In-Person Professional Testimony in Opposition to Senate Bill SB 560
The Medical Marijuana Regulation Act

Eric A. Voth, M.D., FACP
Internal Medicine, Pain, Addiction Medicine
785-640-7064 eavmdtop@aol.com
President and Chairman of the Board
The International Academy on the Science and Impact of Cannabis
IASIC at https://iasic1.org

Mr. Chairman, Members of the Senate:
I am speaking today in opposition to Senate Bill 560 and in specific and general opposition to allowing marijuana by legislative vote to be used as a medicine. This legislation bypasses tried and true processes for assuring the safety and efficacy of medicines. What if the next move is to legalize and allow fentanyl products from surreptitious labs to sell their deadly products simply because of "alleged" safety and helping suffering citizens? The marijuana movement in the United States has clearly demonstrated that **marijuana as a medicine is flawed, poorly regulated, and is a Trojan Horse for marijuana legalization.**

If the legislature proceeds against our strong concerns **and recommendations to reject it**, I have proposed a Medical Standard of Care (Attached) that Health Care providers should adhere to. Providers recommending marijuana MUST be held to the same standards that other medical practitioners are held to and must NOT be given immunity from malpractice nor punitive measures for substandard care nor deviations from the Standard of Care. Furthermore, the allowed conditions listed in the legislation **far exceed evidence in the medical literature**. Marijuana, in fact, is actually **contraindicated** in the medical literature for some disorders like underlying psychiatric conditions.

Furthermore, I along with other experts strongly urge that any THC levels be held **at less than 10% for any form of marijuana that is allowed.** Research suggests that 10% is the apparent threshold beyond which substantial risk of psychosis and psychiatric complications exists. In addition, we have outlined the standard of care for evaluation, testing, and follow-up that are essential to maintaining reasonable safety for the citizens of Kansas.

Finally, such laws to legalize or liberalize marijuana use are crossing the nation, and they represent one of the most heinous examples of **manipulation of the public and lawmakers** by a self-serving industry that has the same lack of regard for the health of our citizens as the tobacco industry. Hopefully you will stop this movement in Kansas.

Dr. Voth is a specialist in Internal Medicine, Pain Management, and Addiction Medicine for 36 years and was formerly Vice-President of Primary Care at Stormont-Vail HealthCare. He serves as the President and Chairman of the Board of the International Academy on the Science and Impact of Cannabis (IASIC). Dr. Voth is a pioneer in the appropriate prescribing of controlled medications and is recognized as an international authority on drug use, drug policy-related issues, pain management, and appropriate prescribing practices.

Dr. Voth also serves as an advisor on alcohol and drug abuse issues to the Kansas State Board of Healing Arts, is a former member of the National Advisory Committee for the Center for Substance Abuse Treatment of HHS, and is a Clinical Professor of Internal Medicine at the University of Kansas School of Medicine.

Dr. Voth has advised Reagan, Clinton, both Bush, and Obama administrations, and has advised or testified for numerous Congressional offices on drug related issues. He has appeared on or consulted to, numerous other radio media, and has been quoted by numerous international print media.

Standard of Care Considerations When Recommending Cannabis (Marijuana) as a Medicine
The International Academy on the Science
and Impact of Cannabis-IASIC-https://iasic1.org

From the Board of Directors of IASIC: Eric A. Voth, M.D., FACP
Ken Finn, M.D. -
Catherine Antley, M.D.

Elizabeth Stuyt, M.D.

Statutes that allow the recommendation of medical marijuana present a real malpractice risk to physicians and medical providers. Despite a rapidly growing medical and recreational marijuana industry, there has been no definition of a standard of care for the use and recommendation of marijuana for medicinal purposes. This issue has been essentially ignored by the federal government and Congress has limited the ability of the Food and Drug Administration to enforce federal food and drugs law when it comes to "medical" marijuana. The marijuana industry has been allowed to run rampant.

Most of the medical opposition to medical marijuana is borne from concern over serious medical and social consequences in patients resulting from marijuana use. Additionally, the medicinal use of marijuana has been used by marijuana advocates as an intentional stair-step to legalization of the drug.

When considering what constitutes the "standard of care," it is important to embrace practices that reduce the risk to patients as well as reducing the risk of potential malpractice litigation of providers. Defining the standard of care should assist providers in determining appropriate therapeutic decisions. By necessity, providers must consider whether they have deviated from the standard of care and thus risk malpractice claims.

In legal terms, the "Standard of Care" is the level at which the average, prudent provider in a given community would practice. It is how **similarly qualified practitioners would have managed the patient's care under the same or similar circumstances.** In order to pursue litigation, the medical malpractice plaintiff must establish the appropriate standard of care and demonstrate that the standard of care has been breached (1).

Pure Cannabis-based medicines such as Marinol, Cesamet, Epidiolex, and Sativex are already FDA approved and on the market as medications that may be prescribed. Providers "recommending" state-approved cannabis are clearly recommending a non-FDA approved substance. **The recommendation of marijuana as a medicine generally has malpractice risk because "recommendations" for the use of marijuana are lacking the standard safe practices required of modern-day medicine**.

_____

Thirty-six states and four provinces have bypassed the Federal FDA authority and now allow medical marijuana "recommendations" well-beyond indications that have research to support them. For instance, Kansas is considering both House and Senate "Medical Marijuana" legislation that allows the following "qualifying" medical conditions:

Kansas Senate Bill 158 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"

Research demonstrates that the use of marijuana even for pain has fallen into question (2). Extensive literature review and several international organizations have concluded that the use of cannabinoids for chronic non-cancer pain is not yet supported nor proven by research and its use for pain is considered limited (3,4).

Questions must also be answered as to what form of the drug is to be provided (smoked, vaped, gummies, oils etc.), what doses are safe and effective, what side effects should be expected, and what long-term side effects might be experienced. Patients must also be notified and cautioned of these side effects and the problem that such delivery vehicles present unreliable doses to the patient.

Several of the elements necessary for the standard of care to be met are listed below. Failure to meet these individual required elements of appropriate medical care open the door to malpractice claims:

_____

Medical Evaluation- History and Physical Examination- As with any medical disorder, a thorough and complete medical evaluation must be performed, documented, and updated regularly by a licensed medical provider. This is a central and essential part of any medical evaluation. This process should also include specific documentation of other medical treatments and other successful or failed medications. The documentation of these elements must be entered into the patient's medical record which is appropriately retained, stored and made readily available for other providers also treating the patient. The patient's mental health history must be explored as cannabis use can damage mental health. (5)

The few Cannabinoid products that have been approved for use by the FDA, including Epidiolex (a CBD product) and Marinol and Cesamet (synthetic THC) have extensive warnings of the many risks of use. The FDA drug label for Marinol issues a warning that the drug "may cause psychiatric and cognitive effects and impair mental and/or physical abilities. Avoid use in patients with psychiatric history." (Table 1) While these boxed warning exist on low potency prescription cannabis products, there may be no warnings on much higher potency federally illegal marijuana products sold at state marijuana stores or dispensaries.

