

# Literature Review on Marijuana Use and Health Effects

## Summary and Key Findings

Retail Marijuana Public Health Advisory Committee  
Final Approval: January 12, 2015

## Introduction

In C.R.S. 25-1.5-110, the Colorado Department of Public Health and Environment (CDPHE) was given statutory responsibility to:

- "...monitor changes in drug use patterns, broken down by county and race and ethnicity, and the emerging science and medical information relevant to the health effects associated with marijuana use."
- "...appoint a panel of health care professionals with expertise in cannabinoid physiology to monitor the relevant information."

Based on this charge, CDPHE appointed a 13-member committee, the Retail Marijuana Public Health Advisory Committee (RMPHAC), to review scientific literature on the health effects of marijuana. Members of this committee (see Appendix, Retail Marijuana Public Health Advisory Committee Membership Roster) consisted of individuals in the fields of public health, medicine, epidemiology, and medical toxicology who had demonstrated expertise related to marijuana through their work, training, or research. This committee was charged with the duties as outlined in C.R.S. 25-1.1-110 to "...establish criteria for studies to be reviewed, reviewing studies and other data, and making recommendations, as appropriate, for policies intended to protect consumers of marijuana or marijuana products and the general public." The Committee conducted nine public meetings between May 2014 and January 2015 to complete these duties. The overall goal of the committee was to implement an unbiased and transparent process for evaluating scientific literature as well as marijuana use and health outcome data. The committee was particularly interested in ensuring quality information is shared about the known physical and mental health effects associated with marijuana use - and also about what is unknown at present. The official committee bylaws of this committee are included in the Appendix, Retail Marijuana Public Health Advisory Committee By-laws.

The committee used a standardized systematic literature review process to search and grade the existing scientific literature on health effects of marijuana. Findings were synthesized into evidence statements that summarize the quantity and quality of supporting scientific evidence. These evidence statements were classified as follows:

- **Substantial evidence** which indicates robust scientific findings that support the outcome and no credible opposing scientific evidence.
- **Moderate evidence** which indicates that scientific findings support the outcome, but these findings have some limitations.
- **Limited evidence** which indicates modest scientific findings that support the outcome, but these findings have significant limitations.
- **Mixed evidence** which indicates both supporting and opposing scientific findings for the outcome with neither direction dominating.
- **Insufficient evidence** which indicates that the outcome has not been sufficiently studied.

The committee also translated these evidence statements into lay language understandable by the general public for future use in public health messaging. In addition, the committee was asked to develop public health recommendations based on potential concerns identified

through the review process and to articulate research gaps based on common limitations of existing research. All of these were presented to the full committee during open public meetings with opportunities for stakeholder input. Final statements, recommendations, and research gaps were formally approved by a vote of the committee.

The topics for review were chosen based on recently published peer-reviewed publications outlining the potential health effects of marijuana use, and public health priorities identified from key informant interviews of local public health officials across Colorado, including in urban, rural, and resort communities. Key findings for each topic are presented below.

An important note for all key findings is that the available research evaluated the *association* between marijuana use and potential adverse health outcomes. This *association* does not prove that the marijuana use alone *caused* the effect. Despite the best efforts of researchers to account for confounding factors, there may be other important factors related to *causality* that were not identified. In addition, marijuana use was illegal everywhere in the United States prior to 1996. Research funding, when appropriated, was commonly sought to identify adverse effects from marijuana use. This legal fact introduces both funding bias and publication bias into the body of literature related to marijuana use.

The Retail Marijuana Public Health Advisory Committee recognizes the limitations and biases inherent in the published literature and made efforts to ensure the information reviewed and synthesized is reflective of the current state of medical knowledge. Where information was lacking - for whatever reason - the Committee identified this knowledge gap and recommended further research. This information will be updated as new research becomes available.

### Marijuana Use During Pregnancy and Breastfeeding

The committee reviewed the literature for marijuana use during pregnancy and while breastfeeding. Outcomes reviewed included those apparent at birth as well as physical, neurocognitive, and mental health findings throughout childhood and adolescence. We found moderate evidence that maternal use of marijuana during pregnancy is associated with negative effects on exposed offspring, including decreased academic ability, cognitive function and attention. Importantly, these effects may not appear until adolescence. We also found moderate evidence that maternal use of marijuana during pregnancy is associated with decreased growth in exposed offspring.

### Unintentional Marijuana Exposures in Children

The committee found moderate evidence that more unintentional marijuana exposures of children occur in states with increased legal access to marijuana; and the exposures can lead to significant clinical effects requiring medical attention. Additionally, we found moderate evidence that use of child resistant packaging reduces unintentional pediatric poisoning.

