fischer et al., 2011. *Lower risk cannabis use guidelines for Canada*)
- Experienced users become tolerant
  - "Experienced smokers who drive on a set course show **almost no functional impairment** under the influence of marijuana."(Sewell et al., 2009. *The effect of cannabis compared with alcohol on driving*)
  - "Patients … develop tolerance to the impairment of psychomotor performance, **so that they can drive vehicles safely**." (Grotenhermen and Mueller Vahl. 2012. *The therapeutic potential of cannabis and cannabinoids*)

175

Accident Analysis and Prevention 60 (2013) 254–267
Contents lists available at ScienceDirect
Accident Analysis and Prevention
journal homepage: www.elsevier.com/locate/aap

Risk of road accident associated with the use of drugs: A systematic review and meta-analysis of evidence from epidemiological studies

Rune Elvik

Table 6
Summary estimates of relative risk of accident involvement associated with the use of various drugs. Based on meta-analysis.

Drug	Accident severity	Number of estimates	Best estimate of odds ratio[a]	95% confidence interval	Best estimate adjusted for publication bias[a]	95% confidence interval
Amphetamine	Fatal	8	**5.61**	(2.74, 11.49)	**5.17**	(2.56, 10.42)
	Injury	2	**6.19**	(3.46, 11.06)	**6.19**	(3.46, 11.06)
	Property damage	1	**8.67**	(3.23, 23.32)	**8.67**	(3.23, 23.32)
Analgesics	Injury	8	1.06	(0.92, 1.21)	1.02	(0.89, 1.16)
Anti-asthmatics	Injury	6	**1.33**	(1.09, 1.62)	**1.31**	(1.07, 1.59)
Anti-depressives	Injury	20	**1.39**	(1.17, 1.70)	**1.35**	(1.11, 1.65)
	Property damage	5	1.28	(0.90, 1.80)	1.28	(0.90, 1.80)
Anti-histamines	Injury	7	**1.12**	(1.02, 1.22)	**1.12**	(1.02, 1.22)
Benzodiazepines	Fatal	10	**2.30**	(1.59, 3.32)	**2.30**	(1.59, 3.32)
	Injury	51	**1.65**	(1.49, 1.82)	**1.17**	(1.08, 1.28)
	Property damage	4	**1.35**	(1.04, 1.76)	**1.35**	(1.04, 1.76)
Cannabis	Fatal	10	1.31	(0.91, 1.88)	1.26	(0.88, 1.81)
	Injury	15	1.26	(0.99, 1.60)	1.10	(0.88, 1.39)
	Property damage	17	**1.48**	(1.28, 1.72)	**1.26**	(1.10, 1.44)
Cocaine	Fatal	4	**2.96**	(1.18, 7.38)	**2.96**	(1.18, 7.38)
	Injury	3	1.66	(0.91, 3.02)	1.66	(0.91, 3.02)
	Property damage	4	1.44	(0.93, 2.23)	1.44	(0.93, 2.23)
Opiates	Fatal	7	**2.13**	(1.23, 3.72)	**1.68**	(1.01, 2.81)
	Injury	18	**1.94**	(1.51, 2.50)	**1.91**	(1.48, 2.45)
	Property damage	1	**4.76**	(2.10, 10.80)	**4.76**	(2.10, 10.80)
Penicillin	Injury	5	1.12	(0.91, 1.39)	1.12	(0.91, 1.39)
Zopiclone	Fatal	1	2.60	(0.89, 7.56)	2.60	(0.89, 7.56)
	Injury	4	1.42	(0.87, 2.31)	1.42	(0.87, 2.31)
	Property damage	1	**4.00**	(1.31, 12.21)	**4.00**	(1.31, 12.21)

[a] Estimates shown in bold are statistically significant at the 5% level.