Concentration/Dose- Research is now suggesting that THC concentrations should not exceed 10% (4), and that higher concentrations have been associated with psychosis and other psychiatric disorders. It is worth also noting that state statutes allowing "medical" applications of marijuana include smoking, oils, vaping for example that can be 70-90% THC concentrations. Typically, street preparations do not contain stable nor predictable doses of Delta-9-THC, **In no other medical realm would we accept a general guess as to the potency of a medication, or would we not specify a concentration/dose at all, particularly when the incorrect dose may have such severe and possibly irreversible, deleterious consequences,** yet that is exactly what is allowed with cannabis.

Failure to warn - Beyond the question of what indications fall within the standard of care for recommending marijuana is the question of side effects and whether a less problematic and less toxic medication might be an available alternative. Furthermore, that information must be made available to the patient, and there must also be a rationale provided if the practitioner proceeds in recommending marijuana over a less toxic medication. The patient must be warned on any drug drug interaction which may harm them or render a medically necessary drug for the patient (such as coumadin) dangerous or ineffective. This rationale and patient notification must be clearly documented in the medical record. A failure to do so by the practitioner constitutes a deviation from the standard of care.

Failure to monitor- Ongoing monitoring of symptoms, toxicity, need for dosage change, need for additional medication are all elements of good medical care. These monitored elements should then be documented in a readily available medical record as well.

REMS- Risk Evaluation and Mitigation Strategies are widely used for high-risk therapies such as opiates. While a REMS for marijuana administration are not widely used, as they become

available it is strongly recommended to be a requirement for prescribing/recommending

providers.

None of these elements are generally required at this time in medical marijuana statutes.

Summary:

1. In legal terms, the "Standard of Care" is the level at which the average, prudent provider

   in a given community would practice. It is how **similarly qualified practitioners would have managed the patient's care under the same or similar circumstances.** The medical malpractice plaintiff would seek to establish the appropriate standard of care and demonstrate that the standard of care has been breached

2. Standard of care: A diagnostic and treatment process that a clinician should follow for a certain type of patient, illness, or clinical circumstance (6).
3. The fact that several states allow "Medical" marijuana should not impact a Standard of Care determination. It may, however, raise a question of conspiracy to harm such as with tobacco that could be pursued by plaintiff litigants.
4. Current medial marijuana statutes are generally in violation of the basic principle of "First Do No Harm". Intrinsic risks to the patient exist for marijuana use, and in order to avoid violating the standard of care, statutes should require the provider to notify and educate the patient on potential harms and risks of:
   1. Impact on driving
   2. Psychosis
   3. Depression/suicide
   4. Violence
   5. Mania
   6. Persistent and uncontrolled vomiting (cannabis hyperemesis syndrome)
   7. Association with opiate abuse and overdose
   8. Cannabis Use Disorder and addiction

5. Marijuana is not an FDA-approved medication, and as such it should be used only under strict research protocols. There exist no clear guidelines for dosing nor contraindications nor precautions.
6. Marijuana is highly impure, and the THC concentrations vary widely.
    1. The impact of dose may be significant for such complications as psychosis where there is a higher likelihood of psychosis with THC concentrations exceeding 10%
    2. Evidence exists that use of over 10% THC has increased side effects (4). Thus, vaped forms, oils, or highly concentrated forms of THC delivery have known complications.
7. Grounds exist for malpractice suits.
    1. Most prominent is failure to warn patients of potential direct harms
    2. Failure to use less problematic medications first
    3. Failure to monitor
    4. Knowingly exposing patients to a toxic substance.
    5. Failure to provide a thorough medical History and Physical examination
    6. Failure to document these elements in medical record.

Bibliography

1. Moffett P, Moore G. The standard of care: legal history and definitions: the bad and good news. *West J Emerg Med*. 2011;12(1):109-112.

2. Why Marijuana Will Not Fix the Opioid Epidemic, by Kenneth Finn, MD. https://www.msma.org/uploads/6/2/5/3/62530417/why_marijuana_will_not_fix_the_opioid_epidemic_mayjune_2018_momed.pdf

3. Boland EG,Bennett MI, Allgar V, *et al. BMJ Supportive & Palliative Care* 2020;**10**:14–24.

4. Pratt et al. Systematic Reviews (2019) 8:320 https://doi.org/10.1186/s13643-019-1243-x
5. Di Forti et al Lancet Psychiatry 2019; 6: 427–36 Published Online March 19, 2019. http://dx.doi.org/10.1016/ S2215-0366(19)30048-3

6. Lieblich LM. N Engl J Med. 2004 Apr 22;350(17):1798. PMID: 15106274

Table 1.

Cesamet - has the potential to affect the central nervous system which might manifest itself in dizziness, drowsiness, euphoria "high", ataxia, anxiety, disorientation, depression, hallucinations and psychosis.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s011lbl.pdf

Marinol -
https://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018651s025s026lbl.pdf

Epidiolex - https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/210365lbl.pdf

Authors:

Eric A. Voth, MD, FACP is the President and Chairman of the Board of IASIC. He is a specialist in Internal Medicine, Pain management, and Addiction Medicine., is recognized as an international authority on drug use, and lectures on drug policy-related issues, pain management, and appropriate prescribing practices. He has been quoted by numerous international news media. Dr. Voth is a former member of the National Advisory Committee for the Center for Substance Abuse Treatment of HHS and has advised Reagan, Clinton, both Bush, and Obama administrations. He also advises on alcohol and drug abuse issues to the Kansas State Board of Healing Arts

Catherine Antley, M.D. is Treasurer of IASIC. She is board certified in Anatomic and Clinical Pathology and in Dermatopathology and was elected a Fellow of the American Society of Dermatopathology in December 2001. For 20 years she has served as laboratory director of Vermont Dermatopathology, the only independent dermatopathology lab in Vermont serving VT, NH and NY. She has a strong interest in public health and effective prevention as well as

exploring the impact of policy on the prevention of use disorder and resulting health care costs. Dr. Antley has co-authored several Vermont Medical Society resolutions on cannabis. She recently contributed a chapter "Cannabis in Dermatology" to the textbook "Cannabis in Medicine, an Evidence Based Approach" edited by Dr. Ken Finn and published by Springer Nature.

Ken Finn, M.D., Pain Medicine and Drug Policy- is Vice-President of IASIC
Practicing medicine in Colorado Springs since 1994, Finn serves on the American
Board of Pain Medicine Exam Council ('01) and is then President-Elect of the American Board of Pain Medicine ('20)., serves on the Appeals Committee ('14), and Executive Board ('14). Finn served on the Colorado Governor's Task Force on Amendment 64, Consumer Safety and Social Issues Work Group ('12) and served 4 years on the Colorado Medical Marijuana Scientific Advisory Council ('14-'18). He was an Executive Board member of El Paso County Medical Society ('14-'18) and helped Colorado Medical Society andColorado Pain Society develop their position statement on cannabis ('18) as well as the El Paso County Board of Health ('14) and Medical Society ('14) on their statements. Finn is a voluntary clinical instructor for the University of Colorado Medical School-Colorado Springs Branch ('17-'20).

Elizabeth Stuyt, M.D., Addiction Psychiatry is Secretary of IASIC

Dr. Stuyt is a board-certified Addiction Psychiatrist and has worked in the addiction/behavioral health field since 1990. She was the Medical Director for the Circle Program, a 90-day inpatient treatment program, funded by the state of Colorado, for persons with co-occurring mental illness and substance abuse who have failed other levels of treatment from June 1999 to May 2020. She was instrumental in helping the Circle Program to become tobacco free in January 2000 and has been a strong advocate of the need to address all addictions at the same time, including tobacco, to improve outcomes. She has been actively incorporating complementary treatments into treatment programs, including the 5-point ear acupuncture NADA (National Acupuncture Detoxification Association) protocol and BST (Brain Synchronization Therapy), to help patients recover from addiction as well as trauma which often underlie addiction and chronic pain issues. Her current mission is to educate as many people as possible on the un-intended consequences of the commercialization of marijuana in Colorado, focusing primarily on the deleterious effects of high potency THC on the developing brain.

