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# Recreational cannabinoid use: The hazards behind the “high”

Marijuana use can cause concerning physical, psychomotor, cognitive, and psychiatric effects, not to mention a near-doubling of car accidents.

## **PRACTICE RECOMMENDATIONS**

- › Screen all patients for use of addiction-prone substances. **(A)**
- › Screen cannabis users with a validated secondary screen for problematic use. **(A)**
- › Counsel patients that there is no evidence that use of recreational cannabis is safe; advise them that it can cause numerous physical, psychomotor, cognitive, and psychiatric effects. **(C)**

### Strength of recommendation (SOR)

- (A)** Good-quality patient-oriented evidence
- (B)** Inconsistent or limited-quality patient-oriented evidence
- (C)** Consensus, usual practice, opinion, disease-oriented evidence, case series

Approximately 156 million Americans (49% of the population) have tried cannabis.<sup>1</sup> About 5.7 million people ages 12 years and older use it daily or almost daily, a number that has nearly doubled since 2006.<sup>2</sup> There are 6600 new users in the United States every day,<sup>2</sup> and almost half of all high school students will have tried it by graduation.<sup>3</sup>

There is limited evidence that cannabis may have medical benefit in some circumstances.<sup>4</sup> (See “Medical marijuana: A treatment worth trying?” *J Fam Pract.* 2016;65:178-185 or <http://www.mdedge.com/jfponline/article/106836/medical-marijuana-treatment-worth-trying>.) As a result, it is now legal for medical purposes in 25 states. Recreational use by adults is also legal in 4 states and the District of Columbia.<sup>5</sup> The US Food and Drug Administration, however, has reaffirmed its stance that marijuana is a Schedule I drug on the basis of its “high potential for abuse” and the absence of “currently accepted medical uses.”<sup>6</sup>

The effects of legalizing the medical and recreational use of cannabis for individuals—and society as a whole—are uncertain. Debate is ongoing about the risks, benefits, and rights of individuals. Some argue it is safer than alcohol or that criminalization has been ineffective and even harmful. Others make the case for personal liberty and autonomy. Still, others are convinced legalization is a misdirected experiment that will result in diverse adverse outcomes. Regardless, it is important that primary care providers understand the ramifications of marijuana use. This evidence-based narrative highlights major negative consequences of non-medical cannabinoid use.

## **Potential adverse consequences of cannabis use**

Although the potential adverse consequences are vast, the literature on this subject is limited for various reasons:

- Many studies are observational with a small sample size.

TABLE 1

Quality of life, socioeconomic issues associated with recreational cannabis use

Lower quality of life <sup>9</sup>	Poor school attendance <sup>10</sup>
Relationship problems <sup>9,10</sup>	Lower educational achievement <sup>9,10</sup>
Lower income, financial instability, greater welfare dependence <sup>9,10</sup>	More discipline problems <sup>11</sup>
Decreased work commitment, performance, success <sup>9-11</sup>	More youth involved in crime <sup>12</sup>
Increased work absenteeism, presenteeism <sup>10,11</sup>	More involvement with other illicit drugs <sup>12</sup>

- Most studies examine smoked cannabis—not other routes of delivery.
- When smoked, the dose, frequency, duration, and smoking technique are variable.
- The quantity of Δ-9-tetrahydrocannabinol (THC), the primary psychoactive component in cannabis, is variable. (For more on the chemical properties of the marijuana plant, see “Cannabinoids: A diverse group of chemicals”<sup>7</sup> on page 773.)
- Most studies do not examine medical users, who are expected to use less cannabis or lower doses of THC.
- There are confounding effects of other drugs, notably tobacco, which is used by up to 90% of cannabis users.<sup>8</sup>

■ **Lower quality of life.** In general, regular non-medical cannabis use is associated with a lower quality of life and poorer socioeconomic outcomes (TABLE 1).<sup>9-12</sup> Physical and mental health is ranked lower by heavy users as compared to extremely low users.<sup>9</sup> Some who attempt butane extraction of THC from the plant have experienced explosions and severe burns.<sup>13</sup>