- Driving with two or more passengers (OR = 2.2) (McEvoy et al., 2007)
- Exceeding the speed limit by 3+ mph (OR = 1.89) (Kloeden et al., 2002)
- Using a mobile phone (OR = 4.1) (Redelmeier and Tibshirani, 1997)

176

February, 2017

AJPH RESEARCH

US Traffic Fatalities, 1985–2014, and Their Relationship to Medical Marijuana Laws

Julian Santaella-Tenorio, DVM, MSc, Christine M. Mauro, PhD, Melanie M. Wall, PhD, June H. Kim, MPhil, MHS, Magdalena Cerdá, DrPH, Katherine M. Keyes, PhD, Deborah S. Hasin, PhD, Sandro Galea, MD, DrPH, and Silvia S. Martins, MD, PhD

"Medical marijuana laws were associated with immediate reductions in traffic fatalities in those aged 15 to 44 years …Dispensaries were also associated with traffic fatality reductions in those aged 25 to 44 years."

177

Lower-risk guidelines

AJPH POLICY

Lower-Risk Cannabis Use Guidelines: A Comprehensive Update of Evidence and Recommendations

Benedikt Fischer, PhD, Cayley Russell, MA, Pamela Sabioni, PhD, Wim van den Brink, MD, PhD, Bernard Le Foll, MD, PhD, Wayne Hall, PhD, Jürgen Rehm, PhD, and Robin Room, PhD

RECOMMENDATIONS

Recommendation 1: The most effective way to avoid any risks of cannabis use is to abstain from use. Those who decide to use need to recognize that they incur risks of a variety of—acute and long-term—adverse health and social outcomes. These risks will vary in their likelihood and severity with user characteristics, use patterns, and product qualities, and so may not be the same from user to user or use episode to another. *[Evidence Grade: None required.]*

Recommendation 2: Early initiation of cannabis use (i.e., most clearly that which begins before age 16 years) is associated with multiple subsequent adverse health and social effects in young adult life. These effects are particularly pronounced in early-onset users who also engage in intensive and frequent use. This may be in part because frequent cannabis use affects the developing brain. Prevention messages should emphasize that, the later cannabis use is initiated, the lower the risks will be for adverse effects on the user's general health and welfare throughout later life. *[Evidence Grade: Substantial.]*

Recommendation 3: High THC-content products are generally associated with higher risks of various (acute and chronic) mental and behavioral problem outcomes. Users should know the nature and composition of the cannabis products that they use, and ideally use cannabis products with low THC content. Given the evidence of CBD's attenuating effects on some THC-related outcomes, it is advisable to use cannabis containing high CBD:THC ratios. *[Evidence Grade: Substantial.]*

Recommendation 4: Recent reviews on synthetic cannabinoids indicate markedly more acute and severe adverse health effects from the use of these products (including instances of death). The use of these products should be avoided. *[Evidence Grade: Limited.]*

Recommendation 5: Regular inhalation of combusted cannabis adversely affects respiratory health outcomes. While alternative delivery methods come with their own risks, it is generally preferable to avoid routes of administration that involve smoking combusted cannabis material (e.g., by using vaporizers or edibles). Use of edibles eliminates respiratory risks, but the delayed onset of psychoactive effect may result in the use of larger than intended doses and subsequently increased (mainly acute, e.g., from impairment) adverse effects. *[Evidence Grade: Substantial.]*

178

Lower-risk guidelines

AJPH POLICY

Lower-Risk Cannabis Use Guidelines: A Comprehensive Update of Evidence and Recommendations

Benedikt Fischer, PhD, Cayley Russell, MA, Pamela Sabioni, PhD, Wim van den Brink, MD, PhD, Bernard Le Foll, MD, PhD, Wayne Hall, PhD, Jürgen Rehm, PhD, and Robin Room, PhD

Recommendation 6: Users should avoid practices such as "deep inhalation," breath-holding, or the Valsalva maneuver to increase psychoactive ingredient absorption when smoking cannabis, as these practices disproportionately increase the intake of toxic material into the pulmonary system. *[Evidence Grade: Limited.]*

Recommendation 7: Frequent or intensive (e.g., daily or near-daily) cannabis use is strongly associated with higher risks of experiencing adverse health and social outcomes related to cannabis use. Users should be aware and vigilant to keep their own cannabis use—and that of friends, peers, or fellow users—occasional (e.g., use only on 1 day/week, weekend use only, etc.) at most. *[Evidence Grade: Substantial.]*

