

Prioritizing Mental Health in an Emerging Market



**A Framework for Maintaining Public Health and
Expanding Knowledge on Cannabis and Mental Health**



A Note



FROM ANDREW FREEDMAN, the Executive Director of the Coalition for Cannabis Policy, Education, and Regulation (CPEAR):

Some reading this policy paper may be surprised that it highlights potential negative effects from cannabis use. Those readers might believe that highlighting mental health issues will be counterproductive to our goal of progressing cannabis policy and regulation. Opponents of a tax and regulate system often point to a tragic incident of cannabis use as an argument for prohibition, full stop.

Our CPEAR Center of Excellence believes that this line of argumentation misses the point. Data and research may well illustrate negative effects of cannabis, as well as beneficial uses. However, Americans will continue to use cannabis, regardless of what any study suggests or individual may think of cannabis use. Congress is not deciding on a world with or without cannabis. With fully half of Americans admitting to trying cannabis¹, Congress is deciding on what the role of government should be in protecting these consumers, patients, and the communities where they reside.

As we have stated many times: cannabis and cannabis reform are already here, we exist to get it right. To do so, we need to take a sober look at the data and research, and shape best practices, as responsible use must be part of any version of responsible regulation.

We are deeply indebted to everyone who helped make this paper possible.



Executive Director Andrew Freedman made history in 2014 when then-Governor John Hickenlooper tapped him to become Colorado's cannabis czar, in charge of implementing the world's first adult-use cannabis market. Since then, he has advised 19 different governments in establishing their cannabis regulatory frameworks. Andrew holds a J.D. from Harvard Law School and a B.A. from Tufts University.

¹ <https://www.usnews.com/news/national-news/articles/2021-08-17/record-high-more-americans-are-trying-marijuana-gallup-poll-finds>

About the Authors



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Dr. Staci Gruber is the Director of the Cognitive and Clinical Neuroimaging Core at McLean Hospital's Brain Imaging Center and an Associate Professor of Psychiatry at Harvard Medical School. Dr. Gruber's clinical research focuses on the application of neurocognitive models and brain imaging to better characterize risk factors for substance abuse and psychiatric conditions. She has been studying the impact of cannabis on the brain for over two decades using neurocognitive, clinical and diagnostic assessments and multimodal brain imaging techniques. Her work examining the etiologic bases of neural models of dysfunction in cannabis-using adolescents and adults has been published in numerous peer reviewed journals and been the basis of national and international symposia, documentaries, news stories and press conferences, including features in the New York Times, NPR, and CNN's documentary series "WEED" with Dr. Sanjay Gupta.

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Currently, Dr. Sagar's research is focused on examining the impact of cannabinoid use utilizing neuropsychological measures, clinical assessments, and multimodal neuroimaging techniques. She is particularly interested in the differential impact of recreational versus medical cannabis use, and how factors such as age of onset and exposure to individual cannabinoids mediate cognitive and clinical effects.

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Drs. Gruber and Sagar conducted this work as paid consultants and are publishing in that capacity.

Executive Summary

The regulatory structure governing cannabis use must be rooted in science, evidence, and data to inform a responsible marketplace and utilize reasonable guardrails. Our understanding of the potential harms of use and therapeutic applications of cannabis will continue to evolve over time through continued and advanced research. Officials should design a regulatory framework that allows common-sense rules to be responsive to evolving policy and market environments. To that end, individuals and the communities in which they live will benefit from a federal regulatory system designed to manage mental health outcomes regarding the use of cannabis products. Ultimately, these components should serve as the foundation upon which a comprehensive federal regulatory system is built. This white paper seeks to define the fault lines in the current understanding of cannabis and its impact on mental health and provides recommendations to advance an evidence-based regulatory system.



Claims regarding the effects of cannabis on mental health appear to fall on seemingly opposite ends of the spectrum. One side believes that cannabis use causes psychosis, worsens psychiatric symptoms, and poses a significant risk for developing cannabis use disorder. The other side often dismisses any claim of potential harm or side effects from cannabis use, instead focusing exclusively on the potential therapeutic aspects, particularly mental health conditions. *The truth is likely somewhere in the middle:*

- **CANNABIS & PSYCHOSIS:** Cannabis may be one of many factors related to the manifestation of psychosis, and products with moderate or even low amounts of THC may exacerbate symptoms. Clinical trials of CBD products have shown therapeutic *benefits* in those with psychosis.
- **CANNABIS & ANXIETY:** Mixed research findings reflect a complex relationship heavily influenced by the unique effects of individual cannabinoids and the doses used. While low doses of THC and mid-range doses of CBD may alleviate anxiety, higher doses of THC often produce or exacerbate anxiety.
- **CANNABIS & PTSD:** Some research studies have corroborated anecdotal findings of symptom relief, while other studies report that cannabis use is related to more severe symptoms and problematic use patterns. Cannabis use may provide short-term relief, but long-term use could potentially result in poorer outcomes in those with PTSD.
- **CANNABIS & MOOD:** While associations between cannabis use and mood disorders have been documented, additional research is needed to more clearly delineate this relationship. Given evidence that some cannabinoids may provide clinical benefit for at least a subset of individuals with mood disorders, controlled clinical trials are needed.
- **CANNABIS & CANNABIS USE DISORDER (CUD):** Although some individuals develop CUD, the majority of recreational cannabis consumers do not develop problematic patterns of use. Preliminary data suggest CBD may protect against development of CUD.

Where should research go from here?

There are dozens of pertinent and pressing questions that should be addressed as quickly as possible with rigorous research. Most relevant to overseeing cannabis use, the federal government should promote and fund research behind two critical areas:

First: Defining Responsible Use

Although additional research is needed to delineate the specific parameters with the most significant impact, existing data can be used to help to shape a framework for responsible use. Important considerations include:

- **AGE:** Children and adolescents are particularly vulnerable to the adverse effects of cannabis, as they are with any drug.
- **THC AND CBD CONTENT:** While THC has therapeutic benefits, it is also associated with adverse outcomes, particularly for children and adolescents. CBD, which has a range of therapeutic properties, has an acceptable safety profile and may protect against adverse outcomes associated with THC.
- **PRODUCT CHOICE & MODE OF USE:** Different modes, or ways of using cannabis, are associated with unique characteristics regarding how much of the active ingredients enter the body, how long it takes to feel or get an effect, and how long effects will last.
- **CUD PREVENTION:** Those with mental illness are more likely to use high potency products, but these products are most likely to be associated with CUD; harm reduction efforts are key.
- **FAMILY HISTORY/GENETIC LIABILITY:** Individuals with a personal or family history of mental illness, particularly psychotic disorders, are likely at higher risk for adverse outcomes associated with cannabis use. Specific genes influence an individual's ability to metabolize drugs including cannabinoids, which also leaves some at increased risk for adverse effects.
- **OTHER MEDICATION USE:** Cannabinoids can interfere with the metabolism of certain medications, making them more or less potent.

