

Marijuana Resources and Citations

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Addiction to Other Drugs (Gateway Effect)

<http://jama.jamanetwork.com/article.aspx?articleid=195839> .Individuals who used cannabis by age 17 years had odds of other drug use, alcohol dependence, and drug abuse/dependence that were 2.1 to 5.2 times higher than those of their co-twin, who did not use cannabis before age 17 years. Journal of the American Medical Association (JAMA). 2003. Escalation of Drug Use in Early-Onset Cannabis Users vs. Co-twin Controls. Lynskey PhD, Michael, et al. Pgs 427-433

Is Cannabis a Gateway drug? Testing Hypotheses about the relationship between cannabis use and the use of other illicit drugs. Hall, Wayne, et al. Drug and Alcohol Review: 2005, Vol 24, No. 1, Pages 39-48.

<http://informahealthcare.com/doi/abs/10.1080/09595230500126698>

Psychological Medicine; October 2004, pp 1227-1237; Cambridge University Press. A twin study of early cannabis use and subsequent use and abuse/dependence of other illicit drugs. ARPANA AGRAWAL ^{a1c1}, MICHAEL C. NEALE ^{a1}, CAROL A. PRESCOTT ^{a1} and KENNETH, S. KENDLER

<http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=255447&fileId=S0033291704002545>

Cannabis use and other illicit drug use: testing the cannabis gateway hypothesis:

<http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2005.01322.x/abstract;jsessionid=68FCB7AFE6988249DAD42D588499AE79.f01t01?systemMessage=Wiley+Online+Library+will+be+disrupted+9th+Aug+from+10-2+BST+for+essential+maintenance.+Pay+Per+View+will+be+unavailable+from+10-6+BST.&userIsAuthenticated=false&deniedAccessCustomisedMessage=>

Fergusson, David; Boden, Joseph; Horwood, L. John; Addiction: Volume 101, Issue 4, pages 556-569, April 2006;

Aim To examine the associations between the frequency of cannabis use and the use of other illicit drugs.

Design A 25-year longitudinal study of the health, development and adjustment of a birth cohort of 1265 New Zealand children.

Measurements Annual assessments of the frequency of cannabis use were obtained for the period 14–25 years, together with measures of the use of other illicit drugs from the same time period.

Findings The frequency of cannabis use was associated significantly with the use of other illicit drugs, other illicit drug abuse/dependence and the use of a diversity of other drugs. This association was found to be particularly strong during adolescence but declined rapidly as age increased. Statistical control for confounding by both fixed and time dynamic factors using random- and fixed-effects regression models reduced the strength of association between frequency of cannabis use and other illicit drug use, but a strong association between frequency of cannabis use and other illicit drug use remained even after control for non-observed and time-dynamic sources of confounding.

Conclusions Regular or heavy cannabis use was associated with an increased risk of using other illicit drugs, abusing or becoming dependent upon other illicit drugs, and using a wider variety of other illicit drugs. The risks of use, abuse/dependence, and use of a diversity of other drugs declined with increasing age. The findings may support a general causal model such as the cannabis gateway hypothesis, but the actual causal mechanisms underlying such a gateway, and the extent to which these causal mechanisms are direct or indirect, remain unclear.

Adolescent Health

PNAS Study: **“Persistent cannabis users show neuropsychological decline from childhood to midlife”**

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Accumulating evidence suggests that long-term, heavy cannabis use may cause enduring neuropsychological impairment— impairment that persists beyond the period of acute intoxication (2). Studies of long-term, heavy cannabis users fairly consistently show that these individuals perform worse on neuropsychological tests (2–5), and some (6–8) but not all (9) studies suggest that impairment may remain even after extended periods of abstinence. The magnitude and persistence of impairment may depend on factors such as the quantity, frequency, duration, and age-of-onset of cannabis use (2), as more severe and enduring impairment is evident among individuals with more frequent and prolonged heavy use and a younger age-of-onset (3, 6, 8, 10–16).

Corpus callosum damage in heavy marijuana use: Preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. *NeuroImage*; 2008; 41:1067-1074. Arnone, Barrick, Chengappa

1 in 6 Adolescents who try marijuana will become addicted to it (1 in 10 for adults). The adolescent brain is especially susceptible to marijuana use. When kids use, they have a greater chance of addiction since their brains are being primed. **Source:** Anthony, J.C., Warner, L.A., & Kessler, R.C. (1994); *Source: Giedd. J. N. (2004). Structural magnetic resonance imaging of the adolescent brain. Annals of the New York Academy of Sciences, 1021, 77-85.*

The average reported past month marijuana use for young adults (ages 18-25) in 2011: The national average = **18.78 percent**. The Colorado average = **27.26 percent**. The average reported past month marijuana use for young adults (ages 18 – 25) in Colorado has increased from **21.43** percent in 2006 to **27.26** percent in 2011. That is a **27** percent increase. SOURCE: National Survey on Drug Use and Health (NSDUH) - Substance Abuse and Mental Health Services Administration

Adolescents who use marijuana have a 2-4 fold increase risk of developing psychosis and this risk is dose-dependent (Hall and Degenhardt, 2009)

Adolescents **who use marijuana heavily have up to an 8-point drop in IQ** and this risk is also dose-dependent (Meier et al., 2012)

Marijuana, especially high potency marijuana, may cause acute anxiety attacks and psychosis (Hall and Degenhardt, 2009). **MJ accounted for 461,028 ED visits in 2012** (DAWN, 2013). Symptoms of withdrawal include anxiety and depression (Budney et al., 2002).

Controlling for other possible confounds, **those who use marijuana are twice as likely to have had a suicide attempt requiring hospitalization** (Hall and Degenhardt, 2009).

Marijuana withdrawal causes a doubling in aggressive episodes compared to controls (Kouri et al., 1999; Smith et al., 2013).

Death of Levi Pongi: "...Police reports released Thursday said 19-year-old Levy Thamba Pongi consumed a little more than one cookie that his friend purchased from a pot shop...An autopsy report from the **March 11 incident lists marijuana intoxication as a significant contributing factor in the death.**" Associated Press, April 17, 2014; 250 drug panel screen – only substance present in system was THC.