Recommendation 8: Driving while impaired from cannabis is associated with an increased risk of involvement in motor-vehicle accidents. It is recommended that users categorically refrain from driving (or operating other machinery or mobility devices) for at least 6 hours after using cannabis. This wait time may need to be longer, depending on the user and the properties of the specific cannabis product used. Besides these behavioral recommendations, users are bound by locally applicable legal limits concerning cannabis impairment and driving. The use of both cannabis and alcohol results in multiply increased impairment and risks for driving, and categorically should be avoided. *[Evidence Grade: Substantial.]*

Recommendation 9: There are some populations at probable higher risk for cannabis-related adverse effects who should refrain from using cannabis. These include individuals with predisposition for, or a first-degree family history of, psychosis and substance use disorders, as well as pregnant women (primarily to avoid adverse effects on the fetus or newborn). These recommendations, in part, are based on precautionary principles. *[Evidence Grade: Substantial.]*

Recommendation 10: While data are sparse, it is likely that the combination of some of the risk behaviors listed above will magnify the risk of adverse outcomes from cannabis use. For example, early-onset use involving frequent use of high-potency cannabis is likely to disproportionately increase the risks of experiencing acute or chronic problems. Preventing these combined high-risk patterns of use should be avoided by the user and a policy focus. *[Evidence Grade: Limited.]*

179

Cannabis

https://www.ncbi.nlm.nih.gov/books/NBK423845/pdf/Bookshelf_NBK423845.pdf

CANNABIS : SUMMARY REPORT

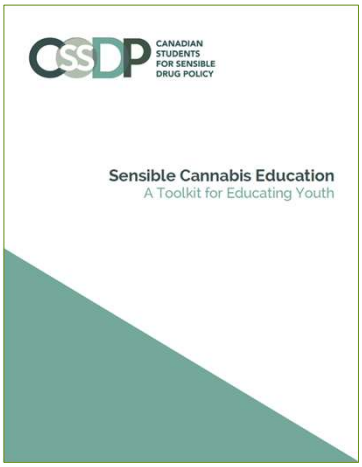
Proposed Criteria for Differentiating Use Types

	Environment	Quantity	Frequency	Period of use and intensity
Experimental / Occasional	Curiosity	Variable	A few times over lifetime	None
Regular	Recreational, social Mainly in evening Mainly in a group	A few joints Less than one gram per month	A few times per month	Spread over several years but rarely intensive
At-risk	Recreational and occupational (to go to school, to go to work, for sport…) Alone, in the morning Under 16 years of age	Between 0.1 and 1 gram per day	A few times per week, evenings, especially weekends	Spread over several years with high intensity periods
Excessive	Occupational and personal problems No self regulation of use	Over one gram per day	More than once per day	Spread over several years with several months at a time of high intensity use

Even if **cannabis itself poses very little danger to the user and to society as a whole, some types of use involve risks**. It is time for our public policy to recognize this and to **focus on preventing at-risk use and on providing treatment for excessive cannabis users**.

180

Cannabis – Young adults



www.cssdp.org/youthtoolkit

1. 10 Principles for Approaching Cannabis Education with Young People

2. Pull Away Curriculum
   a. Cannabis 101
   b. Why Youth Use and Don't Use Cannabis
   c. Harm Reduction
   d. Legislative Overview
   e. Literature Review of Health Harms (as of Dec 2017

181

TEN GUIDING PRINCIPLES

- 1. Education grounded in evidence-based information rather than fear
- 2. Open dialogue that is non-judgmental and use interactive approaches
- 3. Meaningful inclusion
- 4. Delivery by a trained facilitator or peer
- 5. Starting earlier with age-appropriate content

182

TEN GUIDING PRINCIPLES

- 6. Supporting parents to have age appropriate and open conversations
- 7. The inclusion of harm reduction
- 8. Education tailored to the specific context
- 9. Ongoing education available to youth
- 10. Attention to overlapping issues of racism, social justice, and stigma

183

SUPPORT PARENTS TO HAVE OPEN AND INFORMED CONVERSATIONS

- Families also need support to initiate and encourage ongoing conversations around cannabis
- Parents are often left out of educational efforts for drug education, but can be a key component to ensuring consistent messaging around cannabis, particularly in a legalized context[1]
- Supporting parents' access to information is an essential, but often overlooked piece