Studies regarding cannabis use and weight are conflicting. Appetite and weight may increase initially, and young adults who increase their use of the drug are more likely to find themselves on an increasing obesity trajectory.<sup>14</sup> However, in an observational study of nearly 11,000 participants ages 20 to 59 years, cannabis users had a lower body mass index, better lipid parameters, and were less likely to have diabetes than non-using counterparts.<sup>15</sup>

■ **Elevated rates of MI.** Chronic effects may include oral health problems,<sup>16</sup> gynec-

comastia, and changes in sexual function.<sup>17</sup> Elevated rates of myocardial infarction, cardiomyopathy, limb arteritis, and stroke have been observed.<sup>18</sup> Synthetic cannabinoids have been associated with heart attacks and acute renal injury in youth,<sup>19,20</sup> however, plant-based marijuana does not affect the kidneys. In addition, high doses of plant-based marijuana can result in cannabinoid hyperemesis syndrome, characterized by cyclic vomiting and compulsive bathing that resolves with cessation of the drug.<sup>21</sup>

■ **No major pulmonary effects.** Interestingly, cannabis does not appear to have major negative pulmonary effects. Acutely, smoking marijuana causes bronchodilation.<sup>22</sup> Chronic, low-level use over 20 years is associated with an increase in forced expiratory volume in one second (FEV<sub>1</sub>), but this upward trend diminishes and may reverse in high-level users.<sup>23</sup> Although higher lung volumes are observed, cannabis does not appear to contribute to the development of chronic obstructive pulmonary disease, but can cause chronic bronchitis that resolves with smoking cessation.<sup>22</sup> Chronic use has also been tied to airway infection. Lastly, fungal growth has been found on marijuana plants, which is concerning because of the potential to expose people to *Aspergillus*.<sup>22,24</sup>

■ **Cannabis and cancer? The jury is out.** Cannabis contains at least 33 carcinogens<sup>25</sup> and may be contaminated with pesticides,<sup>26</sup> but research about its relationship with cancer is incomplete. Although smoking results in histopathologic changes of the bronchial mucosa, evidence of lung cancer is mixed.<sup>22,25,27</sup> Some studies have suggested associations with cancers of the brain, testis, prostate, and cervix,<sup>25,27</sup> as well as certain rare cancers in children due to parental exposure.<sup>25,27</sup>

➤ Cannabis users have a lower body mass index, better lipid parameters, and are less likely to have diabetes than their non-using counterparts.

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TABLE 2

## Outcomes associated with cannabis use during pregnancy and/or breastfeeding

Pediatric cancers: neuroblastoma, astrocytoma, rhabdomyosarcoma, leukemia <sup>22,25</sup>	Decreased attention, memory, cognitive function <sup>41,42</sup>
Birth defects (mixed data): anencephaly, gastroschisis, ventricular septal defects <sup>41</sup>	Decreased learning ability and educational attainment <sup>41,42</sup>
Decreased growth <sup>41</sup>	Increased impulsivity, behavior problems <sup>41,42</sup>
Neonatal cannabis withdrawal syndrome <sup>42</sup>	Increased risk of tobacco or cannabis initiation as adolescents <sup>42</sup>

**>**  
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There are conflicting data about associations with head and neck squamous cell carcinoma,<sup>25,27,28</sup> bladder cancer,<sup>25,29</sup> and non-Hodgkin's lymphoma.<sup>25,30</sup> Some studies suggest marijuana offers protection against certain types of cancer. In fact, it appears that some cannabinoids found in marijuana, such as cannabidiol (CBD), may be antineoplastic.<sup>31</sup> The potential oncogenic effects of edible and topical cannabinoid products have not been investigated.