Cannabis use in college students with psychiatric disorders is high and appears to have a significantly greater negative impact on function in this population, new research suggests. Overall, 25% of the study sample was on leave from college. However, the investigators found that those with cannabis use disorder were significantly more likely to be on leave compared with their counterparts who did not have a cannabis use disorder — 46% vs 13%. American Psychiatric Association's 2014 Annual Meeting. Abstract NR7-1 Presented May 6, 2014. <http://www.medscape.com/viewarticle/824878>

Young adults who used marijuana only recreationally showed significant abnormalities in two key brain regions that are important in emotion and motivation, scientists report. It showed the degree of brain abnormalities in these regions is directly related to the number of joints a person smoked per week. Scientists examined regions for emotion and motivation, and associated with addiction – “People think a little recreational use shouldn’t cause a problem, if someone is doing OK with work or school. Our data directly says this is not the case.” SOURCE: www.northwestern.edu/newscenter/stories/2014/04/casual-marijuana-use-linked-to-brain-abnormalities-in-students.html#sthash.3bY7IXtZ.dpuf The study was published April 16 in the Journal of Neuroscience. - See more at: <http://www.northwestern.edu/newscenter/stories/2014/04/casual-marijuana-use-linked-to-brain-abnormalities-in-students.html#sthash.3bY7IXtZ.dpuf>

Cancer

The intersection between cannabis and cancer in the United States. Bowles D. et al. Critical Reviews in Oncology Hematology 2012; 83:1-10. This is an excellent review written by Dr. Daniel Bowles from the University of Colorado School of Medicine at the Anschutz Medical Campus. Although much of this review deals with the efficacy of medical marijuana on symptoms in the cancer patient, it also nicely summarizes the evidence of connections between marijuana use and risk of getting cancer. Cannabinoids are not carcinogenic, but marijuana smoke contains many hundreds of combustion products that could increase cancer risk. Some epidemiologic studies have suggested increased risk for lung cancer, while others have not. Although it is hard to separate-out effects of tobacco from those of marijuana, research do date suggests that marijuana smoke is substantially less carcinogenic than tobacco.

The association between marijuana smoking and lung cancer. A systematic review. Mehra R. et al. Archives of Internal Medicine 2006; 166:1359-67. From this review of 19 studies on this question, there is not a pattern suggesting marijuana causes lung cancer, but studies do show increased inflammation of bronchial mucosa, so there is a biologic basis for concern.

Marijuana use and risk of lung cancer: a 40-year cohort study. Callaghan R et al. Cancer Causes and Control 2013;24:1811-1820. This is a single study, included here because it is both recent and large, though an earlier study of about this same size was null. This is a follow-up of about 50,000 military recruits in Sweden. Heavy marijuana use at the time of recruitment (1.7% of the cohort) was found to be associated with a 2.1-fold increased risk of lung cancer after 40 years, after adjusting for baseline tobacco use. Lower levels of marijuana use were not associated with increased risk. It is important to note that there was no assessment of tobacco cessation over time, so any association between heavy marijuana use and persistent tobacco use would confound the marijuana association.

Association of marijuana smoking with oropharyngeal and oral tongue cancers: Pooled analysis from the INHANCE Consortium. Marks M et al. Cancer Epidemiology, Biomarkers, and Prevention 2013; 23:160-71. The pooled analysis of 1,921 oropharyngeal cancer cases, 356 tongue cancer cases, and 7,639 controls found a 24% higher risk for oropharyngeal cancer, but no increased risk (actually 53% lower risk) for tongue cancer. After adjusting for potential human papilloma virus infection (a major risk factor for oropharyngeal cancer) the association with marijuana disappeared. Although this is interpreted by the authors as evidence that cannabinoids may be both pro-carcinogenic and anti-carcinogenic, it is probably best regarded as evidence that any association between cannabis use and increased risk of cancers in the mouth would be quite small.

Child Exposures to Marijuana

Pediatric marijuana exposures in a medical marijuana state. Wang GS. JAMA Pediatrics 2013; 167:630-33. This is a timely report by George Sam Wang about increases noted in unintentional marijuana poisonings showing up in the emergency department of Childrens' Hospital Colorado subsequent to the legalization of medical marijuana in Colorado in 2009. See also accompanying editorials in this same issue of JAMA Pediatrics by Sharon Levy from Harvard (pp 60-61) and William Hurley from Seattle (pp 602-603) commenting on the potentially large impact on children of more widely available cannabis products in homes.

Association of unintentional pediatric exposures with decriminalization of marijuana in the United States. Wang GS et al. Annals of Emergency Medicine 2014; 63:1450-55. This is an analysis of national data from poison control centers, showing that although unintentional marijuana ingestion is uncommon, it has increased more in states that have legalized medical marijuana than in states that have not over time.

Drug Dependency

Cannabis use disorder: epidemiology and management. Copeland J et al. International Review of Psychiatry. 2009;21:96-103. Although cannabis is not addictive it can induce dependency. This is a review of the definition and treatment of cannabis use disorder. Estimates are that about 1% of US adults meet the definition of

cannabis dependence in the previous year. There are not any medications shown to be helpful for treatment, but brief cognitive behavioral therapy seems to help.

Actions of delta-9-tetrahydrocannabinol in cannabis: relation to use, abuse, dependence. Cooper Z et al. *International Reviews Psychiatry*. 2009; 21:104-112. This is a very technical review that largely covers animal model systems and brain neurochemistry. Although this evidence is not easily applicable to human clinical behavior, it is a good basic science summary of the neurologic effects of cannabinoids that are relevant to dependency and withdrawal.

Primary prevention of cannabis use: A systematic review of randomized controlled trials. Norberg M et al. *PLOS ONE* 2013; 8:e53187. This review included 49 studies. Overall, effects of interventions for preventing marijuana use were characterized as “trivial to small”. Programs that were more universal and more multi-modal were superior to more focused programs. The review criticized much of the research as difficult to evaluate, but concluded that there is not yet any compelling evidence that marijuana prevention programs have any substantial effects.

Reversible and regionally selective down regulation of brain cannabinoid CB1 receptors in chronic daily cannabis smokers, Jussi Hirvonen, MD, PhD1, Robert S. Goodwin, DO, PhD2, Cheng-Ta Li, MD1, Garth E. Terry, PhD1, Sami S. Zoghbi, PhD1, Cheryl Morse, MSc1, Victor W. Pike, PhD1, Nora D. Volkow, MD3, Marilyn A. Huestis, PhD2*, Robert B. Innis, MD, PhD1* Molecular Imaging Branch, National Institute of Mental Health, NIH, Bethesda, MD; Chemistry and Drug Metabolism Section and Director, National Institute on Drug Abuse, NIH, Baltimore, MD

Abstract: Chronic cannabis (marijuana, hashish) smoking can result in dependence. Rodent studies show reversible downregulation of brain cannabinoid CB1 receptors after chronic exposure to cannabis. However, whether downregulation occurs in humans who chronically smoke cannabis is unknown. Here we show, using positron emission tomography (PET) imaging, reversible and regionally selective down-regulation of brain cannabinoid CB1 receptors in human subjects who chronically smoke cannabis. Downregulation correlated with years of cannabis smoking and was selective to cortical brain regions. After about four weeks of continuously monitored abstinence from cannabis on a secure research unit, CB1 receptor density returned to normal levels. This is the first direct demonstration of cortical cannabinoid CB1 receptor downregulation as a neuroadaptation that may promote cannabis dependence in human brain.

