High Potency THC and Justice-Involved Individuals with Mental Illness
MHDCJS White Paper

The intent of this white paper is to make people aware of the potential impact high potency marijuana has on justice involved individuals with mental health disorders and to provide recommendations for people to consider when addressing these issues. The intent is to improve the treatment of mental health and further reduce involvement in the criminal and juvenile justice system.

Abstract

With the legalization of medical marijuana in Colorado, justice-involved individuals with mental health disorders can receive medical marijuana recommendations for a variety of health problems, despite a dearth of empirical science about their efficacy. Medical marijuana products currently available in Colorado include flower with an average THC concentration of 20% and hash oil concentrates that can have a THC concentration of up to 90%. There is an increasing body of literature that indicates psychotic symptoms can result from the use of high potency THC products. Other literature exposes the link between addiction, depression, anxiety, violence, and suicide and regular cannabis use. Cannabis use can impair the ability to make an accurate psychiatric diagnosis and can affect the medications often used for treatment. These destabilizing impacts can place justice-involved individuals with mental health disorders at greater risk of continued criminal justice involvement. Since justice-involved populations have higher rates of mental illness and substance use disorders, it is imperative to understand how high potency THC medical marijuana use can impact these individual's community stability. The following recommendations are provided for the purpose of addressing health and behavioral health related issues, to prevent or reduce these individuals' further involvement in the criminal and juvenile justice system and better assist those affected by high potency marijuana.

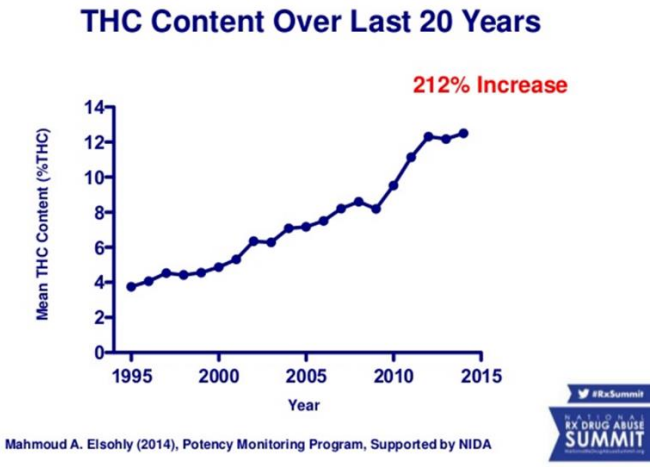
Summary Overview and Recommendations

In November 2000, Colorado voters passed Amendment 20, which legalized medical use of marijuana for debilitating medical conditions, effective June 2001. Use remained somewhat limited: However, several factors increased medical marijuana use around 2010.[1] Then, in November 2012, Colorado passed Amendment 64, which legalized retail sales of marijuana. Personal use was legalized on December 10, 2012, after the Governor certified the election results. As the earliest state to legalize marijuana, Colorado leads policy development in this area. It is incumbent upon the state to evaluate and refine these policies as it gains more experience in legalization, policy application and unforeseen consequences. The recommendations in this white paper will primarily focus on medical marijuana and are based on available research and clinical observation.

In the two decades since medical legalization, Tetrahydrocannabinol (THC) potency, the most psychoactive component in cannabis, has significantly increased in marijuana products. While the marijuana available in the 1960s and 1970s had an average THC content of less than 2%, a study of the changes in cannabis potency from 1995-2014 by the National Center for Natural Products Research,

[1] Events included: Denver District Court decision in 2007, the US Department of Justice issued the 2009 Ogden memo stating federal prosecutors "should not focus federal resources in your States on individuals whose actions are in clear and unambiguous compliance with existing state laws providing for the medical use of marijuana, and the Colorado Legislature established the Colorado Medical Marijuana Code in 2010 allowing for the legal licensing of medical marijuana businesses.

School of Pharmacy, University of Mississippi, found that the THC percentage in illicit cannabis products seized by the DEA, averaged 4% in 1995 and 12% in 2014.[2]



Elshoy MA et al. Biol Psych 2016 ;79 :613-619

In 2020, in Colorado, there are now legal strains of flower with THC well over 20% and concentrated hash oil products such as wax, shatter, dab that can reach upward of 90% THC.

Research on the benefits of marijuana for medical conditions from the United States and around the world is limited to THC potency of less than 10%. This can be in part because research is difficult since it is a Schedule 1 drug, but also because levels of THC higher than this put people at risk for possible consequences, including psychosis. As a result, Institutional Review Boards (IRBs) may not approve studies of high potency THC marijuana, even if the DEA scheduling were to change.