Second: Improving screening tools for Cannabis Use Disorder (CUD)

Existing screening tools are considered reliable and valid among recreational (non-medical) cannabis consumers, but new metrics designed to assess problematic use in those who (also) use for medical purposes are needed.

Finally, it is incumbent on the federal government to act quickly in order to:

— CREATE A FRAMEWORK FOR RESPONSIBLE USE

- Decision-making tools designed to help consumers identify their level of risk will certainly increase safety and help prevent unnecessary exposure for those least likely to gain benefit and most likely to experience negative effects.
- Provide resources for public education campaigns, screening, and treatment to prevent and mitigate irresponsible cannabis use.
- Grant the appropriate regulatory powers the ability to place restrictions on problematic cannabis products as research and data dictate.

— REDUCE BARRIERS TO CANNABIS RESEARCH

- To thoroughly assess both the potential benefit and risks associated with cannabis and cannabinoid use, researchers should be allowed to study the actual products used by consumers and patients, which is not possible under current Federal law.
- Invest in rigorous research on cannabinoid-based therapeutics for mental health
- Well-designed, empirically sound, and controlled studies offer an important opportunity to customize and optimize cannabis and cannabinoid-based treatments, ultimately changing the narrative and transforming patient care.
- Encourage federal public health and research agency officials to issue joint guidance to research institutions about the opportunities and legality of conducting clinical, observational, and other scientific research focused on cannabis. This will undoubtedly help address the potential chilling effect on some universities given the extremely complex, dynamic set of rules and shifting landscape associated with cannabis

— STANDARDIZE TOOLS FOR CANNABIS RESEARCH

- The wide variety of cannabis/cannabinoid formulations available across the country has led to contradictory results across research studies and misinterpretations about what these findings mean. Standardized metrics to assess cannabinoid exposure and standardized batteries to assess outcomes are needed across research investigations.

Introduction

CANNABIS HAS BEEN USED FOR THOUSANDS OF YEARS, with references dating back as far as 2700 BC; however, public opinion has shifted dramatically throughout history and has recently pushed many jurisdictions to reform their cannabis laws. In crafting comprehensive, sensible cannabis policy, one of the most important considerations is ensuring the protection of vulnerable populations. While substantial research has centered on the impact of cannabis use among youth, given the well-documented neurodevelopmental vulnerability associated with childhood and adolescence, far less work has focused on those with mental health issues. For decades, the impact of cannabis on mental health has been hotly debated given concerns about the potential negative effects of cannabis on various psychiatric conditions juxtaposed against claims regarding therapeutic benefits of some cannabinoids for certain psychiatric symptoms. To fully understand the potential impact of cannabis on mental health, it is essential to delineate several key terms, some of which are mistakenly used interchangeably.



Cannabis: Finding Common Language for a Complex Plant

Cannabis or **marijuana** are terms often used to describe *anything* from the plant *Cannabis sativa L.* Importantly, cannabis is actually comprised of hundreds of compounds, including over 100 **cannabinoids**. Cannabinoids are chemicals that interact with the **endocannabinoid system (ECS)**, a series of chemicals and receptors throughout the brain and body known for maintaining homeostasis and other critical functions, including learning and memory, mood, pain perception, movement, pleasure, coordination, and the senses. Of the cannabinoids, delta-9-tetrahydrocannabinol (**THC**) and cannabidiol (**CBD**) are typically the most abundant in the plant, and accordingly, the most widely studied. THC is the primary intoxicating constituent of the plant, often sought by recreational consumers, while CBD is generally considered non-intoxicating. Moreover, CBD has been shown to potentially mitigate negative effects that can occur in the context of THC exposure, including adverse psychological symptoms as well as cognitive decrements and other brain-related changes.¹⁻³

Although both THC and CBD have been noted to have therapeutic properties given the distinct ways they exert their effects, it is not surprising that these cannabinoids appear to impact specific psychiatric symptoms very differently. This is a critical point, as the majority of commercially available cannabis products contain a combination of these compounds. Although most research to date has focused on THC and CBD, it is important to recognize that most cannabis products also contain “minor” or less common cannabinoids (e.g., cannabichromene, cannabigerol, cannabinol, tetrahydrocannabivarin), as well as additional compounds, including terpenes which give cannabis its characteristic scent and taste profile and have been demonstrated to confer their own effects.⁴ Products that contain an array of cannabinoids and other naturally occurring compounds from the plant are referred to as **full-spectrum** or if they contain no detectable THC, **broad-spectrum**. In 2018, the Farm Bill was signed into law which effectively legalized the production of **hemp**, a variety of cannabis with less than <0.3% THC by weight. Hemp-derived products have proliferated over the past several years with demand typically driven by consumers interested in CBD or other cannabinoids. They are widely available online, in retail stores, including licensed cannabis dispensaries, grocery stores, coffee shops, and even gas stations. Therefore, available products may be derived from either cannabis or hemp, further complicating the landscape..

Most cannabis chemovars (also known as cultivars or strains) and cannabis-based products used in the real world contain varying amounts of THC and CBD and other cannabinoids and chemicals, which all work together and account for specific cannabis varieties or products conferring unique effects. Although still somewhat controversial, the **entourage effect** refers to the synergy that occurs when these chemicals work together. It is important to note that all currently FDA-approved medications containing cannabinoids (e.g., nabilone, dronabinol, Epidiolex) are single-compound formulations that may not apply directly to real-world consumers and patients who typically choose full- or broad-spectrum products.