### Marijuana Use Among Adolescents and Young Adults

The committee reviewed the literature on the potential effects of marijuana use among adolescents and young adults including effects on cognitive abilities, learning, memory,

achievement, future use of substances such as marijuana and illicit drugs, and mental health issues. We found substantial evidence for associations between adolescent and young adult marijuana use and future addiction to illicit drugs in adulthood. We found an increased risk for developing psychotic symptoms or psychotic disorders in adulthood among regular adolescent and young adult users. In addition, we found moderate evidence for associations between adolescent and young adult marijuana use and at least short-term impairment of cognitive and academic abilities. We also found moderate evidence indicating that adolescent marijuana users were less likely to graduate from high school and more likely to be addicted to marijuana, alcohol, and tobacco in adulthood. We found beneficial effects related to cessation of use including moderate evidence that adolescent and young adult marijuana users who quit have lower risks of adverse cognitive and mental health outcomes than those who continue to use.

### Marijuana Dose and Drug Interactions

This literature review focused on the dose-response of different methods of marijuana use with regard to THC blood levels and impairment. Additional review was performed to evaluate marijuana's interactions with other drugs and the possibility of a positive drug screen from passive marijuana exposure. In general, we found that substantial evidence that for occasional (less than weekly) marijuana users, smoking, eating, or drinking marijuana containing 10 milligrams or more of THC is likely to cause impairment that affects the ability to drive, bike, or perform other safety sensitive activities. In addition, for these occasional users, waiting at least six hours after smoking marijuana (containing up to 35 milligrams of THC) will likely allow sufficient time for the impairment to resolve. The waiting time is longer for eating or drinking marijuana products. We found it is necessary for occasional users to wait at least eight hours for impairment to resolve after orally ingesting up to 18 milligrams of THC.

A substantial finding, regarding the use of edible marijuana products, is that it can take up to four hours after ingesting marijuana to reach the peak THC blood concentration and perhaps more time to feel the full effects. This has important implications for the time to wait between doses. Using alcohol and marijuana at the same time is likely to result in greater impairment than either one alone. Finally, typical passive exposure to marijuana smoke is unlikely to result in a failed workplace urine test or a failed driving impairment blood test.

### Marijuana Use and Neurological, Cognitive and Mental Health

The committee reviewed the literature on the potential adverse effects of marijuana use among adults including effects on cognitive functioning, memory, and mental health issues such as anxiety, depression, and psychosis. We found substantial evidence for associations between marijuana use and memory impairments lasting at least seven days after last use, as well as the potential for acute psychotic symptoms immediately after use. We found moderate evidence that adults who use marijuana regularly are more likely than non-users to have symptoms or diagnosis of depression.

## Marijuana Use and Respiratory Effects

The committee reviewed literature focused on marijuana use and effects to the respiratory tract. We found substantial evidence that marijuana smoke contains many of the same carcinogens found in tobacco smoke. We also found substantial evidence that acute use - (within the past hour) - results in immediate, short-term improvement in lung airflow. This finding includes use of both smoked and edible marijuana products. However, we found moderate evidence that heavy marijuana smoking is associated with mild airflow obstruction. In addition, we found substantial evidence heavy marijuana smoking is associated with chronic bronchitis, including chronic cough, sputum production, and wheezing. Finally, we found substantial evidence that heavy marijuana smoking is associated with pre-malignant lesions in the airway, but mixed evidence for whether or not marijuana smoking is associated with lung cancer.

## Marijuana Use and Extrapulmonary Effects (non-respiratory body systems)

Unlike other literature reviews outlined in this document, there were relatively few literature reports of marijuana use related to myocardial infarction (heart attacks), ischemic stroke, male infertility, testicular cancer, prostate cancer and bladder cancer. We found limited evidence that marijuana use may increase risk for both heart attack and some forms of stroke. These findings were most closely associated with recent, and in some cases heavy, marijuana use. Limited evidence also suggests an increased risk in both testicular (non-seminoma) and prostate cancers with marijuana use. Evidence was mixed for whether or not marijuana use increased the risk of male infertility.

## Marijuana Use and Injury

Our literature review focused on the increased risk of injury with marijuana use in a variety of settings (occupational, motor vehicle, recreational). The committee found substantial evidence that risk of motor vehicle crash doubles among drivers with recent marijuana use. Additionally, we found substantial evidence for a positive relationship between THC blood level and motor vehicle crash risk - that is, substantial evidence that the higher the level of THC in blood, the higher the crash risk. Finally, the committee found the combined use of marijuana and alcohol increases motor vehicle crash risk more than use of either substance alone. For non-traffic injuries, the evidence is limited, but data suggest the risk of non-traffic workplace injuries may be higher with marijuana use.