Summary of medical marijuana issues for the Senate
Eric Voth MD, FACP
785-272-5872/ eavmdtop@aol.com

1). Medical marijuana is a Trojan horse for legalization.

2). The medical disorders list is far too broad and there is no science to back this and "other serious disorders.

3). Marijuana has significant side effects, and particularly psychosis and psychiatric effects are correlated with the higher concentrations.

4). See the Standard of Care paper re Warnings and Monitoring. There must be appropriate standards of care required of providers.

5). THC is available already and minimally used by physicians.

6). The THC concentrations are not capped and are **dangerous above 10% no matter what form (Leaf, vaped, oils etc).**

7). There **should NOT** be protections from litigation and malpractice for practitioners recommending marijuana. They should be held to same standards, regulations, and standards of care as other practitioners.

8) There need to be requirements for purity and THC concentrations from reputable labs.

CURRENT RESEARCH ON MENTAL HEALTH & HIGH POTENCY THC

1. Young-adult compared to adolescent onset of regular cannabis use: A 20-year prospective cohort study of later consequences
Chan GCK et al. Drug and Alcohol Review (2021) DOI: 10.1111/dar.13239
By the mid-30s, both young-adult and adolescent-onset regular users were more likely than minimal/non-users (63.5%) to have used other illicit drugs (odds ratio [OR] > 20.4), be a high-risk alcohol drinker (OR > 3.7), smoked daily (OR > 7.2) and less likely to be in relationships (OR < 0.4). As the prevalence of the young-adult-onset group was nearly double of the adolescent-onset group, it accounted for a higher proportion of adverse consequences

than the adolescent-onset group. Cannabis users who began regular use in their teens had poorer later life outcomes than non-using peers. The larger group who began regular cannabis use after leaving high school accounted for most cannabis-related harms in adulthood. Given the legalisation of cannabis use in an increasing number of jurisdictions, we should increasingly expect harms from cannabis use to lie in those commencing use in young adulthood.

2. Association of High-Potency Cannabis Use With Mental Health and Substance Use in Adolescence
Hines LA et al. JAMA Psychiatry 2020;77(10):1044-1051.
In this cohort study of 1087 participants who reported cannabis use in the previous year, after adjusting for frequency of cannabis use and early adolescent mental health, use of high-potency cannabis was associated with a significant increase in the frequency of cannabis use, likelihood of cannabis problems, and likelihood of anxiety disorder. Those using high-potency cannabis had a small increase in the likelihood of psychotic experiences; however, this risk was attenuated after adjustment for frequency of cannabis use. Risks for cannabis use problems and anxiety disorders are higher among those reporting use of high-potency cannabis; provision of public health messaging regarding the importance of reducing both frequency of cannabis use and the potency of the drug, as well as limiting the availability of high-potency cannabis,

may be effective for reducing these risks.

3. Association Between Recreational Marijuana Legalization in the United States and Changes in Marijuana Use and Cannabis Use Disorder From 2008 to 2016
Cerda M et al. JAMA Psychiatry. 2020;77(2):165-171.
This study's findings suggest that although marijuana legalization advanced social justice goals, the small post-RML increase in risk for CUD among respondents aged 12 to 17 years and increased frequent use and CUD among adults 26 years or older in this study are a potential public health concern. To undertake prevention efforts, further studies are warranted to assess how these increases occur and to identify subpopulations that may be especially vulnerable.

4. The Effects of Cannabis Use on the Development of Adolescents and Young Adults
Hall W et al. Annu. Rev. Dev. Psychol. 2020. 2:461–83
This review summarizes evidence on the effects of cannabis use on the development

of adolescents and young adults. It draws on epidemiological studies, neuroimaging studies, case-control studies, and twin and Mendelian randomization studies. The acute risks include psychiatric symptoms associated with the use of high THC (tetrahydrocannabinol) products and motor vehicle accidents. Daily cannabis use during adolescence is associated with cannabis dependence and poor cognitive function, which may affect educational attainment and occupational choice. Daily use of highly potent cannabis is associated with more severe psychological symptoms, such as psychoses, mania, and suicidality.

5. Trends in Cannabis Treatment Admissions in Adolescents/Young Adults: Analysis of TEDS-A 1992 to 2016
Standeven LR et al. J Addict Medicine 2020
Treatment admissions for cannabis among adolescents/YAs rose 3-fold from 1992 (49,996) to 1996 (125,858). The majority of referrals came from the criminal justice system (56%). Cannabis is increasingly the sole substance of use, with polysubstance use decreasing from 89% in 1992 to 59% in 2016. While alcohol-related treatment admissions were most common in 1992, admissions for treatment of cannabis use (followed by heroin and alcohol) were highest (38%) by 2016. Being an adolescent (odds ratio [OR] 3.1, 95% confidence interval [CI] 3.1–3.2), non-Hispanic black (OR 6.2, 95% CI 6.2–6.3), male (female OR 0.6, 95% CI 0.6–0.6) with co occurring alcohol use (OR 25.9, 95% CI 25.7–26.1) was associated with admission for treatment of primary cannabis use as compared with other substances.

6. Evaluation of THC-Related Neuropsychiatric Symptoms Among Adults Aged 50 Years and Older A Systematic Review and Metaregression Analysis
Velayudhan et al. JAMA Network Open. 2021;4(2):e2035913. doi:10.1001/jamanetworkopen.2020.35913

We used metaregression analyses to examine any association between THC dose and self-reported neuropsychiatric adverse events (AEs) using data from double masked, randomized clinical trials (RCTs) investigating CBMs in people aged 50 years or older.Higher THC dose was associated with a higher incidence of thinking or perception disorder and dizziness or light-headedness. Self-reported thinking or perception disorders reflect alterations in thinking and

perception typically described under psychotic symptoms and suggest that older adults may also be at risk of psychotomimetic effects from THC.

7. Association of Cannabis Use With Self-harm and Mortality Risk Among Youths With Mood Disorders

Fontenella CA et al. JAMA Pediatrics 2020 doi:10.1001/jamapediatrics.2020.5494

A study of 204,780 (aged 10-24 years)Medicaid-enrolled youths with mood disorders found that the presence of cannabis use disorder was significantly associated with an increased risk of nonfatal self-harm, all-cause mortality, and death by unintentional overdose and homicide. Meaning Cannabis use disorder is common among adolescents and young adults with mood disorders and is associated with an elevated risk of self-harm, overall mortality, and death by unintentional overdose and homicide in this already vulnerable population.

