### Marijuana Beliefs Outstrip Evidence

There is a lot of hype surrounding medical marijuana, but the clinical science is very preliminary. The risks and benefits have not been researched enough to make science-based recommendations.

Steven Novella on July 25, 2018

In the past year not a week has gone by when a patient didn't ask me if marijuana would be useful to treat their neurological condition, with many patients asking me directly for a prescription. This is partly a response to Connecticut, where I work, <u>legalizing medical marijuana</u>. But also there is a lot of hype surrounding marijuana, driving belief that it is safe and effective for many conditions. The truth, however, is that there is little clinical science showing this to be true.

A recent survey, <u>published in the Annals of Internal Medicine</u>, finds that the majority of Americans have a very distorted view of the science behind medical marijuana:

About 81% of U.S. adults believe marijuana has at least 1 benefit, whereas 17% believe it has no benefit. The most common benefit cited was pain management (66%), followed by treatment of diseases, such as epilepsy and multiple sclerosis (48%), and relief from anxiety, stress, and depression (47%). About 91% of U.S. adults believe marijuana has at least 1 risk, whereas 9% believe it has no risks. The most common risk identified by the public was legal problems (51.8%), followed by addiction (50%) and impaired memory (42%). Among U.S. adults, 29.2% agree that smoking marijuana prevents health problems. About 18% believe exposure to secondhand marijuana smoke is somewhat or completely safe for adults, whereas 7.6% indicated that it is somewhat or completely safe for children. Of the respondents, 7.3% agree that marijuana use is somewhat or completely safe during pregnancy. About 22.4% of U.S. adults believe that marijuana is not at all addictive.

The reality is quite different. Cannabinoids are an interesting class of drugs with the potential to be developed into useful pharmaceuticals. But this process takes time, and ultimately we will need to do rigorous clinical trials looking at specific doses of specific preparations to determine safety and efficacy for specific clinical indications.

There is no reason to think that cannabis is a magical plant with special properties. The chemical constituents of marijuana are drugs, and all drugs have side effects, and need to be evaluated for their bioavailability, pharmacokinetics, drug-drug interactions, and toxicity. <u>David Gorski has written about medical marijuana as the new herbalism</u> – he wrote in 2014:

Medical marijuana. It's promoted as a seeming panacea that can cure whatever ails you. While there are potentially useful medicinal compounds in marijuana, in general the medical marijuana movement vastly oversells the promise. The truth is far more prosaic and nuanced.

Let's take an updated look at the science, starting with headaches. A 2017 review concluded:

Currently, there is not enough evidence from well-designed clinical trials to support the use of cannabis for headache, but there are sufficient anecdotal and preliminary results, as well as plausible neurobiological mechanisms, to warrant properly designed clinical trials. Such trials are needed to determine short- and long-term efficacy for specific headache types, compatibility with existing treatments, optimal administration practices, as well as potential risks.

This is also what I find. There are no double-blind placebo controlled trials. Most published studies are retrospective, or uncontrolled observational studies. This is, at best, considered preliminary evidence, which has a very poor track record of predicting ultimate definitive clinical evidence. As the authors above conclude, the plausibility is there, but the current state of evidence only supports doing clinical trials, not recommending its use.

Also, the "encouraging" preliminary evidence is actually not that impressive. One retrospective study found that about 40% of patients who used medical marijuana to treat their migraines found any positive effect. Only 20% reported decreased frequency, which is at about placebo response level.

Further, we need research to tease apart any specific anti-migraine effect from other effects of cannabis that could affect the perception and reporting of pain. It is common for people to gloss over this distinction, with the argument that as long as people feel better, who cares how it works. There is a small point here, in that overall quality of life is an important outcome to measure. But we want to know if any cannabis derivative is actually reducing migraines or other headache types, or if patients just don't care as much because they are sedated or their mood is mellowed.

This is an important distinction (which applies to all pain indications for cannabis) because it impacts whether or not we will be able to disentangle a specific anti-pain effect from the psychoactive effects of these drugs. Further, this factor likely predicts long term effects and addictive potential. The history of using addictive psychoactive drugs to treat chronic pain is not a good one. They tend not to be effective long term, and just make the chronic pain worse and more difficult to treat.

