The “Standard of Care” and Medical Cannabis (Marijuana)

Eric A. Voth, M.D., F.A.C.P-Internal Medicine, Pain, and Addiction Med

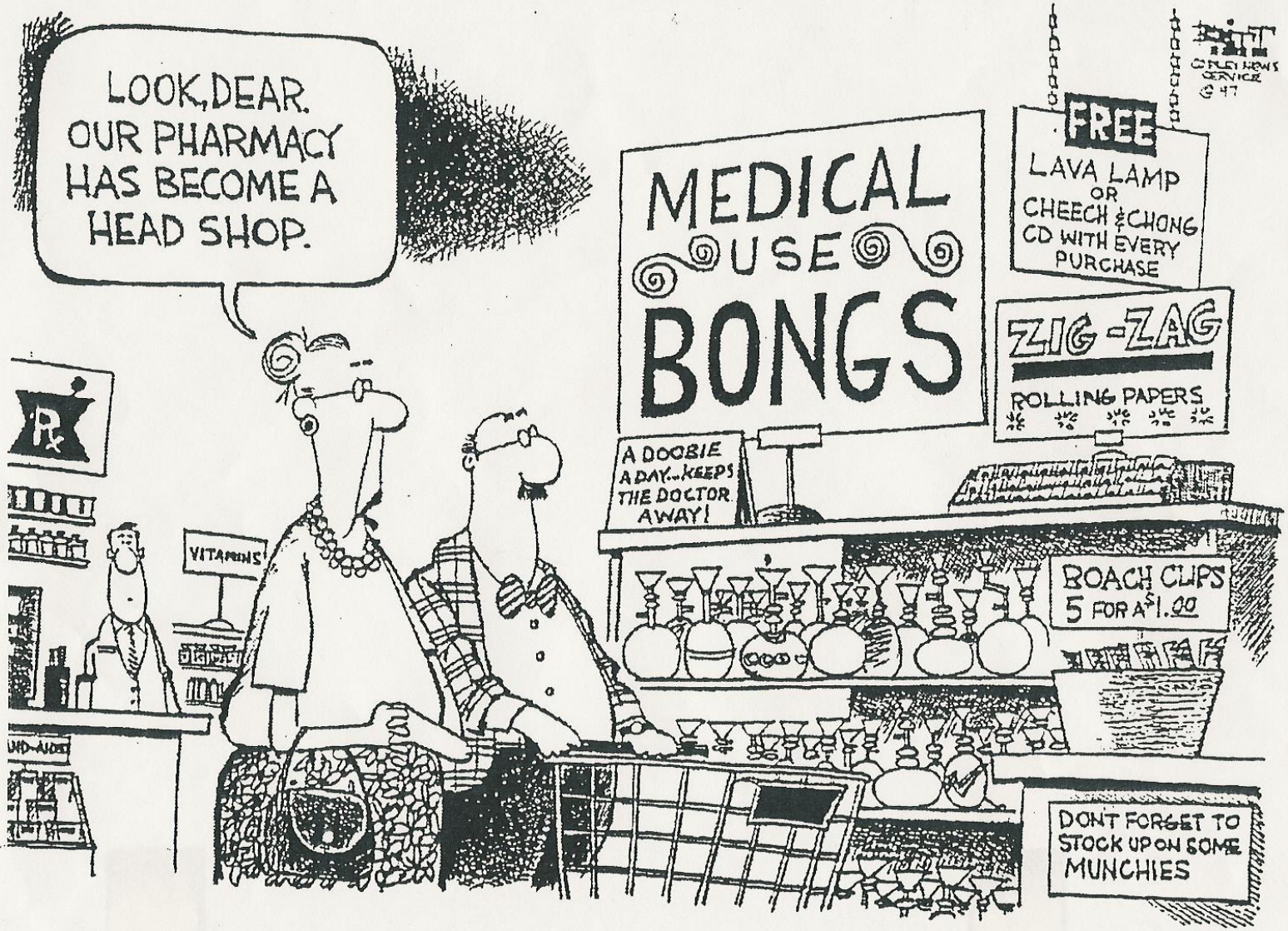
President and Chairman of the Board

The International Academy on the Science and Impact of Cannabis

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

Financial Disclosure

I receive no funding from the cannabis industry nor any of its lobbyists and my presentation is my own production. I furthermore declare that my work with the International Academy on the Science and Impact of Cannabis is voluntary and that I receive no funding nor personal financial benefits.