Individuals who use cannabis recreationally or non-medically (to get high or feel altered) generally seek products high in THC. *In fact, most studies assessing the effects of cannabis have focused on those using products for recreational purposes. As a result, study findings to date largely reflect the impact of products high in THC, which is often associated with negative effects. In contrast, until recently, relatively little empirically sound data have focused on the impact of CBD which is often touted for its therapeutic benefits.* While the provisions of the Hemp Farming Act of 2018 incorporated into that year's Farm Bill generated considerable confusion regarding the legal status of certain products, it also prompted a sharp increase in the use of high-CBD products, predominantly for those with medical or psychiatric symptoms. In addition, expanding legalization of cannabis for medical purposes has also led to increased popularity of products with more varied cannabinoid profiles. Consequently, vastly different outcomes are beginning to be reported among medical cannabis patients relative to recreational/non-medical consumers. Accordingly, as policymakers, clinicians, and other stakeholders consider the impact of legalization, particularly with regard to mental health, it is critical to understand that the term "cannabis" is often used to describe both the whole plant and any of its individual components, which often confer a very wide range of different effects. A review of available literature further underscores this point, with study findings often appearing mixed or inconsistent depending on the population under study, cannabinoid profile of the products being studied, frequency of use and amount of product used, and a number of other variables. For example, while exposure to products high in THC appears to be related to more negative outcomes in general, the use of products high in CBD or other non-intoxicating cannabinoids appears to reduce the likelihood of negative outcomes. As a result, cannabis is anything but "one size fits all."



Part I:

CANNABIS & MENTAL HEALTH: A REVIEW OF THE RESEARCH



Claims regarding the effects of cannabis on mental health appear to fall on seemingly opposite ends of the spectrum. One side believes that cannabis use causes psychosis, worsens psychiatric symptoms, and poses significant risk for developing cannabis use disorder. The other side often dismisses any claim of potential harm or side effects from cannabis use, instead focusing exclusively on the potential therapeutic aspects, particularly for mental health conditions. *While the truth is likely somewhere in the middle, caveats are essential, and additional moderating factors must be considered.*

Over the past decade, cannabis use has increased steadily, most concerning for vulnerable populations, including children and adolescents, older adults, and those struggling with mental health conditions. To put this population into context, in 2019, the National Survey on Drug Use and Health estimated that 51.5 million Americans age 18 or older had a mental health condition, representing approximately 20.6% of the population. Although additional research is needed, existing data can be used to shape policies that will ultimately make cannabis use safer overall, particularly for vulnerable populations.

In 2017, given the controversy regarding both the potential detriments and benefits associated with cannabis use, the National Academy of Sciences, Engineering, and Medicine (NASEM) issued a report summarizing the health impact of cannabinoids.⁵ With regard to mental health, the report concluded that cannabis use may be associated with an increased risk of psychosis, particularly when used more frequently or in higher amounts. However, the report also noted that cannabis use could yield positive

effects in this population, including better learning and memory-related outcomes. In addition, the report concluded that cannabis use does not appear to increase the likelihood of developing depression, anxiety (with the exception of social anxiety disorder), or posttraumatic stress disorder but noted that cannabis use may *exacerbate* symptoms in those already diagnosed with mood/anxiety disorders and that heavy cannabis users are more likely to report thoughts of suicide than non-users. For individuals with bipolar disorder (BPD), NASEM concluded that daily cannabis use may be linked to worse clinical symptoms. Importantly, however, the studies that met NASEM’s rigorous criteria for review were predominantly focused on the impact of THC. *Newer research focused on specific cannabinoids vs. the impact of “cannabis” use in general will ultimately allow for more thoughtfully crafted, informed policies designed to protect the mental health of all Americans.*

It is also important to note that the continued criminalization of cannabis in some jurisdictions across the US has a measurable impact on Americans’ mental health. According to the Federal Bureau of Investigations Uniform Crime Report, just over 350,150 Americans were arrested for cannabis-related crimes in 2020, with 91% of arrests for possession only. The negative impact on mental health associated with interactions with the criminal justice system is well established.⁶ Given this reality, the continued expansion of decriminalization policies and diversion programs at the federal, state, and local levels will increase the opportunities for Americans with mental health conditions to get the help they need.

The discussion that follows is an overview of the research to date on the association of cannabis and various psychiatric disorders organized by commonly discussed topics within each disorder.

Cannabis & Psychosis

Does Cannabis Cause Psychosis?

Psychotic disorders such as schizophrenia are relatively rare, but they are considered chronic and debilitating. The relationship between cannabis use and psychosis has been well-documented; earlier onset of use, use of higher potency products, and increased frequency and amount of cannabis used have all been associated with higher rates of psychosis. It is important to recognize what this association means and what it does not. Although strong evidence indicates that those diagnosed with psychotic disorders, including schizophrenia, have higher rates of cannabis use than the general population, mounting research suggests that cannabis use *alone* is not sufficient to *cause* psychotic disorders.⁷⁻⁹ If this were the case, it would be expected that the observed uptick in cannabis use over recent years would result in an increased prevalence of psychotic disorders, which has not been observed. Therefore, alternative theories have been proposed to explain the relationship between cannabis use and psychosis.

One theory is that cannabis use may be a *contributing* cause of psychosis among many other variables, such as genetic predisposition, poor school performance, use of other drugs (alcohol, tobacco), and

other familial and social factors.^{9,10} While some believe that cannabis is a contributing cause in the model, others suggest that the association between cannabis use and psychosis would not be observed if confounding variables were properly controlled for. In fact, dozens of variables have been identified as potential confounds, making it extremely difficult, if not impossible, to control for in observational research studies. Taken together, psychotic disorders are complex with a multitude of potential underlying causes. *It is therefore unlikely that a single factor, such as cannabis use, can by itself directly cause an individual to develop a psychotic disorder.*

Alternatively, some posit that individuals may have a *shared vulnerability* to psychosis and cannabis use. Interestingly, recent investigations reported higher cannabinoid receptor density and levels of certain chemicals in the endocannabinoid system of individuals diagnosed with schizophrenia. In addition, other studies have uncovered associations between some genes related to cannabinoid receptors and those related to schizophrenia.⁷ These findings indicate that individuals with psychotic disorders may have an underlying biological vulnerability to *both* increased rates of cannabis use and an increased risk for psychosis without cannabis use as a causal factor. Similarly, it is possible that those who have a genetic vulnerability for psychosis may be more susceptible to psychiatric disorders in general.^{11,12} This would mean that those at risk for psychotic disorders are also at increased risk for developing problematic patterns of cannabis use, previously referred to as “addiction” or “dependence”, and more recently termed “cannabis use disorder.”

How Do Cannabis and Cannabinoids Impact Psychotic Symptoms?

