Health Impact Assessment

Marijuana Regulation in Vermont

Appendix:

Annotated Literature Review

Released January 2016

VERMONT
DEPARTMENT OF HEALTH
healthvermont.gov

Author(s) - David et al.

Title - A Case-Control Study of Maternal Periconceptual and Pregnancy Recreational Drug Use and fetal Malformation Using Hair analysis

Year - 2014 (David, Holloway, Thomasson, Syngelaki, & Nicolaides, 2014)

Journal - PLOS ONE

Study Type - Survey/Biological Analysis

Category - Reproductive

Systems Affected - Birth Defects

Strength of Effect/ Direction of Effect - Strong - used analysis of hair to test for the presence of drugs before and during pregnancy. Results were then used to see if recreational drug use was associated with specific fetal abnormalities.

Pull Quotes for Reference - "THC use alone was not significantly associated with any fetal anomaly."

Notes - A very interesting study using a novel technique to test for drug use (hair analysis). Cannabis use reported in 13.2% of the study population.

Country/State of data - UK

Author(s) - El Marroun, Tiemeier, Steegers, Roos-Hesselink, Jaddoe, Hofman, Verhulst, van den Brink, Huizink

Title - A Prospective Study on Intrauterine Cannabis Exposure and Fetal Blood Flow

Year - 2010 (El Marroun, Tiemeier, Steegers, Roos-Hesselink, & Jaddoe, 2010)

Journal - Early Human Development

Study Type - STRONG/MEDIUM - prospective longitudinal cohort study from fetal life until young adulthood in a multi-ethnic urban population

Category - Reproductive

Systems Affected - reproductive (fetal hemodynamics)

Strength of Effect/ Direction of Effect - *Strength of association*: LOW - "cannabis use during pregnancy is indeed associated with adaptations in fetal placental and cardiac blood flow, but not with cerebral blood flow....this association could be explained by the co-occurrence of tobacco use during pregnancy". (p 235) *Meaningfulness of association*: LOW - small sample size; self-reported data may lead to underestimation due to misclassification; "this study may not have enough power for adjustment with multiple confounding factors in the analysis" (p 235) *Direction of association:* difficult to determine - increased/no?

Pull Quotes for Reference - "our findings suggest that intrauterine cannabis exposure is associated with changes in the hemodynamic programming of vascular system in late pregnancy. However, the association found was rather weak and was probably to be induced by tobacco exposure instead of cannabis exposure" (p 235)

Notes -

Country/State of data - The Netherlands

Author(s) - Mark Asbridge, Jill A Hayden, Jennifer L Cartwright

Title - Acute Cannabis Consumption and Motor Vehicle Collision Risk: Systematic Review of Observational Studies and Meta-analysis

Year - 2012 (Asbridge, Hayden, & Cartwright, 2012)

Journal - BMJ

Study Type - Systematic review of observational studies, with meta-analysis.

Category - Motor Vehicle

Systems Affected - Driving

Strength of Effect/ Direction of Effect - Medium - significantly increased risk of motor vehicle collisions compared with unimpaired driving (odds ratio 1.92 (95% confidence interval 1.35 to 2.73); P=0.0003); we noted heterogeneity among the individual study effects (I2=81). Collision risk estimates were higher in case-control studies (2.79 (1.23 to 6.33); P=0.01) and studies of fatal collisions (2.10 (1.31 to 3.36); P=0.002) than in culpability studies (1.65 (1.11 to 2.46); P=0.07) and studies of non-fatal collisions (1.74 (0.88 to 3.46); P=0.11).

Strength of Effect/ Direction of Effect - *Strength of association:* MEDIUM: "Study estimates of the effect of cannabis on collision risk are often confounded by the failure to separate out the effects of alcohol and other psychoactive substances. Therefore, our analyses focused on tetrahydrocannabinol, the main psychoactive component of cannabis. We searched for any positive test for active metabolites of tetrahydrocannabinol, and assessed the presence of tetrahydrocannabinol alone, in the absence of alcohol or other drugs." (p.3) "The overall quality of the evidence on the association between cannabis use and motor vehicle collisions was moderate. Most studies in our meta-analysis consistently showed an increased effect of cannabis use on the risk of motor vehicle collisions." (p.4) "Although we defined high quality studies as those that scored full marks on the Newcastle-Ottawa scale, many of these high and medium quality studies probably did not control for all possible confounders. Although we restricted positive cannabis results to drivers that showed the presence of tetrahydrocannabinol in the absence of other drugs or alcohol, other potentially important confounders were probably not controlled for. These hidden confounders, as well as the differing study designs used, might have affected the results of the individual studies and hence the estimates of the pooled odds ratios." (p. 4-5) *Meaningfulness of association: STRONG. Direction of association:* Increased

Pull Quotes for Reference - Acute cannabis consumption is associated with an increased risk of a motor vehicle crash, especially for fatal collisions.

Pull Quotes for Reference - Primary analysis: "The pooled risk of a motor vehicle collision while driving under the influence of cannabis was almost twice the risk while driving unimpaired (odds ratio 1.92 (95% confidence interval 1.35 to 2.73); P=0.0003)" (p. 3) "To our knowledge, this meta-analysis is the

first to examine the association between acute cannabis use and the risk of motor vehicle collisions in real life settings." (p.4)

Notes - No dose response data. Different ways of measuring how much THC in blood/marijuana concentrations

Notes - Study selection - abstract and full text search of 19 data bases -->use of Newcastle-Ottawa scale. 9 studies included in meta-analysis, four deemed high quality and five medium quality.

Country/State of data -

Author(s) - Thomas et al.

Title - Adverse Cardiovascular, Cerebrovascular, and Peripheral Effects of Marijuana Inhalation: What Cardiologists Need to Know

Year - 2014 (Thomas, Kloner, & Rezkalla, 2014)

Journal - American Journal of Cardiology

Study Type - Review

Category - Physical Health

Systems Affected - Cardiovascular, stc.

Strength of Effect/ Direction of Effect - Moderate - this is a review of a very thin literature and a call for further research.

Pull Quotes for Reference -

Notes - Speculation on mechanism of action.

Country/State of data - NA

Author(s) - Middlekauff HR, Park J, Moheimani RS

Title - Adverse Effects of Cigarette and Non-cigarette Smoke Exposure on the Autonomic Nervous System

Year - 2014 (Middlekauff, Park, & Moheimani, 2014)

Journal - Journal of the American College of Cardiology

Study Type - Review

Category - Physical Health

Systems Affected - Autonomic Nervous System

Strength of Effect/ Direction of Effect - n/a

Pull Quotes for Reference - In the only published report of the effects of marijuana on the autonomic nervous system, HRV was compared between 72 chronic marijuana users and 72 nonusers, and somewhat surprisingly, an increase in HRV was reported, consistent with an increase in vagal over sympathetic tone. Confirmatory studies are warranted.

Notes - The quote references the only study of the effects of marijuana on the autonomic nervous system (Schmid K, Schönlebe J, Drexler H, Mueck-Weymann M; The effects of cannabis on heart rate variability and well-being in young men)

Country/State of data - Western Europe? That single study on the effects of marijuana on the autonomic nervous system may have been conducted in Europe. I can't quickly confirm because there is a cost associated with the manuscript

Author(s) - Nora D. Volkow, M.D., Ruben D. Baler, Ph.D., Wilson M. Compton, M.D., and Susan R.B. Weiss, Ph.D.

Title - Adverse Health Effects of Marijuana Use

Year - 2014 (Volkow, Baler, Compton, & Weiss, 2014)

Journal - New England Journal of Medicine

Study Type - Review

Category – YOUTH

Systems Affected - Youth Health

Strength of Effect/ Direction of Effect – Strong – Review of the evidence of the physical and mental health effects of marijuana particularly on youth.

Pull Quotes for Reference – "Marijuana use has been associated with substantial adverse effects, some of which have been determined with a high level of confidence (Table 2). Marijuana, like other drugs of abuse, can result in addiction. During intoxication, marijuana can interfere with cognitive function (e.g., memory and perception of time) and motor function (e.g., coordination), and these effects can have detrimental consequences (e.g., motor-vehicle accidents). Repeated marijuana use during adolescence may result in long-lasting changes in brain function that can jeopardize educational, professional, and social achievements."

Three responses to this article were also reviewed:

Author(s) - Wolff, Valerie; Rouyer, Olivier; Bernard, Geny (bernard.geny@chru-strasbourg.fr)

Strength of Effect/ Direction of Effect - Use of marijuana (natural or synthetic) increases stroke in young people (Unknown--Cited new literature)

Pull Quotes for Reference - "Simultaneously, the presence of multifocal intracranial arterial vasoconstriction was observed, which was reversible in some cases after cessation of cannabis exposure." | "THC, a major component of cannabis, has been shown experimentally to impair function of the mitochondrial respiratory chain and to increase the production of reactive oxygen species in the brain. Both of these processes are key events during stroke, suggesting that THC may also increase a patient's vulnerability to stroke."

Author(s) - Thompson III, George; Tuscano, Joseph (grthompson@ucdavis.edu)

Strength of Effect/ Direction of Effect - Recreational Use of Marijuana Increases Infectious Risks (Unknown--Cited new literature)

Pull Quotes for Reference - "Recreational use of marijuana has been associated with a multistate outbreak of salmonellosis, illustrating the potential for widespread exposure through either inadvertent contamination during growing and storage or purposeful adulteration" "Prior reports have documented the frequent contamination of marijuana with fungal organisms and the potential for severe complications, including deaths. These risks are not well studied and thus are poorly defined."

Author(s) - Collins, Carol (carolc3@u.washington.edu)

Strength of Effect/ Direction of Effect - Marijuana Use Increases Risk of Pharmacokinetic Interactions (Unknown--Cited new literature)

Pull Quotes for Reference - "Case reports support the risk of pharmacokinetic interactions; however, clinical studies have been equivocal. Notably these studies have not replicated the long-term high potency and high dose achieved by some marijuana users (e.g., hashish users).

Notes - Selected Literature Cited: Yamaori S, Koeda K, Kushihara M, Hada Y, Yamamoto I, Watanabe K. Comparison in the in vitro inhibitory effects of major phytocannabinoids and polycyclic aromatic hydrocarbons contained in marijuana smoke on cytochrome P450 2C9 activity. Drug Metab Pharmacokinet 2012; 27:294-300.

Author(s) - Palamar, Joseph; Fenstermaker, Michael; Kamboukos, Dimita, et al. (joseph.palamar@nyumc.org)

Title - Adverse Psychosocial Outcomes Associated with Drug Use Among US High School Seniors: Comparisons of Alcohol and Marijuana.

Year - 2014 (Palamar J. , Fenstermaker, Kamboukos, Ompad, & Cleland, 2014)

Journal - Am J Drug Alcohol Abuse

Study Type - Random Sampling of High School Seniors in 5 national cohorts (Monitoring the Future, 2007-2011)

Category - YOUTH

Systems Affected - Psychosocial

Strength of Effect/ Direction of Effect - Marijuana Users Are More Likely to Report No Adverse Psychosocial Outcomes Compared to Alcohol Users. All alcohol-related outcomes were significantly more prevalent among those who also used marijuana in their lifetime. Marijuana Users Reported Having Less Energy or Less Interest in Activities Compared to Alcohol Users. Marijuana Users Reported Marijuana to be associated with Involvement with People Who Are a "Bad Influence More So than Alcohol. Marijuana Users More Likely To Report Decreased Work/School Performance, Bad Psychological Effects, and Hurt Relationships with Parents, Teachers, or Supervisors Compared to Alcohol Users. Marijuana Users More Likely to Report No Problems Associated with Use Compared to Alcohol Users. White Marijuana Users were more Likely to Report Use Interfering with Ability to Think Clearly and Unsafe Driving Compared to Black and Hispanic Marijuana Users. Females were More Likely to Most Adverse Outcomes Related to Alcohol and Marijuana Use. Sex Differences Not as Large for Marijuana Compared to Alcohol, however, Female Marijuana Users were more likely to Report Less Energy and Less Emotional Stability, and More Psychological Effects Compared to Male Marijuana Users.

Pull Quotes for Reference -

Notes - HAS TONS OF Adjusted Odds Ratios for the Various Adverse Psychosocial For Alcohol / Marijuana.

Country/State of data -

Author(s) - Palamar et al.

Title - Adverse Psychosocial Outcomes Associated with Drug Use Among US High School Seniors: A Comparison of Alcohol and Marijuana

Year - 2014 (Palamar J. J., Fenstermaker, Kamboukos, Ompad, & Cleland, 2014)

Journal - The American Journal of Drug and Alcohol Abuse

Study Type - Survey

Category - YOUTH

Systems Affected - Adverse consequences

Strength of Effect/ Direction of Effect - Moderate - alcohol was found to have more self-reported adverse consequences than marijuana among high school seniors

Pull Quotes for Reference - "As marijuana use gains greater acceptance among the US population, special attention should be given to the unique differences in adverse outcomes among adolescents who use marijuana and/or alcohol."

Notes - This is not particularly informative. The fact that monitoring the future HS seniors report more adverse consequences for alcohol and marijuana has been already established.

Country/State of data - USA

Author(s) - Stefanis et al.

Title - Age at Initiation of Cannabis Use Predicts Age at Onset of Psychosis: The 7 to 8 Year Trend

Year - 2013 (Stefanis, Dragovic, Power, Jablensky, & Castle, 2013)

Journal - Schizophrenia Bulletin

Study Type - Retrospective

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - This study demonstrates a consistent 7-8 year duration of premorbid exposure to cannabis and age of onset of psychosis in a large sample of individuals with a confirmed diagnosis of psychosis.

Pull Quotes for Reference - While the mechanisms by which cannabis may exert such delayed effects are unclear, several authors have suggested a mechanism involving sensitization of the mesolimbic dopaminergic system, triggered by repeated stimulation with cannabis, to which susceptible individuals may be especially vulnerable, possibly due to heightened, genetically determined sensitivity to the psychotomimetic effects of cannabis.

Notes - does not appear to demonstrate an adolescent vulnerability since age of initiation of cannabis use ranged from 12-21.

Country/State of data - Australia

Author(s) - Pacula et al.

Title - Assessing the Effects of Medical Marijuana Laws on Marijuana Use: The Devil is in the Details

Year - 2014 (Pacula, Powell, Heaton, & Sevigny, 2014)

Journal - Journal of Policy Analysis and Management

Study Type - Survey

Category - YOUTH

Systems Affected - Marijuana use among adults and youth

Strength of Effect/ Direction of Effect - Moderate - specific MMLs appear to contribute to an increase in marijuana use, but not an increase in more serious problems associated with marijuana use.

Pull Quotes for Reference - "It is clear from the analyses presented in this paper that not all MMLs are created equally. There are important nuances to these policies that have differential effects on marijuana consumption, particularly heavy users and youth."

Notes –

Country/State of data -

Author(s) - Hall W, Weier M

Title - Assessing the Public Health Impacts of Legalizing Recreational Cannabis Use in the USA

Year - 2015 (Hall & Weier, 2015)

Journal - Clinical Pharmacology & Therapeutics

Study Type - Systematic review, policy analysis

Category - HEALTH

Systems Affected -

Strength of Effect/ Direction of Effect - Decriminalization in states, Netherlands (1980s), Australia (1980s-90s), Europe did not significantly increase cannabis use. Dutch coffee shops prohibited from advertising, selling amounts greater than a specified quantity; number of licenses and locations are limited, local government preempts. Evidence mixed on whether Dutch legalization increased use; some say similar to other European countries & US but others say cannabis increased when number of licensees increased, then decreased when decreased, Dutch initiation is earlier, and have higher rates of treatment.
Legalization of medical marijuana may be associated with increased adolescent use but results are mixed confounded because these states may have had higher rates to begin with. Motor vehicle fatalities increased after medical marijuana legalized, but could have been affected by increase in testing. Steeper decline in young male suicides in medical marijuana states; lower opioid deaths; increases in cannabis potency highest in states where dispensaries commercialized. WA and CO tax on weight, not THC level, which incentivizes more potent products. Taxation proposed there will not maintain cannabis prices at current black market levels, and use will increase as price falls. May be a time lag of up to 10 years before effects become clear on use and health harms. Precursor is often reduced perception of risk and increased frequency among current youth users. Ready and cheaper access likely to increase use over legal age (no magnitude given). May reduce alcohol harms if young men substitute.

Pull Quotes for Reference - Of recent Australian decriminalization studies: "Their findings suggest that criminal penalties may marginally discourage some people from using cannabis but do not influence how much cannabis is consumed by those who use." (p. 608)

"Alcohol policy analysts would argue that most alcohol regulatory regimes give a low priority to protecting the public health. They have often been captured by alcohol producers and sellers who manipulate these regimes to maximize their profits and protect their interests. Others argue that cannabis legalization will be exploited by the tobacco industry and other large-scale commercial interests to promote cannabis use in much the same way that they promoted tobacco smoking. Commercialization of sales and an expansion of cannabis production and distribution are likely

outcomes of licensed sellers seeking to maximize their incomes by promoting cannabis use, increasing the number of new users and increasing levels of use among existing users." (p. 611)

"The proposed regulatory schemes in Colorado and Washington, in short, do not apply any of the lessons learned from regulating alcohol and tobacco to protect public health, namely, the desirability of restricting the number of producers and sellers, tightly regulating promotion, and using taxes to discourage heavy use of the most potent products." (p. 611)
"It is accordingly a safe prediction that cannabis use will increase after the legalization of recreational use. What is uncertain is by how much, which type of users will increase their use the most (e.g. current users, new users, or some mix of the two), and over what period of time will any such increases be expected to occur." (pp. 611-612)

Notes - Table 1 is a nice model for summarizing cannabis health effects.

Country/State of data - Review

Author(s) - McGrath et al.

Title - Association between Cannabis Use and Psychosis-Related Outcomes Using sibling Pair Analysis in a Cohort of Young Adults

Year - 2010 (McGrath, Welham, Scott, Varghese, & Degenhardt, 2010)

Journal - Archives of General Psychiatry

Study Type - Retrospective

Category - Psychosis

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - Greater than 6 years use of cannabis predicted 3 psychosis-related outcomes

Pull Quotes for Reference - Longer duration since first cannabis use was associated with multiple psychosis-related outcomes in young adults. Furthermore, we report for the first time, to our knowledge, that this association persisted when examined in sibling pairs, thus reducing the likelihood that the association was due to unmeasured shared genetic and/or environmental influences. There was a "dose-response" relationship between the variables of interest: the longer the duration since first cannabis use, the higher the risk of psychosis-related outcomes. The key findings were robust in the face of various planned sensitivity analyses and conservative tests related to attrition.

Notes - This is a methodologically sound study providing strong support for the duration of cannabis use-psychosis relationship.

Country/State of data - Australia

Author(s) - Daling JR, Doody DR, Sun X, Trabert BL, Weiss NS, Chen C, Biggs ML, Starr JR, Dey SK, Schwartz SM

Title - Association of Marijuana Use and the Incidence of Testicular Germ Cell Tumors

Year - 2009 (Daling, Doody, Sun, Trabert, & Weiss, 2009)

Journal - Cancer

Study Type - Population-based, case-control

Category - Cancer

Systems Affected - Testicular Germ Cell Tumors

Strength of Effect/ Direction of Effect - Current cannabis use is associated with an increased risk of Nonseminoma and mixed testicular germ cell tumors. OR = 2.3. Age of first use (<18), length of use (>=10 yrs) and frequency of use (daily or more) were also associated with increased risk.

Pull Quotes for Reference - An association was observed between marijuana use and the occurrence of nonseminoma TGCTs. Additional studies of TGCTs will be needed to test this hypothesis…

Notes - Strong study. Strengths: Resulting association was specific to a classification of tumors, validation of marijuana use in controls by comparison to National data (NSDUH). Weaknesses: Selection bias, residual confounding, no other supporting evidence or studies.

Country/State of data - Washington

Author(s) - Hayatbakhsh MR, Flenady VJ, Gibbons KS, Kongsbury AM, Hurrion E, Mamun AA, Najman JM

Title - Birth Outcomes Associated with Cannabis Use Before and During Pregnancy

Year - 2011 (Hayatbakhsh, Flenady, Gibbons, Kingsbury, & Hurrion, 2011)

Journal - Pediatric Research

Study Type - Cross-sectional analysis of large retrospective cohort, seven-year sample from one Australian public hospital. Sample size 24,874

Category - Reproductive

Systems Affected - Reproductive

Strength of Effect/ Direction of Effect - 26.3% ever-use among women with live births from 2000-2006, 9.5% ever regular users, 2.6% cannabis use during pregnancy. During pregnancy common among younger women (<20 years 6.2%), lower levels of education (incomplete high school 5.1%), single (6.4%), indigenous (7.6%), three or more kids (3.2%).
Unadjusted: Babies of women who smoked during pregnancy an average of 375g (13.2 oz) lighter, lower gestational age, shorter body length, more likely to be small for gestational age, and admitted to NICU. Ever regular use also associated with lower birth weight, lower birth length, SGA, NICU admission.
Adjusted for sociodemographics, smoking, alcohol consumption, other illicit drugs: Higher LBW (OR 2.4, 2.0-2.9), preterm birth (OR 1.7, 1.4-2.1), SGA (OR 3.1, 2.5-3.7), NICU (OR 2.3, 1.9-2.7)
No association between use of cannabis before or during pregnancy and neonatal nursery stay, neonatal death, or mechanical ventilation. **Using ORs from multivariate adjust analysis, PAR for low birth weight, preterm birth, and ICU admission were 2.5%, 1.5%, 2.7%.** Because retrospective, could either underestimate or overestimate the results.