LOOK, DEAR. OUR PHARMACY HAS BECOME A HEAD SHOP.
MEDICAL USE BONGS
FREE LAVA LAMP OR CHEECH & CHONG CD WITH EVERY PURCHASE
ZIG-ZAG ROLLING PAPERS
A DOOBIE A DAY... KEEPS THE DOCTOR AWAY!
ROACH CLIPS 5 FOR A $1.00
DON'T FORGET TO STOCK UP ON SOME MUNCHIES
VITAMINS

Medical Excuse Marijuana

- No compelling evidence that there is a significant group of untreated or inadequately treated patients for which Marijuana is proven useful.
- Support is vastly anecdotal.
- **Marijuana lobby getting its "nose under the tent"**

Fundamental Problems with Medical Cannabis

- **Safe, effective reliable medicines are best for patients, and they are available**
- **Cannabis is impure, unreliable, full of contaminants, high side effect rate.**
- **Defense to possession bypasses FDA and jeopardizes consumer protection**
- **Non-FDA approved Cannabis creates “medicine by popular vote.”**
- **Cannabis is a delivery vehicle for Delta-9-THC (known medicine) and as such should be regulated by the FDA**
- **Conduit for recreational Use**

Definition of "The Standard of Care"

Definition:

The care that **qualified practitioners would have used to manage the patient's care under the same or similar circumstances.**

Guiding principle:

First, do no harm.

Innov Clin Neurosci. 2021;18(7–9):50–51

West J Emerg Med. 2011;12(1):109-112.]

DEA Controlled Med Schedules

- **Schedule I**-Schedule I drugs, substances, or chemicals are defined as drugs with **no currently accepted medical use and a high potential for abuse**.
- **Schedule II-** Schedule II drugs, substances, or chemicals are defined as drugs **with a high potential for abuse, with use potentially leading to severe psychological or physical dependence**. These drugs are also considered dangerous. Some examples of Schedule II drugs are: cocaine, methamphetamine, methadone, hydromorphone (Dilaudid), meperidine (Demerol), oxycodone (OxyContin), fentanyl, Dexedrine, Adderall, and Ritalin
- **Schedule III-** drugs, substances, or chemicals are defined as drugs with a moderate to **low potential for physical and psychological dependence**. Schedule III drugs abuse potential is less than Schedule I and Schedule II drugs but more than Schedule IV. Some examples of Schedule III drugs are: Marinol (Tylenol with codeine), ketamine, anabolic steroids, testosterone

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

Patterns of Use

- 1500 participants-709 cannabis users
- Mean age 30.19
- 61.4% Used exclusively recreationally
- 38.6 % Perceived medical use
- 23.4 % of medical users had health care authorize
- 80.6 % of medical users used recreationally

- Comprehensive Psychiatry 102 (2020) 152188

Deviation from the Standard of Care

- Malpractice Risk
- Medical Disciplinary action
- Criminal prosecution especially if intentional harm (knowledge of risk)
  - Examples: sale or recommendation to individual that becomes psychotic and kills people
  - Traffic fatalities
  - Development of persistent psychosis
  - Hyperemesis complications

Medical Excuse Marijuana

As with any medication that possesses significant side effects, it is imperative to understand that there are important medical, legal, and social consequences to the use of marijuana for medicinal applications.

All “medicines” should be approved by the FDA

Elements of the Standard of Care: Typical Medical Evaluation

- Review of diagnosis for indication
- Detailed Medical History
  - History of present illness
  - Past Medical History
    - Potentially complicating disorders
    - Contraindications to Marijuana
  - Social History (and employment)
  - Family History
  - Review of Systems

"Standard of Care" - cont.