Marijuana accounted for 4.5 million of the 7.1 million Americans dependent on or abusing drugs. In 2009 approx. 18% of people 12 and older entering drug abuse treatment programs reported MJ as their primary drug of abuse. 61% of person under age 15 reported MJ as their primary drug of abuse. 2010 National Study on Drug Use and Health (NSDUH). Center for Behavioral Health Statistics and Quality.

<https://nsduhweb.rti.org/respweb>

LINKS: <http://www.webmd.com/mental-health/addiction/marijuana-use-and-its-effects>

General Health

Marijuana: current concepts. Greydanus A. et al. *Frontiers in Public Health* 2013; 1:1-17.

This is really a more general overview paper about cannabis but it emphasizes mental health issues more than other issues, so it is best regarded as a cannabis and mental health review.

The pharmacologic and clinical effects of medical cannabis. Borgelt L et al. *Pharmacotherapy* 2013; 33:195-209. This is an excellent non-systematic review written by Dr. Laura Borgelt from the Skaggs School of Pharmacy at the Anschutz Medical Campus. Although this review focuses on medical marijuana, it is an excellent summary of cannabis pharmacology and toxicology, including a summary of evidence on potential adverse health effects.

The global epidemiology and contribution of cannabis use and dependence to the global burden of disease: Results from the GBD 2010 Study. Degenhardt L et al. *PLOS ONE* 2013. 8:e76635. This is only one aspect of a much larger study, the Global Burden of Disease Study, funded by the Gates Foundation. This aspect reviewed the literature on health effects of cannabis use and concluded there were two meaningful hazards: **dependence per se as an adverse outcome, and contribution to schizophrenia risk.** The size of the impact on schizophrenia was tiny (only .04% of all schizophrenia being caused by cannabis), but the size of the impact on dependence was larger (about 0.2% of the North American population).

Does cannabis use increase the risk of death? Systematic review of epidemiologic evidence on adverse effects of cannabis use. Calabria B et al. *Drug and Alcohol Review* 2010; 29:318-30. This systematic review of all studies linking mortality to cannabis use was based on 19 studies. The data presentation and discussion are not particularly enlightened. They concluded mostly that evidence was inconclusive except for death from traffic crashes, and that better long-term cohort studies are needed.

The adverse health effects of chronic cannabis use. Hall W et al. *Drug Testing and Analysis* 2013. 6:39-45. This is a general review of adverse health effects associated with chronic use. Although this paper is not very systematically written and is inferior to the other general reviews in terms of its scientific quality, it is included here because it is succinct and recent.

Drug Abuse Warning Network: National Estimates of Drug-Related Emergency Department Visits SAMHSA. (2013). Rockville, MD: Substance Abuse and Mental Health Safety Administration. Marijuana is the #1 substance listed as reason for ED visits over any other substances combined

Evidence on the carcinogenicity of marijuana smoke. 2009. California Environmental Protection Agency. Tomar, Rajpal PhD, et al. 3x the carcinogens of tobacco cigarettes. Studies reporting results for direct marijuana smoking have observed **statistically significant associations with cancers of the lung, head and neck, bladder, brain, and testis.** The strongest evidence of a **causal association was for head and neck cancer,** with two of four studies reporting statistically significant associations. The evidence was **less strong but suggestive for lung cancer, with one of three studies conducted in populations that did not mix marijuana and tobacco reporting a significant association. Suggestive evidence also was seen for bladder cancer,** with one of two studies reporting a significant association. For **brain and testicular cancers, the single studies conducted of each of these endpoints reported significant associations.**

NHTSA: Side Effect Profile: Fatigue, paranoia, possible psychosis, memory problems, depersonalization, mood alterations, urinary retention, constipation, decreased motor coordination, lethargy, slurred speech, and dizziness. Impaired health including lung damage, behavioral changes, and reproductive, cardiovascular and immunological effects have been associated with regular marijuana use. Regular and chronic marijuana smokers may have many of the same respiratory problems that tobacco smokers have (daily cough and phlegm, symptoms of chronic bronchitis), as the amount of tar inhaled and the level of carbon monoxide

absorbed by marijuana **smokers is 3 to 5 times greater than among tobacco smokers**. Smoking marijuana while shooting up cocaine has the potential to cause severe increases in heart rate and blood pressure.

<http://www.nhtsa.gov/people/injury/research/job185drugs/cannabis.htm>

Child Welfare endangerment case: Drug use, fire danger documented as risks in Sterling home where toddler Levi Welton died in fire. Levi was found dead Monday by firefighters, Jan 18, 2014.

<http://www.thedenverchannel.com/news/call7-investigators/drug-use-fire-danger-documented-as-risks-in-sterling-home-where-toddler-levi-welton-died-in-fire>

Recommended Source Studies from NHTSA website (Includes various topics of cross-over subjects):

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- Heishman SJ. Effects of abused drugs on human performance: Laboratory assessment. In: *Drug Abuse Handbook*. Karch SB, ed. New York, NY: CRC Press, 1998, p219.
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- Huestis MA, Henningfield JE, Cone EJ. Blood cannabinoids II: Models for the prediction of time of marijuana exposure from plasma concentrations of Δ -9-tetrahydrocannabinol (THC) and 11-nor-9-carboxy- Δ -9-tetrahydrocannabinol (THC-COOH). *J Anal Toxicol* 1992;16(5):283-90.
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- Varma VK, Malhotra AK, Dang R, Das K, Nehra R. Cannabis and cognitive functions: a prospective study. *Drug Alcohol Depend* 1988;21(2):147-52.
- WHO Division of Mental Health and Prevention of Substance Abuse: Cannabis: a health perspective and research agenda. World Health Organization 1997.

CNN: Dr. Gitlow regarding marijuana "safety" and the harm in legalizing a harmful drug:
http://www.cnn.com/2014/07/30/opinion/gitlow-marijuana-use/index.html?hpt=hp_c3

Heart Disease

At the heart of the matter: the endocannabinoid system in cardiovascular function and dysfunction.

Montecucco, F et al. *Trends in pharmacological sciences* 2012; 33:331-40. This is a very technical and dense article that explains the functioning of the endocannabinoid system, which has complex regulatory functions in various parts of the body, including the brain and circulatory system. Although this is a very technical review, it does help in understanding the various neurologic and physiologic effects of cannabis as reviewed in other papers.

Cannabinoids and atherosclerotic coronary heart disease. Singla, S et al. *Clinical Cardiology* 2012; 35:329-35. This is also a technical review, including many details of molecular biology. It nicely covers the questions of effects of cannabinoids on various conditions, such as blood pressure, insulin resistance, and circulating lipid levels. The acute increases in heart rate and blood pressure are correlated with increased myocardial infarction risk in the first hour after use among those with pre-existing coronary artery disease. The authors also discuss the apparent paradox observed in from animal studies of adverse acute effects but beneficial long-term effects on cardiovascular disease risk.

