

## Public Policy Statement on Marijuana, Cannabinoids and Legalization

## **Background**

In recent years, many states have considered or enacted policies to legalize cannabis use. As of this writing, Alaska, Colorado, Oregon, and Washington and Washington, D.C. have legalized cannabis use for adults, and 23 states and Washington, D.C. have legalized cannabis for non-FDA-approved medicinal uses under state law.<sup>1</sup> This expansion of access to legal cannabis use has occurred partly because of the perception among the public and lawmakers that marijuana use is harmless or that the harms are not significant, especially compared to the harms associated with the use of currently legal drugs, alcohol and tobacco. Indeed, the 2014 *Monitoring the Future* survey reported a five-year decline in the perceived harm of regularly smoking marijuana, from 52.4% of high school seniors to 36.1%.<sup>2</sup> However, as detailed below, recent research has revealed numerous medical harms associated with cannabis use, not the least of which is the likelihood of developing addiction<sup>a</sup> related to cannabis use. As such, this increasing public access to legal cannabis use calls for a response from the field of addiction medicine.

Cannabis is a plant that has been used as a psychoactive recreational drug for a century in the United States and for longer in other cultures. Its use for purported medicinal benefits also has a long recorded history around the globe, and its use for medical indications has recently expanded in the United States as a non-FDA-approved medical product. Botanical cannabis is usually referred to as marijuana but it also goes by various nicknames, among them "pot" or "weed." The primary psychoactive compound in cannabis is delta-9-tetrahydrocannabinol (THC), which is a partial agonist at cannabinoid receptors in the body. The THC content in botanical marijuana sold illicitly for recreational use in America has increased from roughly 3.4% in 1993 to roughly 8.8% in 2008.3 THC is also the active ingredient in many derivatives of cannabis, including hashish and hash oil, and it is more recently found combined with other substances in high-potency, harder-to-identify products. Other synthetic cannabinoid receptor agonists, such as JWH-018 and HU-210, have recently been gaining popularity as psychoactive substances. These synthetic substances are full agonists at cannabinoid receptors, are more potent than THC, and seem to have more intense and toxic clinical effects. They are used as alternatives to marijuana and some persons elect to use them since they can be obtained legally in many parts of the United States and are not detected by drug tests that solely analyze for THC.4 Cannabis has been found to be the most frequently used drug in the U.S. after alcohol, tobacco and caffeine. Moreover, marijuana is the most widely used illegal drug in the United States and it is estimated that it is used by 61% of all persons suffering from a substance use disorder related to drugs other than alcohol.5

<sup>&</sup>lt;sup>a</sup> Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

Empirical evidence associates THC with cannabis dependence<sup>b</sup> (moderate to severe cannabis use disorder in DSM-V). In one study, 9.1% of users of cannabis developed cannabis dependence. 6 A more recent study confirmed the risk of developing cannabis dependence to be about 8%, and demonstrated that the likelihood of using alcohol, nicotine and illicit drugs is significantly higher for continuous cannabis users as well as ex-users of cannabis as compared to those who have never used cannabis. The risk of developing addiction associated with cannabis use has been reported to increase to about 17% among those who start using marijuana in adolescence, and to 25-50% among those who smoke marijuana daily.8 For example, a twin study found that individuals who used cannabis by age 17 were about twice as likely as their twin to develop cannabis abuse<sup>c</sup> or dependence, and 2.1 to 5.2 times as likely to use other drugs, develop alcohol dependence, or develop other drug abuse or dependence.9 While the prevalence of past-year marijuana use among the U.S. adult population appears to have remained stable at about 4.0% from 1991-1992 to 2001-2002, the percentage of past-year marijuana smokers who displayed evidence of abuse or dependence rose from 30.2% to 35.6%: some have hypothesized that this is related to the increased concentration of THC in marijuana available in the United States in recent years. 10, 11, 12

