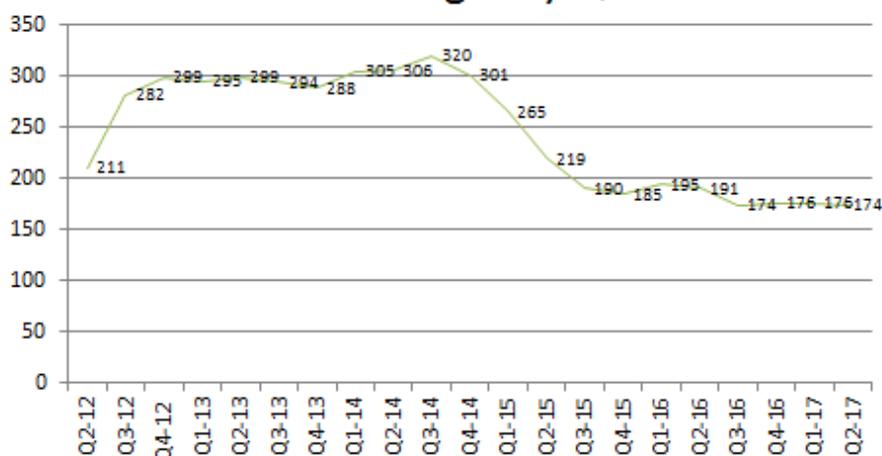


National Drug Shortages – Active Shortages by Quarter



Note: Each column represents the number of active shortages at the end of each quarter.
University of Utah Drug Information Service
Erin.Fox@hsc.utah.edu, @foxerinr

5. CLINICAL IMPLICATIONS AND POLICY CONSIDERATIONS OF CANNABIS USE (RESOLUTION 907-I-16)

Reference committee hearing: see report of Reference Committee K.

**HOUSE ACTION: RECOMMENDATIONS ADOPTED AS FOLLOWS
IN LIEU OF RESOLUTIONS 907-I-16 AND 915
REMAINDER OF REPORT FILED**

See Policies H-95.923, H-95.924, H-95.936, H-95.952 and D-95.969

INTRODUCTION

Resolution 907-I-16, “Clinical Implications and Policy Considerations of Cannabis Use,” introduced by the Resident and Fellow Section and referred by the House of Delegates, asked that our AMA amend Policy H-95.998 by addition and deletion to read as follows:

H-95.998 AMA Policy Statement on Cannabis

Our AMA believes that (1) cannabis is a dangerous drug and as such is a public health concern; (2) ~~sale of cannabis should not be legalized;~~ (3) public health based strategies, rather than incarceration, should be utilized in the handling of individuals possessing cannabis for personal use; and (4) (3) additional research should be encouraged,

and amend Policy D-95.976 by deletion to read as follows:

D-95.976 Cannabis - Expanded AMA Advocacy

1. Our AMA will educate the media and legislators as to the health effects of cannabis use as elucidated in CSAPH Report 2-I-13, A Contemporary View of National Drug Control Policy, and CSAPH Report 3-I-09, Use of Cannabis for Medicinal Purposes, and as additional scientific evidence becomes available. 2. Our AMA urges legislatures to delay initiating full legalization of any cannabis product until further research is completed on the public health, medical, economic and social consequences of use of cannabis and, instead, support the expansion of such research. 3. Our AMA will also increase its efforts to educate the press, legislators and the public regarding its policy position that stresses a “public health”, as contrasted with a

“criminal,” approach to cannabis. 4. Our AMA shall encourage model legislation that would require placing the following warning on all cannabis products not approved by the U.S. Food and Drug Administration: “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.~~”

The Council on Science and Public Health (Council) has issued four previous reports on cannabis (1997, 2001, 2009, and 2013) establishing a broad policy base.¹⁻⁴ This report focuses on the health effects (both therapeutic and harmful) of cannabis and reviews available data on the impact of legalization. While the AMA prefers to use the scientific term “cannabis,” the colloquial term “marijuana” is used interchangeably in this report, for example, when quoting a source or identifying the official name of a committee.

METHODS

English language reports were selected from searches of the PubMed, Google Scholar, and Cochrane Library databases from March 2013 to July 2017 using the search terms “marijuana or cannabis” in combination with “health,” “mental health,” “health effects,” “therapeutic use,” “therapeutic benefits,” “legalization,” “youth or adolescents,” “edibles,” “driving,” “taxes,” and “treatment.” Additional articles were identified by manual review of the reference lists of pertinent publications. Websites managed by federal and state agencies and applicable regulatory and advocacy organizations were reviewed for relevant information.

CURRENT AMA AND FEDERATION POLICY

Existing AMA policy on cannabis states that it is a dangerous drug and as such is a public health concern (H-95.998). The AMA calls for further adequate and well-controlled studies of marijuana and related cannabinoids in patients who have serious conditions for which preclinical, anecdotal, or controlled evidence suggests possible efficacy (D-95.952). The AMA also urges that marijuana’s status as a federal schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical research and development of cannabinoid-based medicines (D-95.952). The AMA also believes that public health based strategies, rather than incarceration, should be utilized in the handling of individuals possessing cannabis for personal use (H-95.998).

The AMA believes that the sale of cannabis should not be legalized (H-95.998) and urges legislatures to delay initiating full legalization of any cannabis product until further research is completed on the public health, medical, economic, and social consequences of recreational use (D-95.976). The AMA supports requiring the following warning on all cannabis products not approved by the U.S. Food and Drug Administration, “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” (D-95.976). The AMA also advocates for regulations requiring point-of-sale warnings and product labeling for cannabis and cannabis-based products regarding the potential dangers of use during pregnancy and breastfeeding (H-95.936). The AMA supports increased educational programs relating to use and abuse of alcohol, marijuana, and controlled substances (H-170.992). (see Appendix A)

Many medical societies in the Federation have taken positions that are consistent with AMA policy. The California Medical Association (CMA) is one exception. It is on record as urging the legalization and regulation of cannabis to allow for greater clinical research, oversight, accountability, and quality control.⁵ CMA believes that the most effective way to protect the public’s health is to tightly control, track, and regulate cannabis and to comprehensively research and educate the public on its health impacts, not through ineffective prohibition.⁵

STATE LAWS ON CANNABIS

At the state level, trends in law have moved from decriminalization, to the legalization of medical use of cannabis, to cannabis regulated for adult recreational use.⁶ California was the first jurisdiction in the United States (U.S.) to legalize the medical use of cannabis. Today, 29 states, the District of Columbia (D.C.), Guam, and Puerto Rico have legalized the medical use of cannabis through either the legislative process or ballot measures.⁷ These laws vary greatly by jurisdiction from how patients access the product (home cultivated or dispensary), to qualifying conditions, product safety and testing requirements, packaging and labeling requirements, and consumption method (some states prohibit smoking the product). In jurisdictions that have legalized cannabis for medicinal use, physicians can “certify” or “recommend” a qualifying patient for the medicinal use of cannabis, but physicians cannot prescribe cannabis for medical purposes because it is illegal under federal law. In recent years, an additional