**■ Use linked to car accidents.** More recent work indicates cannabis use is associated with injuries in motor vehicle,<sup>32</sup> non-traffic,<sup>33</sup> and workplace<sup>34</sup> settings. In fact, a meta-analysis found a near-doubling of motor vehicle accidents with recent use.<sup>32</sup> Risk is dose-dependent and heightened with alcohol.<sup>35-37</sup> Psychomotor impairment persists for at least 6 hours after smoking cannabis,<sup>38</sup> at least 10 hours after ingesting it,<sup>37</sup> and may last up to 24 hours, as indicated by a study involving pilots using a flight simulator.<sup>39</sup>

In contrast to alcohol, there is a greater decrement in routine vs complex driving tasks in experimental studies.<sup>35,36</sup> Behavioral strategies, like driving slowly, are employed to compensate for impairment, but the ability to do so is lost with alcohol co-ingestion.<sup>35</sup> Importantly, individuals using marijuana may not recognize the presence or extent of the impairment they are experiencing,<sup>37,39</sup> placing themselves and others in danger.

Data are insufficient to ascribe to marijuana an increase in overall mortality,<sup>40</sup> and there have been no reported overdose deaths from respiratory depression. However, a

few deaths and a greater number of hospitalizations, due mainly to central nervous system effects including agitation, depression, coma, delirium, and toxic psychosis, have been attributed to the use of synthetic cannabinoids.<sup>20</sup>

**■ Cannabis use can pose a risk to the fetus.** About 5% of pregnant women report recent marijuana use<sup>2</sup> for recreational or medical reasons (eg, morning sickness), and there is concern about its effects on the developing fetus. Certain rare pediatric cancers<sup>22,25</sup> and birth defects<sup>41</sup> have been reported with cannabis use (TABLE 2<sup>22,25,41,42</sup>). Neonatal withdrawal is minor, if present at all.<sup>42</sup> Moderate evidence indicates prenatal and breastfeeding exposure can result in multiple developmental problems, as well as an increased likelihood of initiating tobacco and marijuana use as teens.<sup>41,42</sup>

**■ Cognitive effects of cannabis are a concern.** The central nervous system is not fully myelinated until the age of 18, and complete maturation continues beyond that. Due to neuroplasticity, life experiences and exogenous agents may result in further changes. Cannabis produces changes in brain structure and function that are evident on neuroimaging.<sup>43</sup> Although accidental pediatric intoxication is alarming, negative consequences are likely to be of short duration.

Regular use by youth, on the other hand, negatively affects cognition and delays brain maturation, especially for younger initiates.<sup>9,38,44</sup> With abstinence, deficits tend to normalize, but they may last indefinitely among young people who continue to use marijuana.<sup>44</sup>

## Cannabinoids: A diverse group of chemicals

*Cannabis*, the genus name for 3 species of marijuana plant (*sativa*, *indica*, *ruderalis*), has come to mean any psychoactive part of the plant and is used interchangeably with “marijuana.” There are at least 85 different cannabinoids in the native plant.<sup>7</sup>

Cannabinoids are a diverse group of chemicals that have activity at cannabinoid receptors.  $\Delta$ -9-tetrahydrocannabinol (THC), a partial agonist of the CB1 receptor, is the primary psychoactive component and is found in larger quantities in *Cannabis sativa*, which is preferred by non-medical users. Cannabidiol (CBD), a weak partial CB1 antagonist, exhibits few, if any, psychotropic properties and is more plentiful in *Cannabis indica*.

Synthetic cannabinoids are a heterogeneous group of manufactured drugs that are full CB1 agonists and that are more potent than THC, yet are often assumed to be safe by users. Typically, they are dissolved in solvents, sprayed onto inert plant materials, and marketed as herbal products like “K2” and “spice.”

Dyscognition is less severe and is more likely to resolve with abstinence in adults,<sup>44</sup> which may tip the scale for adults weighing whether to use cannabis for a medical purpose.<sup>45</sup> Keep in mind that individuals may not be aware of their cognitive deficits,<sup>46</sup> even though nearly all domains (from basic motor coordination to more complex executive function tasks, such as the ability to control emotions and behavior) are affected.<sup>44</sup> A possible exception may be improvement in attention with acute use in daily, but not occasional, users.<sup>44</sup> Highly focused attention, however, is not always beneficial if it delays redirection toward a new urgent stimulus.