Pull Quotes for Reference - "If we assume there is a causal relationship between the exposure and outcome, 2.5% of low birth weight, 1.5% of preterm delivery, and 2.7% of admission to the NICU could be prevented if pregnant women did not use cannabis during pregnancy in this tertiary hospital setting." (p.218)

Notes - Population is low to middle income; private hospitals see mostly higher income patients. Questions administered between 12-16 weeks gestation.

Country/State of data - Australia

Author(s) - SuW. HII,1 Jeff D. C. TAM,2 Bruce R. THOMPSON1 AND Matthew T. NAUGHTON1

Title - Bullous Lung Disease Due to Marijuana

Year - 2008 (Hii, Tam, Thompson, & Haughton, 2008)

Journal - Respirology

Study Type - Case review

Category - Respiratory

Systems Affected - Lungs

Strength of Effect/ Direction of Effect - Low - Case review at one institution. Shows there is some potential connection between smoking marijuana and asymmetrical bullous disease. 10 patients.

Pull Quotes for Reference -

Notes - Small case review, not sure we should consider

Country/State of data – Australia

Author(s) - Lubman DI, Cheetham A, Yucel M

Title - Cannabis and Adolescent Brain Development

Year - 2014 (Lubman, Cheetham, & Yucel, 2014)

Journal - Pharmacology and Therapeutics

Study Type - Systematic review of animals and humans

Category - Brain

Systems Affected - Brain development

Strength of Effect/ Direction of Effect - Animal studies show greater effects on young animals of acute exposure, including cell death and reduced learning and memory. Chronic exposure seems to counteract short-term positive effects of cannabinoids, and chronic exposure in adolescent animals has longer impact. Impacts memory and disrupts social behavior, play, depressive-like behaviors. May also interact with existing risk factors for worse outcomes in adulthood. In adult humans, both positive and negative acute effects, though positive acute effects attenuated in light chronic users. Negative impacts on working memory, attention, learning, executive functions, attentional processes. Positive effects of acute exposure may include antipsychotic (cannabidiol). Abstinent ex-users show long-term effects on brain function and cognition, but may not affect performance. May also be normalization after some period of time. Deficits in attention, memory, executive function are vulnerability markers for schizophrenia. Heavy users show some brain abnormalities. Prenatal exposure impairs central nervous system development, cognitive, behavioral deficits. Heavy, regular adolescent use also associated with cognitive impairments and may persist after abstinence. Many studies looking at age of onset retrospective but some longitudinal studies have similar findings. Interaction b/w other risk factors, e.g. childhood trauma, genetics, other substance use. Evidence linking to schizophrenia is mixed.

Pull Quotes for Reference - "This [interaction between early cannabis exposure and other risk factors] is of particular relevance to human research, given that early cannabis use frequently occurs in conjunction with other risky behaviors and/or adverse experiences that may have similar additive or interactive effects on later mental health." (p. 4) "More broadly, it is consistent with studies in adults demonstrating that an earlier age of onset is associated with greater cognitive impairment and more pronounced morphological alterations." (p.6). The potential influence of cannabis use on brain development has important policy implications, as it underscores the need for prevention programs that specifically focus on delaying the onset of cannabis experimentation. Together with early intervention programs that aim to reduce the prevalence of regular or harmful use amongst young people, efforts to delay onset or minimize exposure during this period of development may be of particular importance in reducing long-term harm." (p. 11)

Notes - This review article is a very comprehensive summary but doesn't have magnitude estimates.

Country/State of data – Review

Author(s) - Fernández-Artamendi S, Fernández-Hermida JR, Secades-Villa R, García-Portilla P

Title - Cannabis and Mental Health

Year - 2011 (Fernandez-Artamend, Fernandez-Hermida, Secades-Villa, & Garcia-Portilla, 2011)

Journal - Actas Españolas de Psiquiatría

Study Type - Review

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - n/a

Pull Quotes for Reference - Although the investigation has not found a causality relation between use and long-term alterations, a risk for mental health seems to exist for regular users with a certain vulnerability or predisposition, in which cannabis use significantly increases the risks of presenting mental disorders, particularly psychotic disorders. The younger the age of onset and the greater the amount of cannabis consumed, the greater the probability is that cannabis use will cause harm. ...disorders of the affective spectrum show only a weak relation with cannabis use that is susceptible to moderation by a variety of cultural and contextual variables.

Notes - Solid summary, but the primary literature should be reviewed in order to critically assess the validity of studies that are relevant to the current undertaking.

Country/State of data - Unknown: Each of the studies referenced by the manuscript would need to be reviewed

Author(s) - Katherine M. Boydell, PhD, Catherine Willinsky, MHSc, Natalie Baker, MSc,

Cristina Boydell, MSc

Title – Cannabis and Psychosis Awareness Project A Pan-Canadian Study of Youth Experiences

Year - 2011 (Boydell, Willinsky, Baker, & Boydell, 2011)

Journal - Report

Study Type - Qualitative

Category - Psychosis

Systems Affected - Psychosis

Strength of Effect/ Direction of Effect - Low - Interesting study on youth who have psychosis and their experiences with marijuana

Pull Quotes for Reference -

Notes - This is a qualitative study. Interesting to see what youth who have experienced psychosis think about marijuana use, but not a causal or association.

Country/State of data - Canada

Author(s) - Damjanovic et al.

Title - Cannabis and Psychosis Revisited

Year - 2015 (Damjanovi, Pantovi, Damjanovi, Dunji-Kosti, & Ivkovi, 2015)

Journal - Psychiatria Danubina

Study Type - Review

Category - Psychosis

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - Reviews major research articles on the association between early marijuana use and the development of psychotic symptomatology.

Pull Quotes for Reference - The reviewed studies clearly suggest that cannabis predicts an incresed risk for schizophrenia, particularly in young adults.

Notes - Good and current list of references on this topic

Country/State of data - N/A

Author(s) - D'Souza et al.

Title - Cannabis and Psychosis/Schizophrenia: Human Studies

Year - 2007 (D'Souza, Sewell, & Ranganathan, 2007)

Journal - European Archives of Psychiatry and Clinical Neuroscience

Study Type - Review

Category - Psychosis

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - Reviews major research articles on the association between early marijuana use and the development of psychotic symptomatology.

Pull Quotes for Reference - Taken collectively, exposure to cannabis is neither a necessary nor a sufficient cause of schizophrenia - similar to cigarette smoking being neither necessary nor sufficient to cause lung cancer

Notes - This review includes 242 citations and discusses all aspects of the psychosis-cannabis link from epidemiology to potential mechanisms of action

Country/State of data - N/A

Author(s) - Hackman DG

Title - Cannabis and Stroke Systematic Appraisal of Case Reports

Year - 2015 (Hackman, 2015)

Journal - Stroke

Study Type - Review of case reports

Category - Physical Health

Systems Affected - Cerebrovascular

Strength of Effect/ Direction of Effect - n/a

Pull Quotes for Reference - Two epidemiological studies have studied this association. In a large study of hospital admissions in Texas, cannabis exposure was associated with ischemic stroke even after adjusting for alcohol and tobacco (adjusted odds ratio, 1.76; 95% confidence interval, 1.15–2.71). Second, in a prospective case–control study with adjustment for age, sex, and ethnicity, cannabis was associated with the composite of cerebrovascular events (odds ratio, 2.30; 95% confidence interval, 1.08–5.08). Yet after further adjustment for tobacco, the association was weakened (odds ratio, 1.59; 95% confidence interval, 0.71–3.70).

Notes - Though the author concludes: "...it seems clear that physiological, clinical, and epidemiological data converge on an increased stroke risk from cannabis exposure", the evidence presented in the manuscript is not strong. A review of the studies mentioned in the quote might be warranted (Westover AN, Bride S, Haley RW. Stroke in young adults who abuse amphetamines or cocaine: a population-based study of hospitalized patients. Arch Gen Psychiatry. 2007;64:495–502. doi: 10.1001/archpsyc.64.4.495. Barber PA, Pridmore HM, Krishnamurthy V, Roberts S, Spriggs DA, Carter KN, et al. Cannabis, ischemic stroke, and transient ischemic attack: a case-control study. Stroke. 2013;44:2327–2329. doi: 10.1161/STROKEAHA.113.001562.)

Country/State of data - Unknown: Each of the 34 case reports assessed in the manuscript would need to be reviewed

Author(s) - Rebecca Hartman and Marilyn Huestis

Title - Cannabis Effects on Driving Skills

Year - 2013 (Hartman & Huestis, 2013)

Journal - Clinical Chemistry

Study Type - Review

Category - Motor Vehicle

Systems Affected – Driving

Systems Affected - Psychological / Cognitive

Strength of Effect/ Direction of Effect - Strong - Epidemiologic data show that the srsik involvement in a motor vehicle accident increases approximately 2-fold after cannabis smoking. The adjusted risk of driver culpability also increases substantially, particularly with increased blood THC concentrations.

Strength of Effect/ Direction of Effect - Addiction Patients With More Frequent Cannabis Exposure Had Increased Risk Motor Vehicle Accidents (RR 1.49) | Marijuana Users Using Cannabis More Than Once Per Week and >4 Days Per Week Had Increased MVA Risk (OR 2.76, 2.5 respectively) | Driving Under Influence of Cannabis Within 1 hour After Smoking Increases MVA Risk Compared to DUIC 3 hours After Smoking.

Pull Quotes for Reference - Evidence suggests recent smoking and/or blood THC concentration 2-5 ng/mL are associated with substantial driving impairment, particularly in occasional smokers.

Pull Quotes for Reference - MVA-Driver Injured AOR: 1.22 (95% CI 0.55-2.73, Adjusted for Demographics, Drugs, Time of Day, Season) | MVA-Driver Fatality OR: 13.9 (95% CI 6.6-29.2, Crude) | MVA-DF AOR: 8.6 (95% CI 3.9-19.3, Adjusted for Demographics, Time Period, Season) | MVA-DF (Cannabis Only) OR: 1.9 (95% CI 0.3-13.7, Crude) | MVA-DF (Cannabis Only) AOR: 0.9 (95% 0.1-7.3, Adjusted for Demographics, Time Period, Season) | Single Vehicle Accident (SVA)-DF (No Cannabis Only Cases) OR: 18.9 (95% CI 6.5-54.6, Crude) | SVA-DF (No Cannabis Only Cases) AOR: 9.0 (95% CI 2.7-30.3, Adjusted by Demographics, Time Period, and Season) | "Evidence suggests recent smoking and/or blood THC concentrations 2-5 ng/mL are associated with substantial driving impairment, particularly in occasional smokers" | "One of the greatest challenges is dealing with public attitudes toward DUIC. One fourth (26.3%) of 320 drivers who smoked cannabis in the previous year indicated a >90% likelihood of future DUIC, even after having been shown data on increased crash risk...Past experiences had convinced them that they could compensate for cannabis-associated performance decrements. Most believed cannabis caused minimal driving impairment; a few considered it to have no or even positive effect on driving. A high likelihood of apprehension and punishment was a better deterrent...." | "Low

(100 ug/kg) and moderate (200 ug/kg) THC doses, combined with a 0.04% BAC produced road-tracking impairment to a degree similar to BACs of 0.09% and 0.14%. Because consuming alcohol and cannabis

Notes - This is a review. It has multiple tables we could reference with the number of studies showing each direction.

Notes - Many more OR/AOR in article--no meta-analysis conducted in this article, though some of the OR/AORs are pulled from meta-analyses.

Country/State of data - NA

Author(s) - McLaren et al.

Title - Cannabis Potency and Contamination: A Review of the Literature

Year - 2008 (McLaren, Swift, Dillon, & Allsop, 2008)

Journal - Addiction

Study Type - Review

Category - HEALTH

Systems Affected - Mental and physical health

Strength of Effect/ Direction of Effect - Low - Authors found significant variability in extant literature reports of both potency and contamination effects and their respective effects on health

Pull Quotes for Reference - "Overall, evidence for cannabis potency and contamination is fragmented and fraught with methodological problems."

Notes -

Country/State of data - N/A

Author(s) - Sayantan Bhattacharyya & Syamsundar Mandal & Samir Banerjee & Gautam Kumar Mandal & Anup Kumar Bhowmick & Nabendu Murmu

Title - Cannabis Smoke Can Be a Major Risk Factor for Early-age Laryngeal Cancer—a Molecular Signaling-based Approach

Year - 2014 (Bhattacharyya, Mandal, Banerjee, Mandal, & Bhowmick, 2014)

Journal - Tumor Biology

Study Type - Case review

Category - Cancer

Systems Affected - Cancer

Strength of Effect/ Direction of Effect - Medium - They show an association between marijuana use and a protein expression on the causal pathway of laryngeal cancer.

Pull Quotes for Reference - This study provides evidence for a direct association between cannabis smoking and increased risk of laryngeal cancer.

Notes - total n = 83

Country/State of data - India

Author(s) - Alshaarawy, Omayma; Anthony, James (janthony@msu.edu)

Title - Cannabis Smoking and Diabetes Mellitus (Results from Meta-Analysis with Eight Independent Replication Samples)

Year - 2015 (Omayma & Anthony, 2015)

Journal - Epidemiology

Study Type - Meta Analysis (8 independent replications of NHANES / NSDUH data)

Category - Physical Health

Systems Affected - Endocrine

Strength of Effect/ Direction of Effect - Cannabis Smoking And Diabetes Mellitus Are Inversely Associated (Meta Analytic Covariate-Adjusted OR is 0.7, 95% CI 0.6-0.8)

Pull Quotes for Reference - "Current evidence is too weak for causal inference, but there now is a more stable evidence base for new lines of clinical translational research on a possibly protective (or spurious) cannabis smoking-diabetes mellitus association suggested in prior research." | "In general, cannabis smoking preceded diabetes mellitus. Estimated mean age of "first diagnosis" of diabetes mellitus was 40 years in the aggregate NHANES samples; mean age for "first cannabis smoking" was earlier, at 17 years. NSDUH did not assess age at onset for diabetes mellitus age at onset, but its mean age at onset for cannabis smoking was 18 years."

Notes - NHANES, 2005-2012 | NSDUH, 2005-2012 | NHANES includes a mix of self-report items about diabetes mellitus but adds information on current insulin and/or oral hypoglycemic medicine use and lab-derived glycohemoglobin levels for a composite diabetes mellitus indicator.

Country/State of data -

Author(s) - Gates et al.

Title - Cannabis Smoking and Respiratory Health: Consideration of the Literature

Year - 2014 (Gates, Jaffe, & Copeland, 2014)

Journal - Respirology

Study Type - Review

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Mixed for lung cancer, COPD, and emphysema primarily due to methodological issues. Strong for Airway inflammation and infection.

Pull Quotes for Reference - Overall, the literature suggests that smoking cannabis can have a negative impact on respiratory health.

Notes - Balanced review

Country/State of data - N/A

Author(s) - Biehl JR, Burnham EL

Title - Cannabis Smoking in 2015: A Concern for Lung Health?

Year - 2015 (Biehl & Burnham, 2015)

Journal - Chest

Study Type - Systematic review

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Increased cannabis use has paralleled legislative changes. Does-response relationship between prolonged heavy use and airflow limitation. Symptoms similar to chronic bronchitis appear in cannabis smokers after less intense use. Cannabis often smoked concurrently with tobacco. Cannabis smoke contains more ammonia, hydrogen cyanide, NO, and NOx than cigarette smoke. Association b/w heavy cannabis use and lung cancer ranges from RR 1.08 in case control/OR 7.87 in cross-sectional/HR 2.12 in longitudinal cohort to nonsignificant pooled OR of 0.95 from six case control studies.

Pull Quotes for Reference –

Notes - Table 1 summarizes association between lung capacity and cannabis and tobacco. **Good reference if we want these outcomes** - results are mixed.

Country/State of data - Review

Author(s) - Emilie Jouanjus, PharmD, PhD; Maryse Lapeyre-Mestre, MD, PhD; Joelle Micallef, MD, PhD; The French Association of the Regional Abuse and Dependence Monitoring Centres (CEIP-A) Working Group on Cannabis Complications

Title - Cannabis Use: Signal of Increasing Risk of Serious Cardiovascular Disorders

Year - 2014 (Jouanjus, Lapeyre-Mestre, & Micallef, Cannabis Use: Signal of Increasing Risk of Serious Cardiovascular Disorders, 2014)

Journal - Journal of the American Heart Association

Study Type - Case Review

Category - Physical Health

Systems Affected – Cardiovascular Disorders

Strength of Effect/ Direction of Effect - Low - This is a review of 39 cases. So numbers are very, very small. 1.8% of all cannabis-related reports (35/1979) were cardiovascular complications, with patients being mostly men (85.7%) and of an average age of 34.3 years. In 9 cases, the event led to patient death.

Pull Quotes for Reference - Practitioners should be aware that cannabis may be a potential triggering factor for cardiovascular complications in young people.

Notes - Interesting study. They use a reporting system in France that requires serious cases related to substances be reported. They looked those cases involving cardiovascular events.

Country/State of data - France

Author(s) - Danielsson, Anna-Karin; Falkstedt, Daniel; et al. (anna-karin.danielsson@ki.se)

Title - Cannabis Use Among Swedish Men in Adolescence and the Risk of Adverse Life Course Outcomes: Results From a 20 Year-follow-up Study

Year - Peer Reviewed/Accepted for Publication (Danielsson, Falkstedt, Hemmingsson, Allebeck, & Agardh)

Journal - ?

Study Type - Longitudinal Cohort Study (Examine Associations of Cannabis Use at 18-20 and Unemployment/Social Welfare Assistance at Age 40 in Swedish Men)

Category - YOUTH

Systems Affected -

Strength of Effect/ Direction of Effect - Individuals who used cannabis at high levels in adolescence (>50 times) had increased risk of future unemployment (Adjusted RR 1.26 95% CI 1.04-1.53, adjusted for social background, psychological functioning, health-behaviors, education level, and psychiatric disorders) | Individuals who used cannabis 1-10 times in adolescence had increased risk of future social welfare assistance (Adjusted RR 1.15 95% CI 1.06-1.26) | Individuals who used cannabis 11-50 times in adolescence had increased risk of future social welfare assistance (Adjusted RR 1.21 95% CI 1.04-1.42) | Individuals who used cannabis >50 times had increased risk of future social welfare assistance (Adjusted RR 1.38 95% CI 1.19-1.62)

Pull Quotes for Reference - "Heavy cannabis use among Swedish men in late adolescence appears to be associated with unemployment and being in need of social welfare assistance in adulthood."

Notes - 49,321 Swedish men born 1949-1951 and who were conscripted to compulsory military service at 18-20 years of age. | Life-time exposure to cannabis was assessed at conscription with the question on frequency of cannabis use, which had fixed responding alternatives: Never, 1 time, 2-4 times, 5-10 times, 11-50 times, and >50 times. 1 time, 2-4 times, and 5-10 times responses were combined to create 1-10 times category for analysis. Follow Up outcomes were collected from the Longitudinal Register of Education and Labor Market Statistics (LISA) between the years 1990-1995 (when men were 39-46 years of age). Unique personal identification numbers were used to link the conscript cohort data to the LISA data. Unemployment was defined as having received any income from Unemployment Insurance between 1990 - 1995 (yes/no). Social welfare assistance was categorized as having received it at least once during 1990-1995 (yes/no). Social background was a composite indicator comprised of: 1) Childhood socio-economic position as defined by father's occupational category in 1960: non-manual workers, manual workers, and no occupation. 2) Having divorced parents (yes/no) 3) Having been in contact with the police and/or childcare authorities (yes/no) Mental Function was measured on a stanine scale of general intelligence and social maturity. Low scores would indicate possible adjustment

problems. Diagnosis with Psychiatric disease (using ICD-8 codes) at conscription were also included in analysis. Health Behaviors were measured by Tobacco Smoking (None, 1-10 cigarettes per day, >10 cigarettes per day); Alcohol Consumption defined as "risky use" including one of the following: Ever been apprehended by the police for drunkenness, ever consumed alcohol during a hangover, been drunk often/quite often, drinking > or = 250 g of alcohol per week); Having used other illicit drugs such as amphetamine, morphine, LSD, and Opium (None, yes, yes/injected). Adulthood Education Level was categorized into primary (>or = 9 years), secondary (>or=12 years), and tertiary (> 12 years). Adulthood Psychiatric / Drug Disorders were defined as having been diagnosed and hospitalized due to psychiatric and/or drug-related disorder during the years 1973-1989 (yes/no)

Country/State of data -

Author(s) - Donoghue et al.

Title - Cannabis Use and Age of Onset of Schizophrenia: Data from the AESOP Study

Year - 2014 (Donoghue K. , Doody, Murray, Jones, & Morgan, 2014)

Journal - Psychiatry Research

Study Type - Retrospective

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - Analyzed gender differences in early onset schizophrenia in users and non-users of cannabis. Gender gap of schizophrenia onset significantly less in cannabis group

Pull Quotes for Reference - The current study lends further support to evidence that the use of cannabis is associated with an earlier onset of schizophrenia, which is not explained by confounding whereby cannabis and other illegal drug use is more common in males.