17 states have enacted laws allowing access to low delta-9-tetrahydrocannabinol (THC)/high cannabidiol (CBD) products for children with epilepsy.⁷

In 2012, Colorado (CO) and Washington (WA) were the first U.S. jurisdictions to legalize the adult use of cannabis for recreational purposes.^{8,9} Today, a total of 8 states and D.C. have legalized cannabis for recreational purposes, all through the ballot measure process.⁷ (Figure 1) Most of these jurisdictions have created for-profit, commercial cannabis production and distribution markets where the product is sold and taxed. D.C. is the exception; they have adopted a “grow and give” model whereby residents are permitted to possess, use, grow, and give away cannabis, but they cannot sell it.¹⁰ In 2017, legislatures in 20 states introduced legislation to legalize cannabis for recreational use. Vermont’s legislature was the first in the country to vote in favor of legalizing cannabis for recreational use.¹¹ The bill was ultimately vetoed by the governor due to the lack of provisions to protect public health and safety. Specifically, he called on policymakers to hold off on moving forward with commercialization until the state could:

...detect and measure impairment on our roadways, fund and implement additional substance abuse prevention education, keep our children safe and penalize those who do not, [and] measure how legalization impacts mental health and substance abuse issues our communities are already facing.¹²

RELEVANT FEDERAL LAW AND POLICY

Under the U.S. Controlled Substances Act (CSA) of 1970, cannabis is classified as a Schedule I controlled substance, meaning it has no currently accepted medical use in treatment in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse.¹³ In 2011, the governors of Washington and Rhode Island petitioned the Drug Enforcement Administration (DEA) asking it to change cannabis from a Schedule I to a Schedule II drug under the CSA. In August of 2016, the DEA announced that cannabis would remain a Schedule I controlled substance.¹⁴ The notice stated that:

The DEA and FDA continue to believe that scientifically valid and well-controlled clinical trials conducted under investigational new drug applications are the proper way to research all potential new medicines, including marijuana. Furthermore, we believe that the drug approval process is the proper way to assess whether a product derived from marijuana or its constituent parts is safe and effective for medical use.¹⁴

Cannabis is not FDA-approved as a safe and effective drug for any indication. However, the agency has approved three drug products containing synthetic versions of the main psychoactive ingredient of cannabis, THC. Marinol[®] and Syndros[™], which include the active ingredient dronabinol, are indicated for nausea and vomiting associated with cancer chemotherapy and anorexia associated with weight loss in patients with AIDS.¹⁵ Cesamet[®], which contains the active ingredient nabilone, also is indicated for the treatment of the nausea and vomiting associated with cancer chemotherapy.¹⁵ Clinical investigations are underway for one CBD-based product, Epidiolex[®] for Lennox-Gastaut syndrome and Dravet syndrome and the THC/CBD combination product Sativex[®] for cancer pain.^{15,16}

In 2016, the DEA announced a change in policy designed to increase the number of DEA-registered cannabis manufacturers. Currently the University of Mississippi is the only entity authorized to produce cannabis for research purposes in the United States. The new policy will allow additional entities to submit applications and become registered with the DEA to grow and distribute cannabis for FDA-authorized research purposes.¹⁷

Under the Obama Administration, a memorandum to all U.S. Attorneys outlined cannabis enforcement priorities for the federal government. The memo explained that jurisdictions enacting laws legalizing cannabis that also have strong regulatory enforcement systems would be less likely to be threatened with federal enforcement.¹⁸ Federal priorities include preventing: (1) the distribution of cannabis to minors; (2) revenue from the sale of cannabis from going to criminal enterprises, gangs, and cartels; (3) the diversion of cannabis from states where it is legal under state law in some form to other states; (4) state-authorized cannabis activity from being used as a cover or pretext for the trafficking of other illegal drugs or other illegal activity; (5) violence and the use of firearms in the cultivation and distribution of cannabis; (6) drugged driving and the exacerbation of other adverse public health consequences associated with cannabis use; (7) the growing of cannabis on public lands and the attendant public safety and environmental dangers posed by cannabis production on public lands; and, (8) cannabis possession or use on federal property.¹⁸ Accordingly, if particular conduct threatens federal priorities, that person or entity would be subject to federal enforcement actions.

While the Obama Administration tolerated state laws legalizing cannabis, it is still unclear how the Trump Administration will handle the issue.¹⁹ In July of 2017, the Attorney General sent letters to four governors warning them that he had “serious concerns” about the effects of cannabis legalization, raising questions as to whether the current compromise on enforcement with the Justice Department may be under reconsideration.²⁰

THE HEALTH EFFECTS OF CANNABIS

The National Academies of Sciences, Engineering, and Medicine (National Academies) published a comprehensive report in January 2017 commissioned by federal, state, philanthropic, and nongovernmental organizations, entitled “The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and the Recommendations for Research.”⁶ The report’s recommendations outline priorities for a research agenda and highlight the potential for improvements in data collection efforts and enhanced surveillance capacity.⁶ The report also contained 98 conclusions based on the accumulated evidence related to cannabis or cannabinoid use and health.⁶ (see Appendix B)

The report examined a broad range of possible health effects of cannabis and cannabinoids. Health effects examined included those related to cancer; cardiometabolic risk; respiratory disease; immunity; injury and death; prenatal, perinatal, and neonatal exposure; psychosocial and mental health; problem cannabis use; and cannabis use and the misuse of other substances. The findings are organized into 5 evidence categories: conclusive, substantial, moderate, limited, and no/insufficient evidence. The report found conclusive or substantial evidence that cannabis or cannabinoids are effective: (1) for the treatment of chronic pain in adults (cannabis); (2) as antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids); and (3) for improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids).⁶ The report also found substantial evidence of a statistical association between cannabis smoking and: (1) more frequent chronic bronchitis episodes (long-term cannabis smoking); (2) increased risk of motor vehicle crashes; (3) lower birth weight of offspring (maternal cannabis smoking); and (4) the development of schizophrenia or other psychoses, with the highest risk among the most frequent users.⁶

A systematic review published subsequent to the National Academies report examined 27 clinical trials involving patients with chronic pain and found limited evidence that cannabis may alleviate neuropathic pain in some patients, but that insufficient evidence exists to demonstrate analgesic effects in patients with other types of chronic pain.²¹ This conclusion contradicts the finding of the National Academies report and is an example of how research findings on the therapeutic effects of cannabis remain inconsistent, leading to confusion among physicians, patients, the media, policy makers, and others.