In addition to the risk of developing addiction, several other harmful long-term effects of marijuana use on health have been documented, including adverse psychiatric effects from its use. Specifically, the long-term effects of marijuana use include altered brain development and cognitive impairment, including impaired neural connectivity in specific brain regions, decreased activity in prefrontal regions, and reduced volumes in the hippocampus. 13 These effects have been found to be more profound in users who began marijuana use in adolescence or young adulthood. 14, 15 Other studies have found a correlation between the use of cannabis and the appearance of psychotic symptoms and the prevalence of psychotic disorders. <sup>16</sup> Moreover, even prenatal exposure to marijuana has been shown to be predictive of psychotic symptoms in voung adulthood.<sup>17</sup> There is also evidence of a correlation between cannabis use and decreased academic performance, in addition to an increased likelihood of dropping out of school. 13 A review of multiple studies found consistent associations between cannabis use and lower educational attainment.<sup>18</sup> Another study found an association between cannabis use disorder and nonmedical use of prescription stimulants for studying, reduced class attendance and declining academic performance.<sup>19</sup> Along with lower educational attainment, research on employed individuals has found consistent associations between cannabis use and reduced workplace productivity.<sup>20</sup> Many of these studies await replication. However, collectively, these data are sufficient to suggest that children, pregnant women, and youth with still-developing brains should not use cannabis or cannabinoids due to a variety of neuropsychiatric health effects and impacts on cognitive functioning.

Cannabis is most commonly consumed through smoking, a route of drug delivery that predictably has a variety of negative effects on pulmonary function. Smoke from marijuana combustion has been shown to contain a number of carcinogens and cocarcinogens,<sup>21</sup> as well as many of the toxins, irritants, and carcinogens as tobacco smoke. <sup>22</sup> Additionally, marijuana smokers tend to inhale more deeply and hold their breath longer than cigarette smokers, which

<sup>&</sup>lt;sup>b</sup> Marijuana dependence is defined in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) as increased tolerance, compulsive use, impaired control, and continued use despite physical and psychological problems caused or exacerbated by use.

<sup>&</sup>lt;sup>c</sup> *Marijuana abuse* is defined in *DSM-IV* as repeated instances of use under hazardous conditions; repeated, clinically meaningful impairment in social/occupational/educational functioning, or legal problems related to marijuana use.

leads to a greater exposure per breath to "tar" (the carcinogenic solids in smoke).<sup>23</sup> Regular smoking of marijuana, in the absence of tobacco, produces visible and microscopic injury to the large airways.<sup>24</sup>

Short-term exposure to marijuana smoking is associated with bronchodilation, while long-term marijuana smoking is associated with increased respiratory symptoms suggestive of obstructive lung disease. <sup>25</sup> Yet, there is no clear link between marijuana smoking and obstructive pulmonary disease, <sup>26</sup> such as bronchitis and emphysema, and there is no conclusive evidence of marijuana smoking-induced lower respiratory tract infection. <sup>27</sup> Whereas evidence is mixed concerning possible carcinogenic risks of heavy, long-term marijuana smoking, <sup>28</sup> epidemiological findings to date do not suggest an increased risk for the development of either lung or upper airway cancer from light or moderate use. In fact, the findings of one study that had reported increased rates of lung, upper respiratory and digestive tract cancers in users who smoked the equivalent of no more than one joint or one pipeful of hashish per day were found to be not valid once cigarette smoking and other confounders were taken into account. <sup>29</sup>

An increasingly popular route of administration for THC has been the incorporation of marijuana into edible products, including baked goods, candies and marijuana-infused beverages, which are readily available at retail outlets in states that have legalized cannabis use. For example, in Colorado, marijuana-infused edibles account for 45% of the legal marijuana marketplace.<sup>30</sup> Given their appearance and current trends in packaging and product names, edibles are often particularly attractive to young adults and even children. The absence of any quality control, consumer labeling, or predictability in dosing in edibles has led to appropriate cautionary commentaries and calls for action to protect the public health.<sup>31</sup> The THC content of such products has a wide range, and a given edible can contain several individual doses-worth of THC. Importantly, research has found these products are not consistently labeled; in one study, of 75 products purchased, only 17% were accurately labeled.<sup>32</sup> In part because consumers may be unaware of the THC content in edibles, hospital emergency departments are treating more children and adults who develop paranoia, anxiety and/or psychosis following intentional or accidental ingestion of marijuana edibles.<sup>33,34</sup>