For parents and guardians, this means discussions around cannabis use should be ongoing, open, and non-judgmental

1 Soole D, Mazerolle L, Rombouts S. School Based Drug Prevention Programs: A Review of What Works. *Aus NZ J Crim*. 2008; 41(2): 258-286

184

INCLUDE HARM REDUCTION

- Harm reduction strategies also address the needs of young people who may already be using
- Most effective with older youth (senior high school and above) and heavy youth cannabis users[1]
- Teaching harm reduction strategies doesn't encourage youth to use cannabis, and is an effective approach in a range of contexts[2]
- Brief Interventions - short and easy to administer interventions; can be delivered in medical (e.g., GP'S offices) or more general, non-medical settings[3]

2 Kohler PK, Manhart LE, Lafferty WE. Abstinence-Only and Comprehensive Sex Education and the Initiation of Sexual Activity and Teen Pregnancy. *J Adolesc Health*. 2007; 42(4): 344-51.

185

YOUTH REVISED HR TIPS - TOOLKIT

1. Start low and go slow
2. Consider appropriate time and place
3. Choose less risky cannabis products
4. Choose safer methods of consumption
5. Utilize safer smoking practices
6. Reduce the amount of cannabis used, and how frequently its used
7. Avoid synthetic cannabis altogether
8. Avoid mixing cannabis with tobacco and alcohol
9. Don't drive high and be informed about changing driving laws (e.g. zero tolerance under 21)
10. Consider your risk profile and avoid if pregnant

186

Treatment- Cannabis Check-Up

- In-School MET Intervention
- Individual Sessions
- Brief
- Not Treatment
- No pressure, no judgment
- Computerized Assessment
- No Parental Consent

Walker, Roffman, Stephens, Berghius, & Kim (2006)

187

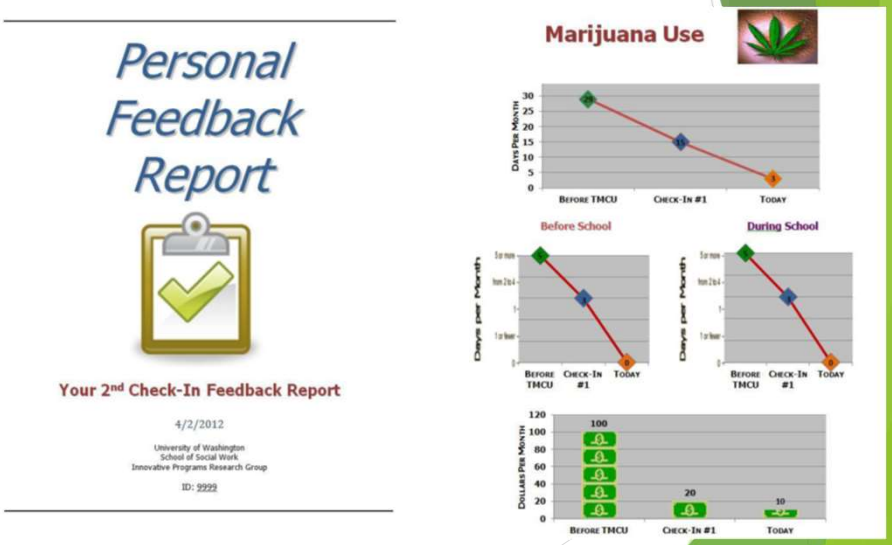
Treatment- Cannabis Check-Up

- Two individual sessions (30-60 minutes)
- Motivational Interviewing
- Review of Personal Feedback Report
- Personal Feedback Report included:
  - Normative data
  - Summaries of
    - Recent use patterns
    - Abuse and dependence symptoms
    - Goals
    - Social supports
    - Benefits of Quitting

Walker, Roffman, Stephens, Berghius, & Kim (2006)