8. Comorbid Cannabis Use Disorder with Major Depression and Generalized Anxiety Disorder: A Systematic Review with Meta-analysis of Nationally Representative Epidemiological Surveys

Onaemo VN et al. Journal of Affective Disorders 2021;281:467-475

In summary, our study findings provide further evidence on the strength of comorbid association of CUD with MD and CUD with GAD in the general population. The rates of comorbid MD and GAD is three times higher among those with CUD. This evidence should help guide clinical management of patients with comorbid CUD and mental health illness, which has often been associated with inadequate treatment, poor prognosis, and high levels of health service utilization (Hasin et al., 2016; Kessler, 2004). A thorough understanding of the way and reasons CUD co-occur with GAD and MD may provide effective prevention and treatment guidelines that focus on integrated shared-care approaches and/or psychosocial treatment in parallel systems (Horsfall et al., 2009; Mills et al., 2012; Tiet and Mausbach, 2007), as well as mitigate barriers

in clinical management of patients with a comorbid diagnosis (Mills et al., 2012). Given the increasing prominence of cannabis use along with ongoing changes in cannabis legalization in legalization in many countries (Statistics Canada, 2019; Hawley et al., 2020), it is imperative to mitigate the serious health-related harms of CUD, such as increased risk of comorbid anxiety or depression (Patton et al., 2002); high risk of myocardial infarction, stroke, and transient ischemic attacks (Thomas et al., 2014); increased ER visits and fatal car accident (Brady and Li, 2014)); and crime (Schauer et al., 2016). There is a great need for stronger evidence-based policy interventions that include, public health education about potential harms and responsible use (Murray et al., 2007); increased clinicians training about treatment prognosis; more

health care funding due to increase service utilization of comorbidity; and reduce social stigmatization of individuals who seek treatment.

9. Understanding Opioid Use Disorder (OUD) using tree-based classifiers

Wadekar AS. Drug and Alcohol Dependence 2020

https://doi.org/10.1016/j.drugalcdep.2020.107839

The proposed machine learning approach predicts adults at risk for OUD with remarkable accuracy. **The dominant predictor of OUD is first use of marijuana before the age of 18**

years. Socioeconomic and demographic groups affected by such early initiation are also identified.The machine learning models are capable of finding a "needle in a haystack", given the low number of observations with OUD. Finally, it is shown how a combination of different machine learning methods can be used to comprehensively and synergistically predict Opioid UseDisorder in adults.

10. Examining Associations Between Licensed and Unlicensed Outlet Density and Cannabis Outcomes From Pre Opening to Postopening of Recreational Cannabis Outlets
Pedersen ER et al. American Journal of Addiction 2020 DOI: 10.1111/ajad.13132

This study expands beyond studies of outlet prevalence to find that, after controlling

for outcomes 1 year prior, licensed and unlicensed outlets were associated with young adults' cannabis outcomes. The current study is among the first to find associations between cannabis use outcomes and density of cannabis outlets among young adults using data from two time points: pre opening and post opening of recreational cannabis retailers. Findings can inform policies around the density and placement of cannabis outlets.

11. Mapping cannabis potency in medical and recreational programs in the United States

Cash MC et al. PLOS ONE 2020 h ttps://doi.org/10.1371/journal.pone.0230167
A total of 8,505 cannabis products across 653 dispensaries were sampled.
Despite the clear differences between medicinal and recreational uses of cannabis, the average THC concentration advertised online in medicinal programs was similar (19.2% ±6.2) to recreational programs (21.5% ±6.0) when compared between states with different programs, or between medicinal and recreational programs within the same states (CO or WA). Lower CBD concentrations accompanied higher THC products. The majority of products, regardless of medicinal or recreational programs, were advertised to have >15% THC

(70.3% - 91.4% of products). These stated concentrations seem unsuitable for medicinal purposes, particularly for patients with chronic neuropathic pain. Therefore, this information could induce the misconception that high potency cannabis is safe to treat pain. This data is consistent with reports in which THC and CBD in products from legal dispensaries or in nationwide products from the illegal market were actually measured, which indicates that patients consuming these products may be at risk of acute intoxication or long-term side effects. Our study offers grounds to develop policies that help prevent misconceptions toward cannabis and reduce risks in pain patients.

12. Risk of Persistence and Progression of Use of 5 Cannabis Products After Experimentation Among Adolescents
Barrington-Trimis JL et al. JAMA Network Open. 2020;3(1):e1919792
In this cohort study of 2685 adolescents with no history of heavy cannabis use, after accounting for polyuse of multiple products, the association of baseline experimental use with persistent use and progression of use of that product during a 12-month follow-up period was significantly stronger for cannabis concentrate than for other cannabis products. The rate of persistence and progression after experimentation among adolescents may be amplified with the use of cannabis concentrate compared with other cannabis products.

13. Knowledge of Tetrahydrocannabinol and Cannabidiol Levels Among Cannabis Consumers in the United States and Canada

Hammond D, Goodman S. Cannabis and Cannabinoid Research 2020 DOI: 10.1089/can.2020.0092

Few consumers knew and were able to report the numeric THC or CBD levels of their usual cannabis products. For example, only 10% of dried herb consumers reported the THC level, approximately 30% of whom reported implausible values. A greater proportion of consumers reported a descriptive THC:CBD ratio of their usual product, ranging from 50.9% of edible users to 78.2% of orally ingested oil users. Consumers were substantially more likely to report

products high in THC versus low in THC for all products except topicals and tinctures, whereas similar proportions reported using products high and low in CBD. Despite some evidence of greater knowledge in legal jurisdictions, knowledge was still low in states with legal cannabis markets.

14. Prevalence of Cannabis Withdrawal Symptoms Among People With Regular or Dependent Use of Cannabinoids A Systematic Review and Meta-analysis

Bahji A et al. JAMA Network Open. 2020;3(4):e202370

In this meta-analysis of observational studies including 23 518 participants, the prevalence of cannabis withdrawal syndrome was found to be 47%. Factors that were associated with higher cannabis withdrawal syndrome were clinical settings (particularly inpatient and outpatient vs population settings), concurrent tobacco or other substance use, and daily cannabis use. Cannabis withdrawal syndrome appears to be common among regular users of cannabis, particularly those in outpatient and inpatient settings and individuals with substance use disorders; clinicians should be aware of the high prevalence of cannabis withdrawal syndrome to counsel patients and support individuals who are reducing their use of cannabis

15. Progression of cannabis withdrawal symptoms in people using medical cannabis for chronic pain

Coughlin LN et al. Addiction 2021 doi:10.1111/add.15370

Adults with chronic pain seeking medical cannabis certification or recertification appear to experience mild to severe withdrawal symptoms. Withdrawal symptoms tend to be stable over a 2-year period, but younger age is predictive of worse symptoms and of an escalating withdrawal trajectory.

16. Association of Naturalistic Administration of Cannabis Flower and Concentrates With Intoxication and Impairment

Bidwell LC et al. JAMA Psychiatry 2020;77(8):787-796.

This study provides information about the association of pharmacological and neurobehavioral outcomes with legal market cannabis. Short-term use of concentrates was associated with higher levels of THC exposure. Across forms of cannabis and potencies, users' domains of verbal memory and proprioception-focused postural stability was primarily associated with THC administration.