Notes –

Country/State of data - UK

Author(s) - Wittchen , Hans-Ulrich; Frohlich, Christine; Behrendt, Silke; et al. (wittchen@psychologie.tu-dresden.de)

Title - Cannabis Use and Cannabis Use Disorders and their Relationship to Mental Disorders: A 10-year Prospective-longitudinal Community Study in Adolescents

Year - 2007 (Wittchen, Frohlich, Behrendt, Gunther, & Rehm, 2007)

Journal - Drug and Alcohol Dependence

Study Type - Longitudinal Cohort Study (Examine Associations of Anxiety and Mood Disorders with Cannabis Use and Cannabis Use Disorders with 14-17 year old subjects from the Munich region of Germany with a three waves of follow up over 10 years)

Category - Brain

Systems Affected - Neurological

Strength of Effect/ Direction of Effect - Cannabis Use was associated with having any mental disorder at baseline (AOR: 3.1, 95% CI 2.3-4.0, Adjusting for Gender), any anxiety disorder at baseline (AOR: 1.7, 95% CI 1.2-2.3), other substance use disorders (AOR ranged from 6.2 to 10.9), as well as with ADHD (AOR: 2.1, 95% CI 1.0-4.1)|Cannabis Use was associated with major depression (AOR: 2.7, 95% CI 1.6-4.4), dysthymia (AOR: 6.0, 95% CI 2.6-13.8), hypomania/mania (AOR: 4.7, 95% CI 2.2-10.0), panic-anxiety disorders (AOR: 5.2, 95% CI 2.6-10.2)| Having any mental disorder at Baseline was associated with Increased Rates of Future Cannabis Use (AOR: 2.1, 95% CI 1.6-2.7)

Pull Quotes for Reference -

Notes - 1395 Community subjects aged 14-17 at baseline | Data collected as part of Early Developmental Stages of Psychopathology study | Baseline survey conducted in 1995 with follow ups occurring at approximately 1.5, 4 and 10 years later | Participants were 21-27 during the final wave of follow up | Participants who denied the mandatory commitment probes to answer questions on illicit drug use and disorders truthfully/openly at one or more waves, were excluded from the analyses referring to illicit substances resulting in an N= 1324 at baseline and N=1310 in the longitudinal sample

Country/State of data -

Author(s) - Matthew Large, BSc(Med), MBBS, FRANZCP; Swapnil Sharma, MBBS, FRANZCP; Michael T. Compton, MD, MPH; Tim Slade, PhD; Olav Nielssen, MBBS, MCrim, FRANZCP

Title - Cannabis Use and Earlier Onset of Psychosis

Year - 2011 (Large, Sharma, Compton, Slade, & Nielssen, 2011)

Journal - ARCH GEN PSYCHIATRY/VOL 68 (NO. 6) (JAMA Psychiatry)

Study Type - Meta-Analysis

Category - Psychosis

Systems Affected – Psychosis, mental health

Strength of Effect/ Direction of Effect - Strong - Meta-analysis found that the age at onset of psychosis for cannabis users was 2.70 years younger (standardized mean difference=−0.414) than for nonusers; for those with broadly defined substance use, the age at onset of psychosis was 2.00 years younger (standardized mean difference=−0.315) than for nonusers.

Pull Quotes for Reference - We found that the use of cannabis and other illicit substances was associated with an earlier age at onset of psychotic disorders. In contrast, alcohol use alone did not appear to be significantly associated with a younger age at onset of psychosis. "The results of this study provide strong evidence that reducing cannabis use could delay or even prevent some cases of psychosis"

Notes - With regard to our a priori hypothesis, we found that a higher proportion of cannabis users in the substance-using groups significantly contributed to the heterogeneity in the effect size, indicating an earlier mean age at onset of psychosis in samples with more cannabis users.

Notes - this is a meta-analysis of 83 studies

Country/State of data - Australia, USA (included results from studies done all over the world)

Author(s) - van Ours, Jan; Williams, Jenny

Title - Cannabis Use and its Effects on Health, Education and Labor Market Success

Year - 2014 (van Ours & Williams, 2014)

Journal - van Ours, J. C., & Williams, J. (2014). Cannabis Use and its Effects on Health, Education and Labor Market Success. (CentER Discussion Paper; Vol. 2014-024). Tilburg: Economics.

Study Type - Literature overview

Category - Economics

Systems Affected - Education and labor markets

Strength of Effect/ Direction of Effect - NA

Pull Quotes for Reference - We conclude that there do not appear to be serious harmful health effects of moderate cannabis use. Nevertheless, there is evidence of reduced mental well-being for heavy users who are susceptible to mental health problems. While there is robust evidence that early cannabis use reduces educational attainment, there remains substantial uncertainty as to whether using cannabis has adverse labor market e etc.

Notes - This is a literature overview. Useful to have their table on pages 24 & 25. Unfortunately this is a very selective review and has an obvious pro cannabis bias.

Country/State of data - NA

Author(s) - J. van Os

Title - Cannabis Use and Psychosis: A Longitudinal Population-based Study

Year - 2002 (Van Os, Bak, Hanssen, Bijl, & de Graaf, 2002)

Journal - American Journal of Epidemiology

Study Type - epidemiological study

Category - Psychosis

Systems Affected - mental health

Strength of Effect/ Direction of Effect - strong evidence

Pull Quotes for Reference - "Results confirm previous suggestions that cannabis use increases the risk of both the incidence of psychosis in psychosis-free persons and a poor prognosis for those with an established vulnerability to psychotic disorder. "We found that the use of cannabis and other illicit substances was associated with an earlier age at onset of psychotic disorders. In contrast, alcohol use alone did not appear to be significantly associated with a younger age at onset of psychosis" "The results of this study provide strong evidence that reducing cannabis use could delay or even prevent some cases of psychosis"

Notes - study included 4000 people selected from general population samples

Country/State of data - Netherlands

Author(s) - Sarah Aldington1, Matire Harwood1, Brian Cox2, Mark Weatherall3, Lutz Beckert1, Anna Hansell4, Alison Pritchard1, Geoffrey Robinson1, and Richard Beasley1,5 On behalf of the Cannabis and Respiratory Disease Research Group

Title – Cannabis Use and Risk of Lung Cancer: A Case Control Study

Year - 2008 (Aldington S. , Harwood, Cox, Weatherall, & Beckert, 2008)

Journal - Eur Respir J. 2008 February; 31(2): 280–286.

Study Type - population-based case-control study

Category - Respiratory

Systems Affected - Lung cancer

Strength of Effect/ Direction of Effect - Medium - The risk of lung cancer increased 8% (95% CI 2% to 15%) for each joint-year of cannabis smoking, after adjustment for confounding variables including cigarette smoking, and 7% (95% CI 5% to 9%) for each pack year of cigarette smoking, after adjustment for confounding variables including cannabis smoking. The highest tertile of cannabis use was associated with an increased risk of lung cancer RR=5.7 (95% CI 1.5 to 21.6), after adjustment for confounding variables including cigarette smoking.

Pull Quotes for Reference - Long term cannabis use increases the risk of lung cancer in young adults.

Notes - Note - relatively small N (~400 total people) - and retrospective data collection on marijuana use.

Country/State of data -

Author(s) - Aldington et al.

Title - Cannabis Use and Risk of Lung cancer: A Case-control Study

Year - 2008 (Aldington S. , Harwood, Cox, Weatherall, & Beckert, 2008)

Journal - European Respiratory Journal

Study Type - survey, case-control

Category - Respiratory

Systems Affected - lung cancer

Strength of Effect/ Direction of Effect - Strong - Used a case control design to examine RR of cannabis use in the etiology of lung cancer and found the risk of lung cancer increased 8% for each joint-year of cannabis smoking controlling for confounding variables such as tobacco use, alcohol use, diet, etc.

Pull Quotes for Reference - "The major finding from the present study was that for each joint year of cannabis exposure, the risk of lung cancer increased by 8%, after adjustment for confounding variables including tobacco smoking. A major differential risk between cannabis and cigarette smoking was observed, with one joint of cannabis being similar to, 20 cigarettes for risk of lung cancer."

Notes - No difference in early (<16) vs late(>21) onset cannabis in RR for lung cancer. Only factor relevant was amount smoked.

Country/State of data - New Zealand

Author(s) - Theresa Moore et. al.

Title - Cannabis Use and Risk of psychotic of affective mental health outcomes: a systematic review

Year - 2007 (Moore, Zammit, Lingford-Hughes, Barnes, & Jones, 2007)

Journal - Lancet

Study Type - meta-analysis

Category - Psychosis

Systems Affected - mental health

Strength of Effect/ Direction of Effect - strong evidence

Pull Quotes for Reference - "In conclusion, we have described a consistent associations between cannabis use and psychotic symptoms, including disabling psychotic disorders." "We believe that there is now enough evidence to inform people that using cannabis could increase their lifetime risk of developing a psychotic illness later in life."

Notes - includes results from prominent large epidemiological studies

Country/State of data - world wide

Author(s) - Merel F. H. Griffith-Lendering1, Johanna T. W. Wigman2,3, Andrea Prince van Leeuwen4, Stephan C. J. Huijbregts1,5, Anja C. Huizink4, Johan Ormel6, Frank C. Verhulst7, Jim van Os3,8, Hanna Swaab1,5 & Wilma A. M. Vollebergh2

Title - Cannabis Use and Vulnerability for Psychosis in Early Adolescence—A TRAILS Study

Year - 2012 (Griffith-Lendering, Wigman, Prince van Leeuwen, Huijbregts, & Huizink, 2012)

Journal - Addiction

Study Type - Prospective longitudinal

Category - Psychosis

Systems Affected - Psychosis

Strength of Effect/ Direction of Effect - Strong - the present study showed that cannabis use at age 16 predicted psychosis vulnerability at age 19 and psychosis vulnerability at age 13 and 16 predicted cannabis use at, respectively, age 16 and 19, thereby providing evidence for both the damage hypothesis and self-medication hypotheses.

Pull Quotes for Reference - Cannabis use predicts psychosis vulnerability in adolescents and vice versa, which suggests that there is a bidirectional causal association between the two.

Notes –

Country/State of data - Netherlands

Author(s) - van Gastel et al.

Title - Cannabis Use as an Indicator of Risk for Mental Health Problems in adolescents: A Population-based Study at Secondary Schools

Year - 2013 (van Gastel, Tempelaar, Bun, Schubart, & Kahn, 2013)

Journal - Psychological Medicine

Study Type - Survey

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Weak - This study uses nonstandard measures and then dichotomizes them. There is an error in Table 1.

Pull Quotes for Reference - "Despite its limitations, we consider that the present study is important because it demonstrates the relevance of cannabis use as a risk factor for poor psychosocial functioning in secondary school children."

Notes - A methodologically questionable study

Country/State of data - Netherlands

Author(s) - Fontes et al.

Title - Cannabis Use Before Age 15 and Subsequent Executive Functioning

Year - 2011 (Fontes, Bolla, Cunha, Almeida, & Jungerman, 2011)

Journal - British Journal of Psychiatry

Study Type - Survey/experimental

Category - YOUTH

Systems Affected - cognitive functioning

Strength of Effect/ Direction of Effect - Strong - investigated early vs late onset of marijuana use in terms of cognitive functioning at age 30. Early onset group performed significantly worse on all neuropsychological tests compared to controls.

Pull Quotes for Reference - "Our findings indicate that early-onset chronic cannabis users are cognitively impaired compared with controls, suggesting that early exposure to cannabis is associated with more adverse effects on the brain."

Notes -

Country/State of data - Brazil

Author(s) - Stinson FS, Ruan WJ, Pickering R, Grant BF

Title - Cannabis Use Disorders in the USA: Prevalence, Correlates and Co-morbidity

Year - 2006 (Stinson, Ruan, Pickering, & Grant, 2006)

Journal - Psychological Medicine

Study Type - National Epidemiologic Survey on Alcohol and Related Conditions - cross-sectional, nationally representative sample. Civilians aged 18+ in households and group quarters. Face-to-face interviews.

Category - YOUTH

Systems Affected - Substance used disorders (cannabis, nicotine, alcohol), **psychiatric disorders** (panic disorder with agoraphobia, panic disorder without agoraphobia, social phobia, specific phobia, generalized anxiety disorder, dysthymia, major depressive disorder, bipolar I and II), **drug treatment**

Strength of Effect/ Direction of Effect - 2001-2002: 1.5% of adults experienced a cannabis use disorder and 8.5% lifetime prevalence. Mean age of onset cannabis abuse - 19.3. Mean age of onset cannabis dependence - 19.0. Interval b/w abuse onset and treatment 5.5 years, dependence 3.1 years. Males more likely to have any cannabis use disorder (11.8% OR 2.5, 2.25-2.79); whites 9.3% more likely to use than Black/Asian/Hispanic but less than Native American (15.4% OR 1.6, 1.21-2.1), 18-29 age group most likely though NSD with 30-44; widowed/separated/divorced more likely (7.7% 1.6, 1.41-1.81); low income most likely ($0-19,000 7.8% OR 1.4, 1.11-1.65 and $20K-34,999 9.0% OR 1.2, 1.01-1.46), Northeast less likely compared to West (7.8% any disorder). Among those with any 12-month cannabis use disorder 57.4% had alcohol use disorder (OR 7.8, 6.21-9.89), 53.1% had nicotine dependence (OR 5.1, 4.19-6.31). Among those with 12-month any cannabis use disorder, increased risk of any mood disorder (29.9% OR 2.9, 2.28-3.6), any anxiety disorder (24.1%, OR 2.4, 1.9-3.15), any personality disorder (48.4%, OR 3.9, 3.18-4.66)

Pull Quotes for Reference - "This study confirmed that cannabis use and dependence are often disorders of adolescence and early adulthood. Individuals at greatest risk for onset of cannabis abuse and dependence are between ages 15 and 20 and onsets of cannabis abuse and dependence after age 30 are rare." (p.1454) "This study also highlighted the continued lack of treatment for many individuals with cannabis abuse and dependence." (p.1454) "That the odds of cannabis abuse did not decrease linearly with age, while the odds of dependence did, underscores the need for further research on transitions from use to abuse to dependence on cannabis." (p. 1455) "The results on cannabis use disorders and mood and anxiety disorder co-morbidity showed that bipolar disorders were more strongly related to cannabis use and dependence than were major depression and dysthymia, and that panic disorder with agoraphobia and generalized anxiety disorder were more strongly associated with cannabis abuse and dependence than any other anxiety disorder." (p. 1455)

Notes - Figure 1 - hazard rates for cannabis abuse & dependence by age. Peaks at age 18. Has info on treatment types and access if necessary. No urban/rural differences. There was a follow-up NESARC three-years later.

Country/State of data - National

Author(s) - Benjamin Chadwick 1†, Michael L. Miller 1† and Yasmin L. Hurd1,2,3

Title - Cannabis Use During Adolescent Development: Susceptibility to Psychiatric Illness

Year - 2013 (Chadwick, Miller, & Hurd, 2013)

Journal - Frontiers in Psychiatry

Study Type - review article

Category - Psychosis

Systems Affected - mental health

Strength of Effect/ Direction of Effect - strong evidence

Pull Quotes for Reference - "Numerous human studies, including prospective longitudinal studies, demonstrate that early cannabis use is associated with major depressive disorder and drug addiction. A strong association between schizophrenia and cannabis use is also apparent, especially when considering genetic factors that interact with this environmental exposure. These human studies set a foundation for carefully controlled animal studies which demonstrate similar patterns following early cannabinoid exposure. Given the vulnerable nature of adolescent neurodevelopment and the persistent changes that follow early cannabis exposure, the experimental findings outlined should be carefully considered by policymakers. In order to fully address the growing issues of psychiatric illnesses and to ensure a healthy future, measures should be taken to reduce cannabis use among teens. "

Notes - review article some of the same studies cited by other meta-analyses

Country/State of data - USA (studies from around the world were cited)

Author(s) - W. A. van Gastel • J. H. MacCabe •C. D. Schubart • E. van Otterdijk • R. S. Kahn • M. P. M. Boks

Title - Cannabis Use is a Better Indicator of Poor Mental Health in Women than in Men: A Cross-Sectional Study in Young Adults from the General Population

Year - 2014 (van Gastel, MacCabe, Schubart, van Otterdijk, & Kahn, 2014)

Journal - Community Mental Health J (2014) 50:823–830

Study Type - Cross Sectional

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Medium - Data collected over a long period (2006-2001). Cross sectional. Monthly cannabis use was associated with a higher total score on the SCL-90, both in a crude (OR 1.94, 95 % CI 1.57–2.38) and fully adjusted model (OR 1.48, 95 % CI 1.07–2.03). The association between cannabis and mental health was stronger in women and weekly users, and was independent of age at first use of cannabis.

Pull Quotes for Reference - In a large sample of young adults aged 18 to 30 years old, we found that monthly cannabis use was associated with poor general mental health, independent of age at onset of use and of other risk factors. The only modifier for this effect was gender: the association was strongest in women.

Notes - Survey conducted from 2006-2011 which is a really long time

Country/State of data - Netherlands

Author(s) - Gilman et al.

Title - Cannabis Use is Quantitatively Associated with Nucleus Accumbens and Amygdala Abnormalities in Young Adult Recreational Users

Year - 2014 (Gilman, Kuster, Lee, Lee, & Kim, 2014)

Journal - The Journal of Neuroscience

Study Type - Observational

Category - Brain

Systems Affected - Brain abnormalities

Strength of Effect/ Direction of Effect - Strong - using MRI demonstrates dose dependent abnormalities in particular brain regions among young (Mean approx. 21 years) recreational cannabis users compared to non-using controls.

Pull Quotes for Reference - The results of this study indicate that in young, recreational marijuana users, structural abnormalities in gray matter density, volume, and shape of the nucleus accumbens and amygdala can be observed

Notes - Small sample size but controls matched on age, sex, handedness, race, and years of education.

Country/State of data - US

Author(s) - Kim Donoghue a,n, GillianA.Doody

Title - Cannabis Use, Gender and Age of Onset of Schizophrenia: Data from the ÆSOP Study

Year - 2014 (Donoghue K. , Doody, Murray, Jones, & Morgan, 2014)

Journal - Psychiatry Research215 (2014) 528–532

Study Type - New research (epidemiological study)

Category - Psychosis

Systems Affected - mental health

Strength of Effect/ Direction of Effect - strong evidence. Cannabis increases risk of psychosis and prepones the onset of psychosis by a couple of years.

Pull Quotes for Reference - "The use of cannabis is associated with an earlier age of onset of schizophrenia" "A third explanation is that cannabis is a causal factor in the development of schizophrenia. There is growing evidence in favor of this hypothesis, for example, a meta-analysis found that there is a significant increased risk of developing a psychotic disorder in those who have used cannabis (Moore et al., 2007)."

Notes - good study method to look at age of onset but a small number (N) of participants in the study

Country/State of data - three centers in United Kingdom

Author(s) - Manrique-Garcia et al.

Title - Cannabis, Schizophrenia and Other non-affective Psychoses: 35 Years of Follow-Up of a Population-Based Cohort

Year - 2011 (Manrique-Garcia, Zammit, Dalman, Hemmingsson, & Andreasson, 2011)

Journal - Psychological Medicine

Study Type - Prospective Longitudinal

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - a 35 year follow-up of the Swedish Conscription study demonstrates an almost 4 fold increase of schizophrenia diagnosis in individuals reporting using marijuana more than 50 times at baseline.

Pull Quotes for Reference - Our study confirms the strong association between cannabis and psychotic disorders, with a more than three-fold increased risk for schizophrenia, and two-fold increased risk for other psychotic outcomes in those using cannabis most frequently. For schizophrenia, we observed a dose–response association

Notes - Very long-term follow-up demonstrates clear association between early cannabis use and subsequent development of schizophrenia.

Country/State of data - Sweden

Author(s) - Jouanjus, Emilie; Leymarie, Florence; et al. (jouanjus@cict.fr)

Title - Cannabis-related Hospitalizations: Unexpected Serious Events Identified through Hospital Databases

Year - 2010 (Jouanjus, Leymarie, Tubery, & Lapeyri-Mestre, 2010)

Journal - British Journal of Clinical Pharmacology

Study Type - Observational Study Based on Claims Data From Six Public Hospitals of Toulouse, France from 2004 to 2007

Category - Physical Health

Systems Affected - Cannabis-Related Hospitalizations

Strength of Effect/ Direction of Effect - 2.94 per 1000 Recent Users (95% CI 2.41-3.48) and 5.05 per 1000 of Regular Users (4.13-5.97) of Cannabis Experienced Adverse Events Due to Psychiatric Disorders | 2.25 per 1000 Recent Users (95% CI 1.78-2.72) and 3.86 per 1000 Regular Users (95% CI 3.06-4.67) of Cannabis Experienced Adverse Events Due to Central and Peripheral Nervous Systems Disorders | 1.92 per 1000 Recent Users (95% CI 1.49-2.35) and 3.29 per 1000 Regular Users (95% CI 2.55-4.04) of Cannabis Experienced Poison Specific Adverse Events | 1.48 per 1000 Recent Users (95% CI 1.19-1.98) and 2.72 per 1000 Regular Users (95% CI 2.04-3.40) of Cannabis Experienced Respiratory System Related Adverse Events

Pull Quotes for Reference - "Among the 200 included patients, 153 (76.5%) were men. Mean age at admission was 28.0 years (95% CI 26.7-29.3) | "Estimated incidence of cannabis-related hospitalizations in 2007 in Toulouse Urban Unit was 1.9 (95% CI 1.4-2.3) per 1000 recent cannabis users and 3.2 (95% CI 2.5-3.9) per 1000 regular cannabis users." |

Notes - Population sampled included inpatients of all medical and surgical wards of the six Toulouse hospitals for whom ICD-10 terms related to mental and behavioral disorders associated to the use of psychoactive drugs (F10 to F19 codes) | Total Number of Hospitalizations Included: 701 (Based on F12 and F19 codes or Cannabis Disorder and Multiple Drug Use/Use of Other Psychoactive Substances respectively | 172 hospitalizations associated with Use of Cannabinoids Were Included In Data Set | 158 Patients with Cannabis Disorder were Included | 52 Hospitalizations Related to Use of Multiple Drugs Were Included | 42 Patients Using Multiple Drugs Were Included | Incidences were calculated using regional estimates based on the Urban Unit data

Country/State of data -

Author(s) - Matthew J. Smith*,1, Derin J. Cobia1, Lei Wang1,2, Kathryn I. Alpert1, Will J. Cronenwett1, Morris B. Goldman1, Daniel Mamah3, and Deanna M. Barch3–5,7, Hans C. Breiter1,6,7, John G. Csernansky1,7

Title - Cannabis-Related Working Memory Deficits and Associated Subcortical Morphological Differences in Healthy Individuals and Schizophrenia Subjects

Year - 2013 (Smith, Cobia, Wang, Alpert, & Cronenwett, 2013)

Journal - Schizophrenia Bulletin vol. 40 no. 2 pp. 287–299, 2014

Study Type - Brain imaging

Category - Brain

Systems Affected - Brain

Strength of Effect/ Direction of Effect - Medium - they cannot prove causation, just association. Our results suggest that (1) CON-CUD were characterized by subcortical shape that differed from CON-Clean; (2) SCZ-CUD were characterized by subcortical shape that differed from SCZ-Clean and were consistent with the subcortical shape observed in CONCUD and schizophrenia; (3) SCZ-Clean shape findings contrasted prior studies; (4) cannabis-related shape asymmetries were observed in the thalamus; (5) CON-CUD and SCZ-CUD demonstrated parametric deficits in WM performance compared with CON-Clean and SCZ-Clean, respectively; and (6) cannabis-related shape differences were correlated with more severe WM performance deficits and age of CUD onset in CON-CUD and SCZ-CUD.