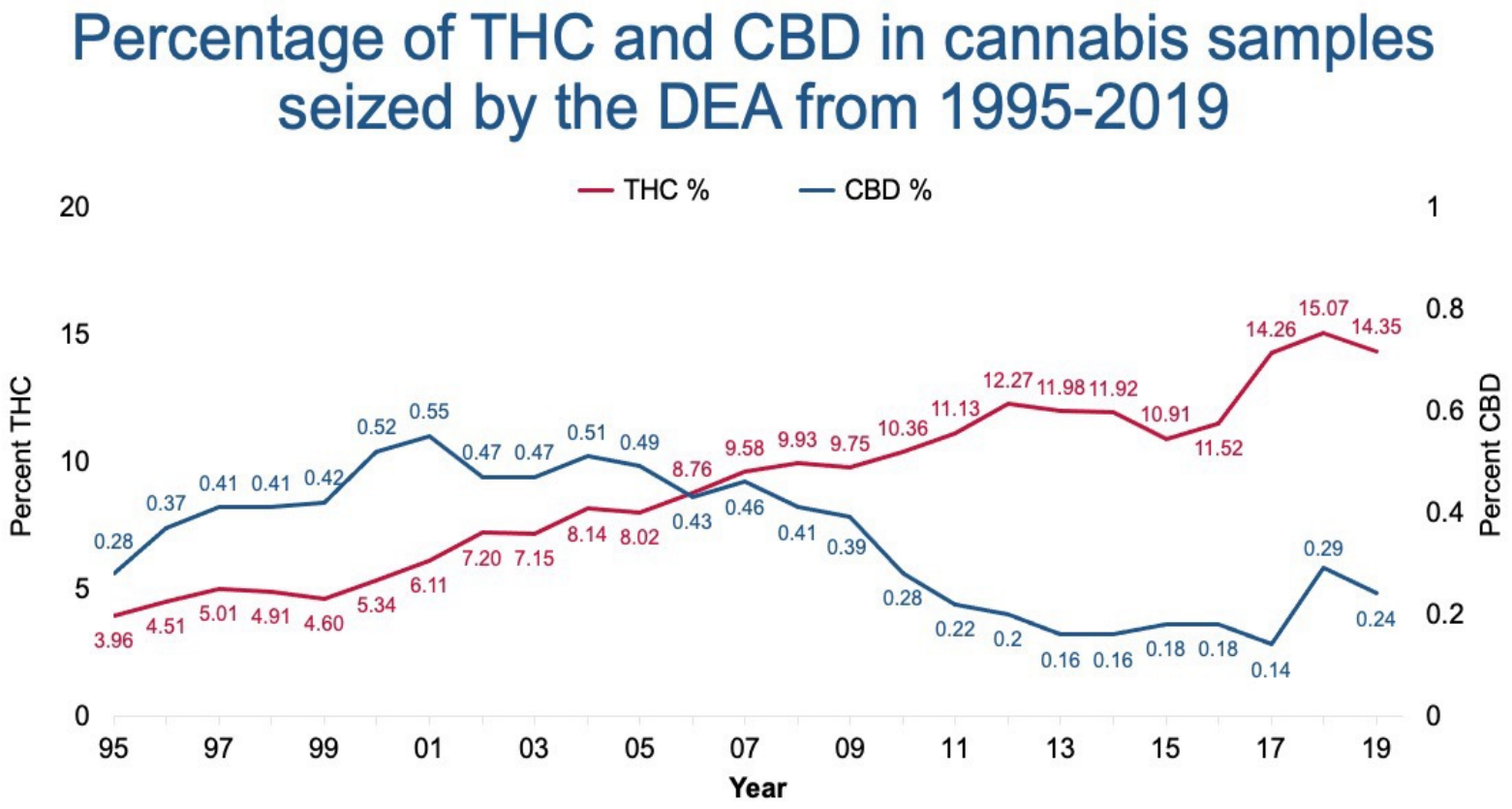
- **Complete** physical examination
- Review of diagnostic studies (e.g. lab, drug testing, radiographic/scans)
- Review and documentation of failed interventions or medications.
- Determination of **exact dose/strength**
- Responsibility to **Warn** of complications
- Responsibility to **Monitor**

Standards of Pharmacotherapy

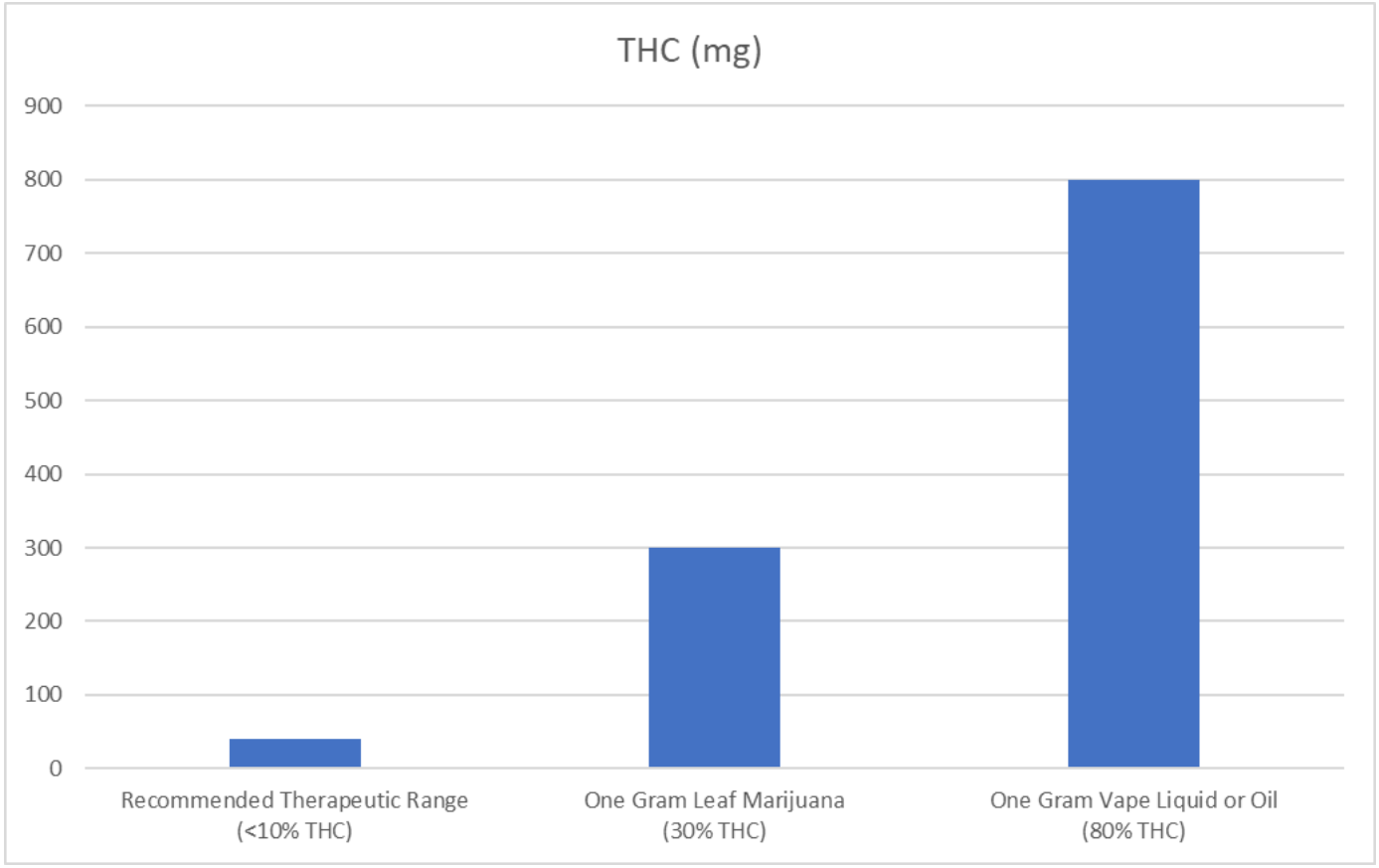
- **Demonstrated and proven efficacy *****
- Predictable dose response ***
- Known dose availability ***
- Known and predictable side effects ***
- Be cautious of reinforcing qualities ***