In the early studies of smoked cannabis for pain, a cannabis naïve participant had a psychotic response to the study cigarette which was 3.56% THC.[3] As a result, subsequent cannabis studies have excluded participants without prior experience smoking cannabis which makes it difficult to have double-blinded studies. There have been several studies that support the use of smoked cannabis for neuropathic pain, however the dose of THC in all these studies has been under 10%.[3-5] In fact, a study in healthy volunteers on the effects of cannabis on capsaicin-induced pain found that there is a window of modest analgesia for smoked cannabis, with 2% THC providing no benefit, 4% THC providing significant decrease in pain but 8% THC resulting in an increase in pain or hyperalgesia.[6]

This has been further supported by a recent study of 989 adults who used cannabis every day for chronic pain.[7] The authors found that high frequency medical marijuana use, especially the higher potency THC products, was associated with worse pain among individuals with chronic pain while those who used less frequently and primarily cannabidiol (CBD) and non-inhalation administration routes had better outcomes. This is important because the primary reason people report purchasing medical marijuana in Colorado is for chronic pain issues.[58] It is also important because, without any regulation on the THC content, medical marijuana products available in Colorado are no different than recreational products where there has yet to be any limits placed on THC potency or any meaningful limits on product types permitted to be sold.

Consequently, people are using high potency THC marijuana that may actually increase their level of pain. Research from other countries provides the best source of information on the consequences of high potency THC, yet, this only provides limited policy guidance and knowledge of impacts on vulnerable populations. Further information is necessary to support responsible policy decisions in the legalization of marijuana.

There is an increasing body of literature that indicates psychotic symptoms can result from the use of high potency THC products. Other literature exposes the link between addiction, depression, anxiety, violence, and suicide and regular cannabis use. Cannabis use can impair the ability to make an accurate psychiatric diagnosis and can affect the medications often used for treatment. Since justice-involved populations have higher rates of mental illness and substance use disorders, it is imperative to understand how high potency THC use might impact these individual's community stability. Therefore, the Colorado Task Force Concerning the Treatment of Individuals with Mental Health Disorders in the Criminal and Juvenile Justice System (MHDCJS) and the Colorado Substance Abuse Trend and Response Task Force (SATRTF) are collaborating on the following recommendations:

1) Improve data on the impacts of high potency THC cannabis in vulnerable populations by encouraging clinical providers in health care, behavioral health, and criminal justice agencies to collect data regarding cannabis use, including questions about THC and CBD, potency, type of products, delivery system (smoke/vape/edibles/oil/ concentrates), type of purchase (i.e. recreational, medical, or home grow).When drug tests are administered with this population, ensure the testing includes THC levels. With routine screening in medical appointments, like questions about tobacco and alcohol use, prescribers can then consider drug interactions and symptoms that may be due to the use of marijuana. This would be for the purpose of addressing health and behavioral health related issues, not for involving individuals in the criminal justice system.
2) Develop provider education materials and training on known impacts of cannabis use on physical and mental health and require that medical marijuana prescribers and vendors receive such education and certification indicating they have completed the education. This would allow them to give consumers accurate information and informed consent regarding the use of medical marijuana
3) Restore funding to the Colorado Department of Public Health and Environment's Retail Marijuana Education Program to develop Public Service Announcements (PSAs) and education materials for the public regarding cannabis use risks.
4) Enforce the rules that strictly limit or eliminate advertising of cannabis products similar to alcohol, tobacco and electronic vape products, including marketing by social media influencers, that appear to be directed to adolescents/young adults.
5) Limit potency of THC to under 10% in **medical** cannabis and eliminate the concentrates such as wax, shatter, dab from **medical** cannabis since there is no research on these products for any **medical** condition.
6) Put Medical Marijuana recommendations on the Prescription Drug Monitoring Program (PDMP) in Colorado. If Colorado is legitimately supporting the use of medical marijuana in people with mental illness for health-related issues, then there needs to be monitoring, especially for those involved in the criminal and juvenile justice system. This is already occurring in several states.

Recommendations:

1. Improve data on the impacts of high potency THC cannabis in vulnerable populations by encouraging clinical providers in health care, behavioral health, and criminal justice agencies to collect data regarding cannabis use, including questions about THC and CBD, potency, type of products, delivery system (smoke/vape/edibles/oil/ concentrates), type of purchase (i.e. recreational, medical, or home grow).When drug tests are administered with this population, ensure testing includes THC levels. With routine screening in medical appointments, like questions about tobacco and alcohol use, prescribers can then consider drug interactions and symptoms that may be due to the use of marijuana. This would be for the purpose of addressing health and behavioral health related issues, not for involving individuals in the criminal justice system.

Rationale:

On November 6, 2012, Colorado voters passed Amendment 64 to legalize recreational marijuana for adults aged 21 and older. The law (CRS 18-16) went into effect on December 2012. Since legalization, some healthcare providers stopped asking questions about cannabis use or including cannabis in drug testing since it is legal. In fact, there is a company out of Florida that provides drug testing panels and offers the "Colorado panel" which tests for all drugs of abuse except for cannabis. When asked why they have this panel they said it was a request by primary care physicians in Colorado who stated they didn't want to know if their patients were using cannabis because they didn't know what to do about it.[8] This limits knowledge of cannabis impacts on vulnerable populations who have mental health or substance use disorders and potential interactions with prescribed psychotropic medications.