Pull Quotes for Reference –

Notes - Future longitudinal studies could help determine whether cannabis use contributes to these observed shape differences or whether they are biomarkers of a vulnerability to the effects of cannabis that predate its misuse.

Country/State of data -

Author(s) - Rebecca J. Evans-Polce a,b,⍰, Sara A. Vasilenko a, Stephanie T. Lanza a,c

Title - Changes in Gender and Racial/Ethnic Disparities in Rates of Cigarette Use, Regular Heavy Episodic Drinking, and Marijuana Use: Ages 14 to 32

Year - 2015 (Evans-Polce, Vasilenk, & Lanza, 2015)

Journal - Addictive Behaviors 41 (2015) 218–222

Study Type - Longitudinal cohort

Category - Risk Factors for use

Systems Affected - Disparities

Strength of Effect/ Direction of Effect - Medium - there are gender and age disparities in marijuana use. The prevalence of marijuana use was not significantly different across gender in early adolescence. However, the prevalence among males rose more sharply and for a longer age period than for females. Use among males and females peaked at 21.5 years (27.5% reporting use) and 19.8 years (18.5% reporting use), respectively. Rates of use among both genders showed a steady decline after their peak, falling to 17.6% for males and 10.1% for females by age 32. The prevalence of marijuana use was similar among White and Black adolescents until age 16 and among White and Hispanic adolescents until age 18.5 (Fig. 2c). However, the prevalence of use among White adolescents continued to rise through age 20.7 (24.7% reporting use). Use among White adolescents began to decline after this age; after age 24 all three groups followed a similar pattern of declining rates, to 10–15% by young adulthood.

Pull Quotes for Reference - Disparities in substance use behaviors fluctuate considerably throughout adolescence and young adulthood, suggesting that targeted intervention programs are more critical at particular ages.

Notes –

Country/State of data -

Author(s) - van Gelder et al.

Title - Characteristics of Pregnant Illicit Drug Users and Associations between Cannabis Use and Perinatal Outcome in a Population-Based Study

Year - 2010 (van Gelder, Reefhuis, Caton, Werler, & Druschel, 2010)

Journal - Drug and Alcohol Dependence

Study Type - Survey/Records search

Category - Reproductive

Systems Affected - Perinatal

Strength of Effect/ Direction of Effect - Moderate - Pregnant individuals who smoked marijuana during pregnancy were less educated and had a lower income than non-users. No difference in birth weight or gestational age at term among marijuana users and nonusers.

Pull Quotes for Reference - "Our findings suggest that prenatal cannabis use overall is not associated with birth weight or gestational age

Notes –

Country/State of data - US

Author(s) - Jon Heron1, Edward D. Barker2, Carol Joinson1, Glyn Lewis1, Matthew Hickman1, Marcus Munafò3 & John Macleod1

Title - Childhood Conduct Disorder Trajectories, Prior Risk Factors and Cannabis Use at Age 16: Birth Cohort Study

Year - 2013 (Heron, Barker, Joinson, Lewis, & Hickman, 2013)

Journal - Addiction

Study Type - Birth cohort

Category - Risk Factors for use

Systems Affected - Conduct problems, SES as RISK FACTORS FOR cannabis use.

Strength of Effect/ Direction of Effect - NOTE: Strong association of risk factors for using cannabis. Early-onset persistent conduct problems were associated strongly with problem cannabis use [odds ratio (OR) = 6.46, 95% confidence interval (CI) = 4.06–10.28]. Residence in subsidized housing (OR = 3.10, 95% CI = 1.95, 4.92); maternal cannabis use (OR 8.84, 95% CI 5.64–13.9) and any maternal smoking in the postnatal period (OR = 2.69, 95% CI = 1.90–3.81) all predicted problem cannabis use. Attributable risks for adolescent problem cannabis use associated with the above factors were 25, 13, 17 and 24%, respectively

Pull Quotes for Reference - Maternal smoking and cannabis use, early material disadvantage and early-onset persistent conduct problems are important risk factors for adolescent problem cannabis use.

Notes - This is a reverse of the many other studies. It details what risk factors are for using marijuana at age 16.

Country/State of data - England

Author(s) - Bechtold et al.

Title - Chronic Adolescent Marijuana Use as a Risk Factor for Physical and Mental Health Problems in Young Adult Men

Year - 2015 (Bechtold, Simpson, White, & Pardini, 2015)

Journal - Psychology of Addictive Behaviors

Study Type - Longitudinal, Prospective

Category - YOUTH

Systems Affected - Physical and Mental Health

Strength of Effect/ Direction of Effect - Weak - Unrepresentative samples of males followed for 20 years show no marijuana associated physical or mental health effects

Pull Quotes for Reference - In conclusion, the health outcomes associated with marijuana use are just one piece of the legalization puzzle. Political debates surrounding the legalization of this drug also need to consider the potential effects on many other domains such as cognitive and intellectual functioning, alterations in brain function and structure, academic and occupational failure, psychosocial adjustment, antisocial and criminal behavior, motor vehicle accidents, and suicidal ideation.

Notes - Reviewed for Harry and Barbara. Problems in methodology, interpretation, and a very selective review of the existing literature.

Country/State of data - USA

Author(s) - Budney AJ

Title - Clinical Epidemiology, Characteristics, Services, and Outcomes for Youth with Cannabis Use Disorders: Status of the Problem and Expectations for the Future

Year - 2014 (Budney, 2014)

Journal - n/a

Study Type - Presentation

Category - YOUTH

Systems Affected - n/a

Strength of Effect/ Direction of Effect - n/a

Pull Quotes for Reference - n/a

Notes - Marijuana/hashish are the most frequently used drugs among 8th and 12th graders (Monitoring the Future Study); Marijuana dependence or abuse most likely among 18 y.o. (NSDUH 2012); Marijuana associated with more treatment admissions than other drugs (TEDS); Comorbidities include MDE, anxiety disorder, bipolar, antisocial beh., obsessive-compulsive, paranoia (Stinson et al);

Country/State of data - Unknown: Each of the studies referenced by the manuscript would need to be reviewed

Author(s) - Timothy I Michaels, BA and Vladan Novakovic, MD

Title - Can Cannabis Cause Psychosis?

Year - 2015 (Michaels & Novakovic, 2015)

Journal - Clinical Neuropharmacology

Study Type - Editorial (citing several studies to make the case)

Category - Psychosis

Systems Affected - mental health

Strength of Effect/ Direction of Effect - strong evidence. Cannabis increases risk of psychosis especially in adolescents. Seems to be especially relevant for those with other risk factors. Psychosis more likely associated than schizophrenia

Pull Quotes for Reference - "The risks associated with cannabis use are particularly high for adolescents because this is a critical period of development in which the brain is especially susceptible to the potentially harmful effects of cannabis" "The use of synthetic cannabis may result in both acute and persistent psychotic experiences."

Notes - although it's an editorial, it's still important because the author cites major studies for every point discussed.

Country/State of data - worldwide (studies quoted from North America, Europe and Australia)

Author(s) - Filbey et al.

Title - Combined Effects of Marijuana and Nicotine on Memory Performance and Hippocampal Volume

Year - 2015 (Filbey, McQueeny, Kadamangudi, Brice, & Ketcherside, 2015)

Journal - Behavioral Brain Research

Study Type - Survey/Experimental

Category - Brain

Systems Affected - Hippocampal size and Memory performance

Strength of Effect/ Direction of Effect - Weak - Found smaller hippocamus size in marijuana only smokers and a significant effect for marijuana and tobacco smokers. Small group sizes

Pull Quotes for Reference - "Overall, results suggest abnormalities in the brain-behavior relationships underlying memory processes with combined use of marijuana and nicotine use."

Notes - Unusual groups - especially the marijuana -only group. Small sample sizes and no corrections for multiple comparisons.

Country/State of data - New Mexico

Author(s) - Lisdahl, K. M., Wright, N. E., Medina-Kirchner, C. et al.

Title - Considering Cannabis: The Effects of Regular Cannabis Use on Neuro-cognition in Adolescents and Young Adults

Year - 2014 (Lisdahl, Wright, Medina-Kirchner, Maple, & Shollenbarger, 2014)

Journal - Current Addiction Reports

Study Type - Review without statement of inclusion/exclusion criteria or methods for choosing cited literature

Category - do not use

Systems Affected - do not use

Strength of Effect/ Direction of Effect - do not use

Pull Quotes for Reference - do not use

Notes - do not use

Country/State of data - USA / Wisconsin

Author(s) - Rebecca Kuepper, Jim van Os, Roselind Lieb, Hans-Ulrich Wittchen, Michael Höfler, Cècile Henquet

Title - Continued Cannabis Use and Risk of Incidence and Persistence of Psychotic Symptoms: 10 Year Follow-up Cohort Study

Year – 2013 (Kuepper, et al., 2013)

Journal - British Medical Journal

Study Type - prospective population based cohort

Category - Psychosis

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - incident cannabis use over the period from baseline to T2 increased the risk of later incident psychotic symptoms over the period from T2 to T3 (adjusted odds ratio 1.9, 95% confidence interval 1.1 to 3.1; P=0.021). Furthermore, continued use of cannabis increased the risk of persistent psychotic symptoms over the period from T2 to T3 (2.2, 1.2 to 4.2; P=0.016). The incidence rate of psychotic symptoms over the period from baseline to T2 was 31% (152) in exposed individuals versus 20% (284) in non-exposed individuals; over the period from T2 to T3 these rates were 14% (108) and 8% (49), respectively.

Strength of Effect/ Direction of Effect - Strong - examined onset and persistence of psychotic symptoms among those not using cannabis at baseline

Pull Quotes for Reference - Cannabis use is a risk factor for the development of incident psychotic symptoms. Continued cannabis use might increase the risk for psychotic disorder by impacting on the persistence of symptoms.

Pull Quotes for Reference - This 10 year follow-up study clearly showed that incident cannabis use significantly increased the risk of incident psychotic experiences. The association was independent of age, sex, socioeconomic status, use of other drugs, urban/rural environment, and childhood trauma; additional adjustment for other psychiatric diagnoses similarly did not change the results

Notes - Adds to a base of international prospective longitudinal studies demonstrating the cannabis-psychosis connection.

Country/State of data - Germany

Author(s) - Hartman, R. L., Brown, T. L., Milavetz, G. et al.

Title - Controlled Cannabis Vaporizer Administration: Blood and Plasma Cannabinoids with and without Alcohol

Year - 2015 (Hartman, Brown, Milavetz, Spurgin, & Gorelick, 2015)

Journal - Clinical Chemistry

Study Type - Observational/Correlational

Category - Risk Factors for use

Systems Affected - Blood and plasma cannabinoids, THCCOOH-glucuronide/THCCOOH ratios

Strength of Effect/ Direction of Effect - Maximum blood concentrations of THC following low-dose or high-dose THC vaporization were significantly increased when alcohol was co-administered with cannabis.

Pull Quotes for Reference - "Alcohol effects on cannabinoid pharmacokinetics are of interest due to the commonality of co-ingestion. Combining these drugs affects performance impairment, possibly in part owing to higher cannabinoid concentrations."

Notes - 32 healthy adult cannabis smokers (of which 22 were men, aged 21-42 years, 72% white) participated; 19 participants completed all 6 sessions; within-individual design so participants received all 6 alcohol/cannabis doses in randomized order (Ethanol + / -, Low-dose THC + / - and High-dose THC + / -)

Country/State of data - USA / Maryland and Iowa

Author(s) - Jacobus, J., Squeglia, L. M., Sorg, S. F. et al.

Title - Cortical Thickness and Neurocognition in Adolescent Marijuana and Alcohol Users Following 28 Days of Monitored Abstinence

Year - 2014 (Jacobus, Squeglia, Sorg, Nguyen-Louie, & Tapert, 2014)

Journal - Journal of Studies on Alcohol and Drugs

Study Type - Observational/Correlational (Neuroimaging [MRI] and Neuropsychological, Substance Abuse and Mental Health Assessments)

Category - Brain

Systems Affected - Cortical Thickness, Neurocognition

Strength of Effect/ Direction of Effect - Increase + Decrease Observed; Increased cortical thickness in left entorhinal cortex only after controlling for alcohol use; Decreased cortical thickness estimates in certain brain regions were associated with more reported lifetime marijuana use (relationships did not change when lifetime alcohol use was held constant). Lack of consistent group differences in cognition across the 5 domains assessed.

Pull Quotes for Reference - "A main effect of group status on cortical thickness estimates was found in four regions (controlling for intracranial volume) in which MJ + Alcohol demonstrated significantly thicker cortices compared to controls … In no region did controls demonstrate thicker cortices than MJ + ALC" but between-group differences did not persist after covarying for alcohol use except in the left entorhinal cortex. "Onset of regular marijuana use was positively related to cortical thickness, in that initiation of regular use at a younger age was linked to thinner cortices at follow-up" in several brain regions.

Notes - Investigated impact of heavy marijuana and alcohol use on cortical thickness in adolescents before and after 28 days of monitored abstinence (n = 54, 24 heavy marijuana users that regularly used alcohol and 30 control teens). Excluded mental disorders, etc. and left-handedness. Sample was predominately male (>70%). Statistically significant differences were identified in baseline participant characteristics, including grade point average & WASI vocabulary score, when control compared to substance-using group. Lifetime alcohol use was statistically adjusted for follow-up post hoc ANCOVAs examining group differences at each time point for regions where a main effect of a group was identified. Bivariate correlations between substance use variables in secondary analyses. Repeated measures ANCOVA used to evaluate neurocognitive performance over time with alcohol as a covariate for each subtest.

Country/State of data - USA / California and Washington

Author(s) - Jérôme Adda, Brendon McConnell, and Imran Rasul

Title - Crime and the Depenalization of Cannabis Possession: Evidence from a Policing Experiment

Year - 2014 (Adda, McConnell, & Rasul, 2014)

Journal - Journal of Political Economy, Vol. 122, No. 5

Study Type - Observational

Category - Regulation

Systems Affected - Crime after decriminalization

Strength of Effect/ Direction of Effect - DECRIMINALIZATION focus - this is not about legalization or health impacts. It does cover changes in crime rates after decriminalization

Pull Quotes for Reference - We find that depenalization in Lambeth led to an increase in cannabis possession offenses that persisted well after the policy experiment ended. We find evidence that the policy enables the police in Lambeth to be able to reallocate their effort toward nondrug crime: there are significant long-run reductions in five nondrug crime types and significant improvements in police effectiveness against such crimes as measured by arrest and clear-up rates.

Notes – DECRIMINALIZATION

Notes - This is about decriminalization, not legalization.

Country/State of data - UK

Author(s) - Fischer et al.

Title - Crude Estimates of Cannabis-Attributable Mortality and Morbidity in Canada - Implications for Public Health Focused Intervention Priorities

Year - 2015 (Fischer, Imtiaz, Rudzinski, & Rehm, 2015)

Journal - Journal of Public Health Advances

Study Type - Report

Category - HEALTH

Systems Affected - MVA, Use Disorders, Mental Health, Cancer

Strength of Effect/ Direction of Effect - Low - these are very imprecise estimates based on extant literature and Canadian population data.

Pull Quotes for Reference - "The overall assessment of the actual burden of cannabis-attributable health problems no a population level should be further developed and refined."

Notes - Two largest burdens attributable to cannabis use are MVA (both fatalities and injuries) and cancer.

Country/State of data - Canada

Author(s) Bossong MG, Jansma JM, van Hell HH, Jager G, Kahn RS, et al.

Title - Default Mode Network in the Effects of D9-Tetrahydrocannabinol (THC) on Human Executive Function

Year - 2013 (Gossong, Jansma, van Hell, Jager, & Kahn, 2013)

Journal - Bossong MG, Jansma JM, van Hell HH, Jager G, Kahn RS, et al. (2013) Default Mode Network in the Effects of D9-Tetrahydrocannabinol (THC) on Human Executive Function. PLoS ONE 8(7): e70074. doi:10.1371/journal.pone.0070074

Study Type - Double-blind, randomized control

Category - Brain

Systems Affected -Task performance and brain function

Strength of Effect/ Direction of Effect - Strong - THC administration significantly decreased the percentage of correctly identified targets (from 83.762.9% to 74.764.3%, t(19) =2.66, p = 0.016) and enhanced the percentage of false
alarms (from 3.560.7% to 5.760.9%, t(19)=23.76, p =0.001). Reaction times on the CPT-IP did not differ between placebo and THC sessions (538.567.1 and 552.0611.0 ms, respectively;
t(19) =21.07, p = 0.296) (all 6 SEM, see Figure 2).

Pull Quotes for Reference - Task performance was impaired after THC administration, reflected in both an increase in false alarms and a reduction in detected targets. This was associated with reduced deactivation in a set of brain regions linked to the default mode network, including posterior cingulate cortex and angular gyrus. Less deactivation was significantly correlated with lower performance after THC.

Notes -This study is complicated and should be reviewed by a provider. However, it shows that task performance decreases with an increase in THC levels.

Country/State of data -

Author(s) - Matthijs G. Bossong, J. Martijn Jansma

Title - Default Mode Network in the Effects of D9-Tetrahydrocannabinol (THC) on Human Executive Function

Year - 2013 (Bossong, Jansma, van Hell, Jager, & Kahn, 2013)

Journal - PLOS (Public Library of Science) One

Study Type - new research (neuroscience)

Category - Brain

Systems Affected - mental health

Strength of Effect/ Direction of Effect - A fair amount of evidence

Pull Quotes for Reference - "After THC administration, subjects showed impaired task performance, reflected in both an increase in false alarms and a reduction in detected targets." "THC-induced impairment of task performance as shown in the present study is expected to result in increased effort to maintain good performance levels, most likely reflected as elevated CES (Central Executive system) activity. However, THC did not affect CES activity during performance of the task."

Notes - small study and it focused on a very narrow functional area - processing of continuously updated information.

Country/State of data - UK

Author(s) - David J Nutt, Leslie A King, Lawrence D Phillips, on behalf of the Independent Scientific Committee on Drugs

Title - Drug Harms in the UK: A Multi-criteria Decision Analysis

Year - 2010 (Nutt, King, & Phillips, 2010)

Journal - Lancet

Study Type - ?

Category - Risk Factors for use

Systems Affected - Harm

Strength of Effect/ Direction of Effect - Medium - This is a very interesting study looking at the overall harm of drugs as they relate to each other. It was done using criterion developed by a committee in the UK. It showed that cannabis does economic harm, but is not among the top five drugs in terms of harm to the individual user or others

Pull Quotes for Reference - heroin, crack cocaine, and methamphetamine were the most harmful drugs to individuals (part scores 34, 37, and 32, respectively), whereas alcohol, heroin, and crack cocaine were the most harmful to others (46, 21, and 17, respectively). Overall, alcohol was the most harmful drug (overall harm score 72), with heroin (55) and crack cocaine (54) in second and third places.

Notes - This is useful in terms of relative harm, but not so much otherwise.

Country/State of data - UK

Author(s) - Zalesky et al.

Title - Effect of Long-Term Cannabis Use on Axonal Fiber Connectivity

Year - 2012 (Zalesky, Solowij, Yücel, Lubman, & Takagi, 2012)

Journal - Brain

Study Type - Observational - MRI

Category - Brain

Systems Affected - Brain abnormalities

Strength of Effect/ Direction of Effect - Strong - Axonal connectivity in heavy, long-term cannabis users found to be impaired compared to matched controls. Amount of impairment was a direct function of age of regular use.

Pull Quotes for Reference - Our results suggest that long-term cannabis use is hazardous to white matter in the developing brain. Given the association between cannabis-related harms and age of onset of regular use, delaying use may minimize such harmful effects. Disturbed brain connectivity in cannabis users may underlie cognitive impairment and vulnerability to psychosis, depression and anxiety disorders (Lim et al., 2002), all of which are significant public health concerns.