IMPACT OF STATE LEGALIZATION OF CANNABIS

In 2012, CO and WA were the first states to legalize cannabis for recreational use. As jurisdictions continue to follow in their footsteps, many are looking at data from these states to determine the impact of legalization on public health and safety. Issues being examined include the impact of legalization on patterns of use by adults, children and adolescents, and pregnant women; cannabis-related exposures; cannabis-related hospital or emergency department visits; cannabis-related treatment admissions; impaired driving; crime; opioid use; and governmental costs and revenue. Since regulatory structures governing cannabis vary by jurisdiction and continue to evolve, the impact on health and safety is difficult to discern. It is also worth noting that although recreational use of cannabis was first legalized in 2012, cannabis products for recreational use were not commercially available for sale in CO or WA until 2014. Alaska (AK), D.C., and Oregon (OR) voted to legalize recreational use in 2014. While OR allowed limited sales of cannabis through medical dispensaries in 2015, cannabis dispensaries for recreational users did not open in AK or OR until 2016 (Figure 2). As a result, limited data are currently available to determine the overall impact of legalizing recreational cannabis use on specific outcome measures.

The Colorado Department of Public Health and Environment (CDPHE) appointed a Retail Marijuana Public Health Advisory Committee (RMPHAC), to review scientific literature on the health effects of cannabis and state-specific health outcomes and patterns of use.²² The RMPHAC report was informed by state-based data and national surveys such as the Substance Abuse and Mental Health Services Administration’s (SAMHSA) National Survey on Drug Use and Health (NSDUH) and the Center for Disease Control and Prevention’s (CDC) Behavioral Risk Factor Surveillance System (BRFSS) and Pregnancy Risk Assessment Monitoring System (PRAMS). The Washington State Institute for Public Policy (WSIPP) has conducted a benefit-cost analysis of the implementation of WA

Initiative 502 as required by law.²³ The Northwest High Intensity Drug Trafficking Area (NWHIDTA) and the Rocky Mountain High Intensity Drug Trafficking Area (RMHIDTA) have also issued reports on the impacts of the legalization of cannabis in WA and CO, respectively.^{24,25} The results from these reports were utilized in examining the impact of cannabis legalization on public health and safety.

Use among Adults

In the United States, cannabis is the most commonly used illicit drug.²⁶ Overall, from 2002-2014, the prevalence of cannabis use during the past month, past year, and daily or almost daily increased among persons aged 18 years and older.²⁷ In 2016, the percentage of young adults (18-25 years) who were current marijuana users (past month) was similar to the percentages in 2014 and 2015, while the percentage of older adults (≥ 26 years) who were current users continued to increase.²⁸

The percentage of young Coloradan adults aged 18 to 25 years reporting cannabis use within the past year increased significantly after “medical” cannabis legalization (35 percent in 2007 to 2008 to 43 percent in 2010 to 2011).²⁹ The latest data available suggest cannabis use has remained fairly constant in CO (45 percent in 2013-2014). In 2015, based on the BRFSS data, 13 percent of CO adults ages 18 and up had used cannabis in the past-month.²² The NSDUH estimate for past-month use is higher, at 17 percent.²² However, neither survey showed a statistical change from 2014 to 2015.²² According to NSDUH data, adult use of cannabis in CO has continued to be higher than the national average, which was 8 percent.²² In WA, young adults’ (18-25 years) past-year cannabis use was 6 percent higher than the nation’s in 2012-2013, and adults’ use (≥ 26 years) was 5 percent higher.²⁴ Past month use of cannabis was 5 percent higher than the nation’s average for young adults and adults in 2012-2013.²⁴ Statewide BRFSS data indicate that since the legalization of recreational cannabis in WA, use has increased among adults.²³

Use among Pregnant Women

Cannabis is the most commonly used illicit drug during pregnancy.³⁰ The movement toward the legalization of cannabis may result in more women using cannabis during pregnancy.³¹ Cannabis crosses the placenta and is found in breast milk.³⁰ It may have adverse effects on both perinatal outcomes and fetal neurodevelopment, though evidence is limited.³¹ In 2015, the American College of Obstetricians and Gynecologists issued a committee opinion discouraging physicians from suggesting the use of marijuana during preconception, pregnancy, and lactation.³⁰

Overall, cannabis use during pregnancy is increasing with 3.85 percent of pregnant women between the ages of 18 and 44 years reporting past-month cannabis use in 2014, compared with 2.37 percent in 2002.³² PRAMS data for CO showed that among new mothers, 11.2 percent used cannabis prior to pregnancy, 5.7 percent used cannabis during pregnancy, and 4.5 percent of breastfeeding mothers used cannabis after delivery.²² Cannabis use during pregnancy was statistically higher among women with an unintended pregnancy (9.1 percent) than among women who intended to become pregnant (4.0 percent).²² When cannabis use during pregnancy was compared among different demographics, both education and age showed statistical differences, whereas race and ethnicity did not.²²

Use among Adolescents

Adolescents are of particular interest in cannabis-policy discussions because the negative health effects of the drug are heightened when use begins in adolescence.³³ In addition to the health effects, including the increased risk of addiction, evidence also suggests that cannabis use in adolescence and early adulthood is associated with poor social outcomes, including unemployment, lower income, and lower levels of life and relationship satisfaction.³³⁻³⁵ Changes in the legal status of cannabis may affect use among adolescents by decreasing the perceived risk of harm or through the marketing of legal cannabis. Studies examining the impact of “medical” cannabis laws found no measurable effect on the patterns of adolescent cannabis use.³⁶⁻³⁸ States with recreational or adult use cannabis laws also have not experienced an increase in adolescent use in the short term.^{22,23} However, further surveillance is necessary to determine long-term results.

NSDUH data for 2016 suggest that 6.5 percent or 1.6 million adolescents (12-17 years) were current (past month) users of cannabis.²⁸ The percentage of adolescents who were current cannabis users in 2016 was lower than the percentages in most years from 2009 to 2014, but was similar to the percentage in 2015.²⁸ In CO, estimates of current cannabis use (2002-2015) among high school students have fluctuated between approximately 20 percent and 25 percent.²² Survey results from 2015 indicate that approximately 38 percent of CO high school students

reported having ever used cannabis and 21 percent reported use in the past 30 days.²² These estimates are similar to national estimates of ever and current cannabis use among high school students. Among CO middle school students in 2015, an estimated 7.6 percent had ever used cannabis and an estimated 4.4 percent reported currently using cannabis.²² In WA, the Healthy Youth Survey, found that cannabis use indicators across grades 6, 8, 10, and 12, have been stable or fallen slightly since the legalization of recreational cannabis.²³

Cannabis-Related Exposures

Cannabis-related exposures generally refer to the number of human exposures related to accidental or excessive consumption or inhalation of cannabis and cannabis edibles. Early data from states that have legalized cannabis have shown an increase in calls to poison control centers related to cannabis exposures. According to the WA State Poison Control Center (WAPC), calls related to cannabis exposure nearly doubled from 2011 (n=146) to 2016 (n=286).³⁹ In 2016, over 42 percent (n=120) of the total cannabis-related calls involved individuals 13-29 years of age who had been exposed to some form of cannabis.³⁹ Over 70 percent (n=226) of patients were exposed to cannabis through ingestion.³⁹