■ **Mood benefit? Research suggests otherwise.** The psychiatric effects of cannabis are not fully understood. Users may claim mood benefit, but research suggests mari-

juana prompts the development or worsening of anxiety, depression, and suicidality.<sup>12,47</sup> Violence, paranoia, and borderline personality features have also been associated with use.<sup>38,47</sup> Amotivational syndrome, a disorder that includes apathy, callousness, and anti-social behavior, has been described, but the interplay between cannabis and motivation beyond recent use is unclear.<sup>48</sup>

Lifetime cannabis use is related to panic,<sup>49</sup> yet correlational studies suggest both benefit and problems for individuals who use cannabis for posttraumatic stress disorder.<sup>50</sup> It is now well established that marijuana use is an independent causal risk factor for the development of psychosis, particularly in vulnerable youth, and that it worsens schizophrenia in those who suffer from it.<sup>51</sup> Human experimental studies suggest this may be because the effect of THC is counteracted by CBD.<sup>52</sup> Synthetic cannabinoids are even more potent anxiogenic and psychogenic agents than plant-based marijuana.<sup>19,20</sup>

### Cannabis Use Disorder

About 9% of those who try cannabis develop Cannabis Use Disorder, which is characterized by continued use of the substance despite significant distress or impairment.<sup>53</sup> Cannabis Use Disorder is essentially an addiction. Primary risk factors include male gender, younger age at marijuana initiation, and personal or family history of other substance or psychiatric problems.<sup>53</sup>

Although cannabis use often precedes use of other addiction-prone substances, it remains unclear if it is a “gateway” to the use of other illicit drugs.<sup>54</sup> Marijuana withdrawal is relatively minor and is comparable to that for tobacco.<sup>55</sup> While there are no known effective pharmacotherapies for discontinuing cannabis use, addiction therapy—including cognitive behavioral therapy and trigger management—is effective.<sup>56</sup>

### So how should the evidence inform your care?

Screen all patients for use of cannabinoids and other addiction-prone substances.<sup>57</sup> Follow any affirmative answers to your questions about cannabis use by asking about potential

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negative consequences of use. For example, ask patients:

- How often during the past 6 months did you find that you were unable to stop using cannabis once you started?
- How often during the past 6 months did you fail to do what was expected of you because of using cannabis? (For more questions, see the Cannabis Use Disorder Identification Test available at: <http://www.otago.ac.nz/national-addictioncentre/pdfs/cudit-r.pdf>.)

Other validated screening tools include the Severity of Dependence Scale, the Cannabis Abuse Screening Test, and the Problematic Use of Marijuana.<sup>58</sup>

Counsel patients about possible adverse effects and inform them there is no evidence that recreational marijuana or synthetic cannabinoids can be used safely over time. Consider medical use requests only if there is a favorable risk/benefit balance, other recognized treatment options have been exhausted, and you have a strong understanding of the use of cannabis in the medical condition being considered.<sup>4</sup>

Since brief interventions using motivational interviewing to reduce or eliminate recreational use have not been found to be effective,<sup>59</sup> referral to an addiction specialist may be indicated. If a diagnosis of cannabis use disorder is established, then abstinence from addiction-prone substances including marijuana, programs like Marijuana Anonymous (Available at: <https://www.marijuana-anonymous.org/>), and individualized addiction therapy scaled to the severity of the condition can be effective.<sup>56</sup> Because psychiatric conditions frequently co-occur and complicate addiction,<sup>53</sup> they should be screened for and managed, as well.

**■ Drug testing.** Cannabis Use Disorder has significant relapse potential.<sup>60</sup> Abstinence and treatment adherence should be ascertained through regular follow-up that includes a clinical interview, exam, and body fluid drug testing. Point-of-care urine analysis for substances of potential addiction has limited utility. Definitive testing of urine with gas chromatography/mass spectrometry (GC/MS) or liquid chroma-

tography (LC/MS-MS) can eliminate THC false-positives and false-negatives that can occur with point-of-care urine immunoassays. In addition, GCMS and LC/MS-MS can identify synthetic cannabinoids; in-office immunoassays cannot.

If the patient relapses, subsequent medical care should be coordinated with an addiction specialist with the goal of helping the patient to abstain from cannabis. **JFP**

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