Notes

Country/State of data - Australia

Author(s) - Andra M. Smith & Carmelinda A. Longo & Peter A. Fried & Matthew J. Hogan & Ian Cameron

Title - Effects of Marijuana on Visuospatial Working Memory: An MRI Study in Young Adults

Year - 2010 (Smith, Longo, Fried, Hogan, & Cameron, 2010)

Journal - Psychopharmacology (2010) 210:429–438

Study Type -

Category - Brain

Systems Affected - visuospatial working memory

Strength of Effect/ Direction of Effect -

Pull Quotes for Reference -

Notes -

Country/State of data -

Author(s) - Tashkin, Donald (dtashkin@mednet.ucla.edu)

Title - Effects of Marijuana Smoking on the Lung

Year - 2013 (Tashkin, 2013)

Journal - Ann Am Thorac Soc 10(3):239-247

Study Type - REVIEW ARTICLE (Not Systematic Review: No methodology/ inclusion/exclusion criteria; Reviewed studies are a mix of designs, including animal studies)

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Regular Marijuana Smoking Increases Airway Injury & Chronic Bronchitis & Resulting Symptoms (Coughing, Sputum Production, and Wheezing)Though Less than Tobacco Use Alone or Concurrent Tobacco Use (A Fair Amount of Evidence) | Possible Increases in Pneumonia (Not Well Researched) |No Association with Emphysema (Not Well Researched) | No Association with Lung or Upper Airway Cancer with ever or current marijuana use when controlled for concomitant tobacco use (Not Well Researched) | Heavy marijuana use (>10.5 joint years) increased risk for lung cancer (Not Well Researched)

Pull Quotes for Reference - "A 2-year follow-up study of 452 daily marijuana-only smokers and 450 nonsmokers among Kaiser Permanente Medical Care Program participants revealed a small but significant increase in outpatient visits for respiratory illnesses among marijuana smokers (relative risk RR, 1.19; 95% CI, 1.01-1.41)" | US NHANES III Study: "Odds ratios for respiratory symptoms in the 414 marijuana users versus 4,789 nonsmokers (controlling for sex, age, current asthma, and concomitant tobacco use) were 2.17 (1.1-4.26) for chronic cough, 1.89)1.35-2.66) for chronic sputum, and 2.98 (2.05-4.34) for wheeze." | "Although lung and upper airway cancer are relatively uncommon in young individuals (<40-45 yr), several small case series have identified an unusually high proportion of regular marijuana smokers among young persons with these respiratory cancers compared with the proportion of regular smokers of marijuana in the general population." | "The single study showing a positive association between marijuana smoking and upper airway cancer (RR, 2.6; 95% CI, 1.1-6.6) was flawed by inappropriate matching of control subjects to case subjects." | "A retrospective cohort study of nearly 65,000 members of the Kaiser Permanente health maintenance organization in northern California who were monitored for up to 8 years failed to find any increased risk for tobacco-related malignancies, including lung and upper airway cancer, in association with ever or current marijuana use, after adjustment for tobacco smoking. However, limitations of this study include the relatively young age (mean, 48 yr) of the members at the end of the follow-up period and the inclusion of few long-term or heavy smokers of marijuana."

Notes –

Country/State of data -

Author(s) - Sarah D. Lynne-Landsman, PhD; Melvin D. Livingston, BA; Alexander C. Wagenaar PhD

Title - Effects of Medical Marijuana Laws on Adolescent Marijuana Use

Year - 2013 (Lynne-Landsman, Livingston, & Wagenaar, 2013)

Journal - American Journal of Public Health

Study Type - Difference-difference design using YRBS to evaluate effect of passage of state MMLs on adolescent marijuana use. Variables: adjusted for age, ethnicity & gender. Age was included as a continuous variable (12 - 18) looked at 2 questions - lifetime marijuana use and past-month use. Limitations: used only self-reported data; benefit from multiple alternative sources of marijuana use; more data on the effects of MMls on expected mechanisms or mediators between these laws and adolescent use.

Category – Regulation

Category - YOUTH

Systems Affected - Focus of research was only on frequency of use

Strength of Effect/ Direction of Effect - Distribution of responses for both questions highly skewed.

Pull Quotes for Reference - MML may influence the prevalence & frequency of adolescent nonmedical marijuana use half a decade later, despite no evidence of more proximal effects.

Notes - 40 planned comparisons of adolescents exposed and not exposed to MMLs across states and over time, only 2 significant effects were found. Conclusions: in states assessed, MMLs have not measurably affected adolescent marijuana use in the first few years, but longer term results need to be studies.

Country/State of data - MT, RI, MI and DE.

Author(s) - Porath AJ, Fried PA

Title - Effects of Prenatal Cigarette and Marijuana Exposure on Drug Use Among Offspring

Year - 2005 (Porath & Fried, 2005)

Journal - Neurotoxology and Teratology

Study Type - Longitudinal, sample size 152

Category - Reproductive

Systems Affected - Reproductive, epigenetic. Youth aged 16-21.

Strength of Effect/ Direction of Effect - Offspring whose mothers reported smoking (>0 cigs/day) during pregnancy more likely to report ever use of cigarettes (OR 2.16, 1.06, 2.39) after controlling for maternal marijuana & alcohol during pregnancy, maternal age, family income. Daily smoking not significantly different. Offspring whose mothers reported marijuana (>0 joints/week) more likely to report ever use of cigarettes (OR 2.58, 1.11, 6.00). Daily smoking also significant at 0.05 (OR 2.36, 1.00, 5.57). Dose-response relationship between marijuana joints smoked and cigarettes smoked per day by offspring. Effect more pronounced for male offspring. Offspring with prenatal marijuana more likely to initiate marijuana in adolescence independent of prenatal cigarette/alcohol (OR 2.76, 1.11, 6.86). NSD between prenatal cigarette exposure and adolescent marijuana. Effect larger in males. Dose-response between prenatal joints per week and offspring average joints per week. NSD for prenatal cigarettes and joints per week.

Pull Quotes for Reference - "The present findings indicate that fetal exposure to cigarettes and marijuana may have a significant impact on the initiation of cigarette smoking and marijuana use in adolescent offspring and a number of mechanisms may contribute to this relationship." (p. 275) Therefore, from a public health perspective, a reduction in rates of cigarette smoking and marijuana use may not only yield direct health benefits for the substance users themselves, but it may also have unanticipated benefits for their offspring including reduced risk of subsequent cigarette smoking and marijuana use later in life which may in effect influence the use of other illicit substances." (276) and the inverse is probably also true! (Sarah's editorializing.)

Notes - Caveats: Small sample size. Unable to control for postnatal tobacco exposure and parent's current use of cigarettes or other substances. White, middle class sample. Relatively young cohort, so smoking behavior may not be reflective of adult use.

Country/State of data - Ottawa, Canada

Author(s) - Robert J. Hancox1, Hayden H. Shin1, Andrew R. Gray1, Richie Poulton2 and Malcolm R. Sears3

Title - Effects of Quitting Cannabis on Respiratory Symptoms

Year - 2015 (Hancox, Shin, Gray, Poulton, & Sears, 2015)

Journal - European Respiratory Journal

Study Type - Prospective Longitudinal

Study Type - Birth cohort

Category - Respiratory

Systems Affected – Respiratory

Systems Affected - symptoms of bronchitis

Strength of Effect/ Direction of Effect - Strong effect - quitting cannabis use significantly lessens respiratory symptoms. The effect is independent of tobacco use.

Strength of Effect/ Direction of Effect - Strong - Frequent cannabis use was associated with morning cough (OR 1.97, $p<0.001$), sputum production (OR 2.31, $p<0.001$) and wheeze (OR 1.55, $p<0.001$). Reducing or quitting cannabis use was associated with reductions in the prevalence of cough, sputum and wheeze to levels similar to nonusers.

Pull Quotes for Reference - "In summary, frequent cannabis use is associated with symptoms of cough, sputum production and wheeze independently of tobacco smoking. These symptoms tend to improve in people who quit indicating that the airway inflammation caused by cannabis may be largely reversible"

Pull Quotes for Reference - In this population-based cohort followed through early adulthood, the use of cannabis was associated with symptoms of cough, sputum production, wheeze and dyspnea.

Notes - From the Dunedin Multidisciplinary Health and Research Study

Country/State of data - New Zealand

Author(s) - Morris Beshay, Heiko Kaiser, Dagmar Niedhart, Marc Reymond, Ralph Schmid

Title - Emphysema and Secondary Pneumothorax in Young Adults Smoking Cannabis

Year - 2007 (Beshay, Kaiser, Niedhart, Reymond, & Schmid, 2007)

Journal - European Journal of Cardio-thoracic Surgery

Study Type - Case review

Category - Respiratory

Systems Affected - Emphysema

Strength of Effect/ Direction of Effect - Low - Case review at one institution. Shows there is some potential connection between smoking marijuana and lung emphysema and secondary spontaneous pneumothorax

Pull Quotes for Reference - NA

Notes - This is a case review at one institution. It is a low level of evidence and should not be considered for this HIA.

Country/State of data - Switzerland?

Author(s) - Fernando A. Wilson, PhDa, Jim P. Stimpson, PhDa, José A. Pagán, PhDb

Title - Fatal Crashes from Drivers Testing Positive for Drugs in the U.S., 1993–2010

Year - 2014 (Wilson, Stimpson, & Pagán, 2014)

Journal - Public Health Reports

Study Type - Crossectional

Category - Motor Vehicle

Systems Affected - Motor vehicle

Strength of Effect/ Direction of Effect - Medium - In 2010, 54.9% of drivers testing positive for cannabis only and 70.3% of drivers testing positive for cocaine only were also using alcohol at the time of the motor vehicle crash

Pull Quotes for Reference - the share of drugged drivers in fatal motor vehicle crashes who tested positive for cannabis reached 36.9% in 2010

Notes - Really focused on the rise in Rx drug fatal crashes.

Country/State of data - US

Author(s) - Diana R. Keith, PhD: Carl Hart, PhD; Michael P. Mceil, EdD; Rae Silver, PhD; Renee D. Goodwin, PhD.

Title - Frequent Marijuana Use, Binge Drinking & Mental Health Problems among Undergraduates

Year - 2015 (Keith, Hart, McNeil, Silver, & Goodwin, 2015)

Journal - The American Journal on Addictions

Study Type - Logical regression analyses to examine relationships between frequency of marijuana use and other substance use. Adjusted for demographic differences such as gender, race, year in school and sorority/fraternity memberships. Seven questions used from ACHA-NCHA. Undergraduates had 3 week window to complete; sent multiple emails; students given gift cards if completed survey.

Category - Mental Health

Systems Affected - Frequent marijuana use significantly associated with anxiety, depression and substance use problems. Perceived stress NOT associated with marijuana use. Frequent use associated with binge drinking, trouble with police, regretting, forgetting and having unprotected sex.

Strength of Effect/ Direction of Effect - MJ use more common among males, white seniors and members of fraternities/sororities. Frequent marijuana users more likely to use other substances. Limitation of study is only one university in Northeast with a 30% completion rate. Longitudinal data is needed to infer temporal order of substance use, stress and mental health problems.

Pull Quotes for Reference -

Notes - Frequency of binge drinking, use of both marijuana and alcohol was associated with more negative consequences related to drinking, compared with those who use alcohol but not marijuana. Non marijuana users reported report not binge-drinking. Data pulled from 2009 and legal status of medical and recreational use have dramatically changed. More research about prevalence and correlates of marijuana use change as acceptance of marijuana becomes more widespread and research on investigation of potentially causal relationships between frequent marijuana use and mental health are needed.

Country/State of data - Undergraduates from one university in the Northeast in 2009. N = 5,859 with return of 1,841 surveys; data from 1,776 surveys used.

Author(s) - Shaul Lev-Rana,b,c,∗, Sameer Imtiaza, Benjamin J. Taylord, Kevin D. Shieldd,g, Jürgen Rehmd,e,f,g, Bernard Le Foll

Title - Gender Differences in Health-related Quality of Life among Cannabis Users: Results from the National Epidemiologic Survey on Alcohol and Related Conditions

Year - 2012 (Lev-Rana, Imtiaza, Taylord, Shieldd, & Rehmd, 2012)

Journal - Drug and Alcohol Dependence

Study Type – Cross-sectional

Category - HEALTH

Systems Affected - Quality of life

Strength of Effect/ Direction of Effect - STRONG - The clinical significance of the results can be better appreciated when taking into account the norm-based scoring of the SF-12 (mean = 50, standard deviation = 10). Accordingly, a mean difference of 5.5 points on the MCS scores between female cannabis users and non-users accounts for a difference of 21 percentiles; similarly, a difference of 9.2 points on the MCS scores between females with CUD compared to females without a CUD accounts for a difference of roughly 32 percentiles.

Pull Quotes for Reference - Increasing doses of cannabis consumed were associated with a significant decrease in mental quality of life which was significantly greater in females compared to males.

Notes - Interesting study on mental health quality of life. Big N.

Country/State of data - US

Author(s) - Radhakrishnan et al.

Title - Gone to Pot - a Review of the Association between Cannabis and Psychosis

Year - 2014 (Radhakrishnan, Wilkinson, & D'Souza, 2014)

Journal - Frontiers in Psychiatry

Study Type - Review

Category - Psychosis

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - This is a thorough review (338 references) that covers a broad range of topics on the connection between cannabis use and development of psychoses)

Pull Quotes for Reference - The findings from research reviewed above have profound implications for public health. Aside from alcohol, cannabis is currently the most prevalent drug used worldwide. In the United States, the legal status of cannabis for medical and recreational purposes is changing rapidly. Pertinent findings that are likely to impact public health include high conversion rates from cannabis-induced psychosis to schizophrenia; global and specific domains of cognitive impairment resulting from cannabis use, which may be irreversible; the effects of acute intoxication; the precipitation of psychotic disorders in genetically vulnerable populations, including individuals with a history of childhood abuse or family history of psychotic disorders; and the increased risk of negative effects of cannabis use in prolonged and early exposure.

Notes - This is the most comprehensive review of the literature on this topic.

Country/State of data - Earth

Author(s) - Rajiv Radhakrishnan, SamuelT. Wilkinson et. al.

Title - Gone to Pot – A Review of the Association between Cannabis and Psychosis

Year - 2014 (Radhakrishnanm, Wilkinson, & D'Souza, 2014)

Journal - Frontiers in Psychiatry

Study Type - Review article

Category - Psychosis

Systems Affected - mental health

Strength of Effect/ Direction of Effect - good evidence

Pull Quotes for Reference - "acute exposure to both natural and synthetic cannabinoids can produce a full range of transient symptoms, cognitive deficits, and psychophysiological abnormalities that bear a striking resemblance to some of the features of schizophrenia". "Finally, exposure to cannabinoids in adolescence confers a higher risk for psychosis outcomes in later life and the risk is dose-related. However, it should be remembered that the majority of individuals who consume cannabis do not experience any kind of psychosis."

Notes - the most comprehensive review article I have seen to date on the topic cannabis effect on psychosis.

Country/State of data - worldwide

Author(s) - Rooke et al.

Title - Health Outcomes Associated with Long-Term Regular cannabis and Tobacco smoking

Year - 2013 (Rooke, Norberg, Copeland, & Swift, 2013)

Journal - Addictive Behaviors

Study Type - Survey

Category - HEALTH

Systems Affected - Physical and Mental Health

Strength of Effect/ Direction of Effect - WEAK - Data are from a convenience sample of individuals 40+

Pull Quotes for Reference - "Findings suggest that mixing cannabis with tobacco leads to more detrimental outcomes than smoking cannabis alone."

Notes - Non-random sample; potential "survivor bias"

Country/State of data - Australia

Author(s) - Washburn & Capaldi

Title - Heterogeneity in Men's Marijuana Use in the 20s: Adolescent Antecedents and Consequences in the 30s

Year - 2015 (Washburn & Capaldi, 2015)

Journal - Development and Psychopathology

Study Type - Prospective longitudinal

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Medium - Of three classes of adolescent users (none, decreasing use, and chronic use) the chronic use had significantly worse outcomes for marijuana abuse/dependence, depression, and antisocial behavior in the 30s

Pull Quotes for Reference - A particularly problematic class of chronic users was identified, who were likely to meet criteria for marijuana abuse or dependence in their mid-20s, and show higher engagement in problem behaviors in their mid-30s relative to their peers. Findings indicate that lowering marijuana use for parents, along with increased parental monitoring during their sons' adolescence, may have long-term beneficial effects on early adult marijuana use in men.

Notes - Sample consists of boys recruited at age 9-10 from areas with high incidence of juvenile delinquency. Sample followed to date at age 36.

Country/State of data - USA - Oregon

Author(s) -Olivier Marie Ulf Zölitz

Title – "High" Achievers? Cannabis Access and Academic Performance

Year - 2015 (Marie & Zolitz, 2015)

Journal - Centre for Economic Performance; London School of Economics and Political Science

Study Type (e.g. meta-analysis, convenience sample etc.) - Retrospective/Observational

Category - Academic

Systems Affected - College-level coursework

Strength of Effect/ Direction of Effect - Strong effect - 9 percent of a standard deviation better and were 5.4 percent more likely to pass courses when they were banned from entering cannabis-shops

Pull Quotes for Reference - Our main finding is that the temporary restriction of legal cannabis access had a strong positive effect on course grades of the affected students. These individuals performed, on average, 9 percent of a standard deviation better and were 5.4 percent more likely to pass courses when they were banned from entering cannabis-shops ("coffee shops"). Importantly, we do not detect a change in dropout probability, which could have created complex composition effects. Sub-group analysis reveals that these effects are somewhat stronger for women than men and that they are driven by younger and lower performing students. This can be explained by baseline differences in consumption rates or differences in marginal compliance with the prohibition.4

Notes - Stronger association for math/numeric coursework. Fascinating - legal alcohol access reduces course grades by .033 to .097 standard deviations when including student fixed effects

Country/State of data - Netherlands

Author(s) - Olivier Marie Ulf Zolitz

Title - "High" Achievers? Cannabis Access and Academic Performance

Year - 2015 (Marie & Zolitz, "High" Achievers? Cannabis Access and Academic Performance)

Journal - Centre for Economic Performance

Study Type - Difference in difference approach using administrative panel data on over 54,000 course grades of local students enrolled at Maastricht University before and during the partial cannabis prohibition. Restricted cannabis purchase by nationality - Dutch, German, Belgian. Narrowed down 177 courses to 56 being classified as numerical.

Category - Academic

Systems Affected - Cognitive functioning or quantitative thinking in courses requiring numerical/ mathematical skills. Age was a factor - older students were not as impacted by cannabis use as younger students.

Strength of Effect/ Direction of Effect -

Pull Quotes for Reference - Results clearly show that students who lost the right to buy cannabis legally experienced important performance improvements relative to their peer who could still enter cannabis-shops. Ranganathan and D'Souza (2006) put it in their review of clinical literature, "THC...impairs immediate and delayed free recall of information presented after, but not before, drug administration."

Notes -

Country/State of data - Maastricht University, Maastricht, Netherlands working with Dutch, German and Belgian students.

Author(s) - Deborah A. Cobb-Clark Sonja C. Kassenboehmer Trinh Le, Duncan McVicar, Rong Zhang

Title - "High"-School: The Relationship between Early Marijuana Use and Educational Outcomes

Year - 2013 (Cobb-Clark, Kassenboehmer, Le, McVicar, & Zhang, 2013)

Journal - Institute for the Study of Labor (IZA) in Bonn - discussion paper

Study Type - Combination survey and longitudinal administrative data.

Study Type - Prospective Longitudinal

Category – Academic

Category - HEALTH

Systems Affected - Education - dose response and SES

Strength of Effect/ Direction of Effect - Medium- the study shows decreased academic scores and decreased high school completion. There are some definite methodological concerns.

Pull Quotes for Reference - We find evidence that early marijuana use is related to educational penalties that are compounded by high-intensity use and are larger for young people living in families with a history of welfare receipt.

Notes - A LOT of missing data!!

Country/State of data - Australia

Author(s) - Hutchinson et al.

Title - How Can Data Harmonisation Benefit Mental Health Research? An Example of the Cannabis Cohorts Research Consortium

Year - 2015 (Hutchinson, Silins, Mattick, Patton, & Fergusson, 2015)

Journal - Australia & New Zealand Journal of Psychiatry

Study Type - Review

Category - Mental Health

Systems Affected –

Strength of Effect/ Direction of Effect - Strong - Points out strengths and challenges in combining several long-term prospective studies to increase power

Pull Quotes for Reference - "A data harmonisation approach to combining participant level data from large cohort studies provides a unique opportunity to examine salient cannabis-related or other questions that are not possible to address in individual cohorts or using meta-analytic approaches."

Notes -

Country/State of data - Australia & New Zealand

Author(s) - Hanan El Marrouna, James J. Hudziaka, Henning Tiemeiera, Hanneke Creemersa, Eric A.P. Steegersf, Vincent W.V. Jaddoe, Albert Hofmand, Frank C. Verhulsta, Wim van den Brink, Anja C. Huizinka

Title - Intrauterine Cannabis Exposure Leads to More Aggressive Behavior and Attention Problems in 18-Month-old Girls

Year - 2011 (Marrouna, et al., 2011)

Journal - Drug and Alcohol Dependence 118 (2011) 470– 474

Study Type - Cohort study

Category - Mental Health

Systems Affected - behavior and attention problems

Strength of Effect/ Direction of Effect - Medium - This study showed an association between maternal marijuana use during pregnancy and behavior and attention problems in girls at 18 months.