It is also important to consider how cannabis may impact those already diagnosed with a psychotic disorder. Notably, most studies examining this question have focused on those who smoke cannabis, with the majority conducted prior to the widespread legalization of medical and recreational cannabis use that currently exists in the US. While this makes it difficult to tease out the effects of different types of cannabis products, cannabis sold in the unregulated or “black market” is typically high in THC with very low or undetectable levels of CBD.^{13,14} In general, frequent cannabis use, particularly daily use of high potency products (those with higher THC content),¹⁵ is related to higher rates of relapse, longer hospitalization time, and poorer treatment outcomes.¹⁶ It remains unclear, however, whether these negative consequences are a direct result of cannabis use exacerbating psychotic symptoms or if they may be related to other factors, such as an increased motivation to use cannabis to treat more severe symptoms.

Notably, some studies have reported *fewer* negative outcomes associated with cannabis use in those using products with detectable amounts of CBD.¹⁷ Bolstered by evidence from animal studies demonstrating that CBD has potential antipsychotic effects, a number of clinical trials of CBD have generated promising results.¹⁸⁻²³ Overall, these studies have primarily concluded that CBD appears to *improve* symptoms common in psychotic disorders. CBD has also been shown to have comparable efficacy to other antipsychotic medications, and with fewer side effects than traditional antipsychotic medications.²¹ It is

important to note, however, that further research using adequately-powered, well-controlled trials and an evidence-based balance of risk and benefit reviewed and overseen by the appropriate regulator (i.e., the Food & Drug Administration [FDA]) are needed to reach conclusions on the relationship between psychotic symptoms and cannabis and cannabinoids. Moreover, it is also important to recognize the false belief that using *any* cannabis product containing CBD completely eliminates the risk of THC-related adverse psychiatric effects.²⁴

Cannabis & Psychosis: Conclusions

Overall, the relationship between cannabis use and psychosis is complicated. In considering the evidence, it is clear that although earlier onset of cannabis use (particularly during adolescence and emerging adulthood) and using cannabis more frequently and in higher amounts are each associated with increased risk for psychotic disorders, cannabis use alone is not likely sufficient to cause psychosis *de novo*. Most agree that a number of variables contribute to the manifestation of psychotic disorders, and cannabis use might be considered one of these factors or may be peripherally related to these factors. Additional empirically sound research studies with oversight from the FDA are needed to understand the contribution that each of these variables has on the manifestation of psychosis and identify who may be at greatest risk based on their genetic profile and other potentially associated variables. Given available data, those with a family history of psychosis, particularly among first-degree relatives, should be considered potentially vulnerable to negative outcomes associated with cannabis use. For individuals diagnosed with a psychotic disorder, it is possible that using cannabis or cannabinoid-based products with even low to moderate amounts of THC may exacerbate symptoms. Cannabis use, therefore, represents a modifiable risk factor that should be targeted in those who use cannabis and have poor clinical outcomes. In contrast, products predominantly or exclusively containing CBD may help to address symptoms and provide therapeutic benefit. Given the proliferation of cannabinoid-based products with varied constituent profiles, further research using adequately-powered and well-controlled trials is needed to determine whether specific CBD-based therapeutics could be safe and effective alternatives for those at least a subset of those with psychotic disorders. However, as this population is particularly vulnerable, it is essential to proceed with caution and carefully consider potential risks and benefits.

Cannabis & Anxiety

Does Cannabis Cause Anxiety Disorders?

Everyone experiences some degree of anxiety, and estimates suggest 1/3 of Americans experience an anxiety disorder at some point in their lives, making it the most common mental health condition in the US. Although conventional medications can be effective for some, others do not find relief, and some struggle with unwanted side effects. The growing availability and popularity of legal cannabis

coupled with high rates of anxiety further exacerbated by the COVID-19 pandemic have reignited a long-standing conversation about the potential effects of cannabis on anxiety.

Research suggests that cannabis use is prevalent among individuals with anxiety disorders, yet relaxation and relief from anxiety are among the most commonly reported motives for cannabis use.²⁵ To date, few studies have examined the causal nature of the association, and those that have often failed to control for related factors have led to mixed findings. *Like most psychiatric disorders, most believe the etiology of anxiety disorders is multifactorial and it is not likely caused by a single factor, including cannabis use.*

Does Cannabis Improve or Worsen Anxiety?

The short answer is “it depends,” and again is related to the constituent profile, frequency, and amount of product used. Data suggest that while many find cannabis effective for relaxation and anxiety-related symptom relief, others report that cannabis use worsens symptoms of anxiety. While individual factors such as genetic profile, physiology, other substance use, and previous experience with cannabis likely play a role, *the impact of cannabis and cannabinoid products on anxiety appears to be related to the specific effects of individual cannabinoids.* Research findings suggest that THC and CBD have different effects on anxiety, and that dose is a critical consideration. For example, while low doses of THC have generally been demonstrated to reduce anxiety, high doses of THC often worsen anxiety.²⁶ Conversely, the few studies conducted thus far suggest that CBD does not worsen anxiety at any dose, and it may effectively relieve anxiety at mid-range doses.^{27,28} Accordingly, there is significant interest in pursuing the development of cannabinoid-based therapeutics for anxiety, particularly CBD-based preparations.

While additional research using appropriately powered, controlled clinical and preclinical studies should be conducted, several preliminary investigations assessed the efficacy of CBD for anxiety and reported that CBD appears to be effective for reducing situational anxiety, such as public speaking tasks,^{29,30} and in those with social anxiety.³¹ As all of these studies were conducted using CBD isolate, additional research is needed to determine whether CBD as a single compound is more or less effective than full- or broad-spectrum products (those containing other cannabinoids and chemicals naturally found within cannabis plants), as the latter represents products most often consumed by individuals in the real world, outside of laboratory studies.

Cannabis & Anxiety: Conclusions

Studies have demonstrated a relationship between rates of cannabis use and anxiety; however, it remains unclear whether cannabis use itself leads to anxiety disorders, or those with anxiety are more prone to use cannabis. While many report using cannabis to alleviate symptoms of anxiety, mixed research findings reflect a complex relationship heavily influenced by the unique effects of individual cannabinoids and the doses used – while low doses of THC and mid-range doses of CBD may alleviate anxiety,

higher doses of THC often produce or exacerbate anxiety. Accordingly, several factors play a role in determining how cannabis use impacts anxiety, including the amounts of THC and CBD present within a product, and an individual's unique genetic profile. Although numerous pharmacological treatments are available for anxiety, not everyone achieves adequate symptom relief and many experience unwanted side effects, underscoring the need for safe and effective alternative treatments. A number of investigations are currently focused on the impact of CBD-based products for those with anxiety, and further work in this area is clearly indicated.

