AAME Statement on Medical Marijuana

The American Academy of Medical Ethics (AAME) has developed this policy on "medical marijuana" based on the Hippocratic tradition and the most recent scientific evidence.

Executive Summary

The term "medical marijuana" refers to the insufficiently regulated use of the whole, unprocessed marijuana plant or its extracts to treat symptoms of illness and other conditions. Note that pharmaceutical-grade medications from components of the marijuana plant have been developed according to U.S. Food and Drug Administration (FDA) standards, but these medications are distinct from what is classified here as "medical marijuana." The science supporting "medical marijuana" has been hotly debated and politicized after emerging on state referendums in recent years.

The two main ingredients in marijuana are tetrahydrocannabinol (THC)—the "psychoactive" ingredient, responsible for the euphoria or "high"—and cannabidiol (CBD). Products may contain primarily THC, primarily CBD, or a mixture of both. THC levels are rising substantially in commercially available marijuana, and product containing concentrations greater than 15 percent are being considered for labeling as "hard drugs" in the Netherlands.[1,2]

State legalization of "medical marijuana" has not been accompanied by the rigorous scientific approval process with regulations for dosing, production, packaging and monitoring that have made FDA-approved medications safe and effective. In such states "medical marijuana" is often approved for conditions[3] where research is inadequate.[4] False advertising may mislead vulnerable patients and the public. "Medical" use may inadvertently result in addiction, increased risk of psychosis, mental or psychosocial impairment, lung damage when smoked, and complications for unborn children when used during pregnancy.[4,5] The presence of "medical marijuana" dispensaries may increase access to recreational marijuana for minors.[6] "Medical marijuana" legalization is associated with increased illicit marijuana use,[7] is linked to increased emergency room visits for marijuana-intoxicated children,[8] and has historically been a stepping stone to legalization of recreational marijuana.[9]

AAME maintains that a reasonable and prudent physician should only recommend FDA-approved pharmaceutical-grade medications when the indications are clear, dosing is well-established, risk-benefit ratios have been investigated and can be applied to individual patients, delivery systems are safe, and careful monitoring is agreed upon. Physicians cannot assume that "medical marijuana" has the labeled amount of active ingredient and is devoid of contaminants and harmful additives. Rather than legalizing a drug by popular vote and political lobbying, AAME encourages legalization via FDA approval through formal clinical and scientific studies of any marijuana-based therapeutic that has demonstrated medical efficacy and safety by randomized controlled trials. To augment this process, AAME suggests rescheduling lower potency marijuana to Schedule II[10] to enable medical research into the potential benefits and harms of the use of pharmaceutical-grade marijuana derivatives within established ethical research

guidelines. FDA-approved marijuana medications should be prescribed and regulated like any other FDA-approved medication.

A. **Biological**

1. Cannabinoids: The genus *Cannabis* contains cultivars that are commonly referred to as "marijuana." Although over 100 different cannabinoids as well as other compounds have been found in cannabis species, the two main cannabinoids, or active ingredients, are tetrahydrocannabinol (THC) and cannabidiol (CBD).[4] THC is the "psychoactive" ingredient, responsible for the euphoria or "high" that comes from marijuana due to its partial agonist activity on type-1 cannabinoid receptors (CB_1). CB_1 receptors are found in the brain in high concentrations as well as other non-neural tissues such as the gastrointestinal tract and skeletal muscle. A small number of CB_2 receptors are also in the brain.[4] THC's chemical structure is similar to the endogenous cannabinoids (specifically anandamide) which are neurotransmitters that bind to CB receptors.[5] CBD has low affinity for CB_1 and CB_2 receptors and is not psychoactive; it is an agonist of the serotonin 5-HT1A receptor and appears to have anti-inflammatory, antioxidant, and neuroprotective properties.[4] There are THC-type, CBD-type, and hybrid cannabis plants which have predominantly THC, CBD, or a mixture of both cannabinoids, respectively.[4]