In CO, 7.9 percent of adults with children 1-14 years old in the home reported having cannabis or cannabis products in or around the home (2015).²² It was estimated that approximately 14,000 homes in CO with children 1-14 years old had cannabis in the home with potentially unsafe storage.²² Cannabis-related exposures in CO increased 100 percent in the three-year average (2013-2015) since CO legalized recreational use of cannabis compared to the three-year average (2010-2012) prior to legalization.²⁵ In children (≤ 5 years old), cannabis-related exposures increased 169 percent after legalization of recreational cannabis in CO.²⁵ However, overall human exposures reported to Rocky Mountain Poison Center involving cannabis were marginally lower in 2016 (n=224) compared with 2015 (n=231).²²

A retrospective cohort study of CO children's hospital admissions and regional poison control (RPC) cases for cannabis exposures between January 1, 2009, and December 31, 2015, found that hospital visits and RPC case rates for cannabis exposures in patients under 10 years of age increased between the 2 years prior to and the 2 years after legalization.⁴⁰ During this time period, RPC calls increased at a significantly higher rate in CO than in the rest of the U.S. (34 percent vs. 19 percent per year).⁴⁰ In CO, edible products were responsible for more than half of the exposures.⁴⁰

Cannabis Secondhand Smoke Exposure

For 2014 and 2015 together, 3.2 percent of adults with children 1-14 years old reported cannabis being used inside the home in CO.²² Of these, 83.2 percent reported the cannabis was smoked, vaporized, or dabbled (dabs are a highly concentrated extract of THC).²² It is estimated that approximately 16,000 homes in CO had children 1-14 years old with possible exposure to secondhand cannabis smoke or vapor in the home.²²

Cannabis-Related Emergency Department Visits and Hospital Admissions

In addition to hospitalizations for unexpected pediatric exposure to cannabis, increased cannabis use after legalization has resulted in an increase in the number of ED visits and hospitalizations related to acute marijuana intoxication.²⁹ Retrospective data from the CO Hospital Association has shown that the prevalence of hospitalizations for cannabis exposure in patients aged 9 years and older essentially doubled after the legalization of medical cannabis (15 per 100,000 hospitalizations in 2001 to 2009 versus 28 per 100,000 hospitalizations from 2010 to 2013) and that cannabis-related ED visits nearly doubled after the legalization of recreational cannabis (22 per 100,000 ED visits in 2010 to 2013 versus 38 per 100,000 ED visits from January to June of 2014).²⁹

Cannabis legalization may also eventually contribute to increased ED visits for the sequelae of chronic cannabis use, including cannabinoid hyperemesis syndrome.²⁹ Patients with cannabinoid hyperemesis present to the ED with periodic bouts of intractable vomiting that are unresponsive to traditional antiemetics. CO saw a doubling of ED visits for cyclic vomiting after the legalization of medical cannabis in CO in 2009, although the total number of visits remained small.²⁹

Cannabis-Related Treatment Admissions

Limited data is available regarding the impact of laws legalizing the recreational use of cannabis on cannabis-related treatment admissions,¹ though the early data suggests a decline in treatment admissions. A study of cannabis-related treatment admissions in Denver from 2001-2013 found that such admissions increased from 2005 (2,694) to 2008 (3,295) and then declined by 10.6 percent to 2,887 in 2011.⁴¹ Significant decreases in treatment entries after 2009, a time when access to cannabis through CO's medical cannabis program was increasing, have been hypothesized to be a reflection of an accepting public opinion of cannabis use resulting in fewer individuals seeking treatment.⁴¹ In WA, cannabis-related treatment admissions fell in the three years following legalization of recreational use dropping from 7,843 in 2012, to 7,374 in 2013, 6,885 in 2014, and 6,142 in 2015.²³ Youth treatment admissions for cannabis have remained between 66 percent and 70 percent of overall admissions in WA state since 2010.²⁴

Impaired Driving

A potential unintended consequence of legalizing cannabis use for medical or recreational purposes is increased cannabis-related driving impairment. While the effects of alcohol on driving performance and crash risk are well understood, less is known regarding the effects of cannabis on driving. Research, including direct observations made in a driving simulator, has demonstrated the potential of cannabis to impair driving related skills.⁴²⁻⁴⁴ Individuals driving under the influence of cannabis seem to exhibit a general reckless driving style and cannabis smoking increases the risk of involvement in a motor vehicle accident approximately 2-fold.⁴⁴ Cannabis use is associated with slower driving, an increased tendency to drive below the speed limit, increased following distance, increased lane weaving, and increased mean distance headway to the preceding vehicle.⁴³ These behaviors suggest that those driving under the influence of cannabis are aware of their impairment and decrease their speed to compensate.⁴⁴

Unlike alcohol, THC is not water soluble, but is stored in fatty tissues and released over time. A clear relationship between THC levels and impairment has been difficult to establish, in part, because a urine or even serum level of THC could reflect cannabis used quite remotely from the date of the specimen collection.⁴⁵ Peak THC level can occur when low impairment is measured, and high impairment can be measured when THC level is low.⁴⁵ Additionally, some individuals may demonstrate little or no impairment at a THC level that impairs someone else.⁴⁵

The most recent data from CO show that cannabis-related traffic deaths increased 48 percent in the three-year average (2013-2015) after recreational use of cannabis was legalized compared with the three-year average (2010-2012) prior to legalization.²⁵ Similarly, the WA State Traffic Safety Commission found that the number of drivers with THC in their blood involved in fatal driving accidents increased more than 120 percent from 2010 to 2014.²⁴ Despite data from these individual states, another study found that three years after recreational cannabis legalization, motor vehicle crash fatality rates overall for WA and CO were not statistically different from those in similar states without recreational cannabis legalization.⁴⁶

Criminal Justice

Legalizing cannabis for recreational use could have variable impacts on crime. Some have argued that legalization could result in a decrease in drug-trafficking and possession charges; others contend that the increased use of cannabis could result in increases in violent crime.

Data from WA's Administrative Office of the Courts demonstrated that among adult offenders, misdemeanor cannabis possession convictions declined from 297 convictions in January 2012 to 0 by January 2013.²³ Among youth offenders, misdemeanor cannabis convictions dropped from 1,015 in the first three months of 2012 to 722 in the first quarter of 2013.²³ WA reports that from 2012 through 2014, cannabis seizure offenses reported to the National Incident-Based Reporting System decreased by nearly 62 percent.²⁴ Despite the overall decline in seizures in the state, youth cannabis seizure offenses have not followed this trend. In 2010, youth twelve to seventeen years old represented 28.9 percent (n=855) of all seizures.²⁴ In 2012 (legalization), they represented 37.5 percent (n=2,378) of seizures, and in 2013 they represented 68.6 percent (n=1,840) of total seizures.²⁴ By the end of 2014 (commercialization), 74 percent (n=1,791) of seizures involved youth aged twelve to seventeen years.²⁴

¹ Treatment admissions data as reported by substance abuse treatment facilities for inclusion in the national Treatment Episode Data Set.