Cannabis & Post-Traumatic Stress Disorder (PTSD)

About half of all adults in the US will experience a traumatic event at some point in their lives. Although only a small percentage (4-9%) develop Post-Traumatic Stress Disorder (PTSD), those who do often struggle to find effective treatments. As a result, cannabis use is common among those with PTSD, including Veterans, who often report using cannabis specifically to improve symptoms including anxiety, sleep disturbance, hyperarousal, and to help avoid emotional triggers.³² Although some research studies corroborate these largely anecdotal findings and suggest that patients with PTSD may find relief with cannabinoid use, others caution that cannabis use may be actually be associated with more severe symptoms and may ultimately result in problematic patterns of use.³³ Some work suggests these mixed findings may be due to the fact that cannabis use can provide short-term relief, but it is possible that long-term use could result in poorer outcomes.³⁴ Despite several reviews on the topic, most conclude that comprehensive data assessing the potential benefit and harms of cannabis use for PTSD is lacking; as noted in the NASEM report, most studies to date are limited by small sample sizes and poor control over other related variables.^{5,35} Given the high rates of cannabis use in those with PTSD and the need for alternative treatment options, additional empirically-sound studies are warranted.

Cannabis & Mood Disorders

Does Cannabis Cause Depression or Mood Disorders?

As with the other mental health conditions previously discussed, studies generally show an association between mood disorders and the use of cannabis, but no link has been established to suggest that cannabis use *causes* mood disorders. A number of explanations and additional variables may explain the link between cannabis and depression for example, but it is critical to examine the factors that influence this relationship to understand how cannabis use affects mood overall.²⁵

Does Cannabis Improve or Worsen Mood or Depressive Symptoms?

It is quite common for cannabis consumers to report that they use cannabis/cannabinoids to relieve negative mood, but many question whether cannabis improves mood or if it could have detrimental long-term effects.

While difficult situations in life can lead individuals to feel sad, down, or lonely, when these feelings become severe and persistent, an individual may be suffering from **depression**. Depression affects approximately 7% of adults and is the leading cause of disability among Americans ages 15-44. The majority of studies conducted thus far suggests that individuals with depression who use cannabis or cannabinoid-based products for non-medical purposes (which typically contain considerable THC) may be at increased risk for more severe symptoms, have higher rates of suicidal ideation, lower utilization of psychiatric services, and a higher chance of developing problematic cannabis use.³⁶ These risks appear to be elevated with increased frequency and higher amounts of cannabis used.¹⁶ A handful of studies, however, also suggest that cannabis users have a better mood and a lower likelihood of experiencing a depressive event.²⁵

Findings are also complicated when it comes to the relationship between cannabis use and suicidality. Overall, data suggest that chronic cannabis use predicts suicidality; among young adults, increased suicidal behaviors (ideation, plan, attempt) have been reported with greater risk for women than men.³⁷ Notably, the relationship between cannabis and suicidality has been questioned given limitations of existing research studies and the possibility that the reverse is true – suicidality may predict cannabis use.³⁸ In addition, adolescent cannabis use has been associated with an increased risk of developing depression or suicidal behaviors later in life, highlighting the need for prevention and harm reduction strategies targeting this population.³⁹ Although few studies have assessed whether very recent use of cannabis could trigger suicidal thoughts, existing data actually suggest that it may lower immediate risk, perhaps as a result of the euphoria experienced during cannabis intoxication.³⁸ More research is needed to understand this phenomenon.

Popular culture has also fueled a stereotype of cannabis users exhibiting a depression-like syndrome characterized by a lack of motivation, lethargy, apathy, and decreased productivity. However, a cannabis-specific “amotivational” syndrome is not supported by actual clinical findings.²⁵ Recent studies of medical cannabis patients have reported significant *improvements* in mood, and preliminary data suggest this may be due to the use of products with considerable amounts of CBD.^{40,41} Additional preclinical work and observational human studies will help pave the way for FDA-approved clinical trials which will further clarify findings thus far and inform best practices.

Bipolar Disorder (BPD) is a debilitating mood disorder characterized by severe changes in mood, including highs (mania) and lows (depression). BPD affects approximately 4.4% of adults at some point during their lives. Rates of substance use are quite high among those diagnosed with BPD, and among substances used by patients with BPD, cannabis is extremely common, second only to alcohol.⁴²

Interestingly, some studies assessing cannabis use among patients with BPD note reduced compliance, higher illness severity, and exacerbation of manic symptoms, while other data indicate that patients with BPD frequently report subjective clinical improvements as a result of cannabis use, underscoring the need for more work in this area.⁴³⁻⁴⁷

Cannabis & Mood: Conclusions

While associations between cannabis use and mood disorders have been documented, additional research is needed to more clearly delineate the relationship between cannabis use, depression, suicidality, mania, and related symptoms. Given evidence that some cannabinoids may provide clinical benefit for at least a subset of individuals with mood disorders, controlled clinical trials are needed to generate more definitive answers regarding whether certain formulations, specifically those containing considerable amounts of CBD, may effectively address at least some mood-related symptoms.

Problematic Use: Cannabis Use Disorder (CUD)

Cannabis Use Disorder (CUD) describes a problematic pattern of cannabis use that leads to significant impairment or distress. In other words, individuals with CUD may exhibit impaired control over their cannabis use; a negative impact on their employment, educational, or social pursuits; elevated risk of harm; and physical dependence (tolerance or withdrawal).

Controversy regarding whether patterns of cannabis can become problematic has been at the forefront of cannabis legalization discussions for years. However, many experts assert that a percentage of individuals who use cannabis may develop patterns of use that have clear negative consequences.⁴⁸ According to national survey studies of recreational users, rates of CUD are highly variable, with estimates ranging from 4-20%^{49,50} in some studies and up to 30% in others.⁵¹ Importantly, there is consensus *that the vast majority of recreational cannabis consumers do not develop problematic patterns of use.* However, given that youth and individuals with psychiatric conditions both tend to have higher rates of cannabis use than the general public, targeted interventions that aim to prevent, delay, and/or limit cannabis use are critical for these vulnerable populations.⁵²