Effect of blockage of the endocannabinoid system by CB1 antagonism on cardiovascular risk. Mach F et al. *Pharmacological Reports* 2009; 61:13-21. This is other review of the physiology of the endocannabinoid system, explaining its effects on blood pressure, glucose metabolism, lipid metabolism, and immune function from the perspective of the documented effects from randomized controlled trials using rimonabant, a cannabinoid receptor antagonist. This drug has multiple beneficial effects, including on weight loss, blood pressure, insulin sensitivity, and lipids, but it has not been approved for use because of a high rate of neurologic side effects (nausea and dizziness).

Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: What cardiologists need to know. Am J Cardiology 2014; 113:187-190. This is only an average-quality review, not very systematic in approach, but included here as a general review since it is recent.

Marijuana and long-term mortality among survivors of acute myocardial infarction. Frost L. et al. Am Heart J 2013;165:170-5. This is a single cohort study of about 3900 survivors of an MI who were followed for 18 years for mortality. There were 22 deaths among the 109 who reported using marijuana at some time during the year before their MI. This was a rate of death that was 29% higher than among who did not report marijuana use, though it was not a statistically significant increase.

Triggering myocardial infarction by marijuana. Mittleman M et al. Circulation 2001; 103:2805-2809. This is a case-only analysis of timing of marijuana use prior to myocardial infarction in 3882 people with a recent myocardial infarction. Marijuana use was reported by only 124 patients (3.9%), and 9 patients reported use in the hour prior to onset of symptoms (0.2%). Although that number was small, the expected number based on usage probability by chance alone was only about 2 people, thus producing an estimate of a 4-fold increase in MI risk acutely after use. This is a figure that is often repeated in literature on the hazards of marijuana use.

Marijuana use may increase heart complications in young, middle-aged adults April 23, 2014

<http://newsroom.heart.org/news/marijuana-use-may-increase-heart-complications-in-young-middle-aged-adults>

“Marijuana use may result in cardiovascular-related complications — even death — among young and middle-aged adults, according to a French study reported in the *Journal of the American Heart Association*”. “There is now compelling evidence on the growing risk of marijuana-associated adverse cardiovascular effects, especially in young people,”

Lasting Effects of Impairment

Carry-over Effects of Marijuana Intoxication on Aircraft Pilot Performance. Yesavage, J., Leirer, V., Denari, M., & Hoillister, L. (1985). *American Journal of Psychiatry*, 142(11):1325-9. Pilots smoked marijuana in a controlled study and were tested at various intervals afterward. 24 hours after ingesting marijuana participants crashed flight simulators, but most did not “feel” impaired. Study showed they were impaired, contrary to how they reported feeling.

Psychomotor Function in Chronic Daily Cannabis Smokers during Sustained Abstinence

Wendy M. Bosker¹, Erin L. Karschner², Dayong Lee², Robert S. Goodwin², Jussi Hirvonen³, Robert B. Innis³, Eef L. Theunissen¹, Kim P. C. Kuypers¹, Marilyn A. Huestis², Johannes G. Ramaekers^{1*}.

¹ Departments of Neuropsychology and Psychopharmacology, Maastricht University, Maastricht, The Netherlands, ² Chemistry and Drug Metabolism, Intramural Research Program, National Institute on Drug Abuse, National Institute of Health, Baltimore, Maryland, United States of America, ³ Molecular Imaging Branch, National Institute of Mental Health, National Institute of Health, Bethesda, Maryland, United States of America. Sustained cannabis abstinence moderately improved critical tracking and divided attention performance in chronic, daily cannabis smokers, but impairment was still observable compared to controls after 3 weeks of abstinence. Between group differences, however, need to be interpreted with caution as chronic smokers and controls were not matched for education, social economic status, life style and race.

Citation: Bosker WM, Karschner EL, Lee D, Goodwin RS, Hirvonen J, et al. (2013) Psychomotor Function in Chronic Daily Cannabis Smokers during Sustained Abstinence. PLoS ONE 8(1): e53127. doi:10.1371/journal.pone.0053127 Editor: Michael Taffe, The Scripps Research Institute, United States of America Received August 30, 2012; Accepted November 27, 2012; Published January 2, 2013 Copyright: © 2013 Bosker et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Lung Diseases

Marijuana and lung diseases. Joshi M et al. *Current Opinions in Pulmonary Medicine*. 2014; 20: online publication. This is a good review. They conclude that despite short-term benefits of cannabis smoking for bronchial dilation, there are potential long-term adverse effects tied to increased inflammation. Chronic marijuana smokers have about a 2-fold increased risk for chronic cough, and bronchial biopsies show clear evidence for increased inflammation. To date no convincing adverse effects have been seen for chronic obstructive pulmonary disease (COPD) or lung cancer, but there are biologic bases for concern for those conditions.

Effects of smoking cannabis on lung function. Lee M. et al. *Expert Rev. Resp. Med.* 2011; 5:537-47. There are short-term benefits of cannabis smoking for bronchial dilation, but potential long-term adverse effects from increased inflammation. It is hard to separate the effects of cannabinoids from the many other constituents of inhaled smoke. There does not seem to be a link between marijuana use and risk for COPD. The review concludes by stating that harm to the lungs is substantially greater from tobacco than from marijuana.

Association between marijuana exposure and pulmonary function over 20 years. Pletcher M et al. *JAMA* 2012; 307:173-181. This is a single cohort study, but one that was very well done and quite recent. They measured pulmonary function in the CARDIA cohort of about 5000 men over 20 years. There was no association between marijuana smoking and declines in lung function, though the expected declines were clearly seen with tobacco smoking.

Effects of Marijuana Smoking on the Lung. Tashkin. *Annals of the American Thoracic Society*, 2013, 10: 239–247. This is the most recent narrative review of research on the effects of marijuana smoking on the lung. It makes the same points covered by Lee et al.

LINKS:

<http://www.lung.org/associations/states/colorado/tobacco/marijuana.html>

Medical Association Positions

[APA Position Statement on Marijuana as Medicine:](#)

“There is no current scientific evidence that marijuana is in any way beneficial for the treatment of any psychiatric disorder. In contrast, current evidence supports, at minimum, a strong association of cannabis use with the onset of psychiatric disorders. Adolescents are particularly vulnerable to harm, given the effects of cannabis on neurological development.” American Psychiatric Association

[ASAM Public Policy Statement on Medical Marijuana:](#)

“ASAM asserts that cannabis, cannabis-based products, and cannabis delivery devices should be subject to the same standards that are applicable to other prescription medications and medical devices and that these products should not be distributed or otherwise provided to patients unless and until such products or devices have received marketing approval from the Food and Drug Administration. ASAM rejects smoking as a means of drug delivery since it is not safe. ASAM rejects a process whereby State and local ballot initiatives approve medicines because these initiatives are being decided by individuals not qualified to make such decisions.”