2. "Medical Marijuana": Cannabis-derived products (dried flowers, resin, oil, sprays, creams, foods, capsules) may be delivered via smoking, inhaling, vaporizing, eating or drinking food products or beverages, topical applications, and suppositories. These products may contain THC alone, CBD alone, or some combination of both.[4] These products are neither FDA-approved nor regulated for consistency in the amount of active compounds or safe processing; they may contain potentially hazardous contaminants or adulterants such as degradation products, microbes, heavy metals, pesticides, fertilizers, glass beads, lead, tobacco, cholinergic compounds, and solvents.[4]

3. Rising THC Levels: The natural levels of THC and CBD in Cannabis are under 1%.[11] Using powerful lights, selective breeding, hydration, chemical fertilizers and special soils, the industry has created a new and more potent marijuana plant than the one of the 1960s and 1970s. The average THC content in the "new" marijuana exceeded 12% nationwide in 2014.[5,11] Marijuana concentrates may contain 75% or more THC;[5] associations of the use of such substances with addictive highs, psychosis, and other effects led one author who works in drug treatment programs to claim they are deserving of the label "hard drug,"[11] like heroin and LSD. Although not yet implemented, recommendations have been made to revise the Netherlands Opium Act to place cannabis containing more than 15% THC in List 1 (hard drugs).[1]

B. Social

1. General: Citizens of a country should consider the known and potential harmful and beneficial effects of marijuana on individuals and society. Experiences with the harms associated with prescription opioids, alcohol, and tobacco are relevant to the consideration of legalizing, prescribing, and dispensing marijuana.

2. Slippery slope to recreational marijuana use: The approval of medical marijuana has historically been a stepping stone to approving recreational marijuana. All states with legal recreational marijuana had prior legalization of medical marijuana.[9] Evidence suggests that overall availability may lead to an increase in recreational usage, which could create a demand for legalization of recreational marijuana. For example, one nationwide study found that medical marijuana laws are associated with "increased prevalence of illicit cannabis use and cannabis use disorders."[7] States with legal medical marijuana have youth rates that

surpass those in states that do not.[12] One study from Oregon suggest that communities with a greater number of medical marijuana patients and licensed growers was associated with a higher prevalence of marijuana use among youth from 2006 to 2015. The authors suggest that changing community attitudes in these areas could be influential in teen behavior as well.[6] Other studies have noted equivocal or contrasting findings.[13,14]

3. Commercialization and social media: Individuals, small businesses, and corporations who profit from medical marijuana sales are looking to increase its usage. To this end, a variety of advertising venues, including social media platforms, are being used; advertising distortions regarding the benefits of marijuana are not uncommon. For example, in one cross-sectional study in Colorado, almost 70% of contacted marijuana dispensaries recommended cannabis products to treat nausea during pregnancy.[15] Another study examined the website marketing practices of medical and recreational marijuana dispensaries across the U.S., finding that only a few advised about side effects and contraindications. 75% did not include age verification, making products available to youth with convenient online ordering.[16] Exposure to medical marijuana advertising has been associated with greater marijuana use in minors.[17] Physicians should warn their patients about false advertising and youth access.

4. Opioid addiction: There has been much hype about marijuana legalization providing a safer replacement for opioid use, with the potential to reduce opioid addiction and overdoses. Evidence is conflicting as to whether this is, in fact, the case,[18] and caution must be used in looking at studies in this area because of bias,[19] unreliability of self-reported use of drugs, the uncertainty of inferring individual substitution behaviors from state-level data relating marijuana legislation and opioid death rates,[20] and other methodological problems. Because societal attitudes may have changed prior to either medical or recreational legalization[6] and because opioid addiction is a complex issue with multiple antecedents that might represent events coinciding with marijuana legalization, it is difficult to define the associations of legalization of marijuana and opioid use. Samples of research:

    a. There are reports that opioid use has increased, rather than decreased, in states legalizing marijuana. In Colorado, for example, opioid use more than doubled among 10 to 19 year-olds after recreational legalization of marijuana.[12]