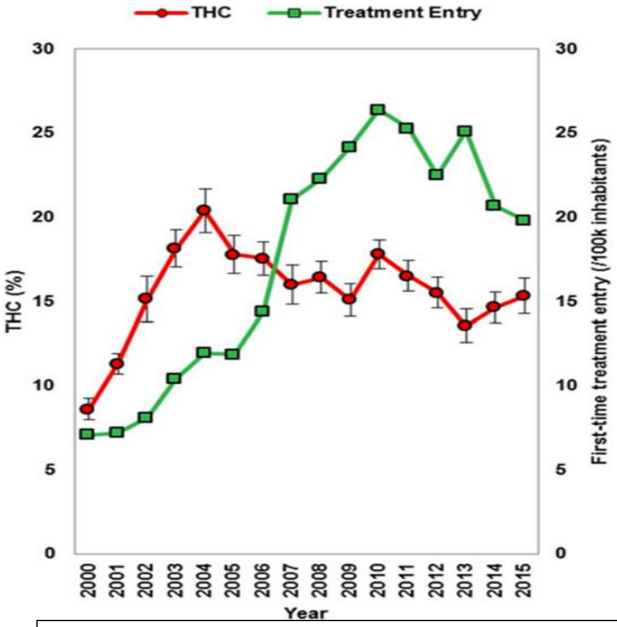
Individuals with serious mental illness (SMI) incarcerated in criminal justice facilities frequently have co-occurring substance use disorders and many may have been using cannabis around the time they were arrested and incarcerated. [9] The use of cannabis is not always inquired about, recorded, or tested for in correctional or healthcare systems in Colorado and is often viewed as "just marijuana". Although jails may ask about other drugs, including alcohol, detainees may not be asked about cannabis use.

Many therapists and treatment providers have expressed concern that high potency THC products may be contributing to psychosis in some of their clients

2. Develop provider education materials and training on known impacts of cannabis use on physical and mental health and require that medical marijuana prescribers and vendors receive such education and certification indicating they have completed the education. This would allow them to give consumers accurate information and informed consent regarding the use of medical marijuana.

Rationale:
Since legalization of cannabis we have seen a 4% percent increase in use in the 18-25-year-old age group from 29% in 2012/2013 to 33.2% in 2017/2018.[10] The biggest increase has been among the 26 and older group, from 10.5% to 15.7% during the same time period. This is in part thought to be due to the decreased perceived risk of harm. A recent study found that residents in recreationally legal states were most likely to believe marijuana has benefits, and that marijuana smoke is safer than tobacco smoke. These states have the highest rates of marijuana use.[11]

Increasing the potency of any drug increases the risk for addiction. A study in the UK in 2015 found that frequent use of Skunk (THC content around 15%) predicted a greater severity of dependence, this effect becoming stronger as age decreased. Whereby in contrast, the use of low potency cannabis (5%) was not associated with dependence.[12] A 16-year observational study in the Netherlands found a positive time dependent association with increased THC potency and increased first-time admissions to drug treatment for cannabis use disorder.[13]



Freeman TP et al. Psychological Med 2018

Approximately 9% of those who experiment with cannabis will become addicted. This number goes up to 1 in 6 who start using cannabis as teenagers and to 25-50% among those who smoke cannabis daily.[14] It used to be thought that marijuana was not addicting and was referred to as a hallucinogen because hallucinogens do not have a withdrawal syndrome associated with their use.[15] We now see a definite withdrawal syndrome from the higher potency cannabis, and it is a criterion for the diagnosis of cannabis use disorder.[16] Cannabis withdrawal syndrome is recognized by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, and requires the presence of at least 3 of the following

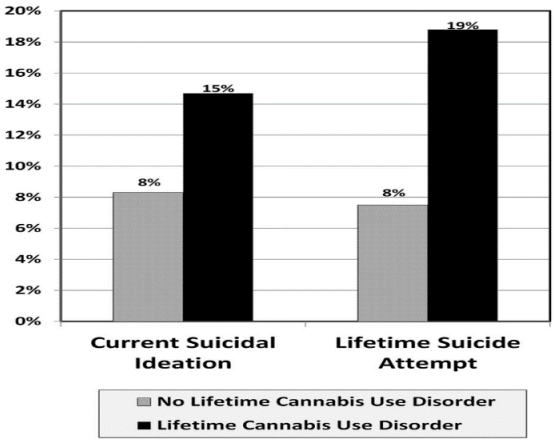
symptoms developing within 7 days of reduced cannabis use: (1) irritability, anger ,or aggression; (2) nervousness or anxiety; (3) sleep disturbance; (4) appetite or weight disturbance; (5) restlessness; (6) depressed mood; and (7) somatic symptoms, such as headaches, sweating, nausea, vomiting, or abdominal pain.[17]

After observing the negative impacts from rising THC potencies, a team of health experts in the Netherlands concluded that THC potencies above 15% should be considered a hard drug.[18]

There is increasingly strong evidence that higher potency cannabis use contributes to increased risk of psychosis. Numerous studies have demonstrated that using cannabis prior to the age of 15-18 significantly increases the risk of developing psychotic symptoms.[19] A landmark study out of the UK analyzed 780 adults, ages 18-65, 410 with their first psychotic episode versus 370 matched healthy controls. It was found that the use of high potency THC >15% resulted in a three times increased risk of psychosis, and if the use was daily there was a five times increased risk. Those using < 5% THC did not exhibit psychotic symptoms.[20] In a recent systematic review and meta-analysis of 15 studies of psychiatric symptoms caused by cannabis constituents, the authors found that acute administration of THC induces significant increases in positive, negative, and other symptoms associated with schizophrenia and other mental disorders with large effect sizes in adults with no history of psychotic or other major psychiatric disorders.[21]