American Society of Addiction Medicine

[American Medical Association](#)

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 consequences of long-term cannabis use through concentrated research, especially among youth and adolescents [...] Our AMA believes that (1) cannabis is a dangerous drug and as such is a public health concern.”

[Medical Journal Articles](#)

[Causal association between cannabis and psychosis: examination of the evidence](#) by Louise Arseneault, Mary Cannon, John Witton and Robin M. Murray in the British Journal of Psychiatry. On an individual level, cannabis use confers an overall twofold increase in the relative risk for later schizophrenia. At the population level, elimination of cannabis use would reduce the incidence of schizophrenia by approximately 8%, assuming a causal relationship. Cannabis use appears to be neither a sufficient nor a necessary cause for psychosis. It is a component cause, part of a complex constellation of factors leading to psychosis. Cases of psychotic disorder could be prevented by discouraging cannabis use among vulnerable youths. Research is needed to understand the mechanisms by which cannabis causes psychosis.

[Psychiatric effects of cannabis](#) by Andrew Johns in the British Journal of Psychiatry.

An appreciable proportion of cannabis users report short-lived adverse effects, including psychotic states following heavy consumption, and regular users are at risk of dependence. People with major mental illnesses such as schizophrenia are especially vulnerable in that cannabis generally provokes relapse and aggravates existing symptoms. Health workers need to recognise, and respond to, the adverse effects of cannabis on mental health.

[Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review](#) by Theresa HM Moore, et al. in The Lancet. The evidence is consistent with the view that cannabis increases risk of psychotic outcomes independently of confounding and transient intoxication effects, although evidence for affective outcomes is less strong. The uncertainty about whether cannabis causes psychosis is unlikely to be resolved by further longitudinal studies such as those reviewed here. However, we conclude that there is now sufficient evidence to warn young people that using cannabis could increase their risk of developing a psychotic illness later in life.

[Adverse Reactions to Marijuana — Classification and Suggested Treatment](#) by Andrew T. Weil in the New England Journal of Medicine. Adverse acute reactions to marijuana are infrequent, but physicians will see more of them as use of the drug increases and reaches new areas of society. Several very distinct types of reactions occur. In persons without a history of mental disorder who have never taken hallucinogenic drugs, marijuana may cause simple depressive reactions, panic reactions (most common) and toxic psychoses. In persons who have previously taken hallucinogens, marijuana may also trigger recurrences of hallucinogenic

effects and may occasionally precipitate delayed psychotic reactions. Finally, in ambulatory schizophrenics, marijuana can cause atypical reactions, frequently marked by derealization. Most of these reactions are self-limited and benign but can be worsened by improper medical management. A few require psychiatric and psychopharmacologic intervention.

Medical Marijuana Issues of Concern

Majority of medical marijuana users report using marijuana to treat ‘chronic or severe pain.’ Source: Colorado Department of Public Health and Environment, 2011; Oregon Public Health Authority, 2011; Montana Department of Public Health and Human Services, 2011

- 96% in Colorado
- 91% in Oregon
- 93% in Montana

After the Compassionate Use Act passed in California in 1996, Allen St. Pierre, the director of NORML admitted in a TV interview that **“in California, marijuana has also been *de facto* legalized under the guise of medical marijuana”** Source: CNN Newsroom 9 May 2009

Source: Emory Wheel Entertainment Staff, 6 February 1979; **“We will use [medical marijuana] as a red-herring to give marijuana a good name.”** —Keith Stroup, *head of NORML to the Emory Wheel, 1979.* Dose? Duration? Patient focused? Know the difference between legitimate cannabis based medicine vs. the medical marijuana movement and industry

In Colorado, 2% reported cancer, less than 1% reported HIV/AIDS, and 1% reported glaucoma as their reason for using medical marijuana. In Oregon, these numbers are less than 4%, 2%, and 1%, respectively. Source: Colorado Department of Public Health and Environment, 2011; Oregon Public Health Authority, 2011

California MMJ: 32-year old white male ; history of alcohol and substance abuse; no history of life-threatening illnesses; Source: O’Connell, T.J. & Bou-Matar, C.B., 2007.

<http://www.harmreductionjournal.com/content/4/1/16> . 87.9% had tried marijuana before age 19; 75% of Caucasian patients had used cocaine and 50% had used methamphetamine in their lifetime.

COLORADO “Medicine” Free Joint Friday for Females (Denver Dispensary ad) How does other medicine compare? If any local pharmacy was offering daily specials on prescription medicine – How would regulators, media, public health/medical officials, and the public react? Why the silence around the “medical” practices of the marijuana industry?

Residents of states with medical marijuana laws have abuse/dependence rates almost twice as high as states with no such laws. Source: Cerda, M., et al., 2012.

MMED Audit Reports Failures:

MEDICAL MARIJUANA REGULATORY SYSTEM, Performance Audit, March 2013

Department of Revenue, Dianne Ray, State Auditor

KEY FACTS AND FINDINGS

- The Division has taken an average of about 23 months to issue final licensing decisions on applications submitted by August 1, 2010, the effective date of a 2-year moratorium on new medical marijuana businesses. The shortest approval time was 436 days, while the longest approval time was 807 days. Of the original business license applications the Division received by August 1, 2010, 41 percent were still pending as of October 2012 and have not received final licensing decisions.
- For 13 (37 percent) of 35 new business application files we reviewed, we found evidence of potentially disqualifying information about the applicants. Ten licenses were issued, however four were questionable based on this evidence. At the time of our audit, the Division had not taken new occupational licensing appointments in the previous 6 months, which creates a burden because individuals cannot legally work at a medical marijuana business without a license.
- The envisioned “seed-to-sale” model for regulating Colorado’s medical marijuana industry does not currently exist. The Division planned to develop a marijuana plant tracking system, spent about \$1.1 million in Fiscal Years 2011 and 2012, but was unable to pay the remaining \$400,000 and implement the system due to financial difficulties. The Division reports that it will implement the system by the end of Calendar Year 2013.
- The Division does not use the prescribed statutory process when taking marijuana related to disciplinary actions against medical marijuana businesses. Additionally, the Division has inadequate controls to ensure that seized marijuana is destroyed properly.
- The Division has not developed a systematic process for setting fees that correspond to its costs of providing regulatory oversight.
- The Division laid off a majority of its staff in Fiscal Year 2012 due to revenue shortfalls. Specifically, in Fiscal Years 2011 and 2012, the Division experienced 19 consecutive months of net losses, including a loss of about \$2.3 million in June 2011 because of large capital purchases, such as furniture, computer equipment, and software for a marijuana plant tracking system. Weaknesses in the Division’s fee-setting, strategic planning, and expense controls contributed to its funding problems.
- The Department of Revenue did not identify all medical marijuana businesses in its sales tax system and underreported sales tax revenue generated by 56 dispensaries by about \$760,000 for Fiscal Years 2011 and 2012 combined.