As noted in a recent review, “the current and pressing challenge with cannabis is to develop well-reasoned policies that consider factual information about risks and potential benefits of cannabis and cannabinoid compounds in service of mitigating potential harm and maximizing potential benefits.”⁴⁸ Along these lines, it is important to recognize that those using cannabis products with higher THC content are likely at *higher risk* for developing a CUD, as THC produces strong reinforcing biologic effects⁵³, which are related to higher addiction severity.⁵⁴ Interestingly, however, initial evidence suggests that CBD, which is non-intoxicating, has a low potential for addiction as it lacks rewarding effects and is not associated with tolerance or withdrawal symptoms.⁵⁵ Recent work suggests that those using cannabis for

medical purposes may be at lower risk for developing CUD, which is likely related to their goals for use (to address symptoms and often to avoid intoxication), their more frequent use of products containing CBD and other non-intoxicating constituents, and other factors which require further exploration.⁵⁶ In addition, CBD may actually have “anti-addiction” properties⁵⁷; preliminary data suggest that CBD may protect against the development of CUD⁵⁸ and has been investigated as a potential treatment for other substance use disorders (i.e., tobacco, opioid, and cocaine). However, it is also important to consider data suggesting that individuals with pain, for example, may be an emerging group vulnerable to CUD,⁵⁹ although additional studies are needed to confirm these findings. Given the evolving knowledge base in this area, further well-designed, comprehensive preclinical and observational studies, as well as clinical trials with oversight by the FDA, are needed to conclude the efficacy of CBD for treatments and for whom it is most effective.



Part II:

RESEARCH SHOULD GUIDE A GOVERNMENT FRAMEWORK FOR RESPONSIBLE USE



In reviewing the state of the science around cannabis use and mental health, it becomes increasingly clear that study findings are mixed not only because there are dozens of variables to consider, but also because for decades, most have treated “cannabis use” as if cannabis is only one thing used in one way. More recently, many have begun to differentiate cannabis from the compounds that comprise it as well as individuals’ goals of cannabis use, which helps clarify the complexities of cannabis and mental health. To more thoroughly understand the effects of cannabis on mental health, more research is needed – but where do we go from here?

As the nation pushes towards cannabis legalization, several key areas must be considered to ensure that vulnerable populations are protected and that all who use or recommend the use of cannabis do so in ways that are likely to maximize benefit and minimize risk and harm.

Defining Responsible Use

Given the overwhelming “green rush” across the US in recent years, clear guidelines will help ensure safer patterns of use in the context of mental health. Although additional research is needed to delineate the specific parameters with the most significant impact, existing data can help shape a framework for responsible use. Importantly, individual differences related to genetics, metabolism, tolerance/experience,

modes of use, product selection, conventional medication use, use of other substances, and additional factors will affect how cannabis and certain cannabinoids interact with each person's body.

Age: As children and adolescents all undergo critical stages of brain development, youth are more vulnerable to the adverse effects of cannabis, as they are with any drug. Accordingly, policymakers should carefully consider age-related guidelines to help prevent or reduce adolescent cannabis use. Earlier onset of recreational cannabis use and higher frequency and more significant amounts of cannabis use have been associated with more negative outcomes than those who begin using later.⁶⁰ To date, there is a paucity of research on the long-term effects of CBD in pediatric/adolescent populations, an area in need of further investigation, including studies specifically focused on whether CBD-based therapeutics could be appropriate for addressing mental health symptoms.

THC and CBD Content: Research suggests that while THC may have medicinal properties, increased exposure to THC is related to negative outcomes (higher risk for mental health problems including development of cannabis use disorder, cognitive decrements, and other brain changes). CBD has been noted to have antipsychotic, antidepressant, antianxiety, anti-craving, and pro-cognitive effects and is generally considered safe, with a few negative effects reported. Accordingly, using products with higher amounts of THC is more likely to confer greater risk, while using products with higher amounts of CBD may lower risk of negative outcomes and may confer significant therapeutic benefit. Further research using appropriately-powered, well-controlled trials is clearly needed. These studies must include an evidence-based assessment of the risks and benefits of each product assessed, which are then reviewed, approved, and monitored by the FDA. Ultimately, this approach will help identify which products and what doses of cannabinoids are best for certain individuals and specific symptoms and conditions. Importantly, guidelines for safer use should stipulate that those using or planning to use cannabis should aim for the lowest effective dose ('start low and go slow'), and should allow ample time for effects to occur before using more product. While no fatal overdoses have been directly related to cannabis use, being overly intoxicated with cannabis can be extremely uncomfortable, disorienting, disturbing, and dangerous as it may lead to risky behaviors.

Product Choice, Mode of Use & Related Risk: Cannabis products are available in many forms including dried flower, concentrates (products designed to deliver a bigger "bang for the buck," which typically contain extremely high levels of THC), oils and extracts, edibles/ingestibles, topical and transdermal preparations, and suppositories, each of which have their own modes of use or routes of administration. Different modes or ways of using cannabis are associated with unique characteristics regarding how much of the active ingredients enter the body, how long it takes to feel or get an effect, and how long effects will last. It is also likely that each way of using cannabis confers different risks in terms of both physical and mental health, but research has only begun to scratch the surface. At this point, however, it has been posited that modes of cannabis use that deliver high doses of THC quickly are more rewarding, reinforcing, and pose a higher risk for negative outcomes. For example,

while traditional methods of inhalation (smoking or vaping) are often used for flower or concentrates, “dabbing” – the vaporization of a small amount of a highly concentrated (usually THC) product (a “dab”) on an extremely hot surface – delivers a single large bolus or dose all at once to the consumer, and it is designed to cause an intense high. As a result, while smoking and conventional vaping allow individuals to titrate their intake relatively easily, “dabbing” may be more difficult to control. Exposure to very high potency products is related to a higher risk of negative outcomes.

CUD Prevention: Individuals diagnosed with mental health conditions are often more likely to use cannabis,⁶¹ yet they are also at higher risk for transitioning from “regular” use to a cannabis use disorder (CUD).^{50,62} How can we work to prevent the potential transition to CUD and change the trajectory in this vulnerable population? One important consideration is the amount of THC and CBD contained in products. Given that THC is closely linked to CUD, potentially limiting THC exposure is key. Although additional research is needed, it is possible that the use of even small amounts of CBD may be protective against developing CUD. Unfortunately, a recent study demonstrated that cannabis consumers with pre-existing mental conditions were more likely to use products with higher THC potency.⁶¹ Accordingly, harm reduction efforts will be beneficial in those with mental health conditions.