Pull Quotes for Reference - The fact that there was no effect in 18-month-old boys was surprising in itself and could be due to chance, but could also be due to the remarkable differences between boys and girls early in neurodevelopment

Notes - Study period is only 18 months after birth. Only showed association in girls without a biological pathway explanation.

Country/State of data - Netherlands

Author(s) - Tamara D. Warner, PhD, Dikea Roussos-Ross, MD.

Title - It's Not Your Mother's Marijuana: Effects on Maternal-Fetal Health and the Developing Child

Year - 2014 (Warner, Roussos-Ross, & Behnke, 2014)

Journal - Clinics of Perinatology

Study Type - Review article

Category - Reproductive

Systems Affected - growth and development

Strength of Effect/ Direction of Effect - good evidence

Pull Quotes for Reference - "From the 1970s to the 2000s, there has been an estimated 6- to 7-fold increase in the potency of cannabis seized in the United States as measured by the percentage of D9-tetrahydrocannabinol (THC), the most psychoactive of the 70 cannabinoids found in cannabis" "Available data to this point do not reveal marijuana-associated fetal teratogenicity." "Results from the Generation R study have shown reduced fetal growth from the second trimester onward, particularly for mothers who used early marijuana during pregnancy or throughout the entire pregnancy". "The results from longitudinal, prospective studies that started in the late 1970s and early 1980s indicate subtle effects on attention, executive functions, and behavior, particularly as marijuana-exposed youth develops into adolescence and early adulthood."

Notes - comprehensive review of cannabis exposure intranatally and developmental effects through adolescence

Country/State of data - US authors citing data from studies worldwide

Author(s) - Friese & Grube

Title - Legalization of Medical Marijuana and Marijuana Use among Youths

Year - 2013 (Friese & Grube, 2013)

Journal - Drugs: Education, Prevention, and Policy

Study Type - Observational

Category - YOUTH

Systems Affected - Marijuana use

Strength of Effect/ Direction of Effect - Moderate - Suggests that the normative environment is more important than MML in youth use of marijuana

Pull Quotes for Reference - "The findings of this study suggest that it may be the normative environment more than the number of medical marijuana cards per se in a community that is related to marijuana use among youths."

Notes - Data limited to one state

Country/State of data - Montana

Author(s) - Justine Renard, Marie-Odile Krebs, GwenaëlleLePen, Thérèse M. Jay

Title - Long-Term Consequences of Adolescent Cannabinoid Exposure in Adult Psychopathology

Year - 2014 (Renard, Krebs, LePen, & Jay, 2014)

Journal - Frontiers in Neuroscience

Study Type -

Category - Mental Health

Systems Affected - Mental health

Strength of Effect/ Direction of Effect - COMING SOON

Pull Quotes for Reference - COMING SOON

Notes - COMING SOON

Country/State of data - COMING SOON

Author(s) - Francesca M. Filbeya , Sina Aslana

Title - Long-Term Effects of Marijuana Use on the Brain

Year - 2014 (Filbey, Aslan, Calhoun, Spence, & Damaraju, 2014)

Journal - PNAS (Proceedings of the Nation Academy of Sciences of the United States)

Study Type - New research (neuroscience)

Category - Brain

Systems Affected - brain structure

Strength of Effect/ Direction of Effect - good evidence

Pull Quotes for Reference - "Our findings provide evidence that heavy, chronic marijuana users have lower OFC (Orbito-Frontal Cortex) gray matter volumes compared with non-using controls". "Functional connectivity analysis revealed greater connectivity within the OFC network in marijuana users compared with controls, which is concordant with existing resting state studies (37) and task-based studies (38, 39). This increased functional connectivity in users may suggest a compensatory mechanism whereby greater network recruitment is engaged to compensate for OFC liability"

Notes - Somewhat larger study (for a neuroimaging study >100 participants

Country/State of data - USA

Author(s) - Tan et al.

Title - Marijuana and Chronic Obstructive Lung Disease: A Population-based Study

Year - 2009 (Tan, Lo, Jong, Xing, & FitzGerald, 2009)

Journal - Canadian Medical Association Journal

Study Type - Survey

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Moderate - found synergistic effects of COPD and respiratory symptoms for individuals who smoke both tobacco and marijuana. No respiratory symptoms for those who smoke marijuana only.

Pull Quotes for Reference - "A dose-related effect of marijuana was suggested by our finding that a self-reported lifetime exposure to marijuana of at least 50 marijuana cigarettes was strongly associated with an increased risk of COPD. The significant interaction term suggested that the effects of marijuana and cigarette smoking were synergistic. We were unable to rule out clinically important respiratory effects of smoking only marijuana, because of insufficient statistical power.

Notes -

Country/State of data - Canada

Author(s) - Manish Joshi, Anita Joshi, and Thaddeus Bartter

Title - Marijuana and Lung Diseases

Year - 2014 (Joshi, Joshi, & Bartter, 2014)

Journal - Curr Opin Pulm Med

Study Type - Review

Category - Respiratory

Systems Affected - Lung cancer

Strength of Effect/ Direction of Effect - Strong - smoking marijuana is associated with chronic bronchitis symptoms and large airway inflammation.

Pull Quotes for Reference - There is unequivocal evidence that habitual or regular marijuana smoking is not harmless. Although it has been difficult to establish a conclusive link between marijuana smoking and cancer development epidemiologically, available evidence definitely warrants caution against regularly heavily (and possible moderate) marijuana use.

Notes - This is a review in the Curren Opinion in Pulmonary Medicine.

Country/State of data -

Author(s) - Bridget Onders, Marcel J. Casavant, MD, Henry A. Spiller, MS, Thiphalak Chounthirath, and Gary A. Smith, MD, DrPH

Title - Marijuana Exposure among Children Younger Than Six Years in the United States

Year - 2015 (Onders, Casavant, Spiller, Chounthirath, & Smith, 2015)

Journal - Clinical Pediatrics

Study Type – Observational

Study Type - Retrospective, time series, cross-sectional, population (National Poison Data System), sample size 1,969 children <6, 2000-2013

Category - Physical Health

Systems Affected - Childhood poisoning

Systems Affected - Accidental ingestion

Strength of Effect/ Direction of Effect - Medium - The rate of marijuana exposure was significantly (2.82 times) higher in states where its use was legalized prior to 2000 compared with states where its use is not legal.

Strength of Effect/ Direction of Effect - National rate of exposure: 5.6 exposures per million children <6 years old. 92.2% of exposures unintentional. 83.0% at child's own residence. Mean age 1.81 years. 77.7% <3 years old. 75.0% exposures were ingestion, 14.5% inhalation/nasal. 41.1% en route to health care facility at time of call. 28.7% managed on site. 47.6% managed at health care facility (29.1% treated & released/11.6% admitted to noncritical care/6.9% admitted to critical care). <2yo most likely to be admitted. Minor effect 24.5% of cases, moderate effect 10.8%, major effect 1.1%, no effect 17.2%. Clinical effects included drowsiness & lethargy, ataxia, agitation or irritability, confusion. Serious effects less common - coma, respiratory depression, seizures. 83.4% (of those with documented effect length) had clinical effects from 2 hours to one day. Rate of exposure for states that had legalized medical marijuana before 2000, rate of exposure higher (2.82, 2.00-3.97). Exposure higher after legalization in states that legalized during study period (2.25, 1.45-3.51).

Pull Quotes for Reference - the percentage of US civilians ≥12 years of age who used marijuana in the past month decreased from 6.2% in 2002 to 5.8% in 2007 before increasing to 7.5% in 2013.15 This suggests that the rate of marijuana exposure among children is associated with the number of marijuana users

Pull Quotes for Reference - "There was a spike in the rate of exposure during the year of legalization compared with several years prior to and several years after legalization." p. 3
"The trend in the rate of marijuana exposure calls in this study parallels the trend in the number of

marijuana users in the United States." p. 4
"The greater proportion of admissions to a health care facility for marijuana exposures also may be related to social indications in addition to medical reasons. A child may be admitted to allow social workers or child protective services time to evaluate the circumstances of exposure before discharging the child home." p. 4
"Legalizing the medical or recreational use of marijuana may have economic or other benefits, but lawmakers also need to be aware of the potential hazard associated with unintentional exposure of young children to marijuana products when considering legalization." p. 4
"It is imperative that commercially available marijuana products be sold in opaque, child-resistant packaging to mitigate the risk of child exposure...child protections must be incorporated in legislation from the beginning to ensure that safety measures are in place when marijuana products first legally go on sale." p. 5

Notes - NOTE: This is based on medical marijuana. They did not differentiate between edibles and smoking and there is no causality here, just the fact that it looks like use is changing in states that have changing medical marijuana laws etc…

Notes - We need current poison control center data for Vermont/New England to predict any increase. Figure 3 is rate of exposure by number of years before and after medical legalization. Child proofing only addresses commercial products - not homemade.

Country/State of data - U.S.

Author(s) - Pacula & Sevigny

Title - Marijuana Liberalization Policies: We Can't Learn Much from Policy Still in Motion

Year - 2014 (Pacula & Sevigny, 2014)

Journal - Journal of Policy Analysis and Management

Study Type - Review

Category - Regulation

Systems Affected - N/A

Strength of Effect/ Direction of Effect - N/A

Pull Quotes for Reference - "It is important to bear in mind that policymakers can take steps to mitigate some of the potential health harms of liberalization policies if public health advocates become engaged. Regulations could be shaped that set limits on the maximum potency or THC to CBD that can be available in the market and requiring regular random testing of samples from producers and growers to ensure compliance. Similarly, rules regarding proper labeling or limited product forms might also be considered. Rules can be put in place to limit opportunities to use marijuana and alcohol together and reduce the commercialization of marijuana. Such ideas that represent attempts to mitigate legitimate public health concerns appear to be missing from current state policy debates, but are desperately needed."

Notes - This paper makes the very important point that MMLs per se did not affect prevalence rates of marijuana, but specific policies (e.g., legal dispensaries) that led to price reductions and increased potency did.

Country/State of data - US

Author(s) - Owen et al.

Title - Marijuana: Respiratory Tract Effects

Year - 2014 (Owen, Sutter, & Albertson, 2014)

Journal - Clinical Review of allergy and Immunology

Study Type - Review

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Low - literature on the effects of marijuana smoking on lung function and associated disorders is highly variable

Pull Quotes for Reference - "Cannabinoids have multiple effects on the pulmonary system, immune system, and on cancer cells. Daily marijuana smoking has been shown to increase the risk for pulmonary symptoms such as wheeze, cough, and sputum production, though the risk for development of COPD is questionable. It is difficult to differentiate the effects of individual cannabinoids with the effect of marijuana smoke."

Notes -

Country/State of data - N/A

Author(s) - Russell C Callaghan, Peter Allebeck, Anna Sidorchuk

Title - Marijuana Use and Risk of Lung Cancer: A 40-year Cohort Study

Year - 2013 (Callaghan, Allebeck, & Sidorchuk, 2013)

Journal - Cancer Causes and Control

Study Type - Longitudinal cohort study

Study Type - Longitudinal cohort, population-based (Swedish conscripts), men

Category - Respiratory

Systems Affected - Lung cancer

Strength of Effect/ Direction of Effect - Strong - "heavy" (used more than 50 times in their lifetime) use associated with a more than twofold risk (hazard ratio 2.12 (1.08-4.14)) of developing lung cancer

Strength of Effect/ Direction of Effect - 91% of those reporting >50x lifetime marijuana use indicated ever tobacco use. Ever marijuana use not significantly associated with lung cancer after adjusting for tobacco use. Heavy cannabis use (>50x lifetime) significantly associated (HR 2.12, 1.08-4.14) after adjusting for tobacco, alcohol, respiratory conditions, and SES.

Pull Quotes for Reference - Our 40-year cohort study, demonstrating increased risk of lung cancer among heavy cannabis smokers, does bolster the few epidemiological studies reporting significant and positive associations between marijuana smoking an lung cancer, as well as the large body of in vivo and in vitro experimental evidence supporting the biological plausibility of a link between the two.

Pull Quotes for Reference - "It is critically important to our modeling and results to note that most individuals reporting marijuana use were also tobacco smokers." p. 1813 "Our primary finding, requiring further replication, does provide initial longitudinal evidence that cannabis use might elevate the risk of lung cancer." p. 1818

Notes - Limitation: Only had data on marijuana use at time of conscription (18-20yo), not after service.

Country/State of data - Sweden

Author(s) - Elickson et al.

Title - Marijuana Use from Adolescence to Young Adulthood: Multiple Developmental Trajectories and Their Associated Outcomes

Year - 2004 (Ehrenreich, Nahapetyan, Orpinas, & Song, 2004)

Journal - Health Psychology

Study Type - Longitudinal

Category - YOUTH

Systems Affected - Physical and mental health

Strength of Effect/ Direction of Effect - Strong - identified 5 robust classes of use from age 13 to age 23 and looked at outcomes at age 29. Abstainers had positive outcomes compared to any of the use trajectories including physical and mental health and life satisfaction.

Pull Quotes for Reference - "However, abstaining from marijuana use altogether or keeping use to experimental levels of no more than three times per year does predict better young adult outcomes. By age 29, abstainers outperformed all other groups with regard to educational achievement, overall health, and life satisfaction; in addition, they had the lowest hard drug use rates and higher earnings..."

Notes - Likely the first study to identify different trajectories of use and associate these trajectories with later outcomes. From RAND

Country/State of data - California and Oregon

Author(s) - Miles K. Light, Adam Orens, Brian Lewandowski, Todd Pickton

Title – Market Size and Demand for Marijuana in Colorado

Year - 2014 (Light, Orens, Lewandowski, & Pickton, 2014)

Journal – State Report

Study Type - Report

Category - Economics

Systems Affected - Economy

Strength of Effect/ Direction of Effect - Our point estimate of demand is 121.4 tons per year for adult residents. This is 31 percent higher than a recent Department of Revenue assessment, 89 percent higher than a study by the Colorado Futures Center, and 111 percent higher than an older study by the Colorado Center for Law and Policy. The primary difference is caused by much heavier dosage amounts consumed by the state's "heavy user" population – those who consume marijuana on a daily basis.

Pull Quotes for Reference - In Colorado, the top 21.8 percent of users account for 66.9 percent of the demand. In contrast, the entire population of rare users (less than once per month), a group that accounts for almost one-third of all users, represents less than 1 percent (0.3 percent) of total demand.

Notes - This is a report done by the Marijuana Policy Group in Colorado. This is not a research study.

Country/State of data - USA

Author(s) - Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD, MS; Colleen L. Barry

Title - Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010

Year - 2014 (Bachhuber, Saloner, Cunningham, & Barry, 2014)

Journal - JAMA

Study Type - ecological

Category - Medical Marijuana

Systems Affected - MEDICAL MARIJUANA: Opioid Overdose

Strength of Effect/ Direction of Effect - Strong - States with medical cannabis laws had a 24.8%lower mean annual opioid overdose mortality rate (95%CI, −37.5%to −9.5%; P = .003) compared with states without medical cannabis laws.

Pull Quotes for Reference - Although the present study provides evidence that medical cannabis laws are associated with reductions in opioid analgesic overdose mortality on a population level, proposed mechanisms for this association are speculative and rely on indirect evidence.

Notes - Very interesting. No mechanism.

Country/State of data - U.S.

Author(s) - Gordon et al.

Title - Medical Consequences of Marijuana Use: A Review of Current Literature

Year – 2013 (Gordon, Conley, & Gordon, 2013)

Journal - Current Psychiatry Reports

Study Type – Review

Category – HEALTH

Systems Affected - All

Strength of Effect/ Direction of Effect - Moderate- Review of infectious disease, cancer, oral cavity, pulmonary function, cardiovascular system, neurologic disorders, ocular disease, renal and urological systems, digestive tract, gynecological disease, hematologic and immunologic disease, and metabolic disorders. Found cannabis associated risks in several systems examined

Pull Quotes for Reference - For example, marijuana use is associated with diseases of the liver (particularly with co-existing hepatitis C), lungs, heart, and vasculature.

Notes - Broad areas superficially covered

Country/State of data - N/A

Author(s) - Kevin P. Hill

Title - Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems A Clinical Review

Year - 2015 (Hill, 2015)

Journal - JAMA

Study Type - Review

Category - Medical Marijuana

Systems Affected - MEDICAL MARIJUANA: Chronic Pain

Strength of Effect/ Direction of Effect - Strong - Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence. Six trials that included 325 patients examined chronic pain, 6 trials that included 396 patients investigated neuropathic pain, and 12 trials that included 1600 patients focused on multiple sclerosis. Several of these trials had positive results, suggesting that marijuana or cannabinoids may be efficacious for these indications.

Pull Quotes for Reference - Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported by high-quality evidence.

Notes - MEDICAL MARIJUANA

Country/State of data -

Author(s) - Deborah S Hasin, Melanie Wall, Katherine M Keyes, Magdalena Cerdá, John Schulenberg, Patrick M O'Malley, Sandro Galea, Rosalie Pacula, Tianshu Feng

Title - Medical Marijuana Laws and Adolescent Marijuana Use in the USA from 1991 to 2014: Results from Annual, Repeated Cross-sectional Surveys

Year - 2015 (Hasin, Wall, Keyes, Cerda, & Schulenberg, 2015)

Journal - Lancet

Study Type - Cross-sectional/observational

Category - Medical Marijuana

Systems Affected - MEDICAL MARIJUANA - Prevalence

Strength of Effect/ Direction of Effect - Strong - No association between medical marijuana laws and increased or decreased use of marijuana among youth.

Pull Quotes for Reference - Our findings, consistent with previous evidence, suggest that passage of state medical marijuana laws does not increase adolescent use of marijuana. However, overall, adolescent use is higher in states that ever passed such a law than in other states.

Notes - MEDICAL MARIJUANA

Country/State of data - US

Author(s) - Cerdá et al.

Title - Medical Marijuana Laws in 50 States: Investigating the Relationship between State Legalization of Medical Marijuana and Marijuana Use, Abuse, and dependence

Year - 2012 (Cerda, Wall, Keyes, Galea, & Hasin, 2012)

Journal - Drug and Alcohol Dependence

Study Type - Observational

Category - Regulation

Systems Affected - Marijuana Use and Marijuana Disorders

Strength of Effect/ Direction of Effect - Moderate - Significantly more use and more marijuana use disorders in states with medical marijuana laws than states without.

Pull Quotes for Reference - "This study indicates that states that legalized marijuana use for medical purposes have significantly higher rates of marijuana use and of marijuana abuse and dependence. The results for marijuana use were found at the state level in two national datasets, the NESARC and the NSDUH, and at the individual level in the NESARC."

Notes –

Country/State of data - US

Author(s) - van der Pol et al.

Title - Mental Health Differences between Frequent Cannabis Users With and Without Dependence and the General Population

Year - 2013 (van der Pol, Liebregts, de Graaf, Have, & Korf, 2013)

Journal - Addiction

Study Type - Retrospective/Observational

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Moderate - Both marijuana groups had worse MH outcomes than the general population group; very few differences of note between dependent and nondependent groups

Pull Quotes for Reference - [Frequent] users with and without dependence had very similar cannabis use patterns

Notes –

Country/State of data - Netherlands

Author(s) - Albertella & Norberg

Title - Mental Health Symptoms and Their Relationship to Cannabis Use in Adolescents Attending Residential Treatment

Year - 2012 (Albertella & Norberg, 2012)

Journal - Journal of Psychoactive Drugs

Study Type - Observational

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Low - compared pretreatment factors with post-treatment cannabis use and mental health outcomes. No control group.

Pull Quotes for Reference - "In Conclusion, the present study demonstrated that pretreatment mental health symptoms are associated with quantity of cannabis use at pre- and post-treatment."

Notes - No control group, quite predictable findings

Country/State of data - Australia

Author(s) - Pacula & Sevigny

Title - Natural Experiments in a Complex and Dynamic Environment: The Need for a Measured Assessment of the Evidence

Year - 2014 (Pacula & Sevigny, Natural Experiments in a Complex and Dynamic Environment: The Need for a Measured Assessment of the Evidence, 2014)

Journal - Journal of Policy Analysis and Management

Study Type - Review

Category - Risk Factors for use

Systems Affected - Rates of use and Attitudes toward marijuana

Strength of Effect/ Direction of Effect - Moderate - makes the case that it is difficult to predict both attitudes and whether legalization will have an overall positive or negative societal impact.

Pull Quotes for Reference - "Numerous factors and critical assumptions come into play, including the characteristics of the user population, consumption practices, potency, structure of the legal regulatory system, level of enforcement, and so forth. Even the relationship between marijuana use and other substances, such as alcohol, could be dramatically different under a legal regime, as income effects and legal risks could shift market demand in unpredictable ways."

Notes –

Country/State of data - N/A

Author(s) - Jutras-Aswad et al.

Title - Neurobiological Consequences of Maternal Cannabis on Human Fetal Development and Its Neuropsychiatric Outcome

Year - 2009 (Jutras-Aswad, DiNieri, Harkany, & Hurd, Neurobiological Consequences of Maternal Cannabis on Human Fetal Development and Its Neuropsychiatric Outcome, 2009)

Journal - European Archives of Psychiatry and Clinical Neuroscience

Study Type - Review

Category - Reproductive

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong across a several neuropsychiatric systems including neurotransmitters, opioid receptors and psychiatric disorders including addiction, mood and anxiety disorders, and psychosis

Pull Quotes for Reference - "Altogether, the existing literature points to significant deficits associated with prenatal cannabis exposure on domains such as attentional behavior, cognitive flexibility, and planning." "However, it is clear that exposure to cannabis during early ontogeny is not benign and potential compensatory mechanisms that might be expected to occur during neurodevelopment appear insufficient to eliminate vulnerability to neuropsychiatric disorders in certain individuals."