In the fiscal year 2012 CO collected \$5.4 million in sales tax on “MMJ” purchases but experienced **\$5.7 million budget shortfall** because of regulatory expenses that could not be covered. Medical Marijuana Licensing. Denver: Office of the City Auditor, 2013. Dennis Gallagher.

Mental Health

Pathways from cannabis to psychosis: a review of the evidence. Burns J. *Frontiers in Psychiatry*. 2013; 4:128-1-12. This is a review of the co-existence of many different types of mental health issues and marijuana. Separating cause from effect in these relationships is hard, as early symptoms of mental illness can lead to use of drugs. Marijuana use is higher among adolescents who are later diagnosed with schizophrenia. Marijuana seems to shorten the time to psychosis. The authors provide a speculative model for cannabis effects on psychosis.

Structural and functional imaging studies in chronic cannabis users: A systematic review of adolescent and adult findings. Battalla A et al. *PLOS ONE* 2013; 8:e55821. This analysis reviews 43 studies, including 8 in adolescents. This very complex article shows several studies have found structural brain changes related to

chronic cannabis use, especially in areas of the brain that are rich in cannabinoid receptor like the hippocampus.

Cannabis use during adolescent development: susceptibility to psychiatric illness. Chadwick B. et al. *Frontiers of Psychiatry* 2013; 4:1-8. This review is not particularly systematic in style, but it does cover the question of brain development. Although it is quite technical on the endocannabinoid system, it documents the reasons for concern that because the adolescent brain is still in active development, drugs such as cannabinoids that alter development of brain signaling pathways and structures, and could thereby have adverse effects on brain development.

Persistent cannabis users show neuropsychological decline from childhood to midlife. Meier M et al. *PNAS (Proceedings of the National Academy of Sciences)* 2012; e2657-64. This is a cohort study of about 1000 New Zealanders followed from birth to age 38. Neurocognitive functioning was measured at age 13 then again at age 38. Although an association was found between marijuana use and cognitive decline, that decline was due to higher IQ scores at age 13 among those who would subsequently use marijuana. IQ scores at age 38 did not differ. Adolescent use had more effect on cognitive decline than did adult use. An accompanying editorial by Raul Gonzalez in that same issue reviews evidence to the contrary, but acknowledges that adolescence may be a particularly sensitive time for adverse effects on brain development.

Cannabis and psychosis: Have we found the missing links? Parakh P et al. *Asian J Psychiatry* 2013;6:281-7. This reviews the literature linking adolescent marijuana use to psychosis onset. This is a thoughtful discussion of the mechanisms of increased risk. They conclude that although marijuana itself may not be causal, it might accelerate the processes leading to psychosis among those who are otherwise susceptible.

The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies. Lev-Ran S et al. *Psychological Medicine* 2014; 44:797-810. This is a systematic review based on 14 cohort studies relating marijuana use to the onset of depression. There was a 17% increased risk for depression onset among all users. Among heavy users (defined as a cannabis use disorder or use at least weekly) risk was increased by 62%. There were no differences noted by age.

Changes in cannabis use among young people: impact on mental health. Copeland J et al. *Curr Opin Psychiatry* 2013;26:325-9. This is a general review summarizing the associations between cannabis use in adolescence and various mental health disorders.

Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: Historical cohort study. Zammit S et al. *BMJ*. 2002;325(7374):1199. Military conscripts who had used cannabis ten or more times by 18 years of age were 2-3 times more likely to later be diagnosed with schizophrenia than those who had not.

Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review. Moore T et al. *Lancet*. 2007;370(9584):319-328. This meta-analysis of longitudinal studies reported a pooled estimate of 40% increased risk of psychotic symptoms or psychotic disorders in those who had ever used cannabis.

Cannabis and anxiety and depression in young adults: A large prospective study. Hayatbakhsh M et al. *J. Am. Acad. Child Adolesc. Psychiatry*. 2007;46(3):408-417. Among about 3200 Australian children followed longitudinally, those who used marijuana in adolescence were 3.4 times more likely to have anxiety disorders.

Does cannabis use predict the first incidence of mood and anxiety disorders in the adult population?

VanLaar M et al. *Addiction*. 2007;102(8):1251-1260. Among a cohort of 3800 adults in the Netherlands, risk for depression and anxiety was increased by 60% among marijuana users. Jan Copeland, Saul Gerber and Wendy Swift., J.; Gerber, Saul; Swift, Wendy (2006). *Evidence-based answers to cannabis questions: a review of the literature*. ANCD Research Paper. Canberra: Australian National Council on Drugs. 1987 study from Sweden published in the British journal *Lancet*. Researchers did a 15-year examination of 45,570 military conscripts and found that those who had used marijuana on more than 50 occasions **had a six-fold** risk for developing schizophrenia relative to non-users

Moore TH, Zammit S, Lingford-Hughes A, et al. **Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review**. *Lancet* 370(9584):319–328, 2007. Also Large, M., Sharma S, Compton M., Slade, T. & O., N. (2011). Cannabis use and earlier onset of psychosis: a systematic meta-analysis. *Archives of General Psychiatry*. 68. Also see Arseneault L, et al. (2002). Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *British Medical Journal*. 325, 1212-1213. Since 2002, almost a dozen studies have shown that regular use of marijuana carries a **significant increased risk** of developing psychotic illnesses like schizophrenia. Higher risk for: Those with a family history of the disorders. Those with a psychosis-prone personality. Those who start using in early adolescence. Risks increase with potency and frequency of use

Potency

Increasing Delta-9-Tetrahydrocannabinol (Delta-9-THC) Content in Herbal Cannabis Over Time: Systematic Review and Meta-Analysis: *Current Drug Abuse Reviews*, 2012, 5, 32-401874-4737/12 © 2012 Bentham Science Publishers Fidelia Cascini, Carola Aiello and GianLuca Di Tanna, 1Istituto di Medicina Legale, Università Cattolica del S. Cuore, largo F. Vito, 1 00168 Roma, Italy, 2Department of Informatics and Systemics, University 'La Sapienza', 00185 Rome, Italy, 3Department of Public Health and Infectious Diseases, University "La Sapienza", 00185, Rome, Italy

Abstract: Aim: The objective of this meta-analysis is to assess the data regarding changes in herbal cannabis potency over time (from 1970 to 2009).