    b. Legalization of marijuana in Colorado is associated with short-term reductions in opioid-related deaths.[21]

    c. Medical legalization appears to be associated with "reductions in both prescriptions and dosages of Schedule III (but not Schedule II) opioids received by Medicaid enrollees."[22]

    d. A study that examined opioid use in patients following musculoskeletal trauma found that self-reported marijuana use during recovery was associated with an increased amount and duration of opioid use. However, many patients in this study had misperceptions that their marijuana use reduced both their pain and the amount of opioids used.[23]

    e. Not only marijuana use but also use of alcohol, illegal methadone, and other opioids was found to increase in pregnant women after legalization of recreational marijuana in Washington State.[24] Cannabis use was associated with an increased risk of developing nonmedical prescription opioid use and opioid use disorder.[25]

D. Medical

1. Federal Drug Administration (FDA)-Approved Marijuana-Derived Medications (pharmaceutical-produced, quality-controlled and dose-specific medications):

a. Synthetic THC drugs: Dronabinol (Marinol and Syndros)[26] and nabilone (Cesamet)[27] have FDA approval for the treatment of chemotherapy-induced nausea and vomiting, and dronabinol is also used to treat loss of appetite and weight in patients with AIDS. A systematic review of anti-nausea efficacy of these medications revealed that side effects were greater and efficacy no better than with the use of traditional anti-nausea medications.[28] These drugs are Schedule II or III (see the Table at the end for a description of scheduling categories).

b. Cannabidiol (CBD) drugs: In June of 2018, the FDA approved the first natural marijuana plant-derived drug, Epidiolex, an oil for the treatment of seizures associated with two rare forms of childhood epilepsy (Lennox-Gastaut and Dravet syndromes).[29] Epidiolex does not contain any THC and has been approved as a Schedule V medication. Schedule V substances are the least restrictive schedule of the Controlled Substances Act.[30] (See the Table at the end for a description of scheduling categories.)

c. Currently there are no other FDA-approved uses for any component of the marijuana plant. "Off-label" use of FDA-approved drugs may be indicated in those occasions when the physician determines that there is significant scientific research evidence of benefit that outweighs any potential harm and the patient has failed other FDA-approved therapies; alternatively, there may be appropriate occasions when an FDA-approved drug is used "off-label" in a different form (e.g. oral solution instead of a capsule), for a different (but similar) patient population, or at a different dose.[31]

2. Studies: There are a number of concerns with the research in this area:

a. Poor reliability: The research itself has significant problems which limit its reliability. These include factors such as heterogeneity in the active ingredients and contaminants, lack of standard dosing, inadequate research into effects of highly potent types, and variability in the route of consuming marijuana. As an example of the latter, alterations in the number of puffs or volume inhaled may change with the potency of THC in the marijuana being smoked.[32] It is important to note the nature of marijuana derivatives used in any studies—the THC and/or CBD level, delivery method, and quantity. For example, self-reported amount of smoking provides poor data compared to use of FDA-approved standard-dose pharmaceuticals. Conclusive studies can only be done with FDA-regulated medications or pharmaceutical-grade compounds.

b. Regulatory barriers: Research on marijuana is hampered because of its classification as a Schedule I drug with intimidating bureaucratic regulations to overcome in order to obtain it for research. Much of the federal funding has been earmarked for studying the negative effects of marijuana, and inadequate money is available for investigating potential benefits.[4] Additionally, some academic institutions may fear that conducting research with Schedule I substances could put their federal funding at risk. (See the Table at the end for a description of scheduling categories.)