There is some evidence to suggest an association between persistent cannabis use and risk of violent behavior in individuals with serious psychiatric disorders. In one study 1,136 recently discharged psychiatric patients were followed at 4 10-week time intervals and evaluated for marijuana, alcohol and cocaine use as well as episodes of violence during the period 1992-1995. Persistent cannabis use was associated with an increased risk of subsequent violence, significantly more so than with alcohol or cocaine.[22] In another study, 265 patients with early psychosis were followed prospectively for 36 months and dichotomized based on presence or absence of violent behavior. Cannabis use disorder (CUD) was the strongest risk factor of violent behavior with 61% of those with CUD versus 23% with no CUD exhibiting violent behavior.[23] The age of onset of cannabis use was 15 in violent patients versus 17 in non-violent patients. The use of cannabis was linked to impulsivity and lack of insight. Further research is needed to investigate this association.

There is also increasing evidence that cannabis use is associated with violence towards oneself in the form of suicide. Multiple studies have documented a relationship between cannabis use and suicidality. A large longitudinal study in Australia and New Zealand of over 2000 adolescents and maximum frequency of marijuana use found almost a seven-fold increase in suicide attempts in daily marijuana users compared with non-users.[24] A 2017 cross-sectional multi-site VA study of 3233 Veterans found that cannabis use disorder was significantly associated with both current suicidal ideation ($p<.0001$) and lifetime history of suicide attempts ($p<.0001$) compared to Veterans with no lifetime history of cannabis use disorder.[25] The significance difference continued even after adjusting for sex, PTSD, depression, alcohol use disorder, non-cannabis drug use disorder, history of childhood sexual abuse and combat exposure.



Kimbrel NA et al. J Pyschiatric Res 2017;89:1-5

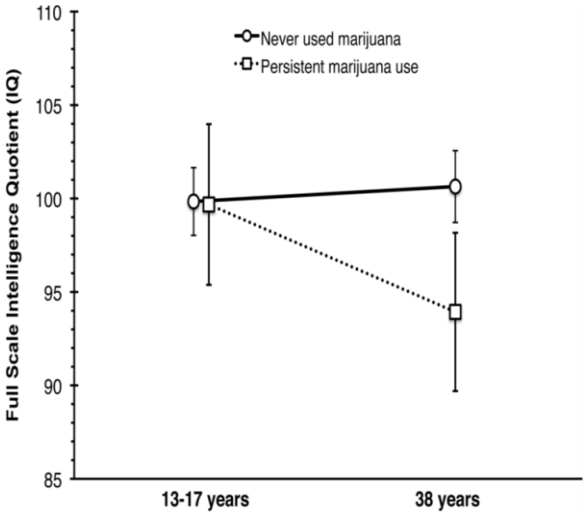
Suicide is the number one cause of death in Colorado for individuals between the ages of 10 and 24 and cannabis is by far the most frequently encountered drug on toxicology screens of suicides among adolescents ages 10-19 and has been increasing over the last eight years according to the Colorado Department of Public Health and Environment.[26] A large systematic review and meta-analysis of 11 studies of 23,327 adolescents found that cannabis use in adolescence significantly increased the risk of depression, anxiety and suicidality in young adulthood with an odds ratio of 3.5 for suicide attempts.[27]

Many people with post-traumatic stress disorder (PTSD) use cannabis to alleviate their symptoms and Colorado has approved PTSD as a condition for medical marijuana. However, this does not cure PTSD any more than alcohol or benzodiazepines cure PTSD. These substances can "numb" the person, so the symptoms are not bothersome but require the person to continue daily use to alleviate the symptoms, putting them at risk for addiction. There is strong evidence that persistent use of cannabis can make the PTSD symptoms worse and increase the risk of violence and suicidal ideation.[28, 29]

An observational study of 2276 veterans treated in PTSD treatment programs of the Veterans Administration around the country found that 4 months after participating in a month-long inpatient treatment program for PTSD, those who never used marijuana had significantly lower symptom severity, those who stopped using marijuana had the lowest level of PTSD symptoms 4 months after treatment and those who started to use marijuana had the highest levels of violent behavior and PTSD symptoms 4 months after treatment.[30]

3) Restore funding to the Colorado Department of Public Health and Environment's Retail Marijuana Education Program to develop Public Service Announcements (PSAs) and education materials for the public regarding cannabis use risks.

Rationale:
The negative effects of cannabis on the developing brain, both in utero and during puberty have been well documented. In a prospective study of 648 children and exposure to cannabis in-utero, women were interviewed about the amount and frequency of cannabis use at 4, and 7 months of pregnancy and at delivery.[31] Their offspring were administered an IQ test at age 6 and examiners were blinded to exposure. They found that in-utero exposure to light to moderate cannabis use approximately three times a week had a significant negative effect on school age intellectual development. In spite of this a study of recommendations from cannabis dispensaries in Colorado found that nearly 70% of the dispensaries contacted for advice for a woman who was 8 weeks pregnant and experiencing morning sickness, recommended cannabis products to treat nausea in the first trimester.[32] Few dispensaries encouraged a discussion with a healthcare provider without prompting. In another prospective study 1,037 individuals were followed for 20 years and were administered neuropsychological testing at age 13 before initiation of cannabis and again at age 38.[33] Those with early persistent teen use of cannabis had an average decrease in IQ by 8 points compared with no change over time by those who never used cannabis. The public needs to have this information in order to make healthy choices.