These concerns are reflected in a 2018 review of cannabis for neuropathic pain:

The potential benefits of cannabis-based medicine (herbal cannabis, plant-derived or synthetic THC, THC/CBD oromucosal spray) in chronic neuropathic pain might be outweighed by their potential harms. The quality of evidence for pain relief outcomes reflects the exclusion of participants with a history of substance abuse and other significant comorbidities from the studies, together with their small sample sizes.

The preliminary evidence for neuropathic pain is actually better than other pain indications, but even here the data is weak, and there are some early indications of potential risk that need to be further explored.

#### A 2015 systematic review of medical marijuana for all chronic pain found:

There is evidence for the use of low-dose medical marijuana in refractory neuropathic pain in conjunction with traditional analgesics. However, trials were limited by short duration, variability in dosing and strength of delta-9-tetrahydrocannabinol, and lack of functional outcomes. Although well tolerated in the short term, the long-term effects of psychoactive and neurocognitive effects of medical marijuana remain unknown. Generalizing the use of medical marijuana to all CNCP [chronic noncancer pain] conditions does not appear to be supported by existing evidence. Clinicians should exercise caution when prescribing medical marijuana for patients, especially in those with nonneuropathic CNCP.

Many experts consider the use of cannabis for the treatment of nausea (specifically chemotherapy-induced nausea) to be the most well-established. A 2015 systematic review found:

Cannabis-based medications may be useful for treating refractory chemotherapy-induced nausea and vomiting. However, methodological limitations of the trials limit our conclusions and further research reflecting current chemotherapy regimens and newer anti-emetic drugs is likely to modify these conclusions.

So even here the results are preliminary and all we can really say is that further research is needed.

Another condition for which there is positive (although still preliminary) evidence is in muscle spasticity from multiple sclerosis (MS). A 2018 review found that:

Based on this review, they concluded that nabiximols (Sativex oral spray), oral cannabis extract (OCE), and synthetic tetrahydrocannabinol (THC) are probably effective at reducing patient-reported symptoms of spasticity in people with MS, but OCE and synthetic THC were not found to be effective for reducing physician-administered measures of spasticity.

I note that they specify "patient-reported" symptoms showed a response, implying a subjective effect, but no real evidence for an objective effect. Again – more research is needed. The same review also cautioned:

However, cannabis use has been associated with an increased risk of psychosis and schizophrenia in at-risk individuals, there is growing evidence that cannabis can increase the risk for cardiovascular diseases, including myocardial infarction (MI), hypertension, heart failure, and stroke, and a recently recognized adverse effect of cannabis is cannabinoid hyperemesis syndrome.

You cannot simultaneously accept the preliminary evidence on efficacy and reject the preliminary evidence on risks. Supporters of medical marijuana might argue that we can separate out the beneficial effects from the unwanted side effects and risks. Possibly. But that is actually the point – we need to do much more research to isolate specific compounds, and study their risks and benefits.

The premature hype surrounding medical marijuana is unfortunate, and actually likely to hamper much needed further research. States are rushing to legalize medical marijuana, and this may also happen at the federal level. If patients can get medical marijuana they are less likely to enroll in a clinical trial where they may be allocated to a placebo group.

The research is likely to continue, however, and we will know in 10-20 years if all the hype was worth it.

# Legalizing Marijuana Not Good for Kids: AAP Policy Explained



By: Claire McCarthy, MD, FAAP

Marijuana has been in the news a lot these days, with more and more states making it legal to use it for medical reasons, and some making it legal to use it for any reason. And while there is a lot of disagreement about these laws, there is one thing that all of us can agree on:

As legal decisions are made about marijuana, we need to think about the health and well-being of our youth.

That's why the American Academy of Pediatrics (AAP) released an updated policy statement, "The Impact of Marijuana Policies on Youth: Clinical, Research and Legal Update," and technical report with all the latest research and information about marijuana. In this time when so many policy decisions about marijuana are being made, it's crucial that everyone understands the impact on youth.

Marijuana use is remarkably common among youth in the US. According to the most recent surveys, about 1 in 5 high school students has used it in the past month. Even more concerning, 1 in 12 has used it at least 20 times in the past month, and 1 in 16 uses it daily.

### The AAP Believes Youth Should Not Use Marijuana

There is a popular perception that marijuana isn't dangerous—but it is dangerous, both in the short term and the long term.