Notes - Excellent review of the effect of cannabis on both fetal and adolescent development.

Country/State of data - N/A

Author(s) - Samantha M. Bitter, Caleb M. Adler et. al.

Title - Neurofunctional Changes in Adolescent Cannabis Users With and Without Bipolar Disorder

Year - 2014 (Bitter, Adler, Eliassen, Weber, & Welge, 2014)

Journal - Society for the Study of Addiction

Study Type - neuroimaging; cross-sectional

Category - Mental Health

Systems Affected - mental health

Strength of Effect/ Direction of Effect - A fair amount of evidence

Pull Quotes for Reference - "Consistent with previous studies, these findings reveal that bipolar adolescents have overactive limbic systems and this greater activation may be a result of dysfunctional pre-frontal–amygdala inhibitory pathways"

Notes - small numbers of people studied.

Country/State of data - USA

Author(s) - Batalla, A., Crippa, J.A., Busatto, G. F. et al.

Title - Neuroimaging Studies of Acute Effects of THC and CBD in Humans and Animals: A Systematic Review

Year - 2014 (Batalla, et al., 2014)

Journal - Current Pharmaceutical Design

Study Type - Systematic Review

Category - Brain

Systems Affected - Cerebral Blood Flow (CBF) in Resting State, Cerebral Blood Flow During Cognitive Tasks, Dopamine Release

Strength of Effect/ Direction of Effect - *Occasional Cannabis Users:* Increase in global cerebral blood flow; dose-dependent increases in regional resting CBF depending on brain region following THC when compared to placebo/marijuana cigarette without THC administration; working memory performance was decreased following THC administration; studies reported inconsistent results regarding whether cannabinoids stimulate dopamine release in striatal areas in humans. *Naive Cannabis Users*: Cannabidiol decreased resting CBF in the amygdala-hippocampal complex and posterior cingulate gyrus and increased activity in the left para-hippocampal gyrus; the attenuating effect of THC on temporal cortical activity was correlated with severity of psychotic symptoms.

Pull Quotes for Reference - "Functional neuroimaging studies comparing CBF during cognitive paradigms before and following THC administration indicate that the perturbation of the endocannabinoid system may affect neural activity" and "Overall, these imaging studies seem to indicate a clear involvement of the endocannabinoid system in learning and memory processes" and "Thereby, these findings do not support a central role for increased striatal dopaminergic activity in THC-induced psychosis"

Notes - 224 studies identified; 45 studies included in review; 24 were in humans and 21 in animals. Methodological differences limit comparison, areas of interest varied and many had small sample sizes.

Country/State of data - Spain, Brazil, UK

Author(s) - Thomas AA, Wallner LP, Quinn VP, Slezak J, Van Den Eeden SK, Chien GW, Jacobsen SJ

Title - Association between Cannabis Use and the Risk of Bladder Cancer: Results from the California Men's Health Study

Year - 2015 (Thomas, Wallner, Quinn, Slezak, & Van Den Eeden, 2015)

Journal - Oncology

Study Type - Prospective Cohort

Category - Cancer

Systems Affected - Bladder Cancer

Strength of Effect/ Direction of Effect - Current cannabis use associated with a decreased risk of bladder cancer. HR = 0.55. There was an implication of cannabis "mediating" the effect of tobacco use on bladder cancer, but this was not explored.

Pull Quotes for Reference - …we observed an inverse association between cannabis use and the development of bladder cancer. Further research is needed to validate these results

Notes - Strengths: population based cohort; use of cancer registry data. Weaknesses: No assessment of former use of cannabis only current use, tobacco use was assessed as current former and never but was dichotomized as any use and non-use in the models (possible confounding effects); other exposures related to bladder cancer were not assessed (possible confounding affects); no other supporting evidence or studies; recall and selection bias.

Country/State of data - California

Author(s) - Baggio et al.

Title - Patterns of Cannabis Use and Prospective Associations with Health Issues Among Young Males

Year - 2014 (Baggio, N'Goran, Deline, Studer, & Dupuis, 2014)

Journal - Addiction

Study Type - Prospective (12-18 months)

Category - YOUTH

Systems Affected - Mental and physical health described in very general terms

Strength of Effect/ Direction of Effect - Weak - likely due to short length of time between assessments

Pull Quotes for Reference - Therefore, interventions dealing with cannabis use and heavy cannabis use should already target teenagers, as by their early 20s users have shown they have settled patterns of use.

Notes - Not a particularly impressive study. Health effects are not well defined and time between assessments very short. No surprise that patterns were stable when measured 12-18 months apart.

Country/State of data -

Author(s) - Romano & Pollini

Title - Patterns of Drug Use in Fatal Crashes

Year - 2013 (Romano & Pollini, 2013)

Journal - Addiction

Study Type - Retrospective/Observational

Category - Motor Vehicle

Systems Affected -

Strength of Effect/ Direction of Effect - Small effect - Cannabis found in 7% of fatally injured drivers in single vehicle crashes.

Pull Quotes for Reference - "Except for cannabinols, alcohol was not associated with the presence of other drugs. The association between alcohol and cannabinols may suggest that drivers tend to consume both drugs simultaneously or that marijuana and alcohol have a synergistic impairment effect leading to fatal crashes."

Notes - Contacted Dr. Romano about VT data appearing anomalous 7/9/15

Country/State of data -

Author(s) - Meier, Caspi, Ambler, Harrington, Houts, Keefe, McDonald, Ward, Poulton, Moffitt

Title - Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife

Year - 2012 (Meier, Caspi, Ambler, Harrington, & Hout, 2012)

Journal - Psychological and Cognitive Sciences

Study Type - STRONG: prospective longitudinal study

Category - Brain

Systems Affected - cognitive, neuropsychological

Strength of Effect/ Direction of Effect - *Strength of Association:* STRONG. *Meaningfulness of Association:* STRONG. *Direction of Association:* INCREASED.

Pull Quotes for Reference - "Persistent cannabis use over 20 y was associated with neuropsychological decline, and greater decline was evident for more persistent users. This effect was concentrated among adolescent onset cannabis users" (p. 5), "In the present study, the most persistent adolescent-onset cannabis users evidenced an average 8-point IQ decline from childhood to adulthood." (p. 6)

Notes - Researchers "ruled out pre-morbid neuropsychological deficit", "showed that the impairment was global and detectable across five domains of neuropsychological functioning", "showed that cannabis-associated neuropsychological decline did not occur solely because cannabis users completed fewer years of education", "showed that impairment was apparent to third-party informants and that persistent cannabis use interfered with everyday cognitive functioning", and that "among adolescent-onset former persistent cannabis users, impairment was still evident after cessation of use for 1 y or more." (p 5)

Country/State of data - New Zealand

Author(s) - Kelly & Rasul

Title - Policing Cannabis and Drug-Related Hospital Admissions: Evidence from Administrative Records

Year - 2014 (Kelly & Rasul, 2014)

Journal - Journal of Public Economics

Study Type - Observational/natural experiment

Category - Physical Health

Systems Affected - Hospitalizations

Strength of Effect/ Direction of Effect - Strong - took advantage of a relaxed cannabis policing effort for 13 months in one borough of London. Found an increase in the number and severity of hospitalizations for hard drugs (e.g., heroin, meth, etc.) up to four years after old policy restored

Pull Quotes for Reference - "in the short-run, during the 13 months in which the LCWS was actually in operation, there are no statistically significant effects on hospitalization rates for any cohort. Hence, as might be expected, any impact of the cannabis depenalization policy on hospitalization rates for Class-A drug use takes time to work through."

Notes - A remarkable study that takes advantage of a time-limited relaxation of cannabis use penalties in a specific London borough as well as the extensive records kept by the centralized health system in the UK. Results based on ICD-10 diagnostic codes.

Country/State of data - London

Author(s) - Mehmedic et al.

Title - Potency Trends of Δ9-THC and Other Cannabinoids in Confiscated Cannabis Preparations from 1993 to 2008

Year - 2010 (Mehmedic, Chandra, Slade, Denham, & Foster, 2010)

Journal - Journal of Forensic Sciences

Study Type - Review

Category - Economics

Systems Affected - Potency of cannabis

Strength of Effect/ Direction of Effect - Strong - Showed an increase of average THC content from 1993 (3.4%) to 2008 (8.4%). Found also that the increase was due mostly from nondomestic samples.

Pull Quotes for Reference - "However, analysis of the available data in conjunction with the PM program results makes a strong case that cannabis is not only more potent than in the past but also that this high potency product's market share is also growing."

Notes -

Country/State of data - N/A

Author(s) - Hill, Reed

Title - Pregnancy, Breast-Feeding, and Marijuana: A Review Article

Year - 2013 (Hill & Reed, 2013)

Journal - Obstetrical and Gynecological Survey

Study Type - STRONG: Review

Category - Reproductive

Systems Affected - Fetal, neonatal, childhood outcomes of maternal cannabis use

Strength of Effect/ Direction of Effect - *Strength of Association:* MEDIUM: Confounders are taken into account, especially polydrug use. *Meaningfulness of Association:* STRONG/MEDIUM - CO study n=756, Jamaica study n = 42, and the Ottawa and Pittsburgh studies were "large prospective cohort studies". *Direction of Association:* None for light to moderate use, increased for heavy use (>5 joints/week)

Pull Quotes for Reference - *Effects of Use on Fetal Outcomes:* "marijuana is not associated with birth defects in humans" (p. 712), "there were no detrimental effects noted on fetal growth or fetal neurodevelopmental outcomes when infants were examined at 24 to 72 hours after birth." (p. 713), "no difference in age at weaning, suggesting that marijuana was not detrimental to the suckling behavior of infants or the maternal production of milk" (p. 713), "Neonatal outcomes were equivalent in the first week after delivery in this cohort. At follow-up 30 days after delivery, no detrimental effects of marijuana use were documented" (p. 713), "These studies did not find an association between marijuana use in pregnancy and immediate pregnancy outcomes such as miscarriage rates, rates of anomalies, mode of delivery, Apgar scores, or meconium-stained fluid." (p. 713), "no apparent withdrawal effects in neonates" (p. 713) *Effects of Use on Childhood Outcomes: "*The problems encountered in these cohorts were the small numbers of ‘‘heavy’’ marijuana users and the confounding introduced by the social determinants of health and use of other drugs concurrently with marijuana. Neither study demonstrated a convincing difference in global IQ of offspring at any age when taking light or moderate use into account." (p 713), "Heavy use of marijuana (95 joints per week) during pregnancy was associated with an increase in omission errors in offspring, highlighting the fact that significant use may be required to produce a cognitive effect" (p. 714), "Executive function seemed affected with omission errors more common in the group of children with heavy exposure to maternal marijuana. IQ was not affected, however" (p. 714) *Effects of Marijuana During Breastfeeding: "*There is inadequate evidence to make a statement about the isolated use of marijuana in breast-feeding mothers. The studies that address this issue are confounded by the fact that few women have isolated use during breast-feeding in the absence of additional prenatal use of marijuana" (p. 714),

Notes - Patients should be cautioned that inhaled marijuana may have effects on fetal growth similar to those of cigarette use. Neurodevelopmental outcomes seem similar between babies of

nonusers and users with no resultant effects on global intelligence quotient. There may be some effects on visuoperceptual ability, reasoning and attention noted in older children. These findings have been reproduced in 2 large cohorts, and the association was statistically significant only with prolonged, heavy maternal use (95 joints per week throughout pregnancy and breast-feeding). If these effects do exist with light, moderate, or sporadic use, they are sufficiently subtle as to not be consistently demonstrated between studies." (p. 716)

Country/State of data - Review of research performed in CO, Jamaica, Pittsburgh, and Ottawa

Author(s) - A.C. Huizink

Title - Prenatal Cannabis Exposure and Infant Outcomes: Overview of Studies☆

Year - 2014 (Huizink, 2014)

Journal - Progress in Neuro-Psychopharmacology & Biological Psychiatry 52 (2014)

Study Type - Review

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Medium - a three study review of longitudinal cohort studies of prenatal exposure to marijuana

Pull Quotes for Reference - there is little evidence that prenatal cannabis exposure affects behavioral or cognitive outcomes in the early period of human life. Beyond infancy, there may be subtle effects on specific cognitive or behavioral outcomes, although more replication studies are needed. With the current evidence from both animal models and human research, in spite of inconsistencies between findings, the evidence does suggest a negative impact of prenatal exposure to cannabis on fetal growth and more subtle effects in infancy and childhood, which may turn into longer-lasting consequences such as altered executive functioning in adolescence

Notes -

Country/State of data - US

Author(s) – Lidush Goldschmidt, Ph.D., Gale A. Richardson, Ph.D., Jennifer Willford, Ph.D., and Nancy L. Day, Ph.D

Title - Prenatal Marijuana Exposure and Intelligence Test Performance at Age 6

Year - 2008 (Goldschmidt, Richardson, Willford, & Day, 2008)

Journal - J. Am. Acad. Child Adolesc. Psychiatry

Study Type - Longitudinal cohort

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Medium - Children who were prenatally exposed to marijuana at the level of 1 or more marijuana cigarettes per day had lower intelligence test scores at age 6 than their non-exposed peers, controlling for significant covariates.

Pull Quotes for Reference - The observed deficits were not linear but were associated with heavy use defined as one or more marijuana cigarettes per day.

Notes - After controlling for these risk factors, PME explained a small but significant portion of the performance on the SBIS measures of child intelligence. These findings are of concern, but they do not by themselves demonstrate causality.

Country/State of data - US

Author(s) - Nancy L. Day, Lidush Goldschmidt & Carrie A. Thomas

Title - Prenatal marijuana exposure contributes to the prediction of marijuana use at age 14

Year - 2006 (Day, Goldschmidt, & Thomas, 2006)

Journal -Addiction

Study Type - Longitudinal cohort

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Low/Medium - Not a super strong association. We have found a marginally significant association between PME and age of onset and a significant association between exposure to marijuana during gestation and the frequency of marijuana use of at age 14

Pull Quotes for Reference – Adolescents with PME have an earlier onset of marijuana use and use marijuana more frequently compared to adolescents who were not exposed.

Notes -

Country/State of data - USA

Author(s) - Kristen E. Sonon , Gale A. Richardson, Jack R. Cornelius, Kevin H. Kim, Nancy L. Day

Title - Prenatal Marijuana Exposure Predicts Marijuana Use in Young Adulthood

Year - 2015 (Sonon, Richardson, Cornelius, Kim, & Day, 2015)

Journal - Neurotoxicology and Teratology 47 (2015) 10–15

Study Type - Longitudinal cohort

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Medium - PME remained a significant predictor of offspring marijuana use ($p = 0.019$; OR = 1.22 (95% CI: 1.02–1.44), controlling for first trimester alcohol exposure and offspring race, gender, and age at the 22-year assessment. Adjusting for these covariates, a one unit increase in PME increased the odds of being in a higher category of use by 1.22.

Pull Quotes for Reference - PME is associated with subsequent marijuana use in young adulthood after considering the effects of other significant factors.

Notes - Strong modeling and good covariates. 77% of the participants were interviewed at last interview. Those lost to follow up did include deaths etc. Unclear that this is a representative sample of the US.

Country/State of data - USA - PA

Author(s) - Haberstick BC, Young SE, Zeiger JS, Lessem JM, Hewitt JK, Hopfer CJ

Title - Prevalence and Correlates of Alcohol and Cannabis Use Disorders in the United States: Results from the National Longitudinal Study of Adolescent Health

Year - 2014 (Haberstick, Young, Zeiger, Lessem, & Hewitt)

Journal - Drug and Alcohol Dependence

Study Type - Add Health Wave IV. Longitudinal nationally representative sample.

Category - Risk Factors for use

Systems Affected - Social

Strength of Effect/ Direction of Effect - Lifetime cannabis abuse: 3.9%. Lifetime cannabis dependence: 8.3%. Abuse and dependence more likely among males.

Pull Quotes for Reference - "One striking finding from this survey of young adults is the prevalence of marijuana use disorder that is higher than in previous reports of population-wide surveys and indicates that in young adults this disorder represents a substantial public health burden. This is of particular importance given the increasingly widespread legalization of marijuana in a number of states either through medical marijuana or recent efforts at outright legalization that may further encourage marijuana use."

Notes -

Country/State of data -

Author(s) - A.C. Huizink

Title - Prenatal Cannabis Exposure and Infant Outcomes: Overview of Studies☆

Year - 2014 (Huizink, Prenatal Cannabis Exposure and Infant Outcomes: Overview of Studies, 2014)

Journal - Progress in Neuro-Psychopharmacology & Biological Psychiatry 52 (2014)

Study Type - Review

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Medium - a three study review of longitudinal cohort studies of prenatal exposure to marijuana

Pull Quotes for Reference - there is little evidence that prenatal cannabis exposure affects behavioral or cognitive outcomes in the early period of human life. Beyond infancy, there may be subtle effects on specific cognitive or behavioral outcomes, although more replication studies are needed. With the current evidence from both animal models and human research, in spite of inconsistencies between findings, the evidence does suggest a negative impact of prenatal exposure to cannabis on fetal growth and more subtle effects in infancy and childhood, which may turn into longer-lasting consequences such as altered executive functioning in adolescence

Notes -

Country/State of data - US

Author(s) - LIDUSH GOLDSCHMIDT, PH.D., GALE A. RICHARDSON, PH.D., JENNIFER WILLFORD, PH.D., AND NANCY L. DAY, PH.D.

Title - Prenatal Marijuana Exposure and Intelligence Test Performance at Age 6

Year - 2008 (Goldschmidt, Richardson, Willford, & Day, Prenatal Marijuana Exposure and Intelligence Test Performance at Age 6, 2008)

Journal - J. Am. Acad. Child Adolesc. Psychiatry

Study Type - Longitudinal cohort

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Medium - Children who were prenatally exposed to marijuana at the level of 1 or more marijuana cigarettes per day had lower intelligence test scores at age 6 than their non-exposed peers, controlling for significant covariates.

Pull Quotes for Reference - The observed deficits were not linear but were associated with heavy use defined as one or more marijuana cigarettes per day.

Notes - After controlling for these risk factors, PME explained a small but significant portion of the performance on the SBIS measures of child intelligence. These findings are of concern, but they do not by themselves demonstrate causality.

Country/State of data - US

Author(s) - Nancy L. Day, Lidush Goldschmidt & Carrie A. Thomas

Title - Prenatal Marijuana Exposure Contributes to the Prediction of Marijuana Use at Age 14

Year - 2006 (Day, Goldschmidt, & Thomas, Prenatal Marijuana Exposure Contributes to the Prediction of Marijuana Use at Age 14, 2006)

Journal -Addiction

Study Type - Longitudinal cohort

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Low/Medium - Not a super strong association. We have found a marginally significant association between PME and age of onset and a significant association between exposure to marijuana during gestation and the frequency of marijuana use of at age 14

Pull Quotes for Reference – Adolescents with PME have an earlier onset of marijuana use and use marijuana more frequently compared to adolescents who were not exposed.

Notes -

Country/State of data - USA

Author(s) - Kristen E. Sonon , Gale A. Richardson, Jack R. Cornelius , Kevin H. Kim, Nancy L. Day

Title - Prenatal Marijuana Exposure Predicts Marijuana Use in Young Adulthood

Year - 2015 (Sonon, Richardson, Cornelius, Kim, & Day, Prenatal Marijuana Exposure Predicts Marijuana Use in Young Adulthood, 2015)

Journal - Neurotoxicology and Teratology 47 (2015) 10–15

Study Type - Longitudinal cohort

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Medium - PME remained a significant predictor of offspring marijuana use ($p = 0.019$; OR = 1.22 (95% CI: 1.02–1.44), controlling for first trimester alcohol exposure and offspring race, gender, and age at the 22-year assessment. Adjusting for these covariates, a one unit increase in PME increased the odds of being in a higher category of use by 1.22.

Pull Quotes for Reference - PME is associated with subsequent marijuana use in young adulthood after considering the effects of other significant factors.

Notes - Strong modeling and good covariates. 77% of the participants were interviewed at last interview. Those lost to follow up did include deaths etc. Unclear that this is a representative sample of the US.

Country/State of data - USA - PA

Author(s) - Haberstick BC, Young SE, Zeiger JS, Lessem JM, Hewitt JK, Hopfer CJ

Title - Prevalence and Correlates of Alcohol and Cannabis Use Disorders in the United States: Results from the National Longitudinal Study of Adolescent Health

Year - 2014 (Haberstick B. , Young, Zeiger, Lessem, & Hewitt, 2014)

Journal - Drug and Alcohol Dependence

Study Type - Add Health Wave IV. Longitudinal nationally representative sample.

Category - Risk Factors for use

Systems Affected - Social

Strength of Effect/ Direction of Effect - Lifetime cannabis abuse: 3.9%. Lifetime cannabis dependence: 8.3%. Abuse and dependence more likely among males.

Pull Quotes for Reference - "One striking finding from this survey of young adults is the prevalence of marijuana use disorder that is higher than in previous reports of population-wide surveys and indicates that in young adults this disorder represents a substantial public health burden. This is of particular importance given the increasingly widespread legalization of marijuana in a number of states either through medical marijuana or recent efforts at outright legalization that may further encourage marijuana use."

Notes -

Country/State of data -

Author(s) - Ferguson et al.