Meier MH et al. PNAS 2012

The pandemic of COVID-19 is the best example of the need for Public Service Announcements. News stories are breaking daily amid this crisis that indicate smoking or vaping tobacco or marijuana, even occasionally, puts people more at risk of getting infected with the virus and if infected, tobacco and marijuana use can result in worse complications from the virus.[34-36]

The public, medical providers, and consumers of cannabis would also benefit from Public Service Announcements regarding Cannabis Hyperemesis Syndrome (CHS) that was once thought to be rare, but is now being seen almost daily in emergency departments around the state.[37] CHS is characterized by frequent bouts of acute nausea, vomiting, and abdominal pain, and often requires emergency medical attention to stop vomiting and rehydrate patients through the use of strong intravenous drugs (like

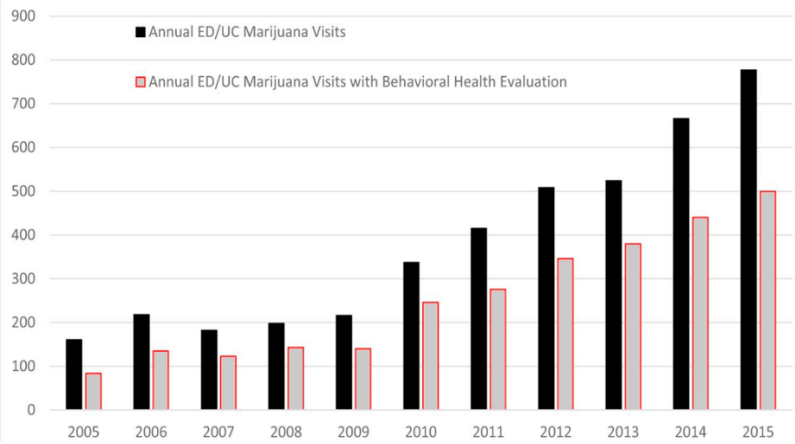
Haloperidol, which has many known side effects) and fluids. CHS is typically seen in people between the ages of 18-40 who use cannabis at least weekly, are under 50 years of age at onset, and started using cannabis in their teenage years.[38] Symptoms include cyclical nausea and vomiting, abdominal pain, compulsive hot water bathing to temporarily ease symptoms, and resolution of symptoms only by stopping cannabis. Although CHS has been documented in medical journals, some medical providers and most consumers of cannabis are unaware of it. Deficient medical information causes confusion and serious repercussions. Patients are skeptical that the cause of their symptoms is cannabis and are reluctant to stop using. They typically undergo multiple costly and time-consuming investigations before diagnosis, while continuing to suffer and accumulate emergency medical bills due to CHS. A 2019 study looked at the number of emergency department visits and costs of CHS to 17 patients who were diagnosed after extensive examinations, x-rays, and emergency treatment.[39] The average was 17.9 emergency department visits, costing an average $76,920.92 per patient. If the public and health care providers understood that the only solution to CHS is the cessation of cannabis, these procedures, costs, and prolonged suffering could be avoided. Broader education regarding CHS is a critical need.

4) Enforce the rules that strictly limit or eliminate advertising of cannabis products similar to alcohol, tobacco and electronic vape products, including marketing by social media influencers, that appear to be directed to adolescents/young adults.

Rationale:
There is a great deal of research documenting the harms of long-term or heavy cannabis use beginning in adolescence and the effects on the developing brain which is not fully developed until the mid-20s.[40] There is evidence that persistent cannabis use can negatively affect neurogenesis in the hippocampus, affecting learning and memory and making it difficult to learn new things.

A study of 40 male and 34 female long-term (15 years) cannabis users versus 37 non-users, healthy controls divided the marijuana users into three groups; those that smoked predominantly THC in the previous three months, those who smoked a combination of THC and CBD in the previous three months and former users with a sustained abstinence of 29 months.[41] They found that cannabis users had smaller hippocampal volumes compared to controls but the users not exposed to CBD had greater (11%) reduced volumes (CBD appears to be somewhat protective). In the former users, the hippocampal integrity was comparable to controls. The conclusion was ongoing cannabis use is associated with harm to brain health, underpinned by chronic exposure to THC. However, such harm was minimized by CBD, and recovery was thought to be possible with extended periods of abstinence. Currently most of the marijuana products available in Colorado dispensaries have significant amounts of THC and negligible amounts of CBD.[54]

Although national survey data indicate that use of marijuana by youth has remained stable, there has been a significant increase in dabbing and use of edibles as the usual method of marijuana use among high school students who reported past 30-day marijuana use in Colorado between 2015 and 2017.[42,59] These products are higher in THC potency and can result in more behavioral health consequences. A recent study from the UK of 1087 participants age 24, who started using cannabis between the ages of 14 and 16, found that those using the higher THC products ($\geq$10% THC) reported significant increased frequency of cannabis use, cannabis problems and increased likelihood of anxiety disorder compared to those using the products with <10% THC.[43] There has been a significant 10-year increase in adolescent marijuana-associated emergency department and urgent care visits in Colorado with a significant increase in behavioral health evaluations, most notably in the years following commercialization of medical (2009) and recreational marijuana (2014).[44]