17. Psychotic disorders hospitalizations associated with cannabis abuse or dependence: A nationwide big data analysis- Portugal

Gonçalves-Pinho M. et al. Int J Methods Psychiatr Res. 2020;29:e1813.
The number of hospitalizations with a primary diagnosis of psychotic disorder (PD) and schizophrenia associated with cannabis use (CU) rose 29.4 times during the study period, from 20 to 588 hospitalizations yearly (2000 and 2015, respectively) with a total of 3,233 hospitalizations and an average episode cost of €3,500. Male patients represented 89.8% of all episodes, and the mean/median age at discharge were 30.66/29.00 years, respectively. From all hospitalizations with a primary diagnosis of PD or schizophrenia, the ones with a secondary

diagnosis of CU rose from 0.87% in 2000 to 10.60% in 2015. Conclusions: The increase on secondary diagnosis coding and the change on cannabis patterns of consumption in Portuguese population with an increasing frequency of moderate/high dosage cannabis consumers may explain the rise on PD Hospitalizations.

18. A genetically informed study on the association of cannabis, alcohol, and tobacco smoking with suicide attempt

Orri M et al. Molecular Psychiatry 2020 https://doi.org/10.1038/s41380-020-0785-6
To evaluate the potential causal contributions of cannabis use, alcohol use, and tobacco smoking to suicide attempt, we applied two-sample Mendelian randomization, an instrumental variable approach using single-nucleotide polymorphisms (SNPs) as instrumental variables for three exposures: lifetime cannabis use (yes/no; 42 instrument SNPs; GWAS sample size [N] = 162,082), alcohol use (drinks-per-week; 53 instrument SNPs; N = 941,280), and tobacco smoking (initiation, yes/no; 156 instrument SNPs; N = 1,232,091; heaviness; 27 instrument SNPs; N = 337,334). The main outcome was suicide attempt measured from hospital records (N = 50,264).Using multivariable Mendelian randomization, we found that only cannabis showed a direct pathway to suicide attempt (P = 0.001), suggesting that the effect of alcohol and smoking was mediated by the other substance use phenotypes. No evidence was found for reverse causation, i.e., associations of suicide attempt on cannabis (P = 0.483), alcohol (P = 0.234), smoking initiation (P = 0.144), and heaviness (P = 0.601). In conclusion, evidence from this quasiexperimental study based on genetic data from large-scale GWASs are consistent with a causal role of cannabis, alcohol, andtobacco smoking on suicide attempt.

19. Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood-A Systematic Review and Meta-analysis
Gobbi G et al. J AMA Psychiatry 2019 doi:10.1001/jamapsychiatry.2018.4500
In this systematic review and meta-analysis of 11 studies and 23 317 individuals, adolescent cannabis consumption was associated with increased risk of developing depression and suicidal behavior later in life, even in the absence of a premorbid condition. There was no association with anxiety. Preadolescents and adolescents should avoid using cannabis as use is associated with a significantly increased risk of developing depression or suicidality in young adulthood; these findings should inform public health policy and governments to apply preventive strategies to reduce the use of cannabis among youth.

20. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study
Di Forti M et al. The Lancet Psychiatry 2019 http://dx.doi.org/10.1016/S2215-0366(19)30048-3

This multicentre case-control study across ten European and one Brazilian site replicates the strong effect of daily use of high-potency cannabis (>10%THC) on the odds for psychotic disorder in the whole sample—which, to our knowledge, is the largest to date to address this question. This effect was particularly visible in London and Amsterdam. Additionally, we show that, assuming causality, if high-potency cannabis types were no longer available, then 12% of

cases of first-episode psychosis could be prevented across Europe, rising to 30% in London and 50% in Amsterdam. Most importantly, we provide the first direct evidence that cannabis use has an effect on variation in the incidence of psychotic disorders. We show that differences in the prevalence of daily use of cannabis, and in use of high-potency cannabis, among the controls from the different study sites made a major contribution to the striking variations in the incidence rates of psychotic disorder that we have previously reported across the same sites.

21. Association between medical cannabis laws and opioid overdose mortality has reversed over time

Shover CL et al. PNAS 2019 www.pnas.org/cgi/doi/10.1073/pnas.1903434116
Medical cannabis has been touted as a solution to the US opioid overdose crisis since Bachhuber et al. [M. A. Bachhuber, B. Saloner, C. O. Cunningham, C. L. Barry, JAMA Intern. Med. 174,1668–1673] found that from 1999 to 2010 states with medical cannabis laws experienced slower increases in opioid analgesic overdose mortality.In this study, we used the same methods to extend Bachhuber et al.'s analysis through 2017. Not only did findings from the original analysis not hold over the longer period, but the association between state medical cannabis laws and opioid overdose mortality reversed direction from −21% to +23% and remained positive after accounting for recreational cannabis laws. We also uncovered no evidence that either broader (recreational) or more restrictive (low-tetrahydrocannabinol) cannabis laws were associated with changes in opioid overdose mortality. We find it unlikely that medical cannabis—used by about 2.5% of the US population—has exerted large conflicting effects on opioid overdose mortality. A more plausible interpretation is that this association is spurious. Moreover, if such relationships do exist, they cannot be rigorously discerned with aggregate data. Research into therapeutic potential of cannabis should continue, but the claim that enacting medical cannabis laws will reduce opioid overdose death should be met with skepticism.

22. Medical Marijuana Users are More Likely to Use Prescription Drugs Medically and Nonmedically
Caputi TL, Humphreys K. J Addict Med 2018 DOI: 10.1097/ADM.0000000000000405
Medical marijuana users were significantly more likely (RR 1.62, 95% confidence interval [CI] 1.50–1.74) to report medical use of prescription drugs in the past 12 months. Individuals who used medical marijuana were also significantly more likely to report nonmedical use in the past 12 months of any prescription drug (RR 2.12, 95% CI 1.67–2.62), with elevated risks for pain relievers (RR 1.95, 95% CI 1.41–2.62), stimulants (RR 1.86, 95% CI 1.09–3.02), and tranquilizers (RR 2.18, 95% CI 1.45–3.16). Our findings disconfirm the hypothesis that a population-level negative correlation between medical marijuana use and prescription drug harms occurs because medical marijuana users are less likely to use prescription drugs, either medically or nonmedically. Medical marijuana users should be a target population

in efforts to combat nonmedical prescription drug use.

23. Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: findings from a 4-year prospective cohort study
Campbell G et al. www.thelancet.com/public-health Vol 3 July 2018
Cannabis use was common in people with chronic non-cancer pain who had been prescribed opioids, but we found no evidence that cannabis use improved patient outcomes. People who used cannabis had greater pain and lower self-efficacy in managing pain, and there was no evidence that cannabis use reduced pain severity or interference or exerted an opioid-sparing effect. As cannabis use for medicinal purposes increases globally, it is important that large well designed clinical trials, which include people with complex comorbidities, are conducted to determine the efficacy of cannabis for chronic non-cancer pain.

24. Cannabis Use and Risk of Prescription Opioid Use Disorder in the United States
Olfson M et al. AJP in Advance 2017 doi: 10.1176/appi.ajp.2017.17040413
In a nationally representative sample of adults evaluated at waves 3 years apart, cannabis use was strongly associated with subsequent onset of nonmedical prescription opioid use and opioid use disorder. These results remained robust after controlling for the potentially confounding effects of several demographic and clinical covariates that were strongly associated with cannabis use. The association of cannabis use with the development of nonmedical opioid use was evident among adults without cannabis use disorders and among adults with moderate or more severe pain. Among adults with nonmedical prescription opioid use, cannabis use was associated with an increase in the level of nonmedical prescription opioid use at follow-up.