There are several potential medical and public health consequences of marijuana use that require further research. Still under investigation is the potential depressive effect of THC on the immune system.<sup>35</sup> More research is also needed on the impact of cannabis use on driving, motor vehicle collisions, and traffic injuries and fatalities. Evidence shows that marijuana use impairs cognitive function, reaction times, divided-attention tasks, and lane tracking,<sup>36</sup> all of which impact driving ability. A recent National Highway Transportation Safety Administration study found no significant increase in crash risk associated with the presence of marijuana when controlling for age, gender, ethnicity and alcohol use.<sup>37</sup> However, several other studies have reported increased crash and culpability risks, even after adjusting for such confounders as age, sex, risky behaviors, and polypharmacy.<sup>37</sup> Finally, it is worth noting the observed drop in opioid overdose death rates in states where marijuana use is legal for medicinal purposes. One study found that states with "medical marijuana" laws had a 24.8 percent lower average annual opioid overdose death rate compared to states without similar laws.<sup>38</sup> According to the study, in 2010 alone, that translated to about 1,729 fewer deaths than expected.

Marijuana contains at least 85 distinct cannabinoids,<sup>39</sup> several of which are being investigated for their potential therapeutic value. To date, the FDA has approved two pharmaceutical products for human use which contain active ingredients that are present or similar to those present in botanical marijuana: Marinol® and Cesamet®. Marinol®, a Schedule III drug whose active ingredient is a synthetic version of THC, is approved for the treatment of chemotherapy-

induced nausea and vomiting as well as anorexia associated with AIDS and increased intraocular pressure in cases of glaucoma. 40 Cesamet®, a Schedule II drug, contains the synthetic cannabinoid nabilone and is approved for the treatment of nausea and vomiting associated with chemotherapy. 41 Other cannabis-derived or cannabis-like drugs are being developed and have been approved for use in other countries. One example is Sativex®, a fastacting non-synthetic oral-mucosal cannabinoid spray containing 50% THC and 50% cannabidiol, which is available in Canada, New Zealand, the United Kingdom, and several European countries to treat spasticity in multiple sclerosis (MS). 42 Cannabidiol (CBD), a nonpsychoactive cannabinoid, is one of the main known active ingredients in marijuana besides THC that may have desirable medicinal effects. 43 CBD has been shown to have antipsychotic effects. 44 as well as anticonvulsant, neuroprotective and anti-inflammatory effects. 45 The medical literature contains only small and methodologically limited studies of CBD in human epilepsy, the results of which have been inconclusive; there is a clear need for further investigation into its potential in epilepsy and other neuropsychiatric disorders. 46 Pharmaceutical grade cannabidiol is being investigated, along with genetically modified strains of botanical marijuana which contain almost exclusively cannabidiol and essentially no THC,47 and regulatory reform to facilitate research into the potential efficacy and safety of cannabidiol for possible medical uses has been proposed.<sup>48</sup> To date, 15 states have legalized limited access to marijuana products with low THC/high CBD content for medicinal purposes, 49 sometimes in response to reports in the popular media of benefits for neuropsychiatric conditions that are not yet substantiated by well-designed medical research studies.