Crime in Denver and Colorado has increased from 2013 to 2015.²⁵ Since 2014, there has been an increase in organized, large-scale home grows for trafficking to states where cannabis is not legalized.²⁵ Seizures of Colorado marijuana in the U.S. mail increased 471 percent from an average of 129 pounds (2010-2012) to 736 pounds (2013-2015) over the three-year period after recreational use was legalized.²⁵ In addition, in Colorado, property crime increased 6.2 percent, violent crime increased 6.7 percent, and all crime increased 6.2 percent from 2014 to 2015.²⁵

Opioid Use

According to the Centers for Disease Control and Prevention, increases in unintentional overdoses and deaths due to prescription opioids and heroin are the biggest driver of the drug overdose epidemic. Studies have found a decrease in the use of opioids among pain patients provided with medical cannabis.⁴⁷ Furthermore, medical cannabis laws are associated with significantly lower state-level opioid overdose mortality rates.⁴⁷ Additional research is necessary to determine how cannabis laws may impact opioid use, morbidity, and mortality.

Governmental Costs and Revenue

Cannabis tax collections in CO and WA have continued to increase, and, on a national basis, legalization and associated taxation of cannabis could result in billions of dollars per year of tax revenue for states.⁴⁸ In WA, I-502 required the WA State Liquor and Cannabis Board to oversee the recreational cannabis market and imposed a 25% excise tax on producers, processors, and retailers, which was later replaced with a 37% excise tax on retail sales.²³ The Dedicated Marijuana Account was created for cannabis revenues and expenditures.²³ Voters were told legalization could bring in as much as \$1.9 billion over five years, with 40 percent going to the state general fund and local budgets and the remaining 60 percent intended for substance abuse prevention, research, education, and health care. As of April 2016, state sales average over \$2 million a day, which translates into mean excise tax revenue approaching \$270 million per year.⁴⁸

In CO, voters were initially told cannabis excise taxes would boost state revenues by \$70 million per year, with the first \$40 million each year to be allocated to school construction, leaving \$30 million for enforcement and general state funds.⁴⁸ Revenues in calendar year 2016 reached nearly \$200 million. The CO legislature established a Marijuana Tax Cash Fund (MTCF) in 2014, which collects tax revenue from both medical and recreational cannabis sales. Funds in the MTCF have been appropriated to government agencies to address the possible health and safety consequences of legalization such as monitoring the health effects of cannabis, conducting health education campaigns, and providing substance abuse prevention and treatment programs.

The legalization and commercialization of cannabis results in revenue for states through taxes and fees, but it also comes with costs, both in regulating and enforcement actions and in protecting public health and safety. For example, in Colorado, the Marijuana Enforcement Division (MED) is responsible for regulating both medical and recreational cannabis businesses in the state. The MED's four offices and 55 employees are responsible for rulemaking, licensing and inspecting cannabis-related businesses, and taking enforcement actions. The annual budget for the MED is approximately \$10.5 million.

MINIMIZING HEALTH RISKS OF LEGALIZATION

As jurisdictions continue to understand the impact of legalization on health and other outcomes, the regulatory structure governing cannabis will continue to evolve. In CO, CDPHE continues to assess the knowledge gaps related to cannabis and develop policies to protect vulnerable populations.⁴⁹ For example, the issue of child cannabis exposure from edibles has been concerning. In CO, confusion surrounding the serving size for edible products and the delayed onset of the effects of THC are thought to have contributed to overconsumption.⁴⁹ Regulations were changed to ensure easier identification of average serving size in a single edible product.⁴⁹ CO, OR and WA now require a universal symbol to be affixed to edibles. Four states (Alaska, CO, OR, and WA) prohibit the manufacture or packaging of edibles that appeal to youth.⁵⁰ Concerns remain regarding the regulatory gaps that exist in each of these states and whether these regulations are actually informing consumers and keeping the public safe.⁵⁰

To address motor vehicle crashes due to driving under the influence of cannabis, some states have established *per se* limits for driving under the influence of cannabis. For example, CO and WA have established 5 ng/ml of THC as the legal limit for cannabis-impaired driving.⁴⁹ However, little evidence exists to support the enactment of specific *per*

se limits for cannabis.²⁴ As a first step, states are being encouraged to conduct prevalence studies on the number and proportion of drivers testing positive for THC.²⁴

The Vermont Department of Health has conducted a health impact assessment to determine the potential impact of legislation to regulate and tax cannabis for recreational use on the health of Vermonters and to recommend ways to mitigate the adverse health impacts of such legislation. The recommendations include expanding all current tobacco laws to include cannabis, prohibiting the use of cannabis in public places, standardizing and testing packaging and potency, funding prevention and education, restricting advertising, prohibiting infused products on the regulated market, setting a blood level operating limit for THC, expanding screening for substance use disorders in primary care, training health care providers on the health impacts of cannabis, and funding surveillance and research.⁵¹

CONCLUSION

Although the National Academies found conclusive or substantial evidence that cannabis or cannabinoids have some therapeutic benefits, they also found substantial or conclusive evidence of a statistical association between cannabis smoking and health harms. Furthermore, the findings of a systematic review on the analgesic effects of cannabis released subsequent to the National Academies report were inconsistent with the National Academies report, which highlights the lack of agreement on this issue, and serves as a source of confusion among physicians, patients, and the public and demonstrates the need for additional research.

Legalizing the recreational use of cannabis may result in its increased use over time due to changes in perceptions of safety and health risks. Existing data, although limited, have yet to confirm this expectation for children and adolescents. However, cannabis use has increased in adults and pregnant women. Data from jurisdictions that have legalized cannabis demonstrate concerns particularly around unintentional pediatric exposures resulting in increased calls to poison control centers and ED visits as well as an increase in traffic deaths due to cannabis-related impaired driving. Limited data also show a decrease in cannabis-related treatment admissions as well as a possible decrease in the use of opioids for chronic pain. In terms of crime, convictions for the possession of cannabis may decline in states that legalize cannabis. While states have seen an increase in revenue through sales and excise taxes on retail cannabis, the administrative and enforcement costs as well as the costs to society in terms of public health and safety should not be minimized.

Ongoing surveillance to determine the impact of cannabis legalization and commercialization on public health and safety will be critical. Surveillance should include, but not be limited to, the issues covered in this report – impact on patterns of use, traffic fatalities and injuries, emergency department visits and hospitalizations, unintentional exposures, exposure to second-hand smoke, and cannabis-related treatment admissions. There should also be a focus on at-risk populations including pregnant women and children. Continued evaluation of the effectiveness of regulations developed to ensure public health and safety in states that have legalized the medical and/or recreational use of cannabis is necessary. Jurisdictions that have legalized cannabis should allocate a substantial portion of their cannabis tax revenue for public health purposes, including substance abuse prevention and treatment programs, cannabis-related educational campaigns, scientifically rigorous research on the health effects of cannabis, and public health surveillance efforts.

For physicians, legalization may require practice modifications, particularly regarding patient-provider conversations about use and risk. Additional education on counseling patients about the danger of second hand smoke exposure, underage use, safe storage, impaired driving, and the over-consumption of edibles may be warranted.