*****Not available with Marijuana**

Marijuana Potency/Dose



Relative THC Concentrations/Dose



Purity: “Natural Substance”
A Few Cannabis Contaminants

- *Aspergillus* Species
- *Penicillium* Species
- *Penicillium* Species
- *Fusarium Oxysporum*
- *Escherichia coli*
- *Salmonella*
- *Clostridium*
- *Heavy Metals eg Cadmium*

Front Pharmacol. 2020; 11: 571832. PMCID: PMC7516211 Published online 2020 Sep 11. doi: 10.3389/fphar.2020.571832

Marijuana advocates' position: Cannabis is "natural"

Most Commonly Advocated as Treatment for:

- Pain
- Depression
- PTSD

“Qualifying Medical Conditions” Where is the Science??

Kansas Senate Bill 560

Qualifying medical condition” means **any of the following**:

(1) Acquired immune deficiency syndrome;

(2) Alzheimer's disease;

(3) Amyotrophic lateral sclerosis;

(4) Cancer;

(5) Chronic traumatic encephalopathy;

(6) Crohn's disease;

(7) Epilepsy or another seizure disorder;

(8) Fibromyalgia;

(9) Glaucoma;

(10) Hepatitis C;

(11) Inflammatory bowel disease

(12) Multiple sclerosis;
(13) Pain that is either chronic and severe or intractable;
(14) Parkinson's disease;
(15) Positive status for HIV;
(16) Post-traumatic stress disorder;
(17) Sickle cell anemia;

(18) Spinal cord disease or injury;

(19) Tourette's syndrome;
(20) Traumatic brain injury;
(21) Ulcerative colitis;

As well as “any other debilitating condition”

Marijuana For Pain

Marijuana for Neuropathic Pain

- 38 subjects/# who had 30% reduction

Placebo	Medium 3.53	Low 1.29
27%	57%	61%

- Significant dose-related effects on memory and learning
- Both groups reported feeling high, stoned, impaired, medium greater than low dose.
- Massive doses appear unnecessary

- Journal of Pain, Vol 16, No 7 (July), 2015: pp 616-627

Marijuana for Pain-
VA study 2017

- Extensive review of literature on marijuana and pain
- 27 Chronic pain trials, low strength evidence for benefit with neuropathic pain
- 11 reviews and 33 studies-increased risk for motor vehicle accidents, psychosis, and cognitive impairment.

Annals of Internal Med 2017

Doi:10.7326/M17-0155

Marijuana for Pain

- Screening 1975 citations, 72 systematic reviews
- Adverse effects were reported in most reviews comparing cannabis with placebo (49/59, 83%) and in 20/24 (83%)
- Small number of results showed a benefit for reducing pain, considering pain in general.

Pratt et al. Systematic Reviews (2019) 8:320
https://doi.org/10.1186/s13643-019-1243-x

Marijuana for Pain

- IASP Taskforce
- 193 Trials, 129 excluded
- 36 Randomized-controlled studies
- 7217 participants

Conclusion: no reliable evidence to support or refute the use of cannabis, cannabinoids, or cannabis-based medicine in the treatment of chronic, acute, or cancer pain.

Bell, Rae F.A; Kalso, Eija A Cannabinoids for Pain or Profit PAIN

Presidential Taskforce on Cannabis and Cannabinoids for Pain 2021

Conclusion:

Although there is preclinical data supporting the hypothesis of cannabinoid analgesia, uncertainties in the clinical evidence base led the Task Force to not support the general use of Cannabis nor cannabinoids for analgesia.