Herbal marijuana is also increasingly sought out for its purported medicinal effects. However, unlike the above-mentioned regulated pharmaceuticals, which have been tested for safety and efficacy, the potency, purity, and effective does of herbal marijuana and cannabis-infused edible products are unknown. A recent review of cannabinoids for medical use has called into question the efficacy of these types of products, finding only moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity, and only lowquality evidence suggesting cannabinoids were associated with improvements in chemotherapy-related nausea and vomiting, weight gain in HIV, sleep disorders and Tourette syndrome.<sup>50</sup> The review also confirmed cannabinoids were associated with an increased risk of short-term adverse events. Given the uncertain evidence to support the safety and efficacy of cannabis and cannabinoid-products in the treatment of medical conditions, ASAM and a number of other professional medical societies have advised that all cannabis-based medicinal products, like all other medicinal products, should be approved by FDA. And given the current state of medical evidence, the American Medical Association has gone so far as to advise that marijuana and cannabis-containing products such as edibles should be required to be labeled with the statement: "Marijuana has a high potential for abuse. It has no scientifically proven, currently accepted medical use for preventing or treating any disease process in the United States."51

These various responses of professional and research entities to expanding knowledge of the health and public health aspects of marijuana and other cannabinoid use, and to the need for expanded knowledge via increased research, have developed in a larger sociological and political context in which approximately half of Americans support legalization. ASAM recognizes that an important factor in the changes in public attitudes about legalization, as well as philosophical positions held by physicians on such matters, is the perception that the current drug control policy which emphasizes criminalization ("The War on Drugs") hasn't been effective, has expanded incarceration in our nation in non-salutary ways, and is biased against minority citizens. There are indeed public health aspects of criminalization, but these are beyond the scope of this policy statement.

One of the suggested solutions to the problems of criminalization is legalization. In its extreme, legalization includes legal commercialization, with for-profit entities manufacturing, distributing, marketing, and wholesaling cannabis and psychoactive cannabis products for retail sale. The image of major corporations entering "the business" of marijuana is disturbing in its similarity to the presence of major corporations in the promotion and sale of tobacco products. Quite different from a policy of legalization is a policy of decriminalization, in which possession and personal use of cannabis and cannabis products is not tied to criminal penalties. One version of decriminalization has criminal penalties for possession and personal use reduced to lesser offenses such as misdemeanors; but this still results in those convicted of possession having criminal records which can lead to lifelong discrimination against them. Another version of decriminalization would reduce penalties for possession and use to civil offenses only (noncriminal citations, "tickets," or fines), which could be linked to contingencies that would promote public health, such as mandatory clinical assessments, health education related to substance use and substance use disorders, and referral to addiction treatment when indicated. Common models of decriminalization retain criminal penalties for distribution or importation. The nation of Portugal has drawn attention for its drug policy reforms which strive to emphasize public health, including early identification of cases of addiction and referral to clinical interventions in lieu of criminal sanctions. Comparable models for drug policy reform can mandate follow-through with required clinical assessments and escalating civil penalties for individuals who fail to comply with medical recommendations or who become habitual offenders of civil regulations addressing cannabis possession and use. ASAM's intention in developing the current policy statement is to assist health care professionals and the general public, as well as policy makers and the media, to better appreciate current evidence about the biology and health aspects of the use of cannabis, cannabis products, and synthetic cannabinoids. The overall response of American society to cannabis use is undeniably relevant to the medical and public health communities as they address the health aspects of human use of such products.

In light of the evolving legal landscape surrounding cannabis in the United States, which is giving rise to increased availability and use of cannabis and cannabis products, ASAM's viewpoint is that it is imperative that Americans promote and adopt public policies that protect public health and safety as well as protect the integrity of our nation's pharmaceutical approval process, which is grounded in well-designed and executed clinical research. Currently, the legalization of cannabis in some states but not others provides a unique opportunity for a thorough investigation into the societal and public health impact of broader cannabis use. Such research is critical to inform other jurisdictions in how they can best protect and promote public health as they consider the legal status of marijuana use.