RECOMMENDATIONS

The Council on Science and Public Health recommends that the following statements be adopted in lieu of Resolution 907-I-16 and the remainder of this report be filed:

1. That portions of Policies H-95.998, “AMA Policy Statement on Cannabis,” H-95.995 “Cannabis Use,” H-95.938 “Immunity from Federal Prosecution for Physicians Recommending Cannabis,” and D-95-976 “Cannabis – Expanded AMA Advocacy,” be retained and used, in part, to establish the following new policies:

Cannabis Legalization for Recreational Use

Our AMA: (1) believes that cannabis is a dangerous drug and as such is a serious public health concern; (2) believes that the sale of cannabis for recreational use should not be legalized; (3) discourages cannabis use, especially by persons vulnerable to the drug's effects and in high-risk populations such as youth, pregnant women, and women who are breastfeeding; (4) believes states that have already legalized cannabis (for medical or recreational use or both) should be required to take steps to regulate the product effectively in order to protect public health and safety and that laws and regulations related to legalized cannabis use should consistently be evaluated to determine their effectiveness; (5) encourages local, state, and federal public health agencies to improve surveillance efforts to ensure data is available on the short- and long-term health effects of cannabis use; (6) supports public health based strategies, rather than incarceration, in the handling of individuals possessing cannabis for personal use.

Cannabis Legalization for Medicinal Use

Our AMA: (1) believes that scientifically valid and well-controlled clinical trials conducted under federal investigational new drug applications are necessary to assess the safety and effectiveness of all new drugs, including potential cannabis products for medical use; (2) believes that cannabis for medicinal use should not be legalized through the state legislative, ballot initiative, or referendum process; (3) will develop model legislation requiring the following warning on all cannabis products not approved by the U.S. Food and Drug Administration: "Marijuana has a high potential for abuse. This product has not been approved by the Food and Drug Administration for preventing or treating any disease process."; (4) supports legislation ensuring or providing immunity against federal prosecution for physicians who certify that a patient has an approved medical condition or recommend cannabis in accordance with their state's laws; and (5) believes that effective patient care requires the free and unfettered exchange of information on treatment alternatives and that discussion of these alternatives between physicians and patients should not subject either party to criminal sanctions.

2. That the following new policy be adopted:

Taxes on Cannabis Products

Our AMA encourages states and territories to allocate a substantial portion of their cannabis tax revenue for public health purposes, including: substance abuse prevention and treatment programs, cannabis-related educational campaigns, scientifically rigorous research on the health effects of cannabis, and public health surveillance efforts.

3. That Policy H-95.952, "Cannabis for Medicinal Use," be amended by addition and deletion to read as follows:

H-95.952, "Cannabis and Cannabinoid Research for Medicinal Use"

(1) Our AMA calls for further adequate and well-controlled studies of marijuana and related cannabinoids in patients who have serious conditions for which preclinical, anecdotal, or controlled evidence suggests possible efficacy and the application of such results to the understanding and treatment of disease. (2) Our AMA urges that marijuana's status as a federal schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical research and development of cannabinoid-based medicines, and alternate delivery methods. This should not be viewed as an endorsement of state-based medical cannabis programs, the legalization of marijuana, or that scientific evidence on the therapeutic use of cannabis meets the current standards for a prescription drug product. (3) Our AMA urges the National Institutes of Health (NIH), the Drug Enforcement Administration (DEA), and the Food and Drug Administration (FDA) to develop a special schedule and implement administrative procedures to facilitate grant applications and the conduct of well-designed clinical research involving cannabis and its potential medical utility. This effort should include: a) disseminating specific information for researchers on the development of safeguards for cannabis clinical research protocols and the development of a model informed consent form for institutional review board evaluation; b) sufficient funding to support such clinical research and access for qualified investigators to adequate supplies of cannabis for clinical research purposes; c) confirming that cannabis of various and consistent strengths and/or placebo will be supplied by the National Institute on Drug Abuse to investigators registered with the DEA who are conducting bona fide clinical research studies that receive FDA approval, regardless of whether or not the NIH is the primary source of grant support. (4) ~~Our AMA believes that effective patient care requires the free and unfettered exchange of information on treatment alternatives and that discussion of these alternatives between physicians and patients should not subject either party to criminal sanctions.~~ Our AMA supports research to

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APPENDIX A - Existing AMA Policies Related to Cannabis

D-95.976, "Cannabis - Expanded AMA Advocacy"

1. Our AMA will educate the media and legislators as to the health effects of cannabis use as elucidated in CSAPH Report 2, I-13, A Contemporary View of National Drug Control Policy, and CSAPH Report 3, I-09, Use of Cannabis for Medicinal Purposes, and as additional scientific evidence becomes available. 2. Our AMA urges legislatures to delay initiating full legalization of any cannabis product until further research is completed on the public health, medical, economic and social consequences of use of cannabis and, instead, support the expansion of such research. 3. Our AMA will also increase its efforts to educate the press, legislators and the public regarding its policy position that stresses a "public health", as contrasted with a "criminal," approach to cannabis. 4. Our AMA shall encourage model legislation that would require placing the following warning on all cannabis products not approved by the U.S. Food and Drug Administration: "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." Res 213, I-14.

H-95.952, "Cannabis for Medicinal Use"

(1) Our AMA calls for further adequate and well-controlled studies of marijuana and related cannabinoids in patients who have serious conditions for which preclinical, anecdotal, or controlled evidence suggests possible efficacy and the application of such results to the understanding and treatment of disease. (2) Our AMA urges that marijuana's status as a federal schedule I controlled substance be reviewed with the goal of facilitating the conduct of clinical research and development of cannabinoid-based medicines, and alternate delivery methods. This should not be viewed as an endorsement of state-based medical cannabis programs, the legalization of marijuana, or that scientific evidence on the therapeutic use of cannabis meets the current standards for a prescription drug product. (3) Our AMA urges the National Institutes of Health (NIH), the Drug Enforcement Administration (DEA), and the Food and Drug Administration (FDA) to develop a special schedule and implement administrative procedures to facilitate grant applications and the conduct of well-designed clinical research involving cannabis and its potential medical utility. This effort should include: a) disseminating specific information for researchers on the

development of safeguards for cannabis clinical research protocols and the development of a model informed consent form for institutional review board evaluation; b) sufficient funding to support such clinical research and access for qualified investigators to adequate supplies of cannabis for clinical research purposes; c) confirming that cannabis of various and consistent strengths and/or placebo will be supplied by the National Institute on Drug Abuse to investigators registered with the DEA who are conducting bona fide clinical research studies that receive FDA approval, regardless of whether or not the NIH is the primary source of grant support. (4) Our AMA believes that effective patient care requires the free and unfettered exchange of information on treatment alternatives and that discussion of these alternatives between physicians and patients should not subject either party to criminal sanctions. CSA Rep. 10, I-97, Modified: CSA Rep. 6, A-01, Modified: CSAPH Rep. 3, I-09, Modified in lieu of Res. 902, I-10, Reaffirmed in lieu of Res. 523, A-11, Reaffirmed in lieu of Res. 202, I-12, Reaffirmed: CSAPH Rep. 2, I-13.