Methods: Systematic searches of 17 electronic scientific databases identified studies on this topic, within which 21 case series studies satisfied our inclusion criteria of reporting the mean tetrahydrocannabinol (THC) value per number of samples per year. No language, publication date, publication type or status restrictions were imposed. The study selection and data extraction processes were performed independently but uniformly by two authors, included screening, determination of eligibility and inclusion of the eligible studies in the systematic review, and a meta-analysis of the results on THC content in herbal cannabis samples. We considered papers and not monographic scientific publications, rejecting all studies that were not focused on the subject of this review.

Results: Meta-analysis by year was performed on 21 studies containing 75 total mean THC observations from 1979 to 2009 using the random effects model. The results revealed much variability between studies. Further, there was a significant correlation between year and mean THC in herbal cannabis. The combined data indicated the correlation between year and mean THC in herbal cannabis, revealing a temporal trend of increasing potency (5% above the mean THC value in the Poisson regression analysis).

Conclusions: The results of the analysis suggest that there has been a recent and consistent increase in cannabis potency worldwide.

CNBC Dabs - <http://www.cnbc.com/id/101445332>

USA TODAY Edibles - <http://www.usatoday.com/story/news/nation/2014/05/08/marijuana-pot-edibles-thc-legalized-recreational/8463787/>

WSJ Edibles - <http://online.wsj.com/articles/colorado-grapples-with-risks-from-edible-marijuana-1399675707>

Law enforcement from neighboring states agree, Colorado has strongest marijuana in the world. By [Garrison Wells](#) April 14, 2014. <http://gazette.com/law-enforcement-from-neighboring-states-agree-colorado-has-strongest-marijuana-in-the-world/article/1518194#TxA0JLQJs0k7wobD.99>

Vape Pens:

“This is the wave of the future.” whichever (vapor) pen you get, it will produce almost scentless vapor and can be hit easily in a bathroom or on the street. “I like to be able to smoke when I want...Being in Colorado, I can smoke it anywhere – it’s so discreet.” (quotes from Joshua Thomas who oversees Colorado warehouse of Gotvape.com). *The Ipod of Getting Baked*, Rolling Stone, June 20, 2013

Since our first vaporizer buyer's guide in 2011, a plethora of new pen-sized vapes have hit the market – **offering cannabis consumers a stealthy, convenient way to get high in almost any location or situation.”** High Times Magazine March 28, 2013

In California – ABC News highlights Colorado’s celebration/promotion of potent marijuana while California works to control potent marijuana. <http://abcnews.go.com/Nightline/video/wax-colorado-embraces-drug-22693499>

Students Find Way To Secretly Smoke Marijuana In Class. February 5, 2014 10:10 PM LAKEWOOD, Colo. (CBS4)

Pregnancy and Breast Feeding

Cannabis, the pregnant woman, and her child: weeding out the myths. Jaques S et al. J. of Perinatology 2014; 1-8. This is a non-systematic review of various issues tied to cannabis exposures in utero or during lactation. There is no compelling evidence suggesting cannabis causes birth defects or that it is associated with poor birth outcomes, but cannabis does easily cross the placental barrier and is excreted in milk, so there is reason to believe that cannabis may interfere with brain development of the fetus and/or the infant.

Prenatal cannabis exposure and infant outcomes: Overview of studies. Huizink AC. Prog Neuropsychopharmacol Biol Psychiatry. 2013; [Epub ahead of print] This review presents detailed information about three prospective longitudinal studies on prenatal cannabis exposure, including the Generation R study. Preclinical studies and potential mechanisms for marijuana’s effects are also described.

Effect of prenatal marijuana exposure on the cognitive development of offspring at age three, Day NL, Richardson GA, Goldschmidt L, et al. Neurotoxicol. Teratol. 1994;16(2):169-175. Among 655 children examined at age 3 those who had been exposed in utero to marijuana tested lower on the Stanford-Binet test of intelligence.

Effects of prenatal marijuana exposure on child behavior problems at age 10. Goldschmidt L, Day NL, Richardson GA. *Neurotoxicol. Teratol.* 2000;22(3):325-336. This follow-up examination of the cohort above (reference 3) found that at age 10 the children who had been exposed to marijuana in utero had intelligence tests that were not different from children unexposed, but they had more of a tendency to have hyperactivity disorders.

Maternal cannabis use and birth weight: A meta-analysis English DR, Hulse GK, Milne E, Holman CDJ, Bower CI. *Addiction.* 1997;92:1553-1560. This is a meta-analysis of 5 studies done at that time showing considerable heterogeneity in findings. The overall relative risk for low birthweight with marijuana use in pregnancy was 1.09 (not statistically significant). The conclusion was that the overall evidence is inconclusive.

Maternal use of cannabis and pregnancy outcome. Fergusson DM, Horwood LJ, Northstone K. *BJOG: An International Journal of Obstetrics & Gynaecology.* 2002;109:21-27. This is a cohort of about 12,000 women, about 5% of whom reported cannabis use before and/or during pregnancy. Cannabis use in pregnancy was associated with lower birth weights, but that relationship was largely confounded by other factors. The adjusted difference in birth weights was 90 grams (not a statistically significant difference in that study).

Prenatal cannabis exposure and infant outcomes: Overview of studies. Prog. Neuropsychopharmacol. Biol. Psychiatry. Huizink AC. 2013. This is a review of three prospective studies. Cannabis use early in pregnancy resulted in reduced fetal growth, but there is not a consistent pattern of adverse neurological or cognitive outcomes in the early period of life.

A literature review of the consequences of prenatal marijuana exposure: an emerging theme of a deficiency in aspects of executive function. Fried P et al. *Neurotoxicol. Teratol.* 2001;23:1-11.

At 12 years of age, children who were exposed to cannabis did not differ on full-scale intelligence quotient (IQ) scores from those not exposed, but there were small differences in higher cognitive processes (eg, perceptual organization and planning).

Smoking tobacco or marijuana, taking prescription painkillers, or using illegal drugs during pregnancy is associated with double or even triple the risk of stillbirth, according to research funded by the National Institutes of Health. SOURCE: *NIH press release, Tobacco, drug use in pregnancy can double risk of stillbirth, December 11, 2013*

Signs and Symptoms of Use

Comprehensive List: <http://www.nhtsa.gov/people/injury/research/job185drugs/cannabis.htm>

Stroke

Cannabis-related stroke. Myth or reality? Wolff V. et al. *Stroke* 2013; 44:558-63.

This review addresses the question of co-occurrence of strokes and marijuana use, whether this is a causal connection or only coincidental. This paper reviews 59 case reports in the medical literature in which strokes occurred following marijuana use. As cases are reported only when they are unusual, it is important to note that this series is young, with an average age of 33. There is some evidence that a condition similar to

Reversible Cerebral Vasoconstriction Syndrome (RCVS) may be induced by cannabis and may account for some of these strokes. The author concludes that the co-occurrence of strokes and cannabis use reflects a causal connection between the two caused by reversible cerebral narrowing, but the scientific evidence supporting causality is not clear-cut. See also their subsequent response to a critical letter in *Stroke*, 44:e57.