#### Recommendations:

# A. Policy Recommendations

- ASAM supports the "decriminalization" of marijuana, which would reduce penalties for marijuana possession for personal use to civil offenses linked to contingencies, such as mandated referral to clinical assessment, educational activities, and, when indicated, formal treatment for addiction or other substancerelated disorders.
- 2. ASAM does not support the legalization of marijuana and recommends that jurisdictions that have not acted to legalize marijuana be most cautious and

- not adopt a policy of legalization until more can be learned from the "natural experiments" now underway in jurisdictions that have legalized marijuana.
- 3. ASAM recommends that jurisdictions that have already legalized marijuana or that may act to legalize it in the future implement the following public health and safety measures to minimize potential harms to vulnerable populations. ASAM encourages addiction medicine physicians to champion the implementation of these safeguards in all jurisdictions where marijuana has been legalized or may be legalized in the future.
  - a. Prohibit the legal sale of marijuana products to anyone younger than 25 years of age.
  - b. Prohibit marketing and advertising to youth, akin to the current restrictions on tobacco product advertising.
  - c. Require that products made available for retail sale be tested for potency and clearly labeled with THC content.
  - d. Require rotating warning labels to be placed on all marijuana and marijuana products not approved by the U.S. Food and Drug Administration (FDA) which are offered for sale in retail outlets, stating, "Marijuana use increases the risk of serious problems with mental and physical health, including addiction," or "Marijuana should not be used by pregnant women or persons under age 25," or "Marijuana should not be used by persons prior to operating motor vehicles and heavy machinery."
  - e. Require that marijuana products (such as edibles and beverages) be sold only in child-proof packaging and be accompanied by the mandatory distribution of educational flyers regarding the risks of overdose and poisoning in cases of accidental ingestion by children or household pets.
  - f. Earmark taxes placed on marijuana and marijuana product sales, wholesale or retail, such that a majority of tax revenues are required to be devoted to public education about addiction, prevention of addiction, health effects of cannabis and synthetic cannabinoid use, prevention of initiation of cannabis and cannabinoid use by youth, addiction treatment, or research on the health risks and potential benefits of marijuana, "natural" cannabinoids, and synthetic cannabinoids.
  - g. Limit marijuana and marijuana product sales to state-operated outlets, akin to Alcohol Beverage Control regulations existing in several states and Canadian provinces, which preserve both public access and the potential for governmental revenues linked to sales, while limiting the broad commercialization of public sale of potentially harmful but brainrewarding products.
  - h. Implement public awareness campaigns which highlight the risks of marijuana use to discourage vulnerable populations, including youth (i.e., adolescents and young adults), individuals with mental illness, and those with a history of addiction involving alcohol or other drugs, from using marijuana products.

- 4. ASAM supports the use of cannabinoids and cannabis for medicinal purposes only when governed by appropriate safety and monitoring regulations, such as those established by the FDA research and post-marketing surveillance processes.
  - a. ASAM supports the medicinal use of pharmaceuticals that contain cannabinoids that have gone through the FDA-approval process.
  - b. ASAM asserts that cannabis, cannabis-based products, and cannabis delivery devices should be subject to the same safety and efficacy standards that are applicable to other prescription medications and medical devices.<sup>52</sup> Such products should not be distributed or otherwise provided to patients unless and until they have received marketing approval from the FDA.
  - c. In general, any product purported to be medicine should have the appearance of medicine, such as a pill, capsule or wafer, and should not appear to be candy or food.
  - d. Physicians who recommend marijuana use to patients should do so within the context of a patient-physician relationship that includes the creation of a medical record, and follow-up visits to assess the results of physicianrecommended clinical interventions so that treatment plans can be amended, as indicated.
  - e. ASAM rejects smoking as a means of drug delivery.
- 5. ASAM does not support the legalization of synthetic cannabinoid receptor agonists. ASAM supports the establishment of legal controls on the manufacture and sale of synthetic cannabinoid receptor agonist compounds within the framework of controlled substances laws for other highly addictive compounds.