Pain July 2021, vol 162 #7, S3-4

Cannabis Products for Chronic Pain

- Comparison of THC/CBD ratios & effects
- Short term improvements with higher THC/CBD ratios, some sedation and dizziness
- Risk of Bias low to moderate in all studies
- Intervention doses ranged from **1mg/day to 25 mg per day of THC**

Ann Intern Med 2022:175;1143-1153

McDonagh et all

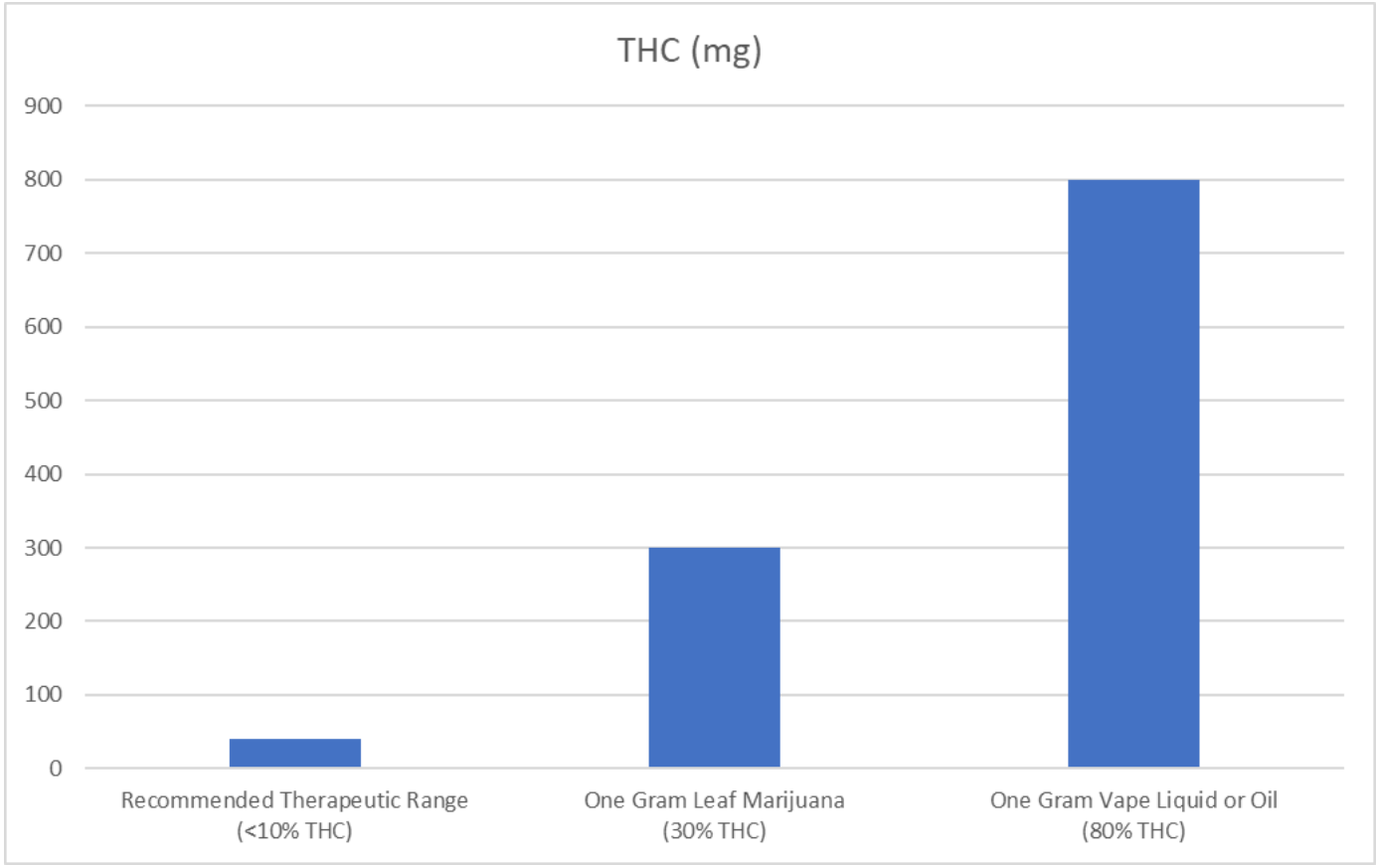
IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

Pain and Placebo Effect

- 20 Studies with 1459 subjects
- Pain Intensity associated with placebo response
- Media attention strong pos bias
- Placebo effect contributes significantly to pain reduction

Gedin et al JAMA Open 2022;5(11):
e2243848 Nov 28, 2022

Relative THC Concentrations/Dose



PTSD and Marijuana Use

- 2000 participants in VA treatment programs
- Non-users had significantly less symptoms
- Prior users who quit had less symptoms
- Users had higher levels of violence,
- New users had higher levels of violence and also turned more to other drugs

Commented: "Most people assume things based on their own experience… People assume that there aren't a lot of risks…..there really are"

Wilkinson Yale University

December 2014 Presented to the AAAP

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

PTSD

In the absence of well-controlled evidence on the long-term efficacy of cannabinoids in improving the symptoms of PTSD (National Academies of Sciences, Engineering, & Medicine, 2017), findings based on the statistically rigorous models utilized in our and other prospective studies **do not support the widespread state sanctioned medical use of cannabis for the treatment of PTSD.** For these individuals, recommending cannabis cessation and seeking evidence-based treatment for PTSD may help improve PTSD outcomes and mitigate the risk of a comorbid CUD.