Wang GS et al. J Adolesc Health 2018;63:239-241

The use of electronic cigarettes (e-cigarettes) and vape devices by youth has rapidly increased, driven in large part by marketing and advertising by e-cigarette companies.[45] In 2017 Colorado was leading the nation in use of nicotine-containing vapor products or vaping among young people under the age of 18 and this use was associated with a number of other risk behaviors including significantly more reports of marijuana use in the past 30 days.[46] Among adolescents reporting use of electronic vapor products, 50.1% reported using marijuana in the past 30 days versus7.6% of those not using vape products.

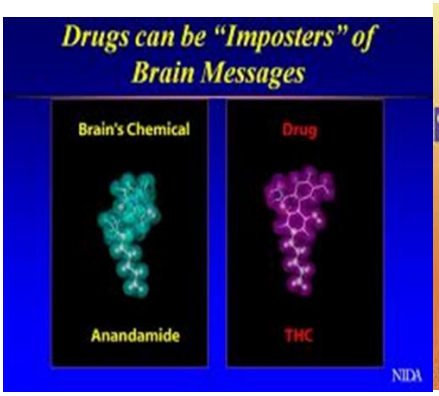
Table 1. Substance Use and Sexual Behavior among Colorado High-School Students, According to Use or Nonuse of Electronic Vapor Products, in 2017.*

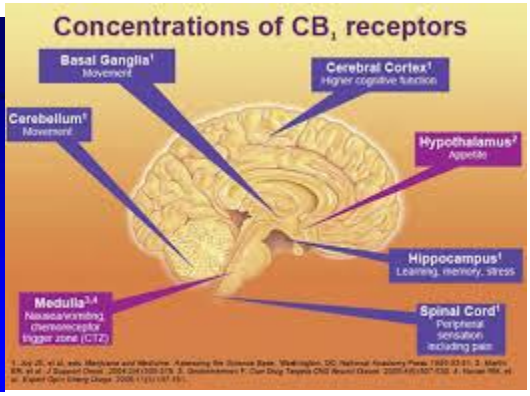
Variable	All Students (N=45,385)	Recent Use of Electronic Vapor Product†	
		No (N=31,991)	Yes (N=13,394)
	percent (95 percent confidence interval)		
Binge drinking on ≥1 day in past 30 days‡	16.0 (15.2–16.8)	6.1 (5.6–6.5)	43.0 (41.3–44.7)
Use of opioid pain medicine without a prescription in lifetime	12.4 (11.8–12.9)	7.1 (6.7–7.5)	26.0 (24.8–27.2)
Use of marijuana in past 30 days	19.4 (18.4–20.4)	7.6 (6.7–8.4)	50.1 (49.2–52.7)
Use of cocaine >1 time in lifetime	5.0 (4.5–5.4)	1.4 (1.1–1.6)	14.2 (13.2–15.2)
Sex with ≥1 partner during past 3 mo	22.9 (21.9–24.0)	14.6 (13.7–15.5)	45.1 (43.8–46.4)
Use of heroin >1 time in lifetime	1.5 (1.3–1.7)	0.5 (0.3–0.6)	3.7 (3.2–4.1)
Use of methamphetamines >1 time in lifetime	2.0 (1.8–2.2)	0.6 (0.5–0.8)	5.0 (4.5–5.6)

* Data are from the Healthy Kids Colorado Survey. Of the 47,146 students who were surveyed, 45,385 provided answers to the questions listed in the table. Data were weighted to reflect the sociodemographic profile of the high school students in Colorado.
† Recent use was defined as the use of an electronic vapor product not including marijuana during the past 30 days.
‡ Binge drinking was defined as four or more drinks per day for female students and five or more for male students.

Ghosh TS et al. NEJM 2019 ;380 :689-690

One positive benefit of research on cannabis has been an increasing understanding of the endocannabinoid system in the brain. It was named as such because it was discovered that THC fit into a receptor in the brain in the 1960s, well before there was any understanding of why we might have such a receptor in the brain.[47] The same lab that discovered this, discovered why we have these receptors. In the 1990s they discovered the brain makes a substance, they named anandamides (which is a Sanskrit word for extreme joy or bliss) which fit into these cannabis receptors (CB1) in the brain.