c. Insufficient data: In a system proven effective over many decades, medicine aims to establish the safety and effectiveness of treatment by requiring rigorous clinical trials before the FDA will recommend or release medications to large numbers of people. There is a lack of studies on the safety, efficacy, and short-term and long-term effects of marijuana, especially the high potency forms. There are also insufficient studies on the potential drug interactions between cannabis compounds and prescription and non-prescription medications. Researchers, scientific organizations, and representatives of the

federal government claim that there is not enough evidence to support the use of marijuana as a beneficial drug and call for more research.[33,34]

d. Impediments: Researcher bias and obtaining properly controlled, adequately-sized, representative samples are among the methodological problems that may be anticipated in this research area.

e. Ethical issues: Adverse health effects of marijuana, especially use of high potency variants and smoking as the means of consumption, highlight ethical problems in exposing research subjects to harm when trying to document the safety or harm of specific consumer products.

f. Caution: Weak or absent evidence about harmful effects of marijuana does not mean they do not exist; caution should be used when even limited evidence suggests a possibility of harm.

3. Health effects of cannabis use: A review of the current literature regarding health effects of cannabis, while representing only a snapshot into a rapidly changing landscape and having some limitations, can be found in a recent report from The National Academies of Sciences, Engineering, and Medicine.[4] According to this report, the therapeutic effects of cannabis or cannabinoids are as follows:

   a. Substantial evidence of effectiveness for treatment of:
      1) Chronic pain in adults (cannabis)
      2) Antiemetics in chemotherapy-induced nausea and vomiting (oral cannabinoids)
      3) Patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)

   b. Moderate evidence of effectiveness for improving short-term sleep outcomes in patients with sleep disturbances associated with obstructive sleep apnea, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols[35])

   c. Limited evidence of effectiveness for:
      1) Improving the wasting syndrome associated with HIV/AIDS (cannabis and oral cannabinoids)
      2) Clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids)
      3) Symptoms of Tourette syndrome (THC capsules)
      4) Improving anxiety symptoms in social anxiety disorders, as assessed by a public speaking test (cannabidiol)
      5) Improving symptoms of posttraumatic stress disorder (nabilone—single, small, fair-quality trial)

   d. Limited evidence of a statistical association between cannabinoids and better outcomes after traumatic brain injury or intracranial hemorrhage

   e. Limited evidence they are ineffective for:
      1) Improving dementia (cannabinoids)
      2) Improving intraocular pressure in glaucoma (cannabinoids)
      3) Reducing depressive symptoms in patients with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone)

   f. Insufficient evidence to support or refute the effectiveness of treatment for cancers, cancer-associated anorexia cachexia syndrome and anorexia nervosa, irritable bowel syndrome

symptoms, epilepsy, spasticity due to spinal cord injury paralysis, symptoms of amyotrophic lateral sclerosis, chorea and certain symptoms of Huntington's disease, motor symptoms of Parkinson's disease, levodopa-induced dyskinesis, and dystonia.

4. Medical complications of marijuana use: Despite the lack of research, some of the short-term and long-term effects of marijuana use are being uncovered. In all associations or lack thereof of marijuana use and health complications listed below, the conclusions are often drawn in the face of insufficient good quality and conflicting data and with the knowledge that research may not reflect the current products being used by consumers. Therefore, future research will be needed to provide more definitive answers to questions about effects of marijuana use.

   a. Cancer: There is limited evidence of a statistical association between current, frequent, or chronic cannabis smoking and one type of testicular tumor, but not current sufficient evidence of associations between marijuana use and other cancer types in adults. There is minimal evidence that cannabis use during pregnancy is associated with a greater risk of cancer in offspring.[4]

   b. Respiratory diseases: There is substantial evidence of an association between chronic marijuana smoking and chronic bronchitis and worsening respiratory symptoms.[36] There is more limited evidence of an association with chronic obstructive pulmonary disease (COPD).[4]

   c. Injury and death: Substantial evidence correlates cannabis use and increased risk of motor vehicle crashes.[4]