Psychological Medicine 52, 446–456. https://doi.org/10.1017/

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

PTSD and Cannabis Use Disorder

Strong Association between PTSD and CUD

Strong Relation between Cannabis use and severity of Trauma

Findings based on the statistically rigorous models utilized in our and other prospective studies **do not support the widespread state-sanctioned medical use of cannabis for the treatment of** PTSD. For these individuals, recommending cannabis cessation and seeking evidence-based treatment for PTSD may help improve PTSD outcomes and mitigate the risk of a comorbid CUD.

Psychological Medicine 52, 446–456.17 June 2020
https://doi.org/10.1017/ S003329172000197X

IASIC

INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS

Doctors Educating on Marijuana

Complications of Marijuana Use

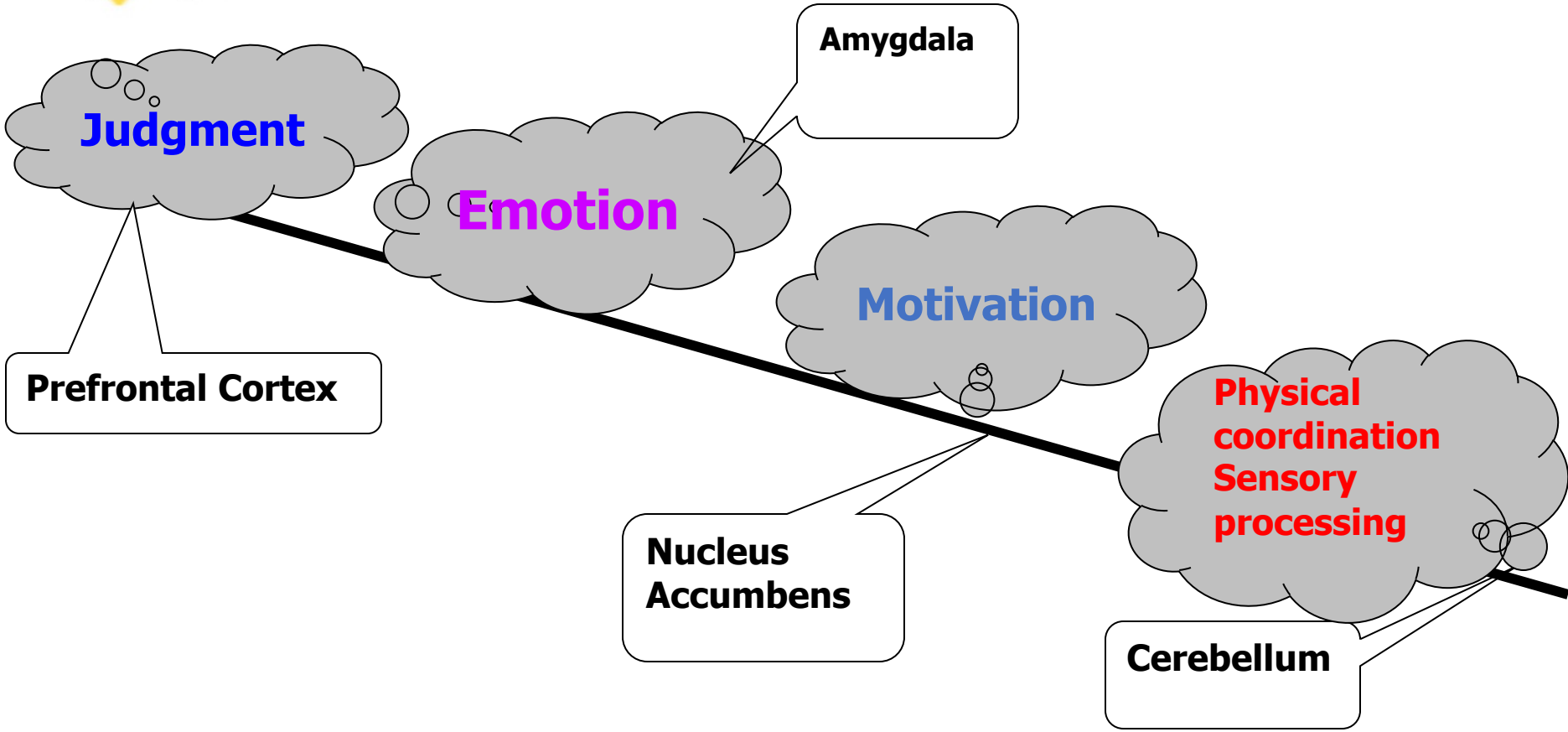
Recent Summary of Cannabis-Associated Disorders

- Acute or chronic psychosis
- Acute anxiety disorder
- Acute violent disorder
- Acute cannabis intoxication
- Acute Cannabis use disorder
- Chronic Cannabis-induced Psychosis
- Cannabis-induced Delirium

- Gorelick
- NEJM 389;24 nejm.org
- December 14, 2023

START TALKING BEFORE THEY START DRINKING
www.stopalcoholabuse.gov

Brain Development



Maturation starts at the back of the brain and moves to the front

Judgment is last to develop!