188

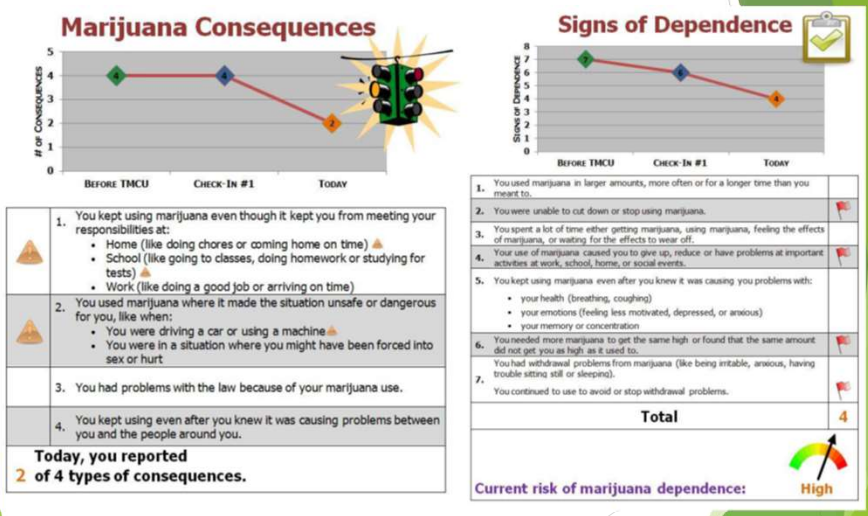
Treatment- Cannabis Check-Up



Walker, Roffman, Stephens, Berghius, & Kim (2006)

189

Treatment- Cannabis Check-Up



Walker, Roffman, Stephens, Berghius, & Kim (2006)

190

Treatment- Cannabis Check-Up

Life Goals

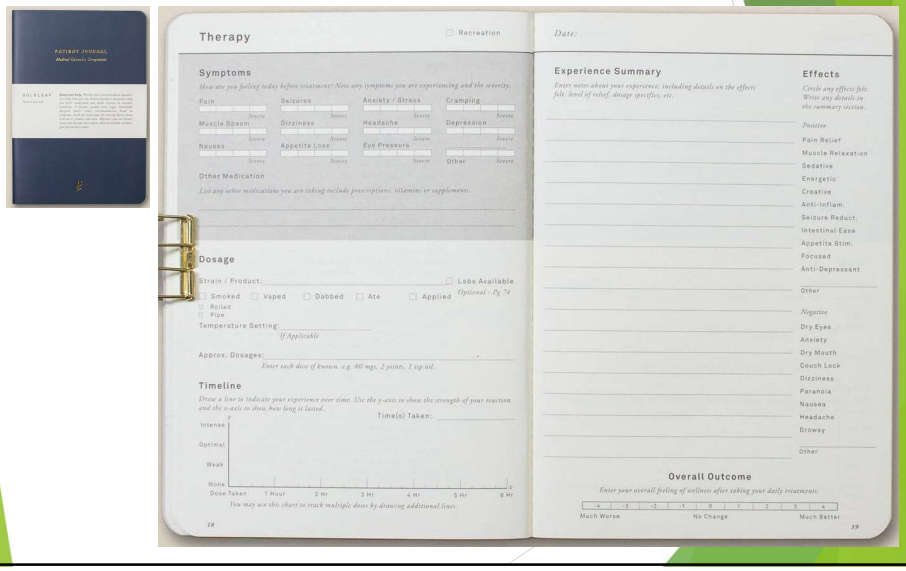
Very Negatively 1	Negatively 2	Not Positively or Negatively 3	Positively 4	Very Positively 5

Your Goals:	Your marijuana use affects this goal:	Reducing your marijuana use would affect this goal:
1)		
2)		
3)		
4)		
5)		

Walker, Roffman, Stephens, Berghius, & Kim (2006)

191

Mindful Cannabis Use



192

Jeffrey Y. Hergenrather, MD
General practice physician
Solo private practice
Cannabis consultations since 1997
Sebastopol, California

SOCIETY of CANNABIS CLINICIANS

President and founding member of
The Society of Cannabis Clinicians

193

Treatment plan

Dosing range: Titrate for desired effect (low and slow)

Micro-dosing 1 ug/kg/day
Average dosing:
"High dose" 1-20 mg/kg/day

Frequency of dosing

- Episodic or as needed
- Daily administration: morning, evening or bedtime
- Multiple or frequent administrations daily
- Holidays

194

Treatment Plan

Method of Admininistration (MOA):

- ☐ Oral tincture, infusion, or spray, alcohol or oil based
- ☐ Full extract cannabis oil, FECO
- ☐ Other ingested flowers, products, or concentrates
- ☐ Vapor or smoke
- ☐ Suppositories
- ☐ Topical

Cannabinoid ratio: Preferred ratio of principle cannabinoids, THC:CBD.