25. Maternal and paternal cannabis use during pregnancy and the risk of psychotic-like experiences in the offspring
Bolhuis K et al. Schizophrenia Research 2018;202: 322-327.
In this prospective cohort, we examined the relationship between parental cannabis use during pregnancy and offspring psychotic-like experiences. Comparisons were made between maternal and paternal cannabis use during pregnancy to investigate causal influences of intrauterine cannabis exposure during foetal neurodevelopmental. This study was embedded in the Generation R birth cohort and included N = 3692 participants.We demonstrated that both maternal and paternal cannabis use were associated with more offspring psychotic-like experiences at age ten years. This may suggest that common aetiologies, rather than solely causal intra-uterine mechanisms, underlie the association between parental cannabis use and offspring psychotic-like experiences. These common backgrounds most likely reflect genetic vulnerabilities and shared familial mechanisms, shedding a potential new light on the debated causal path from cannabis use to psychotic-like phenomena. Our findings indicate that diagnostic screening and preventative measures need to be adapted for young people at risk for severe mental illness

25. Cannabis-associated psychosis: Neural substrate and clinical impact

Murray RM et al. Neuropharmacology 2017 doi.org/10.1016/j.neuropharm.2017.06.018

In our opinion, the epidemiological evidence clearly demonstrates that heavy cannabis use, particularly of high potency types, or of synthetic cannabinoids, increases the risk of psychosis, especially in those who start their use in their early teens.

27. Cannabis induced psychosis and subsequent psychiatric disorders

Shah D et al. Asian Journal of Psychiatry 2017;30:180–184.

Patients who completely abstained from cannabis after the 1st episode had no relapse of psychiatric illness. They showed marked improvement in socio-occupational functioning as well. All those who relapsed to cannabis use had a recurrence of illness. Half the patients with predominantly non-affective psychosis progressed to an independent psychiatric disorder; while only 7.7% of patients with predominantly affective psychosis developed an independent disorder (p = 0.01). Besides this, early onset of cannabis use (≤18 years), younger age at onset of 1 st episode, positive family history of psychiatric illness, being unmarried and lower socio-economic status were associated with poor prognosis. Abstinence later in the course of illness did not improve outcome significantly.

28. Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis
Starzer MSK et al. AJP in Advance (doi: 10.1176/appi.ajp.2017.17020223)
Substance-induced psychosis is strongly associated with the development of severe mental illness, and a long follow-up period is needed to identify the majority of cases.The highest conversion rate (47.4%) was found for cannabis-induced psychosis. Young age was associated with a higher risk of conversion to schizophrenia; the risk was highest for those in the range of 16–25 years.

29. Cannabis use disorder and suicide attempts in Iraq/Afghanistan-era Veterans
Kimbrel NA et al. Journal of Psychiatric Research 2017;89: 1-5
The objective of the present research was to examine the association between lifetime cannabis use disorder (CUD), current suicidal ideation, and lifetime history of suicide attempts in a large and diverse sample of Iraq/Afghanistan-era veterans (N= 3233) using a battery of well-validated instruments. As expected, CUD was associated with both current suicidal ideation (OR= 1.683, p = 0.008) and lifetime suicide attempts (OR = 2.306, p < 0.0001), even after accounting for the effects of sex, posttraumatic stress disorder, depression, alcohol use disorder, non-cannabis drug use disorder, history of childhood sexual abuse, and combat exposure. Thus, the findings from the present study suggest that CUD may be a unique predictor of suicide attempts among Iraq/Afghanistan-era veterans; however, a significant limitation of the present study was its cross-sectional design. Prospective research aimed at understanding the complex relationship between CUD, mental health problems, and suicidal behavior among veterans is clearly needed at the present time.

30. Long Lasting Effects of Chronic Heavy Cannabis Abuse

Nestoros JN et al. The American Journal on Addictions 2017;26:335-342

We provide evidence that chronic and heavy cannabis abuse results in long-lasting brain dysfunction in all users and in long-lasting schizophrenia-like psychotic symptoms in more than

half of all users. These findings suggest a reevaluation of the current classification of cannabis as a "soft narcotic" which erroneously, therefore, is typically considered harmless.

31. U.S. cannabis legalization and use of vaping and edible products among youth
Borodovsky JT et al. Drug Alcohol Depend. 2017; 177: 299–306.
This study examined relations among specific provisions of LCL and cannabis vaping and use of edibles in youth ages 14–18. Consistent with our previous study of adult cannabis users recruited via Facebook, the present analyses indicated that longer LCL duration and higher dispensary density were related to a higher likelihood of lifetime vaping and edible use. The current study extended those findings by showing that provisions for recreational cannabis use and for permitting home cultivation were also related to a higher likelihood of lifetime vaping and edible use. Some of these increased likelihoods were substantial. For example, living in a high dispensary density state doubled the likelihood of trying vaping and tripled the likelihood of trying edibles.

32. The association between regular marijuana use and adult mental health outcomes
Guttmannova K et al. Drug and Alcohol Dependence 2017;179:109–116
Objective: The present study is a prospective examination of the relationship between regular marijuana use from adolescence through young adulthood and mental health outcomes at age 33. Methods: Data came from a gender-balanced, ethnically diverse longitudinal panel of 808 participants from Seattle, Washington. Outcomes included symptom counts for six mental health disorders. Regular marijuana use was tracked during adolescence and young adulthood. Regression analyses controlled for demographics and early environment, behaviors, and individual risk factors. Results: Nonusers of marijuana reported fewer symptoms of alcohol use disorder, nicotine dependence, and generalized anxiety disorder than any category of marijuana users. More persistent regular marijuana use in young adulthood was positively related to more symptoms of cannabis use disorder, alcohol use disorder, and nicotine dependence at age 33. Conclusions: Findings highlight the importance of avoiding regular marijuana use, especially chronic use in young adulthood. Comprehensive prevention and intervention efforts focusing on marijuana and other substance use might be particularly important in the context of recent legalization of recreational marijuana use in Washington and other U.S. states.

33. Patterns of marijuana use among psychiatry patients with depression and its impact on recovery
Bahorik AL et al. Journal of Affective Disorders 2017;213:168–171
Participants were 307 psychiatry outpatients with depression; assessed at baseline, 3-, and 6-months on symptom (PHQ-9 and GAD-7), functioning (SF-12) and past-month marijuana use

for a substance use intervention trial. Longitudinal growth models examined patterns and predictors of marijuana use and its impact on symptom and functional outcomes.
Results: A considerable number of (40.7%; n=125) patients used marijuana within 30-days of baseline. Over 6-months, marijuana use decreased (B=−1.20, p < .001), but patterns varied by demographic and clinical characteristics. Depression (B=0.03, p < .001) symptoms contributed to increased marijuana use over the follow-up, and those aged 50+(B=0.44, p < .001) increased their marijuana use compared to the youngest age group. Marijuana use worsened depression (B=1.24, p < .001) and anxiety (B=0.80, p=.025) symptoms; marijuana use led to poorer mental health (B=−2.03, p=.010) functioning. Medical marijuana (26.8%; n=33) was associated with poorer physical health (B=−3.35, p=.044) functioning.