Complications of Marijuana Use
Cognitive Changes

- Attention
- Concentration
- Decision-making
- Disinhibition
- Impulsivity
- Working memory
- Verbal fluency
- Concept formation and planning

J Addict Med 2011;5:1-8

Structural Change on MRI

- 48 marijuana users
- Abnormal Gray Matter volume
- Abnormal Orbitofrontal Cortex
- Part of the reward network of the brain
- Cumulative deleterious effect on OFC

Filbey et al

Proceedings of the National Academy of Sciences, 2014;111:16913-16918

Neuropsychological Decline

- 1037 individuals
- Pot use at 18,21,26,32,38 y/o
- Neuropsych testing at 13 before pot and 38
- Broad Neuropsychological decline across all domains even controlling for education
- 10% (101-91) IQ difference between never and persistent user.
- **6-point IQ decline age 13-38 w/ persistent use**

Proc Natl Acad Sci U S A. 2012 Aug 27

Cannabis and Opioid Relationship

- Both receptors found at **presynaptic terminals**
- Both receptors co-localize in **GABA-ergic neurons**
- Both systems **share** pharmacologic profiles
- Sedation, antinociception, hypotension, hypothermia, decreased intestinal motility, drug-reward reinforcement
- Naloxone may have effects on the cannabinoid system in several animal models

Cannabis and Opioid Relationship

- The number one risk factor for adolescent opioid misuse is having EVER use marijuana (lifetime use); YRBS, 2020
  - https://www.cdc.gov/mmwr/volumes/69/su/su6901a5.htm?s_cid=su6901a5_w
- The predominant predictor of adult opioid misuse is having used marijuana before the age of 18
  - https://www.sciencedirect.com/science/article/abs/pii/S0376871620300041
- Cannabis use increases the risk of developing opioid use disorder
  - https://pubmed.ncbi.nlm.nih.gov/28946762/

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

Psychiatric and Behavioral Disorders

Depression

- Depressive responses measured
- Lower doses= Serotonin agonist
- Higher doses= Serotonin suppressant
- Effect was the Medial Prefrontal Cortex

J Neuroscience 2007;27:11700-11711

Marijuana and Bipolar Illness

- 166 first-episode bipolar I disorder patients.
- Cannabis and alcohol associated with the first episode of mania

Bipolar Disorder 2008;10:738-741

Persistence of Psychosis

- Risk of psychosis -no prior psychosis who used pot, 1.9 times greater that non-users in avg. 3.5 years.
- Continued pot use risk of future psychosis was 31% vs **20% in those who did not continue use** out to approx. 8.5 years.

BMJ 2011;342: d738

Psychosis Related to Delta-9-THC

- Presence of psychosis related to percentage of THC
- Threshold for **increased psychosis appears about 10% THC concentration**
- Daily use increased risk

***Lancet Psychiatry* 2019; 6: 427–36**
Published **Online** March 19, 2019

Psych and Behavioral Risk

Cannabis use disorder is a common comorbidity and risk marker for **self-harm, all-cause mortality, and death by unintentional overdose and homicide among youths with mood disorders.** These findings should be considered as states contemplate legalizing medical and recreational marijuana, both of which are associated with increased CUD.

Cynthia A. Fontanella, PhD

JAMA Pediatr. doi:10.1001/jamapediatrics.2020.5494

American Psychiatric Association Review of Cannabis 2021

- Need to **follow FDA processes**
- Underlying Psych disorders present risk
- **Can trigger anxiety, depression, suicidal ideation, psychosis, dependence**.
- **Not approved for any medicinal uses**
- Use for Opiate use disorder not approved
- Recreational use and medicinal use should be considered separately.

Suicidal Ideation and Attempts

- 281,650 adults aged 18 to 34 years who participated in the National Surveys on Drug Use and Health
- Cannabis use was associated with higher prevalence of suicidal ideation, plan, and attempt

JAMA Han et al
June 22, 2021 1/15

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

Marijuana and Psychosis

This population-based cohort study found that CUD was associated with an increased risk of psychotic and nonpsychotic bipolar disorder and unipolar depression. 6 651 765 individuals (50.3% female) were followed

Cannabis use disorder associated **unipolar depression** (HR, 1.84; 95% CI, 1.78-1.90), **psychotic unipolar depression** (HR, 1.97; 95% CI, 1.73-2.25), and **nonpsychotic unipolar depression** (HR, 1.83; 95% CI, 1.77-1.89). Cannabis use was associated with an increased risk of **bipolar disorder in men** (HR, 2.96; 95% CI, 2.73-3.21) and women (HR, 2.54; 95% CI, 2.31-2.80), **psychotic bipolar disorder** (HR, 4.05; 95% CI, 3.52-4.65), and nonpsychotic bipolar disorder in men

Oskar Hougaard Jefsen, MD; Annette Erlangsen, PhD; Merete Nordentoft, DMSc; Carsten Hjorthøj

JAMA Psychiatry. doi:10.1001/jamapsychiatry.2023.1256

Published online May 24, 2023.