H-95.998, “AMA Policy Statement on Cannabis”

Our AMA believes that (1) cannabis is a dangerous drug and as such is a public health concern; (2) sale of cannabis should not be legalized; (3) public health based strategies, rather than incarceration, should be utilized in the handling of individuals possessing cannabis for personal use; and (4) additional research should be encouraged. BOT Rep. K, I-69, Reaffirmed: CLRPD Rep. C, A-89, Reaffirmed: Sunset Report, A-00, Reaffirmed: CSAPH Rep. 1, A-10, Reaffirmed in lieu of Res. 202, I-12, Modified: CSAPH Rep. 2, I-13.

H-95.995, “Cannabis Use”

Our AMA (1) discourages cannabis use, especially by persons vulnerable to the drug's effects and in high-risk situations; (2) supports the determination of the consequences of long-term cannabis use through concentrated research, especially among youth and adolescents; and (3) supports the modification of state and federal laws to emphasize public health based strategies to address and reduce cannabis use. CSA Rep. D, I-77, Reaffirmed: CLRPD Rep. C, A-89, Reaffirmed: Sunset Report, A-00, Reaffirmed: CSAPH Rep. 1, A-10, Modified: CSAPH Rep. 2, I-13.

H-95.936, “Cannabis Warnings for Pregnant and Breastfeeding Women”

Our AMA advocates for regulations requiring point-of-sale warnings and product labeling for cannabis and cannabis-based products regarding the potential dangers of use during pregnancy and breastfeeding wherever these products are sold or distributed. Res. 922, I-15.

H-95.938, “Immunity from Federal Prosecution for Physicians Recommending Cannabis”

Our American Medical Association supports legislation ensuring or providing immunity against federal prosecution for physicians who certify that a patient has an approved medical condition or recommend cannabis in accordance with their state's laws. Res. 233, A-15.

H-95.997, “Cannabis Intoxication as a Criminal Defense”

Our AMA believes a plea of cannabis intoxication not be a defense in any criminal proceedings.

BOT Rep. J, A-72 Reaffirmed: CLRPD Rep. C, A-89 Reaffirmed: Sunset Report, A-00 Reaffirmed: CSAPH Rep. 1, A-10 Modified: CSAPH Rep. 2, I-13.

H-170.992, “Alcohol and Drug Abuse Education”

Our AMA: (1) supports continued encouragement for increased educational programs relating to use and abuse of alcohol, marijuana and controlled substances; (2) supports the implementation of alcohol and marijuana education in comprehensive health education curricula, kindergarten through grade twelve; and (3) encourages state medical societies to work with the appropriate agencies to develop a state-funded educational campaign to counteract pressures on young people to use alcohol. Sub. Res. 63, I-80 Reaffirmed: CLRPD Rep. B, I-90 Reaffirmation and Reaffirmed: Sunset Report, I-00 Appended: Res. 415, I-01 Reaffirmed: CSAPH Rep. 1, A-11.

APPENDIX B - The National Academies of Sciences, Engineering, and Medicine

The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research (2017)

EVIDENCE	CONCLUSIONS FOR THERAPEUTIC EFFECTS
There is conclusive or substantial evidence that cannabis or cannabinoids are effective:	<ul style="list-style-type: none"> • For the treatment for chronic pain in adults (cannabis) • Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) • For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids)
There is moderate evidence that cannabis or cannabinoids are effective for:	<ul style="list-style-type: none"> • Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols)

There is limited evidence that cannabis or cannabinoids are effective for:	<ul style="list-style-type: none"> • Increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabis and oral cannabinoids) • Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids) • Improving symptoms of Tourette syndrome (THC capsules) • Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol) • Improving symptoms of posttraumatic stress disorder (nabilone)
There is limited evidence of a statistical association between cannabinoids and:	<ul style="list-style-type: none"> • Better outcomes (i.e., mortality, disability) after a traumatic brain injury or intracranial hemorrhage.
There is limited evidence that cannabis or cannabinoids are ineffective for:	<ul style="list-style-type: none"> • Improving symptoms associated with dementia (cannabinoids) • Improving intraocular pressure associated with glaucoma (cannabinoids) • Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone)
There is no or insufficient evidence to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for:	<ul style="list-style-type: none"> • Cancers, including glioma (cannabinoids) • Cancer-associated anorexia cachexia syndrome and anorexia nervosa (cannabinoids) • Symptoms of irritable bowel syndrome (dronabinol) • Epilepsy (cannabinoids) • Spasticity in patients with paralysis due to spinal cord injury (cannabinoids) • Symptoms associated with amyotrophic lateral sclerosis (cannabinoids) • Chorea and certain neuropsychiatric symptoms associated with Huntington's disease (oral cannabinoids) • Motor system symptoms associated with Parkinson's disease or the levodopa-induced dyskinesia (cannabinoids) • Dystonia (nabilone and dronabinol) • Achieving abstinence in the use of addictive substances (cannabinoids) • Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis (cannabidiol)
EVIDENCE	CONCLUSIONS FOR CANCER
There is moderate evidence of no statistical association between cannabis use and:	<ul style="list-style-type: none"> • Incidence of lung cancer (cannabis smoking) • Incidence of head and neck cancers
There is limited evidence of a statistical association between cannabis smoking and:	<ul style="list-style-type: none"> • Non-seminoma-type testicular germ cell tumors (current, frequent, or chronic cannabis smoking)
There is no or insufficient evidence to support or refute a statistical association between cannabis use and:	<ul style="list-style-type: none"> • Incidence of esophageal cancer (cannabis smoking) • Incidence of prostate cancer, cervical cancer, malignant gliomas, non-Hodgkin lymphoma, penile cancer, anal cancer, Kaposi's sarcoma, or bladder cancer • Subsequent risk of developing acute myeloid leukemia/acute non-lymphoblastic leukemia, acute lymphoblastic leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring (parental cannabis use)
EVIDENCE	CONCLUSIONS FOR CARDIOMETABOLIC RISK
There is limited evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • The triggering of acute myocardial infarction (cannabis smoking) • Ischemic stroke or subarachnoid hemorrhage • Decreased risk of metabolic syndrome and diabetes • Increased risk of prediabetes
There is no evidence to support or refute a statistical association between <i>chronic effects</i> of cannabis use and:	<ul style="list-style-type: none"> • The increased risk of acute myocardial infarction
EVIDENCE	CONCLUSIONS FOR RESPIRATORY DISEASE
There is substantial evidence of a statistical association between cannabis smoking and:	<ul style="list-style-type: none"> • Worse respiratory symptoms and more frequent chronic bronchitis episodes (long-term cannabis smoking)
There is moderate evidence of a statistical association between cannabis smoking and:	<ul style="list-style-type: none"> • Improved airway dynamics with acute use, but not with chronic use • Higher forced vital capacity (FVC)
There is moderate evidence of a statistical association between <i>the cessation</i> of cannabis smoking and:	<ul style="list-style-type: none"> • Improvements in respiratory symptoms.