Cannabis, ischemic stroke, and transient ischemic attack: A case-control study. Barber P. et al. *Stroke* 2013; 44:2327-29. Among 218 consecutive patients ages 18-55 who were admitted to a single New Zealand hospital for ischemic stroke or TIA, 15% tested positive for cannabis in their urine, compared to 8% of people admitted for other reasons. Risk for stroke or TIA was increased 2.3-fold, but marijuana smokers were also more likely to smoke tobacco, so after adjustment for tobacco use risk was only 59% higher (and not a statistically significant increase). This study provides weak evidence in support of the idea that cannabis increases stroke risk.

Traffic Safety

Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. Asbridge M et al. *British Medical Journal* 2012; 344:e536.

This meta-analysis is based on 9 studies, showing a 1.9-fold increased risk for all crashes, and a 2.1-fold increased risk for fatal crashes.

Marijuana use and motor vehicle crashes. Mu-Chen L. et al. *Epidemiologic Reviews* 2012; 34:65-72.

This meta-analysis of 9 studies produced an overall estimate of a 2.7-fold increased risk for car crashes with cannabis use, and a dose-response relationship of higher risk with higher levels of cannabis in the blood.

Risk of road accident associated with the use of drugs: A systematic review and meta-analysis of evidence from epidemiological studies. Elvik, R. *Accident Analysis and Prevention* 2013; 60:254-67.

This systematic review and meta-analysis including 66 studies that have assessed the risk of accident associated with the use of different types of drugs when driving. For fatal crashes, adjusting for publication biases, there was a 31% increased risk from cannabis, compared to 3-fold increase from cocaine, and 2-fold increased risk from benzodiazepine tranquilizers.

Cannabis Effects on Driving Skills. Rebecca L. Hartman^{1,2} and Marilyn A. Huestis¹, *American Assoc for Clinical Chemistry*, 2013; 59:478-92. This meta-analysis is based on 10 studies, concluding a 2-fold increased risk for motor vehicle accidents after marijuana use.

CONTENT: We review and evaluate the current literature on cannabis' effects on driving, highlighting the epidemiologic and experimental data. Epidemiologic data show that the risk of involvement in a motor vehicle accident (MVA) increases approximately 2-fold after cannabis smoking. The adjusted risk of driver culpability also increases substantially, particularly with increased blood THC concentrations. Studies that have used urine as the biological matrix have not shown an association between cannabis and crash risk. Experimental data show that drivers attempt to compensate by driving more slowly after smoking cannabis, but control deteriorates with increasing task complexity.

Cannabis smoking increases lane weaving and impaired cognitive function. Critical-tracking tests, reaction times, divided-attention tasks, and lane-position variability all show cannabis-induced impairment. Despite purported tolerance in frequent smokers, complex tasks still show impairment. Combining cannabis with alcohol enhances impairment, especially lane weaving.

National Institute on Drug Abuse (NIDA) 2013. Healthy Kids survey, 11% of kids say they have driven impaired in the last week.

[A recent University of Colorado School of Medicine study](http://www.denverpost.com/marijuana/ci_25779293/no-doubt-about-dangers-stoned-driving#ixzz3288cUbVD) shows the number of drivers in fatal Colorado crashes testing positive for pot nearly doubled from 2009 to 2011. Read more: [No doubt about the dangers of stoned driving - The Denver Post](http://www.denverpost.com/marijuana/ci_25779293/no-doubt-about-dangers-stoned-driving#ixzz3288cUbVD) http://www.eurekalert.org/pub_releases/2014-05/uocd-mui051514.php (may 14, 2014)

Pot Fuels Surge in Drugged Driving Deaths, February 15, 2014. Tanya Guevara and her son, Adrian, were killed in 2010 when a driver, impaired after smoking marijuana, hit Guevara's car head-on in Colorado. <http://www.nbcnews.com/#/health/health-news/pot-fuels-surge-drugged-driving-deaths-n22991>

Marijuana and Driving Impairment: Barry K. Logan, Forensic Science and Medicine: Marijuana and the Cannabinoids; The School of Pharmacy, The University of Mississippi; ElShohly Laboratories Inc., Oxford, MS; P 277 - 293

OTHER:

Dismal Tax Revenue Income

<http://www.colorado.gov/cs/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobkey=id&blobtable=MungoBlobs&blobwhere=1251999888405&ssbinary=true>

<http://www.coloradofiscal.org/half-a-mile-high-coloradans-not-buying-as-much-pot-as-expected/>

<http://www.colorado.gov/cs/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobkey=id&blobtable=MungoBlobs&blobwhere=1251999888405&ssbinary=true>

Colorado Futures Study:

The Fiscal Impact of Amendment 64 on State Revenues, April 24, 2013; Prepared by: Charles Brown Phyllis Resnick, Director Lead Economist; Colorado Futures Center Colorado Futures Center www.colostate.edu/coloradofutures

LAWS in Colorado

Colorado Unemployment Law:

<http://www.colorado.gov/cs/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobkey=id&blobtable=MungoBlobs&blobwhere=1251874262653&ssbinary=true>

Colorado Worker's Compensation Act:

<http://www.colorado.gov/cs/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobkey=id&blobtable=MungoBlobs&blobwhere=1251874262653&ssbinary=true>

Medical Marijuana Act: <http://www.colorado.gov/cs/Colorado+Constitution+Article+XVIII.pdf>

Social Costs

The Economic Costs of Alcohol Abuse .NIDA. (2000). Washington D.C.: National Institute of Health.

Costs of substance abuse to employers: Substance Abuse and Mental Health and Safety Administration, 2005.
<http://www.samhsa.gov/data/trends/htm>

Marijuana users cost employers more in industrial accidents and injuries: **Testimony on Federal Workplace Drug-Testing**. Washington D.C. DHHS, 1998; Burlington, Bruce D.

Employees who test positive for marijuana have 75% higher absentee rates. National Drug-Free Workplace Alliance, 2010; www.ndwa.org/statistics.php

Cost of tobacco \$200 billion annually, 10x the amount of money collected from taxes. CDC 2007.
www.cdc.gov/tobacco/data_statistics/fact_sheet

Alcohol \$185 billion annually – 10x the amount of money collected from taxes. HHS. The Economic Costs of Alcohol Abuse. Washington D.C. National Institute of Health 2000

For the first time, MJ use is higher than tobacco use amongst teens in the U.S. **Key Findings on Adolescent Drug Use**. Ann Arbor, MI; L. Johnston

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