#### Here's why:

- It interferes with judgment, concentration, reaction time and coordination in ways that can make youth more likely to get into <u>car accidents</u> or otherwise injure themselves while using it.
- The ways that it interferes with brain functions such as memory, attention and problemsolving can make it much harder for youth to learn and succeed in school.
- Contrary to what many people think, it can be addictive.
- Inhaling the smoke can cause lung problems.
- New research shows that marijuana use during adolescence and young adulthood, when the brain is going through many important changes, can lead to permanent problems with memory, learning and thinking.
- Youth who use marijuana regularly are less likely to <u>finish high school</u> or get other degrees, more likely to use <u>other drugs</u>, and more likely to try to commit <u>suicide</u>.

That's why it's really important that laws prevent youth from buying marijuana. Even more, we need to do everything possible to prevent them from using it or being exposed to it.

#### That means:

- Parents, relatives, and other caregivers should not use marijuana around children, both for safety reasons and <u>role-modeling</u> reasons.
- Banning any marijuana marketing to youth.
- Making sure that there is child-safe packaging and other safety measures.
- Creating public health campaigns like the ones we've used against smoking.

## The AAP Believes the Penalties for Using Marijuana Shouldn't Ruin a Child's Future

Hundreds of thousands of youth have been arrested or put in jail for using marijuana. Having a criminal record can make it hard or impossible to get college loans, financial aid, housing, and certain kinds of jobs. While the AAP does not believe that marijuana use should be legal, it does believe that it should be decriminalized so that penalties for marijuana-related offenses are reduced to lesser criminal charges or civil penalties. Our efforts should go into prevention and treatment, not locking kids up; we want to give our youth a good future instead of taking it away.

# If Marijuana is Going to Be Used As a Medicine, the AAP Believes It Must Be Done Carefully—and with Research to Understand All of Its Effects

The AAP believes in using the usual Food and Drug Administration (FDA) processes instead of "medical marijuana" laws. The FDA has a long track record of being sure that medicines are safe and effective (and are dispensed and sold safely); that's what we need if we want to use marijuana as a medication.

We also need more research on the use and safety of marijuana in youth. While studies have shown the chemicals in marijuana do seem to help people with chronic pain, as well as the nausea, vomiting, and appetite problems that are common in <u>cancer</u>, the studies were all done in adults. Youth are different from adults—and may react differently to marijuana. We need to find ways to fund this research and make it easier to do, so that we can really understand everything about how marijuana affects our youth.

Our first responsibility in everything we do as parents and caregivers should be to our children—because they rely on us to keep them safe and well, and because they are our future. Marijuana policies are no different. Let's be careful, thoughtful, and keep our children in mind.

### Additional Information from HealthyChildren.org:

- Marijuana: What Parents Need to Know
- When Teens Use Drugs: Taking Action
- Is Your Child Vulnerable to Substance Abuse?

### About Dr. McCarthy:

Claire McCarthy, MD, FAAP is a primary care pediatrician at Boston Children's Hospital, an Assistant Professor of Pediatrics at Harvard Medical School, a senior editor for Harvard Health Publications, and an official spokesperson for the American Academy of Pediatrics. Along with serving on the HealthyChildren.org Editorial Advisory Board, she writes about health and parenting for Boston.com and Huffington Post.

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POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

#### American Academy of Pediatrics



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### The Impact of Marijuana Policies on Youth: Clinical, Research, and Legal **Update**

COMMITTEE ON SUBSTANCE ABUSE, COMMITTEE ON ADOLESCENCE

#### abstract

This policy statement is an update of the American Academy of Pediatrics policy statement "Legalization of Marijuana: Potential Impact on Youth," published in 2004. Pediatricians have special expertise in the care of children and adolescents and may be called on to advise legislators about the potential impact of changes in the legal status of marijuana on adolescents. Parents also may look to pediatricians for advice as they consider whether to support state-level initiatives that propose to legalize the use of marijuana for medical and nonmedical purposes or to decriminalize the possession of small amounts of marijuana. This policy statement provides the position of the American Academy of Pediatrics on the issue of marijuana legalization. The accompanying technical report reviews what is currently known about the relationships of marijuana use with health and the developing brain and the legal status of marijuana and adolescents' use of marijuana to better understand how change in legal status might influence the degree of marijuana use by adolescents in the future.