   d. Pre-and perinatal exposure to maternal cannabis use: Use of marijuana during pregnancy increased in Washington State after legalization,[24] and is on the rise nationally.[37] According to a recent study, nearly 70 percent of approved marijuana dispensaries in Colorado recommended marijuana to pregnant mothers experiencing morning sickness.[15] Marijuana has potentially serious effects on the developing fetus.[37-39] A recent study documented that prenatal THC exposure adversely affects infant neurobehavior and child development up through the teen years,[40] but other researchers feel data is lacking to draw conclusions about long-term effects.[4] Overall review of current studies suggests a substantial association between maternal smoking of marijuana with lower birth weight babies and more limited evidence of a correlation with pregnancy complications for the mother and admission of the newborn to intensive care.[4]

   e. Teen use: Heavy marijuana use can damage brain development in youth ages 13 to 18. There is evidence of an association between cannabis use and loss of concentration and memory, jumbled thinking, schizophrenia, and early onset paranoid psychosis.[41]

   f. Psychosocial impairment: Moderate evidence correlates acute cannabis use with impaired learning, memory, and attention, and more limited evidence suggests that such impairments may be neurotoxic in that effects are sustained even after prolonged abstinence from cannabis use.[4,42,43] More limited associations exist between cannabis use and impaired academic achievement and outcomes, higher unemployment, lower income, and impaired social functioning.[4] Neurocognitive effects also include a decline in IQ, memory problems, and attentional impairments.[42,43]

   g. Mental health: There is substantial evidence of statistical association between cannabis use and the development of schizophrenia and other psychoses,[44] with greater risk occurring among more frequent users.[4] In two studies of patients with drug-induced psychosis (most

or all being cannabis as the inciting drug), one-third to one-half of the patients later developed a schizophrenia-spectrum disorder.[45,46] Those with drug-induced psychosis were equally as violent as schizophrenia patients who misused drugs.[45] Moderate evidence associates cannabis use with increased incidence of developing depression; suicidal ideation, attempts, and completion; and social anxiety disorder. More limited evidence links cannabis use with certain increased symptoms (e.g. hallucinations) in psychotic disorders, development of bipolar disorder, the development and/or increased symptoms of anxiety disorders, and increased symptoms of posttraumatic stress disorder.[4]

h. High doses or use of some high potency and/or synthetic cannabis derivatives have produced the following effects: psychosis, mood alterations, panic attacks, cognitive impairment, dizziness, cardiovascular effects (tachycardia, hypertension, palpitations), nausea, appetite changes, and others.[5] Mental impairment and distressing emotional states, such as paranoia, hallucinations, and psychosis, have caused people to harm themselves and others.[45,47,48]

i. Addiction: Use of marijuana can become problematic (marijuana use disorder) which may progress to addiction in some cases; when a person cannot stop using the drug despite interference with many aspects of daily life, use disorder is classified as addiction.[5] A 2015 study suggests that "30 percent of those who use marijuana may have some degree of marijuana use disorder."[5] Marijuana use disorder is frequently "associated with dependence—in which a person feels withdrawal symptoms when not taking the drug."[5] A user may be dependent but not be addicted. Studies estimate that 9 percent of adults[49] and 17 percent of teens who use marijuana will become dependent on it.[5] In 2015 roughly 4 million people in the US were found to have a marijuana use disorder, and 138,000 sought treatment.[5] In the same year in the Netherlands, more first-time entrants and more people overall entered treatment programs for cannabis use than for any other drug.[1] Although modulation of smoking technique may partially blunt the effect of use of high potency cannabis,[32] there is evidence that higher potency marijuana use is associated with increased severity of cannabis dependence.[50] There is moderate evidence of an association between cannabis use and the development of substance dependence and/ or a substance abuse disorder for other substances, including tobacco, alcohol, and illegal drugs.[4,51]

j. Delivery method: Smoking is a harmful route of administration for any medicinal compound because of carcinogens and other harmful materials which are known to produce adverse effects on the lungs and other tissues. Marijuana joints may contain "particulate matter, toxic gases, reactive oxygen species, and polycyclic aromatic hydrocarbons at a concentration possibly 20 times that of tobacco smoke."[52] Histopathologic changes in bronchial inflammation that are similar to changes seen with smoking tobacco have been found in marijuana smokers.[52] Only other delivery methods of FDA-approved cannabis compounds should be prescribed.