#### **B. Clinical Recommendations**

- 1. ASAM recommends that addiction medicine physicians and other clinicians educate their patients about the known medical risks of marijuana use, including the use of and accidental exposure to edible products, and the risks of use of synthetic cannabinoid receptor agonists.
- ASAM recommends a significant expansion of opportunities for youth with cannabis use disorder to receive medically necessary treatment as well as for youth to receive appropriate clinical preventive services related to cannabis use, and that private and public insurance coverage be available for youth to be able to access such services.
- 3. ASAM supports the consensus of most addiction professionals that clinicians should counsel persons suffering from addiction about the need for abstinence from marijuana and synthetic cannabinoids and the role of cannabis and cannabinoid use in precipitating relapse, even if the original drug involved in their addiction is a substance other than marijuana.

- 4. ASAM supports the expanded establishment of clinical entities such as Student Assistance Programs in middle schools, high schools, and postsecondary schools, including professional schools, which offer health promotion approaches and support services to persons, especially youth, who have been identified as having cannabis or cannabinoid use disorder or other unhealthy use of such substances.
- 5. ASAM recommends that medical professional societies educate the public, the media, and public policy makers that there is no such thing as a legal "prescription" for marijuana and that laws enacted to date provide for physicians to authorize "permits" for use and possession and nothing more.

#### C. Professionalism Recommendations

- 1. ASAM asserts that in states where physicians are placed in the gate-keeping role of authorizing marijuana use permits, professional licensure authorities should take steps to ensure that physicians who choose to discuss the medical use of cannabis and cannabis-based products with patients:
  - a. Are able to have good-faith discussions with patients without conversations on such topics between clinicians and patients being considered illegal or unprofessional acts.
  - b. Adhere to the established professional tenets of proper patient care, including
    - i. History-taking and good faith examination of the patient;
    - ii. Development of a treatment plan with clinical objectives;
    - iii. Provision of informed consent, including discussion of potential adverse drug effects from use;
    - iv. Periodic review of the treatment's efficacy;
    - v. Consultation, as necessary, with other clinical colleagues; and
    - vi. Proper record keeping that supports the clinical decision to recommend the use of cannabis.
  - c. Have a bona fide patient-physician relationship with the patient, i.e., should establish an ongoing relationship with the patient as a treating physician when there is not a pre-existing relationship, and should offer recommendations regarding the use of marijuana within the context of other indicated treatment for the patient's condition; they should not offer themselves to the public as solely a permitauthorizing individual:
  - d. Ensure that the issuance of "recommendations" is not a disproportionately large aspect of their practice;
  - e. Have adequate training in identifying addiction and unhealthy substance use.

#### D. Research Recommendations

1. ASAM supports research on marijuana, the various cannabinoids present in marijuana, and synthetic cannabinoid agonists and

antagonists, including both basic science and applied clinical studies, as well as the development of pharmaceutical-grade cannabinoids. The mechanisms of action of marijuana and its constituent compounds, its effect on the human body, its addictive properties, and any appropriate medical applications should be investigated, and the results made known for clinical and policy applications. Research should be expanded on functional impairments associated with use of cannabis and related substances including effects on driving, how to distinguish impaired driving due to cannabinoids from impaired driving due to other factors, and effects on educational and occupational performance.

- a. Research should receive increased funding and appropriate access to marijuana for study.
  - i. ASAM recognizes that research into the medical benefits of marijuana is not within the remit of the National Institute on Drug Abuse (NIDA) and encourages other NIH institutes to sponsor additional research on the potential medicinal properties of cannabis and cannabinoids related to specific disease states.
  - ii. ASAM supports the expansion of NIH-approved research sites to grow different strains of marijuana with varying composition and concentration of specific cannabinoids. Thus, ASAM believes NIH should be able to grant multiple contracts to grow marijuana for research purposes.
- 2. ASAM recommends that the federal and state governments establish robust health surveillance related to marijuana use. The data should be made available to public health and health policy researchers to understand the public health impact of marijuana use as well as the relative effectiveness of different policy levers to discourage use among vulnerable populations, especially adolescents and young adults, persons with mental illness, and persons with pre-existing substance use disorders.

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