Family History/Genetic Vulnerability: Individuals with a personal or family history of mental illness, particularly psychotic disorders, are likely at higher risk for adverse outcomes associated with cannabis use. Interestingly, this population is also more likely to use cannabis for the alleviation of symptoms. As a result, it is imperative for these individuals to be aware of the potential risks associated with use, particularly with regard to high-THC products. Further, specific genes influence an individual’s ability to metabolize drugs including cannabinoids, which leaves some at increased risk for adverse effects. For example, someone who is considered a “poor” metabolizer of THC may experience intoxication at significantly lower doses or for longer periods of time.

Other Medication Use: Individuals with mental health conditions are often treated with conventional medications. Importantly, clinical evidence suggests both THC and CBD can inhibit the metabolism of other drugs via interactions with the body’s cytochrome P450 (CYP) enzymes which are involved in the metabolism of drugs and detoxification of foreign chemicals. This means that using cannabinoids could cause certain pharmaceuticals to become more or less potent, both of which may result in adverse outcomes. Research focused on the degree and severity of interactions between cannabinoids, and specific medications is sparse, and greater work in this area is warranted, including studies that focus on how genetics may also influence this relationship.

Improving Screening Tools for CUD

Currently, several screening tools exist that can be used to provide information about whether an individual may be exhibiting symptoms or behaviors consistent with cannabis use disorder (CUD). While these

screening tools have generally been shown to be valid and reliable, they have only been evaluated in recreational/non-medical cannabis users. Importantly, initial work suggests that these tools likely are not appropriate for assessing CUD in those who use cannabis for medical purposes.⁵⁶ One issue is that these tools use frequency of cannabis use as one of the main criteria to assess the presence of CUD, but those who use cannabis as a medication are often expected to use cannabis daily. Therefore, high frequency of use can falsely inflate overall risk for CUD in those using cannabis medically. In addition, these tools could be strengthened if caveats could be issued. For example, the criteria assessing time spent acquiring cannabis may reflect the distance some patients must travel to access a dispensary, or reflect time patients wait to purchase products, rather than flagging a problematic behavior. It is critical to invest in research to develop appropriate tools to assess CUD in medical cannabis patients and conduct research using these tools to better understand the relationship between medical cannabis use and the development of CUD.

Effective Treatments and Approaches for CUD

For those experiencing patterns of problematic cannabis use, a variety of treatment options are available. Standard behavioral treatments include cognitive-behavioral therapy (CBT), motivational enhancement therapy, and contingency management. CBT teaches strategies to correct problematic behaviors, develop coping skills, and pursue prosocial behaviors to help enhance self-control and stop using cannabis. Motivational enhancement therapy is designed to enhance internal motivation to change, encouraging collaborative goal setting and using one's own internal resources to effect behavior change. Contingency management is often used in conjunction with traditional "talk therapy" and is a reward system where individuals achieve tangible rewards for desired behaviors (negative drug screen, attending sessions, etc.)⁶³ Given that each approach has its own unique strengths, studies have actually demonstrated that a *combination* of all three approaches is most effective. Still, abstinence is only maintained in about 20% during treatment, and unfortunately, abstinence rates drop further after treatment is complete.⁶⁴

Several pharmacological options have also been evaluated for initiation of abstinence, relapse prevention, and cannabis withdrawal symptoms, which include irritability, anxiety, relentlessness, sleep disruption, and appetite changes.⁶⁵ Overall, despite years of research, there are currently no clearly efficacious pharmaceutical treatments for CUD.⁶⁴ Nonetheless, studies point to some promising areas for future investigations, and suggest that individual characteristics of those diagnosed with CUD (gender, impulsivity, severity of CUD) will influence which medications are most effective. In addition, while many have shared anecdotal evidence regarding the potential efficacy of CBD for treating CUD, little research has been published thus far, and it is therefore premature to conclude that CBD may confer benefits for those with problematic cannabis use.



Part III:

CREATING A REGULATORY FRAMEWORK TO PROMOTE RESPONSIBLE USE



Despite the fact that cannabis remains illegal at the Federal level, and the noted risks associated with use, especially with regard to products containing THC for some vulnerable populations, rates of use continue to increase across the nation. While a number of factors should be considered when developing a framework for safe and responsible use (see Part II), it is clear that additional resources must be devoted to expand and articulate specific guidelines that inform consumers about best practices for cannabis and cannabinoid use that are least harmful and most beneficial to their mental health. Decision-making tools designed to help consumers identify their level of risk will certainly increase safety and help prevent unnecessary exposure for those least likely to gain benefit and most likely to experience negative effects.

In order to promote responsible use, the government should consider a two-pronged approach that employs both prevention and harm reduction efforts. **Prevention efforts** are needed to protect cannabis consumers that likely have a higher risk for negative outcomes, including children and adolescents, those with certain mental illness or a family history of psychosis, and pregnant or lactating individuals. However, as a significant number of Americans do not fall into high-risk categories, it is prudent to delineate guidelines and enact public health policies focused on **harm reduction** in order to *educate consumers and further encourage responsible use*. Considerations for harm reduction messaging include:

Prevention of “overuse”: Consumers must be aware of the risks of overuse, which can more easily occur when using cannabis in certain ways. High-THC products, particularly concentrates, which are designed to deliver a high dose of THC quickly, can result in unwanted and uncomfortable effects for some. Given what we know about the potential negative impact of cannabis use (and any drug use) during development, age-related restrictions may be considered for high potency products, and marketing of these products should specifically avoid targeting youth. In addition, edibles and other products with slow rise times and longer duration of effects can also raise the risk of consuming more THC than intended, leading to unwanted effects. It is imperative to ensure that consumers are well informed about the risks and benefits associated with different product types and ways of using cannabis.

Encourage using the “lowest effective dose”: For those using cannabis for therapeutic reasons, emphasize using just enough to achieve a therapeutic effect (i.e., the “lowest effective dose”). Educate consumers about the time it takes to feel an effect and how long it can last as a function of specific routes of administration. Further, it is important to ensure all consumers are aware that non-intoxicating products may be an option and that many of these products confer desirable effects for a range of conditions.

Adopt similar strategies as used to promote responsible alcohol use: It is essential to continue to promote messaging that individuals who are intoxicated must refrain from unsafe behavior that puts themselves or others at risk, such as driving/operating vehicles and other machinery, activities requiring critical thinking and decision-making, or caring for children or the elderly. As with alcohol use, consumers must be aware of the risks associated with misuse or overuse, and public health messaging should promote moderate, responsible consumption.