5. Inaccurate public analysis and use of research: Current state medical marijuana laws specifically approve medical marijuana as treatment for illnesses such as HIV, ALS, hepatitis, Parkinson's cancer, and glaucoma,[3] even though the data from scientific studies is weak or even nonexistent in most of these diseases.[4] As an example, multiple states include ALS on their list of approved illnesses for medical marijuana, but there have been only two small randomized double-blind clinical studies and the results of effectiveness were unequivocally negative.[4] Washington D.C. does not restrict medical marijuana use to any specific disease.[3,53] While scientific studies may eventually show benefit from cannabinoids for some of these illnesses, that is clearly not the case at this time. As a result, vulnerable and suffering patients are being misled and deceived.

6. Physician response to "medical marijuana":

    a. Irresponsible behavior: One study found almost one half of cancer doctors say they have recently recommended medical marijuana to their patients, although 70 percent of them admitted they did not have sufficient knowledge to do so.[54] Marijuana should not be discussed with, or prescribed to, patients without clear evidence-based guidelines supporting its use.

    b. Responsible behavior: The Cleveland Clinic and other reputable hospitals have prohibited physicians on staff from recommending "medical marijuana."[55] Dr. Paul Terpeluk, Medical Director at the Cleveland Clinic, summarizes why it does not make sense for physicians to prescribe it: "In the world of healthcare, a medication is a drug that has endured extensive clinical trials, public hearings and approval by the U.S. Food & Drug Administration (FDA). Medications are tested for safety and efficacy. They are closely regulated, from production to distribution. They are accurately dosed, down to the milligram. Medical marijuana is none of those things."[56]

E. Legal and Practical Implications:

1. Marijuana classification: The U.S. still classifies marijuana in the same category as heroin, as a Schedule I Drug, which has "no currently accepted medical use and a high potential for abuse."[57] The United States Food and Drug Administration (FDA) does not recognize, regulate, or approve the marijuana plant as medicine. They state: "researchers haven't conducted enough large-scale clinical trials that show that the benefits of the marijuana plant (as opposed to its cannabinoid ingredients) outweigh its risks in patients it's meant to treat."[18] Because of the vast increase in marijuana potency and the potential for harm and addiction, there is a need for limiting access to marijuana. When medical benefits are established for FDA-approved, pharmaceutical-grade derivatives of marijuana, these substances have been classified as Schedule II (Syndros), III (Marinol),[58] or V (Epidiolex).[30] (See the Table at the end for a description of scheduling categories.)

2. State regulations: As of late 2018, thirty-three states, the District of Columbia, Guam and Puerto Rico have approved medical marijuana.[9] Klieger et al evaluated laws in 28 states (including the District of Columbia) that had approved "medical marijuana," as of February 2017.[53] Besides specifying different qualifying diseases, the states varied in protections for patients against discrimination, in requirements for product safety testing, and in the range of packaging and labeling regulations.[53] Enforcement and adequacy of state regulations is unclear. Although Colorado, for example, has packaging regulations,[53] the number of children under 12 with marijuana ingestion visits to emergency rooms went from 0% to 2.4% of total visits after medical marijuana legalization.[8] After recreational marijuana was legalized in 2014 in Colorado, increases in pediatric hospital visits and calls to poison control due to marijuana ingestion have continued to increase,[59,60] with hospital visits doubling in 2017.[60] The majority of exposures were due to ingestion of medical marijuana in a food product.[8,59,60] State referenda approving the use of "medical marijuana," essentially a form of potentially addictive and harmful herbal therapy, with the inability to monitor or control the dose of active compounds, without clear safety standards or clinical guidelines,[53] and in the absence of evidence of effectiveness and a positive risk/benefit ratio, is unique in modern medicine.