## Public Health Recommendations

The committee made a number of public health recommendations interspersed throughout this report. These recommendations loosely fall into several categories but almost all of the recommendations include some effort to standardize data quality (marijuana use frequency), standardize procedures (roadside THC testing) and improve monitoring of use patterns and health outcomes. Standardized data collection on method of marijuana use, amount and frequency should be encouraged across medical specialties and on survey tools used in Colorado to better characterize use patterns and dose among users. The committee also

recommends data collection on the THC content of Colorado products to better characterize the THC dose of a typical user. In addition, improved information on blood THC levels of drivers is needed to effectively monitor the impact of driving under the influence of marijuana.

The committee recommended many educational interventions ranging from information on safe storage to protect the youngest Coloradans, to information for adult users, their families, and health care providers. Education for health care providers on the known health effects of marijuana use may encourage more open dialog between providers and patients.

## Research Gaps

Important research gaps related to the population-based health effects of marijuana use were identified during the literature and data review process. These research gaps were based on common limitations of existing research (e.g., not enough focus on occasional marijuana use, distinct from regular or heavy use), exposures not sufficiently studied (e.g., dabbing or edibles), outcomes not sufficiently studied, or issues important to public education or policymaking (e.g., defining impairment in frequent users). These research gaps provide an important framework for prioritizing research related to marijuana use and public health. The committee strongly recommends Colorado support research to fill these important gaps in public health knowledge. While outside the scope of this committee's duties, the committee also recognizes more research is needed on the potential therapeutic benefits of marijuana.

Research gaps identified by the committee had five common themes: 1) Additional research using marijuana with THC levels consistent with currently available products; 2) Research on impairment in regular marijuana users who may have developed tolerance; 3) Research to identify improved testing methods for impairment either through alternate biological testing methods or physical tests of impairment; 4) Research to better characterize the pharmacokinetics/pharmacodynamics, potential drug interactions, health effects, and impairment related to newer methods of marijuana use such as edibles and vaporizing as well as other cannabinoids such as CBD; and 5) Research to better characterize possible differences in health effects between heavy (daily or near daily), regular (weekly or more), and occasional (less than weekly) users.

Table 1.  
Substantial and Moderate Findings from Systematic Literature Review

	Substantial	Moderate
Marijuana Use During Pregnancy & Breastfeeding (p.75)		Decreased IQ scores Attention problems Decreased growth Decreased cognitive function Decreased academic ability
Unintentional Marijuana Exposures in Children (p.87)		Legal marijuana access increases unintentional marijuana exposures in children Child resistant packaging reduces unintentional pediatric poisonings
Marijuana Use Among Adolescents and Young Adults (p.94)	Other illicit drug use and addiction after adolescence Psychotic symptoms or disorders like schizophrenia	Impaired cognitive abilities and academic performance after 28 days abstinence Less high school graduation Increased MJ use and addiction after adolescence Alcohol or tobacco use and addiction after adolescence Quitting lowers risks
Marijuana Dose and Drug Interactions (p.103)	Increased risk of driving impairment at blood [THC] 2-5 ng/mL Smoking > 10 mg THC leads to blood [THC] near or > 5 ng/mL within 10 minutes Smoking > 10 mg THC leads to driving impairment	Ingesting $\geq 15$ mg THC may lead to blood [THC] > 5 ng/mL Inhaling vaporized THC leads to blood [THC] similar to smoking same dose Higher blood [THC] in impaired drivers now than in past

Table 1 (Continued).  
Substantial and Moderate Findings from Systematic Literature Review

	Substantial	Moderate
Marijuana Dose and Drug Interactions (p.103)	<p>Ingesting &gt; 10 mg THC leads to driving impairment</p> <p>Waiting at least 6 hrs after smoking &lt; 18 mg resolves/nearly resolves driving impairment</p> <p>Waiting at least 8 hrs after ingesting &lt; 18 mg resolves/nearly resolves driving impairment</p> <p>Time to peak blood [THC] up to four hours post oral ingestion</p> <p>Passive exposure does not lead to positive screen by urine or blood</p>	<p>Waiting at least 6 hrs after smoking &lt; 35 mg resolves/nearly resolves driving impairment</p>
Marijuana Use and Neurological, Cognitive, and Mental Health Effects (p.116)	<p>Impaired memory to at least 7 days abstinence (heavy users)</p> <p>Acute psychotic symptoms during intoxication</p>	<p>Depression [symptoms or diagnosis], (regular users)</p>
Marijuana Use and Respiratory Effects (p.125)	<p>Same carcinogens in marijuana smoke as tobacco smoke</p> <p>Chronic bronchitis with cough/wheeze/sputum</p> <p>Precancerous lesions in airways</p> <p>Acute use improves airflow</p>	<p>Heavy use increases airflow obstruction</p>
Marijuana Use and Injury (p.142)	<p>Increased MV crash risk</p> <p>THC level and MV crash risk</p> <p>Combined use with alcohol increases MV crash risk</p>	