34. Changes in cannabis potency and first-time admissions to drug treatment: a 16-year study in the Netherlands
Freeman TP et al. Psychological Medicine 2017 doi.org/10.1017/S0033291717003877
In this 16-year observational study, we found positive time-dependent associations

between changes in cannabis potency and first-time cannabis admissions to drug treatment. These associations are biologically plausible, but their strength after adjustment suggests that other factors are also important

35. Traditional marijuana, high-potency cannabis and synthetic cannabinoids: increasing risk for psychosis
Murray RM et al. World Psychiatry 2016;15:195–204
Epidemiological evidence demonstrates that cannabis use is associated with an increased risk of psychotic outcomes, and confirms a dose response relationship between the level of use and the risk of later psychosis. High-potency cannabis and synthetic cannabinoids carry the greatest risk.

36. Association of cannabis use with hospital admission and antipsychotic treatment failure in first episode psychosis: an observational study
Patel R et al. BMJ Open 2016;6:e009888. doi:10.1136/bmjopen-2015-009888
Cannabis use in patients with first episode psychosis (FEP) was associated with an increased likelihood of hospital admission. This was linked to the prescription of several different antipsychotic drugs, indicating clinical judgement of antipsychotic treatment failure. Together, this suggests that cannabis use might be associated with worse clinical outcomes in psychosis by contributing towards failure of antipsychotic treatment.

37. Limitations to the Dutch cannabis toleration policy Assumptions underlying the reclassification of cannabis above 15% THC
Van Laar M et al. International Journal of Drug Policy 2016;34:58–64
The purpose of this measure was twofold: to reduce public health risks and to reduce illegal cultivation and export of cannabis by increasing punishment. This paper focuses on the public health aspects and describes the (explicit and implicit) assumptions underlying this '15% THC

measure', as well as to what extent these are supported by scientific research. Based on scientific literature and other sources of information,we conclude that the 15% measure can provide in theory a slight health benefit for specific groups of cannabis users (i.e., frequent users preferring strong cannabis, purchasing from coffee shops, using 'steady quantities' and not changing their smoking behaviour), but certainly not for all cannabis users. These gains should be weighed against the investment in enforcement and the risk of unintended (adverse) effects. Given the many assumptions and uncertainty about the nature and extent of the expected buying and smoking behaviour changes, the measure is a political choice and based on thin evidence.

38. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study
DiForti M. et al. Lancet Psychiatry 2015 http://dx.doi.org/10.1016/S2215-0366(14)00117-5
The association between cannabis use and increased risk of developing schizophrenia-like psychosis has been consistently reported by prospective epidemiological studies.2,3 Our previous study was the first to show that use of high-potency (skunk-like) cannabis (>15% THC)

carries the highest risk for psychotic disorders.8 In the present larger sample analysis, we replicated our previous report and showed that the highest probability to suffer a psychotic disorder is in those who are daily users of high potency cannabis. Indeed, skunk use appears to contribute to 24% of cases of first episode psychosis in south London. Our findings show the importance of raising awareness among young people of the risks associated with the use of high-potency cannabis. The need for such public education is emphasised by the worldwide trend of liberalisation of the legal constraints on cannabis and the fact that high potency varieties are becoming much more widely available. Finally, in both primary care and mental health services, a simple yes-or-no question of whether people use skunk might be more useful to identify those at increased risk to develop psychosis because of their cannabis use.

39. Effects of continuation, frequency, and type of cannabis use on relapse in the first 2 years after onset of psychosis: an observational study
Schoeler T et al. Lancet Psychiatry 2016; 3: 947–53
Continued cannabis use (at least monthly use) after the onset of psychosis, especially use of high-potency cannabis, is associated with a significantly worse outcome in individuals with first episode psychosis. In our study, outcomes were better in those who used cannabis in smaller doses (reduced frequency, lower potency, and shorter duration of continuation) after onset, which suggests that interventions should aim to reduce frequency of use or shift to less potent forms of cannabis when complete cessation of cannabis use might not be a realistic goal.

40. Daily Use, Especially of High-Potency Cannabis, Drives the Earlier Onset of Psychosis in Cannabis Users
Di Forti M et al. Schizophrenia Bulletin vol. 40 no. 6 pp. 1509–1517, 2014
We confirm an association between cannabis use and earlier age onset psychosis (AOP) and further show this to be independent of gender. Moreover, daily cannabis use and the use of high-potency cannabis are independently associated with a significantly higher hazard to make contact with services for psychosis at any given time. Finally, a younger age at first cannabis

use (≤15 years) is associated with a younger AOP only in those who had used cannabis daily. All these findings support a true effect of cannabis use on AOP, which is dose dependent, similar to its effect on risk of developing a psychotic disorder.

41. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence
Freeman TP, Winstock AR. Psychological Medicine 2015; 45: 3181–3189
High-potency cannabis use is associated with an increased severity of dependence, especially in young people. Its profile is strongly defined by negative effects (memory, paranoia), but also positive characteristics (best high, preferred type), which may be important when considering clinical or public health interventions focusing on cannabis potency.

42. Young adult sequelae of adolescent cannabis use: an integrative analysis

Silins E et al. Lancet Psychiatry 2014;1:286–293

We recorded clear and consistent associations and dose-response relations between the frequency of adolescent cannabis use and all adverse young adult outcomes. After covariate adjustment, compared with individuals who had never used cannabis, those who were daily users before age 17 years had clear reductions in the odds of highschool completion (adjusted

odds ratio 0·37, 95% CI 0·20–0·66) and degree attainment (0·38, 0·22–0·66), and substantially increased odds of later cannabis dependence (17·95, 9·44–34·12), use of other illicit drugs (7·80, 4·46–13·63), and suicide attempt (6·83, 2·04–22·90).

43. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research (2017) National Academies of Sciences,Engineering, Medicine
PDF available at h ttp://nap.edu/24625

44. Cannabinoids for Medical Use A Systema*tic Review and Meta-analysis* Whiting PF et al. JAMA. 2015;313(24):2456-2473
Randomized clinical trials of cannabinoids for the following indications:nausea and vomiting due to chemotherapy, appetite stimulation in HIV/AIDS, chronic pain, spasticity due to multiple sclerosis or paraplegia, depression, anxiety disorder, sleep disorder, psychosis, glaucoma, or Tourette syndrome. A total of 79 trials (6462 participants) were included; 4 were judged at low risk of bias. Most trials showed improvement in symptoms associated with cannabinoids but these associations did not reach statistical significance in all trials. There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term AEs.

45. Benefits and harms of medical cannabis: a scoping review of systematic reviews

Pratt M et al. Systematic Reviews (2019) 8:320 https://doi.org/10.1186/s13643-019-1243-x
After screening 1975 citations, 72 systematic reviews were included. The reviews covered many conditions, the most common being pain management. Several reviews focused on management of pain as a symptom of conditions such as multiple sclerosis (MS), injury, and cancer. After pain, the most common symptoms treated were spasticity in MS, movement disturbances, nausea/vomiting, and mental health symptoms. Results from the included reviews were mixed, with most reporting an inability to draw conclusions due to inconsistent findings and a lack of rigorous evidence. Mild harms were frequently reported, and it is possible the harms of cannabis-based medicines may outweigh benefits.