3. Legal dichotomy: When medical marijuana is legally allowed in a state, the state has agreed to allow consumers to purchase marijuana from regulated dispensaries if they have a

physician's prescription. However, because marijuana is a Schedule I Drug, physicians who prescribe medical marijuana (non-pharmaceutical grade, non-standard dose, non-FDA-approved marijuana) from dispensaries are violating federal law, even if they are in compliance with state law. FDA-approved pharmaceutical grade standard dose medications derived from marijuana (e.g. Marinol) are legal in all states and physicians may prescribe them for appropriate indications and patients. The FDA cannot regulate marijuana edibles or any other forms of "medical marijuana" because marijuana is illegal; standard dosing and safety of these potentially pesticide and chemical-laden products[4] are illusory.

4. Practical recommendations: Rescheduling lower potency marijuana to Schedule II to make research easier and to allow FDA involvement in regulating marijuana on a national, rather than state, level seems reasonable. (See the Table at the end for a description of scheduling categories.) There should not be a double standard for prescription medications. All need to be subject to FDA regulations for safety of consumers and the respectability of the medical profession.

F. AAME Recommendations for Healthcare Professionals

1. AAME maintains that a reasonable and prudent physician should only recommend FDA-approved medications when the indications are clear, dosing is well-established, risk benefit ratios have been investigated and can be applied to individual patients, delivery systems are safe, and careful monitoring is agreed upon.

2. State legalization of "medical marijuana" has not been accompanied by the rigorous scientific approval process with regulations for dosing, production, packaging and monitoring that have made FDA-approved medications safe and effective. State-approved dispensaries are marketing a form of potentially addictive and harmful herbal therapy that does not meet modern safety and efficacy standards or clinical guidelines. Physicians cannot assume that "medical marijuana" is safe or effective for state-listed qualifying diseases or conditions, nor can they be sure that it has the labeled amount of active ingredient and is devoid of contaminants and harmful additives.

3. There are risks of significant short-term and long-term complications associated with marijuana use, including addiction; medical, mental health, psychosocial, and cognitive problems; and increasing the likelihood of problems for the unborn, children, and teens. These risks should make any medical use of marijuana a serious decision in which benefits clearly outweigh the risks. Given the inadequate research on marijuana benefits and the few conditions for which there are even moderate or better evidence of effectiveness (often accompanied by significant side effects), indications for prescribing marijuana are limited at this time.

4. Rather than legalizing marijuana for medical use by popular vote and political lobbying, AAME encourages legalization via FDA approval through formal clinical and scientific studies of any marijuana-based therapeutic that has demonstrated medical efficacy and safety by randomized controlled trials. To augment this process, AAME supports rescheduling lower potency marijuana to Schedule II to enable medical research into the potential benefits and harms of the use of pharmaceutical-grade marijuana derivatives within established ethical research guidelines and FDA supervision.

5. AAME recommends that FDA-approved marijuana medications should be regulated and regarded like any other FDA-approved medication. Medications that have been approved by the FDA have been studied extensively and have undergone a lengthy and rigorous process before they are made available to the public. The FDA requires carefully conducted studies (clinical trials) in hundreds to thousands of human subjects to determine the benefits and

risks of a possible medication. These medications have carefully regulated manufacturing processes, quality and purity standards, and standardized dosing and prescribing requirements.