- ☐ **High CBD** strain: CBD:THC (30:1 <-> 10:1) , (ACDC, Charlotte's Web, and others)
- ☐ **Balanced**: 6:1<-> **1:1** <-> 1:2 THC:CBD, nominally 1:1
- ☐ **High THC** strain: (THC:CBD ~ 100:1 <-> 50:1)
- ☐ **Other:** e.g. consider a High CBD tincture in the AM before breakfast and a balanced THC:CBD tincture at bedtime

Frequency: Frequency varies depending therapeutic goal, variations in the rate of hepatic metabolism, and MOA.

- ☐ Once daily
- ☐ Twice daily, AM before breakfast or PM, and bedtime
- ☐ Three times daily, every 8 hours ~ AM before breakfast, PM, and bedtime
- ☐ Other _____

195

Developing the Treatment Plan

Suggested Dose: Wide range in dosing depending on tolerance and individual differences.

Generally dosing is increased by slow titration to effective dose.

- ☐ 2 1/2 mg to 5 mg per dose
- ☐ 5 - 10 mg per dose
- ☐ 10 - 20 mg per dose
- ☐ 20 - 40 mg per dose
- ☐ ~ 50 mg per dose
- ☐ Other: e.g. Increase dose gradually and speadily..

Target dose: (SPECIAL CONDITIONS)

- ☐ Minimum target dose: _____ mg / day, (or mg/dose)
- ☐ Maximum target dose: _____mg / day, (or mg/dose)

Tolerance (a reminder): Develops with a steady, at least daily, dosing with induction of auto-regulation of cannabinoid CB1 receptor population (internalization of CB1 receptors). From onset tolerance develops in ~ 1-2 weeks,

Footnotes:

1. All products are considered to be organically grown and produced.
2. Products have accurately measured cannabinoid content and terpenes when available.
3.. Hold dose if too sleepy
4. Drug-Drug interactions: For nearly all conventional pharmaceuticals there is no significant drug-drug interactions with cannabis/cannabinoids. Clobazam and other anti-epileptics drugs metabolized by the hepatic CYP 2C19 and CYP 3A4 families, with concurrent high doses of cannabis concentrates (> 1 mg/kg/day) should be monitored for safe and effective blood levels of these anti-epileptic medications.

196

Treatment Plan - Precautions

- Anxiety and panic in the neophyte or THC sensitive
- Syncope and/or fall risk especially with high dose "dabs"
- Smoking > bronchitis ~ No COPD, emphysema, or cancers
- Habit Forming ~ Not addictive, minor withdrawal
- Drug Drug interaction: CYP450 2C and 3A families
- Association with schizophrenia and psychosis
- Association with the hyperemesis syndrome

197

Case 1 - Janis

- 27y/o female
- Recently separated
  - 2 & 5 y/o daughters
- Symptoms of anxiety & depressed mood
  - Sleep disturbance
  - Use cannabis -
    - Mild in late teens
    - Currently smoked in pipe
    - 3-5x week evenings
    - sleep
  - Guilt related to use

198

Case 2 - Benedict

- 19y/o male
- Single
- Living with parents
- Part time – service industry
- Referred by parents
  - Use cannabis –
    - Started 14 y/o
    - Daily 3-5x
    - 3-7 grams week
  - Low motivation to change

199

Case 3 - Sunil

- 64 y/o male
- Single
- Living alone
- Chronic pain & d/t MVA 5 years ago
  - depression
- Alcohol and opioid use
  - Referred by children
  - Cannabis naive

200

THANKS

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201