Standardization of Packaging and Doses: In order to help consumers understand how a specific product may affect them, products must be labeled clearly and consistently. All cannabinoids present within a product should be listed and the amount of each cannabinoid clearly noted. Standard unit dosing for each cannabinoid, particularly THC, should be determined and stated in order to provide consumers with a sense of their actual exposure. Overall, standardized labeling will help decrease confusion and assist consumers in making informed, responsible choices. Federal oversight should confirm that products are tested by third parties using reliable methods which yield accurate results, while also ensuring that all products remain free of contaminants, including pesticides, aflatoxins, heavy metals, yeast, and mold.

Companies Must Utilize Responsible Marketing Practices: In the current landscape, cannabis companies typically rely on their own internal studies, which are often observational or anecdotal in nature, underpowered, and lack rigor, to make claims regarding the potential therapeutic effects of their products. It is imperative that statements regarding the potential therapeutic effects of cannabinoid-based products are based on empirically sound data with proper oversight from regulators and other third parties.

Within this proposed framework, the government can and should provide resources for public education campaigns, screening, and treatment to prevent and mitigate cannabis misuse and outline steps for responsible use. Additionally, it should grant the appropriate regulatory powers the ability to place restrictions on problematic cannabis products as research and data dictate.

Reduce Barriers to Cannabis Research

Cannabis researchers must navigate an unprecedented and complex landscape when it comes to conducting cannabis-based research. The discrepant laws across states and the fact that most cannabinoids remain illegal at the Federal level is incredibly complicated. As a result, multiple institutional approvals (i.e. FDA, DEA, and local IRBs) are needed. Further, until recently, the National Center for the Development of Natural Products at the University of Mississippi produced cannabis exclusively for the National Institute on Drug Abuse (NIDA), the only approved source of cannabis for US-based clinical research studies, making it difficult for scientists to access cannabis-based products that are analogous to those used by consumers. With few exceptions, the majority of products currently available to researchers are limited to either conventional flower provided by NIDA with significantly lower potency (amount of THC) relative to products widely available to consumers across the country, or are FDA-approved single-compound products which are essentially pure THC (e.g., dronabinol, nabilone) or CBD (e.g., Epidiolex or other purified formulations). Accordingly, these all lack “ecological validity” and may not reflect real-world outcomes for those using a wide range of “typical” cannabis products or the increasingly popular hemp-derived full- and broad-spectrum products. In order to thoroughly assess both the potential benefit and risks associated with cannabis and cannabinoid use, researchers should be allowed to study the actual products used by consumers and patients, which is not possible under current Federal law.

Invest in Rigorous Research on Cannabinoid-based Therapeutics for Mental Health

Although great discoveries are often initially sparked by anecdotal findings, *well-designed, empirically sound, controlled studies offer an important opportunity to customize and optimize cannabis and cannabinoid-based treatments, ultimately changing the narrative and transforming patient care.* As noted in the NASEM report, THC is an effective option for several indications, including chronic pain, nausea and vomiting associated with chemotherapy, muscle spasticity associated with multiple sclerosis.⁵ It is well-established that CBD has a wide range of purported therapeutic effects that could provide relief for those suffering from mental health conditions. For example, several clinical trials of purified CBD for anxiety have generated positive findings, with additional studies of full- or broad-spectrum products underway, providing hope to the countless individuals seeking alternative treatments for anxiety that are effective and well-tolerated. In addition, CBD presents with an acceptable safety profile (especially relative to THC), and even at high doses CBD generally seems to be well tolerated. A number of “minor” cannabinoids have also been noted to have therapeutic potential, potentially applicable for a range

of mental health conditions.⁴ Harnessing the therapeutic benefits of certain cannabinoids while also mitigating potential harms to create safe cannabinoid-based treatments may be the answer for individuals for whom conventional medicine does not provide adequate symptom alleviation or produces unwanted side effects. All statements touting the efficacy and safety of cannabis and its effect on mental health of the end-user must be supported by thoroughly controlled and comprehensive clinical studies conducted, overseen by an appropriate federal regulator, and independently reviewed by partner public health and safety agencies. Adhering to this standard is particularly critical to patient safety, maintaining public health, and establishing trust between patients and healthcare providers.

Standardizing Tools for Cannabis Research

Currently, the wide variety of cannabis/cannabinoid formulations available across the country has led to contradictory results across research studies and misinterpretations about what these findings mean.⁶⁶ First, it is imperative that researchers clearly denote whether they are studying those who use medically, recreationally/non-medically, or for both reasons and that they define the specific type(s) of cannabis/cannabinoid products under study (product type, mode of administration, content of THC, CBD, and other cannabinoids), and acute versus long-term effects. Observational studies of cannabis use have faced significant difficulty in determining the best way to quantify cannabis use. Assessing even seemingly basic aspects of use including frequency or amount of cannabis used is not easy when considering different product types and modes of use, and the field needs tools to help researchers accurately and systematically assess exposure to cannabinoids using the same metrics. Finally, mixed findings are often related to the outcome measures used. Therefore, it is imperative to develop standardized batteries to assess outcomes in cannabinoid-based research investigations.



Conclusions:



Cannabis is an incredibly polarizing topic. As increasing numbers of states legalize cannabis, the perception of risk and harm has continued to drop, fueling the belief that cannabis is a benign substance. While it is true that many use cannabis without serious consequences, it is important to acknowledge that each person has a unique degree of risk based on factors related to the cannabis products they are using and their own individual characteristics. Current research suggests cannabinoids have great therapeutic potential for some conditions and for some individuals, but what's good for one is not necessarily good for all, and what's good in low doses may not be good in high doses. All sides must be considered in order to avoid both antiquated views from the Reefer Madness era and the more recent push to all but include cannabinoids in the drinking water. The truth and path forward are somewhere in between, and we must allow science, not rhetoric, to lead the way.

Cannabis has been a documented part of history for thousands of years and is likely here to stay. It is critical that commercially-available therapeutic applications of cannabis-derived formulations are subject to U.S. Food & Drug Administration oversight and evidence-based standards, similar to other prescription medicines. Once in place, patients, caregivers, and health care providers can be certain that cannabis-derived products have been manufactured to meet rigorous quality standards, and have undergone comprehensive study regarding safety and efficacy using empirically sound methods, allowing consumers to adequately assess the potential risk-benefit ratio for their own use. Accordingly, we must remove research barriers, dedicate funds for innovative projects, draft well-informed policies, and invest in additional efforts designed to protect our most vulnerable populations. Regardless of any opinion, moral or ethical concern, political or religious views, science and empirically sound data must guide discussions and policies regarding best practices and the safest ways for individuals to use cannabis.

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