F. AAME Recommendations for the Community

Because of inadequate research, potential addiction and health hazards of marijuana use, inadequate regulation in state laws to ensure safety and efficacy, and misleading advertising, AAME recommends the following:

1. Most medical conditions are best treated with FDA-approved medications that are devoid of addictive qualities and significant complications. Indications for prescribing marijuana are limited, and medications with fewer risks are the first line of therapy. However, in cases where primary treatments have not been adequate, and a trial of THC or CBD compounds might be considered, seek medical care from a qualified health professional who can prescribe currently available, pharmaceutical-grade, FDA-approved marijuana derivatives for appropriate conditions with proper monitoring.
2. Be wary of claims made about marijuana "benefits."
3. "Medical marijuana" dispensaries may have products with unknown contaminants and additives, variable amounts of active ingredients, unproven efficacy, unclear short-term and long-term problems, and unsafe packaging. This is not medicine.
4. Smoking any product is never healthy and should not be considered "medicine."
5. Be vigilant to ensure that children do not inadvertently have access to "medical marijuana" when visiting or in someone else's care.
6. Encourage federal government authorities to change lower potency marijuana to Schedule II to enable better research to elucidate potential benefits and harms of pharmaceutical grade marijuana products under the auspices of the FDA.

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Table: Controlled Substances Act Scheduling

Schedule	Description of substances	Examples
I	No accepted medical use and a high potential for abuse	Heroin, LSD, marijuana
II	High potential for abuse with risk of severe psychological or physical dependence	Vicodin, hydromorphone, meperidine, cocaine, fentanyl, Ritalin
III	Moderate to low potential for physical and psychological dependence. Abuse potential less than Schedule I and II, but more than IV.	Products with < 90mg codeine per dose (Tylenol with codeine), ketamine, anabolic steroids
IV	Low potentials for abuse and risk of dependence.	Xanax, Soma, Darvon, Valium, Ativan,, Ambien, Tramadol
V	Lower potential for abuse than Schedule IV; preparations containing limited quantities of certain narcotics. Generally used for antidiarrheal, antitussive, and analgesic purposes.	Cough preparations with < 200 mg codeine or per 100 mL (Robitussin AC), Lomotil, Motofen, Lyrica, Parepectolin

Adapted from: DEA. Drug Scheduling. https://www.dea.gov/drug-scheduling (accessed Feb. 7, 2019)

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10. See the Table at the end of the statement for a description of drug scheduling categories.
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13. A meta-analysis of 11 studies from four large national surveys compared adolescents' past-month marijuana use prevalence pre-and post- changes in state medical marijuana laws (MMLs). Comparison between pre-post MML changes in MML states to changes in non-MML states over comparable time periods yielded non-significant differences between changes in adolescents' past month use prevalence in the two states.(Sarvet AL, Wall MM, Fink DS, et al. Medical marijuana laws and adolescent marijuana use in the United States: a systematic review and meta-analysis. *Addiction* 2018; 113(6): 1003-16.) However, Chu argues that caution is indicated in accepting this conclusion for the following reasons: changes in other measurements of marijuana use, such as increased frequency, could be hidden behind the choice of past-month use as a measure; the large surveys on which Sarvet et al's data was extracted may not be representative at the state level; and the changes in attitudes and usage of marijuana in control non-MML states may actually be driven, and thus contaminated by, changes in MML states.(Chu YL. Commentary on Sarvet et al. (2018): What do we still need to know about the impacts of medical marijuana laws in the United States? *Addiction* 2018; 113(6): 1017-8.)
14. A study comparing pre-post MML differences in teen use of marijuana, cigarettes, binge drinking, and other illicit or non-prescribed drugs found that MML enactment was associated with a decrease in the use of such substances for early adolescents, no change for 10th graders, but an increase in non-medical prescription opioid and cigarette use among 12th graders.The authors suggested that parents of younger children may have been more vigilant about warning about marijuana use after MML passage; limitations to their study were also discussed. Limitations include: substance use was self-reported, study only included school-attending adolescents, specific features of MMLs were not assessed, assumption that the passage of MML in one state did not affect the behaviors of individuals in nearby, non-MML states (perhaps this assumption is

incorrect), concurrent policy changes may have confounded the relationships of interest.(Cerdá M, Sarvet AL, Wall M, et al. Medical marijuana laws and adolescent use of marijuana and other substances: Alcohol, cigarettes, prescription drugs, and other illicit drugs. *Drug & Alcohol Dependence* 2018; 183: 62-8.)
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