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#### **DEFINITIONS**

For the purpose of clarifying terminology, the following are definitions used in this policy statement and the accompanying technical report1:

#### Legalization

Allowing cultivation, sale, and use of cannabis (restricted to adults  $\geq$ 21 years of age).

#### Legalization of Medical Marijuana

Allowing the use of marijuana to treat a medical condition or symptom with a recommendation from a physician.

#### Decriminalization

Reducing penalties for cannabisrelated offenses to lesser criminal charges or to civil penalties.

#### INTRODUCTION

Marijuana is the most commonly used illicit substance among adolescents.2 Recreational sale and possession of marijuana by adults remain illegal in most states and remain illegal under federal law. However, a number of states and local jurisdictions have decriminalized the possession of marijuana for recreational use by adults, reducing penalties to misdemeanors or citations. Many states also have legalized medical marijuana for adults who receive recommendations for use by physicians. Almost all states with medical marijuana laws allow access by minors, though often with greater regulation. States in which marijuana is legal prohibit marijuana sales to and use by minors, but changes in the legal status of marijuana, even if limited to adults, may affect the prevalence of use among adolescents. Although the epidemiologic data are not consistent across states and time periods, with the exception of Michigan and New Mexico, in all states where medical marijuana has been legalized, marijuana use by minors has been stable or has decreased.3 Youth substance use rates depend on a number of factors, including legal status, availability and ease of access of the substance. and perception of harm. For example, although tobacco is easily accessible. youth tobacco use rates have decreased substantially since the 1990s, in conjunction with aggressive public health campaigns warning of the medical consequences of smoking. In Colorado, the passage of the amendment to legalize recreational marijuana occurred in November 2012. Although sales of recreational

marijuana did not start in Colorado until January 1, 2014, the postlegalization 2013 rates of youth use increased.4 It is possible that public health campaigns that effectively communicate the harms associated with teen marijuana use could reduce youth use despite legalization. Legalization campaigns that imply that marijuana is a benign substance present a significant challenge for educating the public about its known risks and adverse effects. Therefore, it is unclear what the impact of legalization of marijuana for adults will have on the prevalence of marijuana use by adolescents, especially if the implementation of legalization includes messaging that minimizes the health and behavioral risks.

Substance abuse by adolescents is an ongoing health concern. Marijuana remains classified in the Controlled Substances Act (21 USC §801-971 [2012]) as a schedule I drug. This classification implies that it has a high potential for abuse, has no currently accepted medical use in the United States, and lacks accepted safety for use under supervision by a physician. Despite this classification by the federal government, marijuana has been legalized for medical purposes in a number of states, in direct opposition to federal law. Since the first policy statement from the American Academy of Pediatrics (AAP) on the legalization of marijuana was published in 2004, limited research has been performed to examine the potential therapeutic effects of marijuana for adults, specifically the class of chemicals known as cannabinoids, which are responsible for most of the medicinal effects of marijuana. This research has demonstrated that both the drugs approved by the US Food and Drug Administration and other pharmaceutical cannabinoids, such as cannabidiol, can be helpful for adults with specific conditions, such as increasing appetite and

decreasing nausea and vomiting in patients with cancer and for chronic pain syndromes,<sup>5,6</sup> although side effects of dizziness and dysphoria may also be experienced. There are no published studies on the use of medicinal marijuana or pharmaceutical cannabinoids in pediatric populations.

#### **EFFECTS OF MARIJUANA**

The adverse effects of marijuana have been well documented, and studies have demonstrated the potential negative consequences of short- and long-term recreational use of marijuana in adolescents. These consequences include impaired shortterm memory and decreased concentration, attention span, and problem solving, which clearly interfere with learning. Alterations in motor control, coordination, judgment, reaction time, and tracking ability have also been documented? these may contribute to unintentional deaths and injuries among adolescents (especially those associated with motor vehicles if adolescents drive while intoxicated by marijuana).8 Negative health effects on lung function associated with smoking marijuana have also been documented, and studies linking marijuana use with higher rates of psychosis in patients with a predisposition to schizophrenia have recently been published,9 raising concerns about longer-term psychiatric effects. New research has also demonstrated that the adolescent brain, particularly the prefrontal cortex areas controlling judgment and decision-making, is not fully developed until the mid-20s, raising questions about how any substance use may affect the developing brain. Research has shown that the younger an adolescent begins using drugs, including marijuana, the more likely it is that drug dependence or addiction will develop in adulthood.10 A recent analysis of 4 large epidemiologic

trials found that marijuana use during adolescence is associated with reductions in the odds of high school completion and degree attainment and increases in the use of other illicit drugs and suicide attempts in a dose-dependent fashion that suggests that marijuana use is causative.<sup>11</sup>