There is limited evidence of a statistical association between cannabis smoking and:	<ul style="list-style-type: none"> • An increased risk of developing chronic obstructive pulmonary disease (COPD) when controlled for tobacco use (occasional cannabis smoking)
There is no or insufficient evidence to support or refute a statistical association between cannabis smoking and:	<ul style="list-style-type: none"> • Hospital admissions for COPD • Asthma development or asthma exacerbation
EVIDENCE	CONCLUSIONS FOR IMMUNITY
There is limited evidence of a statistical association between cannabis smoking and:	<ul style="list-style-type: none"> • A decrease in the production of several inflammatory cytokines in healthy individuals
There is limited evidence of <i>no</i> statistical association between cannabis use and:	<ul style="list-style-type: none"> • The progression of liver fibrosis or hepatic disease in individuals with viral hepatitis C (HCV) (daily cannabis use)
There is no or insufficient evidence to support or refute a statistical association between cannabis use and:	<ul style="list-style-type: none"> • Other adverse immune cell responses in healthy individuals (cannabis smoking) • Adverse effects on immune status in individuals with HIV (cannabis or dronabinol use) • Increased incidence of oral human papilloma virus (HPV) (regular cannabis use)
EVIDENCE	ConclusionS FOR Injury and Death
There is substantial evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • Increased risk of motor vehicle crashes
There is moderate evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • Increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal
There is no or insufficient evidence to support or refute a statistical association between cannabis use and:	<ul style="list-style-type: none"> • All-cause mortality (self-reported cannabis use) • Occupational accidents or injuries (general, nonmedical cannabis use) • Death due to cannabis overdose
EVIDENCE	Conclusions FOR Prenatal, Perinatal, and Neonatal Exposure
There is substantial evidence of a statistical association between maternal cannabis smoking and:	<ul style="list-style-type: none"> • Lower birth weight of the offspring
There is limited evidence of a statistical association between maternal cannabis smoking and:	<ul style="list-style-type: none"> • Pregnancy complications for the mother • Admission of the infant to the neonatal intensive care unit (NICU)
There is insufficient evidence to support or refute a statistical association between maternal cannabis smoking and:	<ul style="list-style-type: none"> • Later outcomes in the offspring (e.g., sudden infant death syndrome, cognition/academic achievement, and later substance use)
EVIDENCE	Conclusions FOR Psychosocial
There is moderate evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • The impairment in the cognitive domains of learning, memory, and attention (acute cannabis use)
There is limited evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • Impaired academic achievement and education outcomes • Increased rates of unemployment and/or low income • Impaired social functioning or engagement in developmentally appropriate social roles
There is limited evidence of a statistical association between <i>sustained abstinence from</i> cannabis use and:	<ul style="list-style-type: none"> • Impairments in the cognitive domains of learning, memory, and attention
EVIDENCE	Conclusions FOR Mental Health
There is substantial evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • The development of schizophrenia or other psychoses, with the highest risk among the most frequent users
There is moderate evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> • Better cognitive performance among individuals with psychotic disorders and a history of cannabis use • Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use) • A small increased risk for the development of depressive disorders • Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users • Increased incidence of suicide completion • Increased incidence of social anxiety disorder (regular cannabis use)

There is moderate evidence of <i>no</i> statistical association between cannabis use and:	<ul style="list-style-type: none"> Worsening of negative symptoms of schizophrenia (e.g., blunted affect) among individuals with psychotic disorders
There is limited evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> An increase in positive symptoms of schizophrenia (e.g., hallucinations) among individuals with psychotic disorders The likelihood of developing bipolar disorder, particularly among regular or daily users The development of any type of anxiety disorder, except social anxiety disorder Increased symptoms of anxiety (near daily cannabis use) Increased severity of posttraumatic stress disorder symptoms among individuals with posttraumatic stress disorder
There is no evidence to support or refute a statistical association between cannabis use and:	<ul style="list-style-type: none"> Changes in the course or symptoms of depressive disorders The development of posttraumatic stress disorder
EVIDENCE	Conclusions FOR Problem Cannabis Use
There is substantial evidence that:	<ul style="list-style-type: none"> Stimulant treatment of attention deficit hyperactivity disorder (ADHD) during adolescence is <i>not</i> a risk factor for the development of problem cannabis use Being male and smoking cigarettes are risk factors for the progression of cannabis use to problem cannabis use Initiating cannabis use at an earlier age is a risk factor for the development of problem cannabis use
There is substantial evidence of a statistical association between:	<ul style="list-style-type: none"> Increases in cannabis use frequency and the progression to developing problem cannabis use Being male and the severity of problem cannabis use, but the recurrence of problem cannabis use does <i>not</i> differ between males and females
There is moderate evidence that:	<ul style="list-style-type: none"> Anxiety, personality disorders, and bipolar disorders are <i>not</i> risk factors for the development of problem cannabis use Major depressive disorder is a risk factor for the development of problem cannabis use Adolescent ADHD is <i>not</i> a risk factor for the development of problem cannabis use Being male is a risk factor for the development of problem cannabis use Exposure to the combined use of abused drugs is a risk factor for the development of problem cannabis use Neither alcohol nor nicotine dependence alone are risk factors for the progression from cannabis use to problem cannabis use During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for the development of problem cannabis use
There is moderate evidence of a statistical association between:	<ul style="list-style-type: none"> A persistence of problem cannabis use and a history of psychiatric treatment Problem cannabis use and increased severity of posttraumatic stress disorder symptoms
There is limited evidence that:	<ul style="list-style-type: none"> Childhood anxiety and childhood depression are risk factors for the development of problem cannabis use
EVIDENCE	Conclusions FOR Cannabis Use and the Abuse of Other Substances
There is moderate evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> The development of substance dependence and/or a substance abuse disorder for substances, including alcohol, tobacco, and other illicit drugs
There is limited evidence of a statistical association between cannabis use and:	<ul style="list-style-type: none"> The initiation of tobacco use Changes in the rates and use patterns of other licit and illicit substances
EVIDENCE	Conclusions FOR Challenges and Barriers in Conducting Cannabis Research
There are several challenges and barriers in conducting cannabis and cannabinoid research, including:	<ul style="list-style-type: none"> There are specific regulatory barriers, including the classification of cannabis as a Schedule I substance, that impede the advancement of cannabis and cannabinoid research It is often difficult for researchers to gain access to the quantity, quality, and type of cannabis product necessary to address specific research questions on the health effects of cannabis use A diverse network of funders is needed to support cannabis and cannabinoid research that explores the beneficial and harmful health effects of cannabis use To develop conclusive evidence for the effects of cannabis use on short- and long-term health outcomes, improvements and standardization in research methodology (including those used in controlled trials and observational studies) are needed