Impulsivity and Hostility

- Impulsivity increased with use on same day and day prior
- Hostility self-rated increased interpersonal hostility
- Hostility perceived in others increased

Drug AlcoholDepend. (2015),
http://dx.doi.org/10.1016/j.drugalcdep.2014.12.029

Sexual Assault/ Victimization

- Alcohol and Marijuana predict violence. Kraanen Journal of Substance Abuse Treatment 46 (2014) 532–539
- Marijuana-associated partner aggression Moore Clinical Psych Review 28 (2008) 247-274
- College Drug Use and Partner Violence

  Nabors Journal of Interpersonal Violence 25(6) 1043–1063
- Dating Aggression by Adolescents

Reyes Journal of Adolescence 37 (2014) 281–289

Cannabis and Violence

- Documents 11 cases of Marijuana-related violence
- "highly documented association between marijuana and violence. A legal standard used for 14. causation can be applied to illustrate this association. A legal cause is 15. "but for" the actions or circumstances, the result would not have occurred. A proximate cause is the result was "foreseeable" based on 16. the facts and actions. The most likely legal and proximate cause of violence in these cases was the use and intoxication from marijuana. 17. No other variables fulfill these requirements."

Miller and Oberbarnscheidt, J Addict Res Ther 2017, S11:014 DOI: 10.4172/2155-6105.1000S11-014

Violence-con't

1. Parkland Shooter (Cruz) and 14 other cases
2. Marijuana use causes violent behavior through increased aggressiveness, paranoia, and personality changes (more suspicious, aggressive, and anger).
3. Recent illicit and "medical marijuana" (especially grown by care givers for medical marijuana) is of much high potency and more likely to cause violent behavior.
4. Marijuana use and its adverse effects should be considered in cases of acts of violence as its role is properly assigned to its high association.
5. Recognize that high potency marijuana is a predictable and preventable cause of tragic violent consequences.

Int. J. Environ. Res. Public Health **2020**, *17*, 1578; doi:10.3390/ijerph17051578
www.mdpi.com/journal/ijerph

Violence cont

- Chris Kyle- Navy Seal hero
  - Murdered 2/2/2013 by PTSD sufferer who smoked marijuana and became psychotic the night before going to shooting range with Kyle and an associate to help with his PTSD

Violence cont.

- **11/20/21 Darrell Brooks, Jr**, 39, **drove through a Christmas parade** in Waukesha, WI, killing 6, including a child. He had a long arrest record including **several arrests for marijuana. Was clearly psychotic at the time. On his social media pages, Brooks describes himself as a "stoner."** https://www. nationalreview.com/corner/was-the-waukesha-killer-a- stoner/ "... Brooks' attorney, public defender Anna Kees, argued that Brooks was high during the incident, noting that officers who arrested him noticed he smelled of marijuana and his eyes were red and glassy...

Violence cont.

- **12/27/21 - Lakewood, Colorado** shooter Lyndon McLeod took out his anger at several massage parlor owners and co-workers, killing 6 people and trying to kill more. He divulged his planning in books, he appears to have been a long-time pot user because a **couple who bought a house from him said he had a large marijuana grow in the** house. https://denver.cbslocal.com/2021/12/29/lyndon-mcleod-couple-home-denver- shooting-spree/#.Yc01SXrLOxo.twitter

Violence cont.

- **5/24/22 Uvalde, Texas** shooter Salvador Ramos killed 21 (19 students, 2 teachers) and injured 18. He was a **marijuana user, which the New York Times first reported and then took down off their website.** https://alexberenson.substack.com/p/urgent-the-new-york-times-has-edited/comments

Violence cont.

- **7/4/22** Bobby Crimo of **Highland Park IL** shot and killed 6 and injured about 20, in a 4th of July parade and injured many. He was described in **social media by a former friend as an "isolated stoner who completely lost touch with reality."** https://twitter.com/mtracey/status/1544248652033654784

IASIC
INTERNATIONAL ACADEMY ON THE SCIENCE AND IMPACT OF CANNABIS
Doctors Educating on Marijuana

Recommendations

- **Require FDA approval process for all cannabis-based medicines or substances**.
- Require much tighter regulatory control of Pot-shops and age limits over 24 y/o
- Require warnings on any preparations over 10% THC or BETTER YET- **prohibit concentrations over 10% and a require daily total limit**