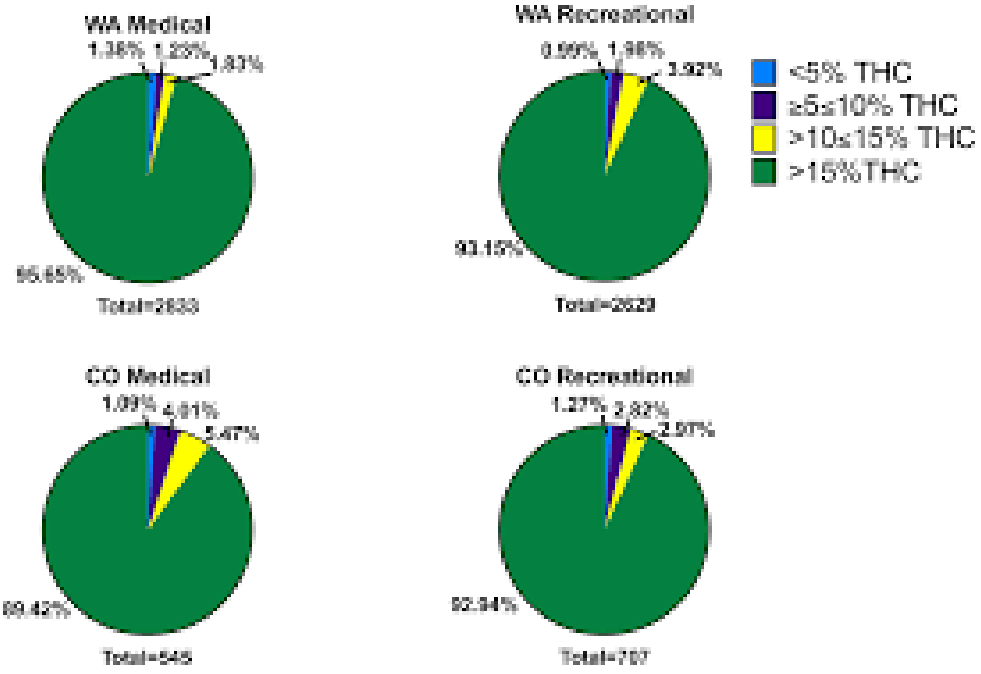


Experimental evidence shows that the cannabinoid system activity is neuroprotective, regulating critical homeostatic processes in the brain.[48] The brain produces anandamides when needed; they are used locally and destroyed when no longer needed. CB1 receptors regulate the balance between excitatory and inhibitory neuronal activity. CB1 receptors play a particularly important role during adolescent brain development. THC fits into the CB1 receptors blocking anandamides and is slow to disappear. Adolescent/young adult exposure to cannabis can disrupt excitatory glutamate functioning in the brain. Glutamate plays an important role in normal brain development by facilitating synaptic pruning in the prefrontal motor cortex during adolescence and young adulthood. This process is not complete until the mid-20s when the brain is considered fully developed. [49] As such the use of marijuana during development can cause long-term or possibly permanent adverse changes in the brain.[33]

5) Limit potency of THC to under 10% in **medical** cannabis and eliminate the concentrates such as wax, shatter, dab from **medical** cannabis since there is no research on these products for any **medical** condition.

Rationale:
Several large systematic reviews and meta-analyses of peer reviewed studies of cannabis for medical conditions done to date used THC percentages at or below 10%.[50-52] There are no controlled studies of the highly concentrated cannabis products such as vaping hash oil, smoking shatter, wax, or dab for any medical condition. Recognizing that higher doses of THC can increase the risk of harm from cannabis, Freeman and Lorenzetti propose that there should be a standardized dose across all cannabis products and methods of administration and that standard units should be based on the quantity of active pharmacological constituents.[53] Since the primary psychoactive constituent of cannabis is THC, standardized doses of THC should form the basis of 'standard THC units' rather than other methods of measuring cannabis exposure (e.g. grams, joints). They propose that the standard THC unit should be fixed at 5 mg of THC. It is important to understand the difference between mg of THC and % of THC. To put this in perspective, several of the pain studies in the systematic reviews demonstrating benefits utilized the pharmaceutical drug Sativex which is an oral mucosal spray with 2.7 mg THC and 2.5 mg CBD per dose. A typical marijuana joint weighs 0.5 g. If the product is 12 – 23% THC then a typical joint contains 60 – 115 mg of THC which is 20 – 40 times the medicinal dose.

A recent analysis of cannabis potency in medical and recreational programs in the United States found the average concentration of THC in all states was two to three times the THC content known to be efficacious in the treatment of pain (i.e. >5–10%) and that a vast majority of products in all states, including medical-only programs, contained THC designed for recreational use (i.e. > 15%).[54] In Colorado, they found that most products available in medical dispensaries have greater than 15% THC.



Cash MC et al. PLOS-ONE

The authors point out that patients who find this information in their online searches may subsequently believe high potency products are suitable for medical purposes, placing themselves at higher risk of cannabis intoxication. This is especially concerning in light of the previously mentioned systematic review and meta-analysis of 15 studies of psychiatric symptoms caused by cannabis constituents.[21] The authors found that acute administration of THC induces significant increases in positive, negative, and other symptoms associated with schizophrenia and other mental disorders with large effect sizes in adults with no history of psychotic or other major psychiatric disorders.

A study in Colorado found a significant increase in cannabis-related visits to emergency departments from 2012 to 2016 including episodes of severe intoxication, hyperemesis, psychiatric symptoms, and severe cardiovascular events.[55] This may very well be due to the increase in potency and availability of cannabis products, without any warnings regarding the possible consequences. There are currently 81,722 patients with an active medical marijuana card in Colorado and there are no significant differences in the products available for medical versus recreational marijuana in dispensaries.