46. Exploring cannabis concentrates on the legal market: User profiles, product strength, and health-related outcomes
Bidwell LC et al. Addictive Behaviors Reports 2018;8:102-106.
Background: Concentrated cannabis products are increasingly available and used, particularly in states with legal cannabis, but little is known about the profiles and characteristics of concentrate users. We aimed to characterize user profiles of cannabis users living in states with legal medical or recreational cannabis who reported using concentrates to those who do not use concentrates. Methods: An anonymous online survey was advertised in California, Colorado, Nevada, Oregon, and Washington. We compared respondents who endorsed frequent concentrate use (FC; N = 67) (i.e. 4 days/week) with cannabis users who never use concentrates (NC; N = 64), and with those who smoke/vaporize cannabis flower frequently but

never or very rarely use concentrates (FF; N = 60), on measures related to cannabis use patterns and cannabinoid product strength, other substance use, and occupational functioning and health. Results: FC endorsed more symptoms of cannabis use disorder as compared to non-concentrate users (p < 0.05), but were similar to FF and NC on other health and occupational outcomes. FC also differed from FF and NC in that they tended to use cannabis that was higher in THC (p < 0.0005), even when using non-concentrated forms of cannabis (p < 0.005). Over half of FC users reported typically using concentrates of at least 80% THC, and 21% endorsed use of (non-concentrated) dry cannabis flower containing at least 30% THC. Conclusions: Concentrate users endorsed higher symptoms of cannabis use disorder and use higher strength cannabis even when using non-concentrated forms. Frequent use of concentrates may be associated with additional risks over and above frequent use of flower forms.

47. Acute Effects of Cannabis Concentrate on Motor Control and Speed: Smartphone-Based Mobile Assessment Hitchcock LN et al. Frontiers in Psychiatry

2021 https://doi.org/10.3389/fpsyt.2020.623672
Use of cannabis concentrates in frequent users impairs movement speed and balance similarly in men and women. The motor impairment is largely uncorrelated with the change in THC plasma levels. These results warrant further refinement of cannabis impairment testing and encourage caution related to use of cannabis concentrates in work and driving settings.

48.Acute effects of naturalistic THC vs. CBD use on recognition memory: a preliminary study Curran T et al. Journal of Cannabis Research 2020 2:28

Thirty-two regular cannabis users consumed cannabis of differing THC and CBD levels purchased from a dispensary and were assessed via blood draw and a verbal recognition memory test both before (pretest) and after (posttest) ad libitum home administration in a mobile laboratory. Memory accuracy decreased as post-use THC blood levels increased (n = 29), whereas performance showed no relationship to CBD blood levels. When controlling for post-use THC blood levels as a covariate, participants using primarily THC-based strains showed significantly worse memory accuracy post-use, whereas subjects using strains containing both THC and CBD showed no differences between pre- and post-use memory performance. Using a brief and sensitive verbal recognition task, our study demonstrated that naturalistic, acute THC use impairs memory in a dose dependent manner, whereas the combination of CBD and THC was not associated with impairment.

49.Association between Friends' Use of Nicotine and Cannabis and Intake of Both Substances among Adolescents
Herold R et al. Int. J. Environ. Res. Public Health 2021, 18, 695
Over one-third of the 517 surveyed adolescents reported using tobacco and one-third reported using cannabis. A significant relationship between friends' substance use and self-use was found. For both tobacco and cannabis, over 90% (p < 0.01) of participants with urinary biomarker levels above cutoff had friends who used the respective substance. Friends' nicotine and friends' cannabis use were each independently associated with urinary biomarker levels for those substances (for nicotine, beta = 88.29, p = 0.03; for cannabis, beta = 163.58, p = 0.03). Friends' use of nicotine and cannabis is associated with adolescents' intake, as well as the

physiological exposure to those substances. These findings underscore the importance of including peer influence in the discussion with adolescents about tobacco and cannabis use.

50. .When Cannabis Use Goes Wrong: Mental Health Side Effects of Cannabis Use That Present to Emergency Services

Crocker CE et al. Frontiers in Psychiatry 2021doi: 10.3389/fpsyt.2021.640222

The situation in Colorado is also interesting from an epidemiological point of view as the past month cannabis use level among native Coloradans has remained constant since recreational legalization but healthcare utilization associated with adverse events due to cannabis has increased (38, 75). Some authors have noted that this may be related to the current market forces being focused on sales with ever increasing concentrations of THC in cannabis products (38). This may suggest a cumulative dose dependency for at least certain types of adverse events associated with cannabis use as has been suggested by others for the development of psychosis (28, 29, 76). The lack of research in these areas is not surprising given the challenges of doing research in urgent care and across disciplines to obtain outcomes for longer term psychiatric care. This lack of information further impacts clinical care as if we knew the frequency of conversion from a severe adverse mental health event related to anxiety symptoms or depressive symptoms with cannabis use to a diagnosed disorder requiring ongoing care, clinical guidelines could be developed. As we move to greater cannabis use with greater acceptance of the product, the ED may be one of the sentinel locations to monitor any

emerging mental health trends. There are also opportunities for public education that may be possible in the ED setting. The effects we present here are, we suspect, more commonly associated with higher (often defined as 12% and greater) THC concentration strains of cannabis with little to no cannabidiol in the material as these are the most commonly sold strains in the marketplace in legalized settings (78, 79). The sale of these higher THC strains is based on consumer preference (80). However, there is evidence that consumers do not understand the significance of the percentages of THC and CBD in sales materials in the legal marketplace (81).

51. Recreational Marijuana Legalization and Use Among California Adolescents: Findings From a Statewide Survey

Paschall MJ et al. J. Stud. Alcohol Drugs 2021; 82: 103–111

We found no overall statistically significant association between RML and frequency of marijuana use among youth who reported any past-30-day use. However, marked increases in marijuana use frequency were observed in 2018–2019 across almost all demographic subgroups. This may reflect the recent substantial increases in vaping of tobacco and marijuana products among adolescents in the United States (Miech et al., 2019b). Our findings also indicate differential effects of RML on marijuana use prevalence among demographic subgroups of adolescents in California, notably having greater effects for those groups with historically lower prevalence rates of marijuana use. For example, stronger associations between RML and lifetime and past-30-day marijuana use were observed among females relative to males, and past-30-day marijuana prevalence use rates have converged in these two subgroups since 2010.Similarly, stronger RML effects on marijuana use were observed among non-Hispanic/Latinx relative to Hispanic/Latinx students, and marijuana use prevalence rates have converged in these two subgroups. Stronger associations between RML and marijuana use were also observed among White youth relative to African American and American Indian/Alaska Native youth, although somewhat higher prevalence rates persisted for these two groups

52. Association Between Recreational Marijuana Legalization in the United States and Changes in Marijuana Use and Cannabis Use Disorder From 2008 to 2016

Cerda M et al. JAMA Psychiatry 2020; 77(2):165-171.

Key Points Question How did marijuana use and cannabis use disorder change during 2008 to 2016 after the legalization of recreational marijuana in the United States? Findings In this multilevel, difference-in-difference survey study with 505 796 respondents comparing marijuana use before and after the legalization of recreational marijuana in the United States, the proportion of respondents aged 12 to 17 years reporting cannabis use disorder increased from 2.18% to 2.72%, while the proportion of respondents 26 years or older reporting frequent marijuana use increased from 2.13% to 2.62% and those with cannabis use disorder, from 0.90% to 1.23%. Meaning This study's findings suggest that possible increases in the risk for cannabis use disorder among adolescent users and increases in frequent use and cannabis use disorder among adults after legalization of recreational marijuana use may raise public health concerns and warrant ongoing study.