### DECRIMINALIZATION EFFORTS AND EFFECTS

The illegality of marijuana has resulted in the incarceration of hundreds of thousands of adolescents, with overrepresentation of minority youth.12 A criminal record can have lifelong negative effects on an adolescent who otherwise has had no criminal justice history. These effects can include ineligibility for college loans, housing, financial aid, and certain kinds of jobs. 13 In states that have passed decriminalization laws, marijuana use is still illegal, although the consequences of possession and use are less punitive. Although these laws are not applicable to adolescents in all states, the changes in the law are intended to address and reduce the long-term effects that felony charges can have on youth and young adults.13 Continued efforts to address this problem are based on issues of social justice, given the disparate rate of adjudication for drug offenses for youth of racial minority groups compared with white youth. Advocates of decriminalization have also sought to increase the availability of drug treatment services.14

#### CONCLUSIONS

Ultimately, the behavioral and health risks associated with marijuana use by youth should be the most salient criteria in determining whether policies that are enacted are effective in minimizing harm. More information, including the legal status of marijuana for both recreational and medical use, the effect of legal status on rates of use by adolescents and young adults, research on

medical marijuana and the adverse effects of marijuana use, the impact of criminal penalties particularly on minority teens and communities, and adolescent brain development related to substance use, is available in the accompanying technical report.<sup>1</sup>

#### **RECOMMENDATIONS**

- Given the data supporting the negative health and brain development effects of marijuana in children and adolescents, ages 0 through 21 years, the AAP is opposed to marijuana use in this population.
- 2. The AAP opposes "medical marijuana" outside the regulatory process of the US Food and Drug Administration. Notwithstanding this opposition to use, the AAP recognizes that marijuana may currently be an option for cannabinoid administration for children with life-limiting or severely debilitating conditions and for whom current therapies are inadequate.
- 3. The AAP opposes legalization of marijuana because of the potential harms to children and adolescents. The AAP supports studying the effects of recent laws legalizing the use of marijuana to better understand the impact and define best policies to reduce adolescent marijuana use.
- 4. In states that have legalized marijuana for recreational purposes, the AAP strongly recommends strict enforcement of rules and regulations that limit access and marketing and advertising to youth.
- 5. The AAP strongly supports research and development of pharmaceutical cannabinoids and supports a review of policies promoting research on the medical use of these compounds. The AAP recommends changing marijuana from a Drug Enforcement Administration schedule I to

- a schedule II drug to facilitate this research.
- Although the AAP does not condone state laws that allow the sale of marijuana products, in states where recreational marijuana is currently legal. pediatricians should advocate that states regulate the product as closely as possible to tobacco and alcohol, with a minimum age of 21 years for purchase. Revenue from this regulation should be used to support research on the health risks and benefits of marijuana. These regulations should include strict penalties for those who sell marijuana or marijuana products to those younger than 21 years, education and diversion programs for people younger than 21 years who possess marijuana, point-of-sale restrictions, and other marketing restrictions.
- 7. In states where marijuana is sold legally, either for medical or recreational purposes, regulations should be enacted to ensure that marijuana in all forms is distributed in childproof packaging, to prevent accidental ingestion.
- 8. The AAP strongly supports the decriminalization of marijuana use for both minors and young adults and encourages pediatricians to advocate for laws that prevent harsh criminal penalties for possession or use of marijuana. A focus on treatment for adolescents with marijuana use problems should be encouraged, and adolescents with marijuana use problems should be referred to treatment.
- The AAP strongly opposes the use of smoked marijuana because smoking is known to cause lung damage,<sup>15</sup> and the effects of secondhand marijuana smoke are unknown.
- The AAP discourages the use of marijuana by adults in the presence of minors because of the important influence of role modeling by adults on child and adolescent behavior.

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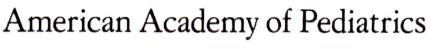
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