Colorado Medical Marijuana Registry Program Statistics March 2020

Condition	# of Patients	Percentage
Cachexia	1,198	1.47%
Cancer	4,267	5.22%
Glaucoma	1,132	1.39%
HIV/AIDS	0	0%
Muscle Spasms	29,945	36.64%
Seizures	3,091	3.78%
Severe Pain	75,731	92.67%
Severe Nausea	15,791	19.32%
PTSD	10,437	12.77%
Autism Spectrum d/o	375	0.46%
In Lieu of an Opioid	2,749	3.36%

**Does not add to 100% as some patients report more than one debilitating or disabling medical condition.

https://www.colorado.gov/pacific/cdphe/2020-medical-marijuana-registry-statistics

6) Put Medical Marijuana recommendations on the Prescription Drug Monitoring Program (PDMP) in Colorado. If Colorado is legitimately supporting the use of medical marijuana in people with mental illness for health-related issues, then there needs to be monitoring, especially for those in the criminal and juvenile justice system. This is already occurring in several states.

Rationale:
Because cannabis can often cause or worsen psychiatric symptoms, it is difficult to diagnose mental health conditions and determine appropriate pharmacological interventions in a patient who is actively using cannabis products, especially the high potent THC products. Drugs are metabolized and eliminated by enzymes in the liver, specifically, the cytochrome P450 (CYP) family of enzymes. Drugs can act as either inhibitors or inducers of these enzymes and as a result, cannabis can have many drug-drug interactions with other drugs.[56,60]

THC and CBD are both metabolized by CYP3A4 and CYP2C9. Some medications can increase cannabinoid levels. For example, drugs that are CYP3A4 inhibitors such as ketoconazole, an antifungal medication, can double THC and CBD concentrations, augmenting the psychoactive effects of THC. This is similar for drugs that inhibit CYP2C9 such as fluoxetine which could be expected to increase THC exposure and psychoactive effects. On the other hand, cannabis can affect the levels of other medications. THC induces CYP1A2 and can reduce levels of drugs metabolized by CYP1A2 such as theophylline or olanzapine. CBD inhibits CYP3A4 and CYP2D6 and can increase levels of drugs metabolized by these isoenzymes. CPY3A4 metabolizes about a quarter of all drugs.

CBD may increase serum concentrations of macrolides, calcium channel blockers, benzodiazepines, cyclosporine, sildenafil (and other PDE5 inhibitors), antihistamines, haloperidol, antiretrovirals, and some statins (atorvastatin and simvastatin, but not pravastatin or rosuvastatin). CYP2D6metabolizes many antidepressants, so CBD may increase serum concentrations of SSRIs, tricyclic antidepressants, antipsychotics, beta blockers and opioids (including codeine and oxycodone). Increased concentrations of these drugs can result in increased side effects.

Currently in Colorado, a physician can make a recommendation that a patient have a medical marijuana card but another physician prescribing for the patient has no way to know that the patient is using medical marijuana unless the patient self-reports his/her use. There are no current requirements that prescribers recommending medical marijuana determine the type, dose, frequency and route of administration nor requirements that the patients' current medications are reviewed nor requirements to document that patients are advised about possible drug-drug interactions. So even if a prescriber recommends a low THC product, there is no "prescription" and the patient can purchase any concentration, including any product the dispensary worker recommends. The patient can purchase high potency edibles, wax, shatter, or dab, even though there is no evidence to support their use for any medical condition.

Equally concerning is the fact that many prescribers have limited knowledge of cannabis and its uses medicinally, or possible consequences from use. A recent report of an on-line survey of 451 health care professionals including neurologists, nurse practitioners/nurses and pharmacists indicated that many health care professionals are not educated enough about medical marijuana to counsel their patient and recommend specific products or dosing.[57] The authors reported "professional cannabinoid education nationwide is immensely needed."

Patient care in Colorado would be improved substantially if medical marijuana is on the PDMP. This information would allow other physicians seeing the patients, who are using medical marijuana, to consider drug to drug interactions with other prescribed medicine. It could also facilitate communication between providers to discuss the best options for the patient. This way the providers would know who was making the recommendation for medical marijuana and how to contact them. Anecdotally in Colorado, very few patients are able to tell a primary care provider or psychiatric provider the name of the physician who signed their medical marijuana card so there is very little communication between providers regarding the use of medical marijuana. Because of the inherent danger in scheduled medications, they should all be on the PDMP.

Conclusion

The Task Force Concerning the Treatment of Persons with Mental Health Disorder in the Criminal and Juvenile Justice System (MHDCJS) and the Substance Abuse Trend and Response Task Force (SATRTF) hope people will carefully consider the recommendations and research that are detailed in this whitepaper. Colorado has taken many steps to responsibly implement marijuana legalization. Despite these efforts, unanticipated consequences emerge. This paper focuses on the medical classification of marijuana and the perception that it is safe and effective for everyone regardless of dosing or method of administration. Yet, legalized marijuana has evolved to higher THC potencies, disproportionate THC to CBD proportions, and concentrated methods of administration. There is no research to prove this new form is safe or effective for medical use. The Colorado marijuana industry can be strengthened by developing safeguards to remedy some of these misunderstandings and their potentially harmful impacts on vulnerable populations. We hope these recommendations can serve as a blueprint to establish those safeguards

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