Title - Psychosocial Sequelae of Cannabis Use and Implications for Policy: Findings from the Christchurch Health and Development Study

Year - 2015 (Fergusson, Boden, & Horwood, 2015)

Journal - Social Psychiatry and Psychiatric Epidemiology

Study Type - Prospective longitudinal

Category - Mental Health

Systems Affected - Psychosocial Outcomes and Mental Health

Strength of Effect/ Direction of Effect - EXTREMELY STRONG - followed birth cohort until age 35; adjusted for observed and unobserved confounders. Found a dose response relationship with marijuana use and adverse psychosocial outcomes as well as a strong direct relationship with psychotic symptomatology

Pull Quotes for Reference - "In summary, it is our conclusion that the accumulated findings of the CHDS suggest that cannabis use, and in particular heavy use and use at younger ages, is associated with increased risks in a number of areas of functioning, including: (a) educational achievement; (b) welfare dependence; (c) unemployment; (d) other illicit drug use; and (e) psychotic symptomatology."

Notes - A remarkable study that addresses important questions on the impact of early and heavy use of marijuana. "Specifically pro-cannabis groups [5–7] and others [2, 87] have consistently argued that the apparent associations between cannabis and adverse outcomes is due to faulty research design and particularly failure to control confounding factors. These comments are reminiscent of the claims of the tobacco industry in its defense of cigarette smoking. The position taken is, in effect, that since research cannot eliminate all possibility that the relationships between cannabis and adverse outcomes are confounded by non-observed factors and processes, any evidence suggesting harmful effects of cannabis can be discounted and ignored. It is our view that this logic is deeply flawed."

Country/State of data - New Zealand

Author(s) - Yucel, M., Solowij, N., Respondek, C. et al.

Title - Regional Brain Abnormalities Associated with Long-term Heavy Cannabis Use

Year - 2008 (Yucel, Solowij, Respondek, Whittle, & Fornito, 2008)

Journal - Archives of General Psychiatry

Study Type - Observational/Correlational (Neuroimaging [MRI] and Mental Health and Auditory Verbal Learning Assessments)

Category - Brain

Systems Affected - Regional gray matter volume, mental health, verbal learning

Strength of Effect/ Direction of Effect - Decreased hippocampal volume, decreased amygdala volume, increase in subthreshold psychotic symptoms (positive and negative) and poorer performance in verbal learning in cannabis users, when compared to non-using controls.

Pull Quotes for Reference - "These findings corroborate previous animal research, suggesting that long-term heavy cannabis use is associated with significant and localized hippocampal volume reductions that relate to increasing cannabis exposure."

Notes - Small sample (n=31, 15 males with long histories of regular and heavy cannabis use, 16 matched non-using healthy males); cannabis-using group had lower Global Assessment of Functioning Scale scores and greater depressive symptoms (measured by the Hamilton Depression Rating Scale) than non-using controls at baseline.

Country/State of data - Australia

Author(s) - Moffitt et al.

Title - Reply to Rogeberg and Daly: No Evidence that SES Status or Personality Differences Confound the Association between Cannabis Use and IQ Decline

Year - 2013 (Moffitt, Meier, Caspi, & Poulton, 2013)

Journal - Proceedings of the National Academy of Sciences

Study Type - Review

Category - YOUTH

Systems Affected - Youth cannabis use and adult drop in IQ

Strength of Effect/ Direction of Effect - Strong - Reply to two critiques of the original study showing an IQ drop of 8 points among early and persistent users of marijuana

Pull Quotes for Reference - "In any event, SES and conscientiousness were raised as potential explanations (2, 4), but here we show they did not account for the finding."

Notes -

Country/State of data - New Zealand

Author(s) - HAYWOOD L. BROWN, MD* and CORNELIA R. GRAVES, MDw

Title - Smoking and Marijuana Use in Pregnancy

Year - 2013 (Brown & Graves, 2013)

Journal – Clinical Obstetrics and Gynecology

Study Type - ?

Category - Reproductive

Systems Affected - Prenatal exposure

Strength of Effect/ Direction of Effect - Low - Neither exposure to cigarette nor marijuana smoke has evidence for teratogenicity, but both have been implicated in developmental and hyperactivity disorders in children.

Pull Quotes for Reference –

Notes - Unclear what this is. Most likely not a systematic review.

Country/State of data - ?

Author(s) - Niemi-Pynttä et al.

Title - Substance-Induced Psychoses Converting into Schizophrenia: A Register-Based Study of 18,478 Finnish Inpatient Cases

Year - 2013 (Niemi-Pynttari, Sund, Putkonen, Worma, & Wahlbeck, 2013)

Journal - Journal of Clinical Psychiatry

Study Type - Retrospective longitudinal

Category - Mental Health

Systems Affected - Mental Health

Strength of Effect/ Direction of Effect - Strong - rate of conversion to schizophrenia from cannabis induced psychoses was higher than any other substance (alcohol, sedatives, opioids, hallucinogens, amphetamines)

Pull Quotes for Reference - The risk for diagnostic conversion to schizophrenia spectrum disorder was remarkable and highest among persons with cannabis-induced psychosis.

Notes - Very large sample size

Country/State of data - Finland

Author(s) - J Riba, M Valle, F Sampedro, A Rodríguez-Pujadas, S Martínez Horta, J Kulisevsky, and A Rodríguez-Fornells

Title - Telling True from False: Cannabis Users Show Increased Susceptibility to False Memories

Year - 2015 (Ribal, Valle, Sampedros, Rodriguez-Pujadas, & Martinez Horta, 2015)

Journal - Molecular Psychiatry

Study Type - fMRI

Category - Brain

Systems Affected - Memory

Strength of Effect/ Direction of Effect - Medium- Strong study methods, but small n (16 cannabis users, 50 non users). significant negative correlation (r = − 0.806, r2 = 0.650, Po0.001) was found between activity in the MTL regions of interest and lifetime cannabis use (log value of the estimated number of cannabis cigarettes smoked).

Pull Quotes for Reference - rather than a compromise of memory structures per se (that is, the hippocampus), our results point to a more diffuse impairment, which leads to a reduced capacity to deal with the retrieval and monitoring demands needed to differentiate between illusory and real events.

Notes - Interesting study regarding specifically what pieces of the brain and memory might be affected. Small n though.

Country/State of data - Spain

Author(s) - Wayne Hall, and Louisa Degenhardt

Title - The Adverse Health Effects of Chronic Cannabis Use

Year - 2014 (Hall & Degenhardt, 2014)

Journal - Drug Test. Analysis

Study Type - Review

Category - HEALTH

Systems Affected - Health generally

Strength of Effect/ Direction of Effect - Strong - This is a strong review demonstrating that there are adverse health outcomes for regular marijuana use.

Pull Quotes for Reference - Chronic cannabis use can produce a dependence syndrome in 1 in 10 users. Regular users have higher risks of chronic bronchitis and possibly impaired respiratory function; and psychotic symptoms and disorders, especially if they have a history of psychotic symptoms or a family history of these disorders. The most probable adverse psychosocial effect among adolescents who become regular users is impaired educational attainment. Regular adolescent cannabis users are more likely to use other illicit drugs although the explanation of this relationship remains contested.

Notes - The lifetime risk of dependence among all cannabis users has been estimated at about 9%.[10] This increases to one in six among those who initiate in adolescence.[10] The equivalent lifetime risks of dependence were 32% for nicotine, 23% for heroin, 17% for cocaine, 15% for alcohol, and 11% for stimulant users.[11,12]

Country/State of data - NA

Author(s) - Mehra R, Moore BA, Crothers K, Tetrault J, Fiellin DA

Title - The Association between Marijuana Smoking and Lung Cancer

Year - 2006 (Mehra, Moore, Crothers, Tetrault, & Fiellin, 2006)

Journal - Archives of Internal Medicine

Study Type - Systematic review

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Quantitative synthesis not possible because of variation in study design. Marijuana smoking associated with increased tar delivery compared with cigarette smoking. Other studies show increased pathology in lungs of marijuana smokers compared with tobacco smokers.

Pull Quotes for Reference - "Given this biological plausibility for the enhanced risk of lung cancer associated with marijuana, the observational studies reported thus far may have failed to find such an association owing to methodological limitations." p. 1365 "The potential for additive of synergistic effects between marijuana and tobacco smoking, as suggested from this literature, deserves rigorous evaluation, especially given the significant comorbid prevalence of these two behaviors." p. 1366

Notes - Swedish study is large and more recent - may be evidence this review was missing.

Country/State of data - Review

Author(s) - Valentina Lorenzetti, Nadia Solowij, Alex Fornito, Dan Ian Lubman and Murat Yücel

Title - The Association between Regular Cannabis Exposure and Alterations of Human Brain Morphology: An Updated Review of the Literature

Year - 2014 (Lorenzetti, Solowij, Fornito, Lubman, & Yucel, 2014)

Journal - Current Pharmaceutical Design

Study Type - Review

Category - Brain

Systems Affected - Brain

Strength of Effect/ Direction of Effect - Medium - Specifically, CB users showed volumetric alterations within regions of the medial temporal lobe (i.e., hippocampus and amygdala) as well as sub regions of the PFC and of the cerebellum. Group differences in brain regions were however not always consistent across studies.

Pull Quotes for Reference - First, there is emerging evidence that regular cannabis use is associated with alterations in the morphology of specific (e.g., medial temporal, PFC, cerebellar), as opposed to global, brain measures. Second, while structural brain alterations were observed particularly in CB samples with heavier patterns of cannabis use, there is mixed evidence for an association between levels of cannabis exposure (i.e., cannabis use patterns) and brain morphology in CB users. Third, there is evidence for preliminary associations between psychopathology/neurocognitive measures with brain structure in CB users. However, the paucity of studies and inconsistency between findings prevented a plausible speculation on their meaning. Overall, there is emerging evidence that regular cannabis exposure may be associated with neuroanatomical abnormalities in brain regions that are high in CB1 receptors and that mediate processes that are altered in CB users.

Notes - Strong review, showing that there are changes in the brain but that the studies are not consistent with what exactly it means.

Country/State of data -

Author(s) - Vinkers et al

Title - The Effect of Childhood Maltreatment and Cannabis Use on Adult Psychotic Symptoms is Modified by the COMT Val158Met Polymorphism

Year – 2013 (Vinkersa, et al., 2013)

Journal - Schizophrenia Research 150 (2013) 303–311

Study Type - Cross-Sectional

Category - Psychosis

Systems Affected - Psychosis & Genetics

Strength of Effect/ Direction of Effect - Medium - There is a relationship between childhood maltreatment, genetics, marijuana use and the outcome of psychosis.

Pull Quotes for Reference - The contributions of cannabis and childhood adversity on psychosis risk may be of particular significance in Val carriers of the COMT Val158Met genotype.

Notes - Interesting study, and meaningful, but not sure how to use it in any VT analysis.

Country/State of data -

Author(s) - van Ours, Jan; Williams, Jenny

Title - The Effects of Cannabis Use on Physical and Mental Health

Year - 2012 (van Ours & Williams, The Effects of Cannabis Use on Physical and Mental Health, 2012)

Journal - Journal of Health Economics

Study Type - Survey/Observational

Category - HEALTH

Systems Affected - All

Strength of Effect/ Direction of Effect - Moderate - found that cannabis use reduces mental health of both genders and the physical health of men only

Pull Quotes for Reference - In order to answer this question, we compare the size of the health effects we find for cannabis use with the size effects reported in the literature for having a single chronic condition or suffering a migraine. Doing so reveals that although statistically significant, the effects of cannabis use on health we estimate are small. This seems reasonable given that the estimates represent an average over all types of users: past, current, long duration, short duration, high intensity, low intensity, and various combination of these types.

Notes - Data collected in 1994

Country/State of data - Netherlands

Author(s) - Kempker et al.

Title - The Effects of Marijuana Exposure on Expiratory Airflow

Year - 2015 (Kempker, Honig, & Martin, 2015)

Journal - Annals of the American Thoracic Society

Study Type - Survey/Observational/Experimental

Category - Respiratory

Systems Affected - Respiratory

Strength of Effect/ Direction of Effect - Strong - Found no effect on airflow with marijuana users up to 20 joint-years (a joint year is equivalent to smoking one joint every day for a year).

Pull Quotes for Reference - "In conclusion, in a large representative sample of U.S. adults, ongoing use of marijuana is associated with increased respiratory symptoms of bronchitis without a significant functional abnormality in spirometry, and cumulative marijuana use under 20 joint-years is not associated with significant effects on lung function."

Notes -

Country/State of data - USA

Author(s) - Yu-Wei Luke Chu

Title - The Effects of Medical Marijuana Laws on Illegal Marijuana Use

Year - 2014 (Chu, 2014)

Journal - Journal of Health Economics

Study Type - Observational

Category - Medical Marijuana

Systems Affected - MEDICAL MARIJUANA - effects on illegal use

Strength of Effect/ Direction of Effect - MEDICAL MARIJUANA - I find that these laws increase marijuana arrests among adult males by about 15–20%. These results are further validated by findings from data on treatment admissions to rehabilitation facilities: marijuana treatments among adult males increased by 10–20% after the passage of medical marijuana laws.

Pull Quotes for Reference -

Notes - This study is interesting, but it is about medical marijuana, so it is outside of the scope of work.

Country/State of data - US

Author(s) - Fonseca et al.

Title - The Endocannabinoid System in the Postimplantation Period: A Role during Decidualization and Placentation

Year - 2013 (Fonseca, Correia-da-Silva, Almada, A., & Teixeira, 2013)

Journal - International Journal of Endocrinology

Study Type - Review

Category - Reproductive

Systems Affected - Reproductive

Strength of Effect/ Direction of Effect - N/A - Describes the natural role of the endocannabinoid system in pregnancy and the possible deleterious effects of exogenous THC on fetal development.

Pull Quotes for Reference - "Thus, exogenous cannabinoid exposure may overwhelm this local protection mechanism and interfere with stromal/decidual cells, trophoblast differentiation/proliferation, and interstitial/ endovascular invasion impairing placental function, which may result in intrauterine retardation and low birth weight, some of the adverse effects of cannabis consumption during pregnancy."

Notes -

Country/State of data - N/A

Author(s) - Williams J, Skeels CL

Title - The Impact of Cannabis and Cigarette Use on Health

Year - 2006 (Williams & Skeels, 2006)

Journal - Department of Economics, University of Melbourne, Research Paper Number 969

Study Type - Cross-sectional, representative of Australian population. Used 2001 and 2004 waves. Only included respondents aged 20-50 years.

Category -HEALTH

Systems Affected -

Strength of Effect/ Direction of Effect - 57% of sample report being in excellent/v. good health, but only 41% of weekly cannabis and 38% of daily cigarette smokers. Daily cigarette and weekly cannabis smokers less likely to be married, more likely to be divorced, live in smaller households, less educated, lower household income than full sample. Weekly cannabis users more likely to live in a state that has decriminalized use.

Pull Quotes for Reference - "We find that cannabis use does reduce self-assessed health status, with the effect of weekly use being of a similar magnitude as smoking cigarettes daily." p. 1 "The relative magnitude of the coefficients for weekly and yearly use suggests that there is a dose-response relationship between cannabis use and health, such that the more frequently cannabis is used, the greater the harm incurred." p. 20

Notes - Methods in this paper a bit above my head - econometrics. Not clear how they controlled for confounding - e.g. people in poor health use cannabis to alleviate other health symptoms.

Country/State of data - Australia

Author(s) - Seth Ammerman, MD, FAAP, Sheryl Ryan, MD, FAAP, William P. Adelman, MD, FAAP, The Committee on Substance Abuse, The Committee on Adolescence

Title - The Impact of Marijuana Policies on Youth: Clinical, Research, and Legal Update

Year - 2015 (Ammerman, Ryan, & Adelman, 2015)

Journal - Pediatrics

Study Type - Technical Report

Category - YOUTH

Systems Affected - Brain development, physical health, social justice

Strength of Effect/ Direction of Effect - NA

Pull Quotes for Reference - Available data have shown that legalization of medical marijuana has not led to a significant increase in the current use of recreational marijuana by adolescents. Marijuana use in pediatric populations remains an ongoing concern, and marijuana use by adolescents has known medical, psychological, and cognitive side effects. Marijuana alters brain development, with detrimental effects on brain structure and function, in ways that are incompletely understood. Furthermore, marijuana smoke contains tar and other harmful chemicals, so it cannot be recommended by physicians.

Notes - NOTE: This is a technical report, so it is more a summary and statement from the AAP. Useful though in terms of defining the issue for adolescents

Country/State of data -

Author(s) - Choo et al.

Title - The Impact of State Medical Marijuana Legislation on Adolescent Marijuana Use

Year - 2014 (Choo, et al., 2014)

Journal - Journal of Adolescent Health

Study Type - Survey (YRBS)

Category - YOUTH

Systems Affected - Rate of youth marijuana use

Strength of Effect/ Direction of Effect - Moderate - examined the impact on youth marijuana use in states that did and did not implement state-level medical marijuana laws - found no differences.

Pull Quotes for Reference - "In conclusion, our study of self-reported marijuana use by adolescents in states with a medical marijuana policy compared with a sample of geographically similar states without a policy does not demonstrate increases in marijuana use among high school students that may be attributed to the policies."

Notes - This study has been methodologically criticized for not using correct MML data

Country/State of data - USA

Author(s) - Monte et al.

Title - The Implications of Marijuana Legalization in Colorado

Year - 2014 (Monte, Zane, & Heard, 2014)

Journal - JAMA

Study Type - Editorial (citing several studies to make the case)

Category - HEALTH

Systems Affected - All but particularly pediatric

Strength of Effect/ Direction of Effect - Strong - evidence from Colorado Eds suggest an increasing rate of marijuana related injuries and diseases. Of particular concern is edibles and pediatric increases of accidental ingestion of marijuana infused products.

Pull Quotes for Reference - "While many users feel they have benefited from marijuana legalization in Colorado, there have also been untoward adverse health effects. The risks of use must be consistently communicated through health care practitioners and public health officials, especially for edible products that pose unique risks for exposed adults and children."

Notes - A well-argued editorial calling for additional research and caution particularly with respect to edible products

Country/State of data - Colorado

Author(s) - Anderson & Rees

Title - The Legalization of Recreational Marijuana: How likely is the Worst-Case Scenario?

Year - 2014 (Anderson & Rees, 2014)

Journal - Journal of Policy Analysis and Management

Study Type - opinion

Category - Motor Vehicle

Systems Affected - Consumption of Alcohol, traffic fatalities and youth consumption

Strength of Effect/ Direction of Effect - Weak - although based on past research, the speculation in this opinion piece is difficult to justify.

Pull Quotes for Reference - "On net, we predict the public-health benefits of legalization to be positive."

Notes -

Country/State of data - N/A

Author(s) - Degenhardt, Coffey, Romaniuk, Swift, Carlin, Hall, Patton

Title - The Persistence of the Association between Adolescent Cannabis Use and Common Mental Disorders into Young Adulthood

Year - 2012 (Degenhardt, Coffey, Romaniuk, Swift, & Carlin, 2012)

Journal - Addiction

Study Type - STRONG: prospective longitudinal study

Category - Mental Health

Systems Affected - Mental health - anxiety disorder, major depressive disorder

Strength of Effect/ Direction of Effect - *Strength of Association:* MEDIUM - Considers possible confounders. "Multiple potential confounders were considered, and the associations for anxiety disorders remained. It is still possible that other confounding variables may explain the observed associations." (p. 130) "Further work is required to replicate this finding and clarify whether there is a causal relationship between early heavy cannabis use and anxiety disorders, or whether this association is better explained by residual confounding by social context or temperament" (p. 132) *Meaningfulness of Association:* STRONG. *Direction of Association:* INCREASED for anxiety, NONE for depressive disorder.

Pull Quotes for Reference - "Regular (particularly daily) adolescent cannabis use is associated consistently with anxiety, but not depressive disorder, in adolescence and late young adulthood, even among regular users who then cease using the drug. It is possible that early cannabis exposure causes enduring mental health risks in the general cannabis-using adolescent population." (p. 124), "Heavier adolescent cannabis use was associated more consistently with a roughly twofold higher risk of anxiety disorder at 29 years, particularly if cannabis use continued at 29 years" (p. 130)

Notes - "A similar level of risk was found at 29 years for people who had not used cannabis regularly (weekly+) in adolescence but who used cannabis at age 29 years. There also appeared to be an increased risk of anxiety disorders at age 29 among adolescent cannabis users, even if they ceased using cannabis in adulthood" (p. 130)

Country/State of data - Australia

Author(s) - Tobacco Control Legal Consortium

Title - (Cork, 2015)

Year - 2015

Journal - REPORT

Study Type - REPORT

Category - Regulation

Systems Affected - Regulation

Strength of Effect/ Direction of Effect - Strong - lessons from tobacco regulation

Pull Quotes for Reference -

Notes - Great review of lessons from tobacco

Country/State of data - USA

Author(s) - Stacy Salomonsen-Sautela,∗, Sung-JoonMina, Joseph T. Sakaia, Christian Thurstonea,b, Christian Hopfera

Title - Trends in fatal motor vehicle crashes before and after marijuana commercialization in Colorado

Year - 2014 (Salomonsen-Sautela, Min, Sakaia, & Thurstonea, 2014)

Journal - Drug and Alcohol Dependence

Study Type – Cross sectional

Category - Motor Vehicle

Systems Affected - Motor vehicle

Strength of Effect/ Direction of Effect - Medium - In Colorado, since mid-2009 when medical marijuana became commercially available and prevalent, the trend became positive in the proportion of drivers in a fatal motor vehicle crash who were marijuana-positive (changeintrend,2.16(0.45), $p < 0.0001$);in contrast, no significant changes were seen in NMMS.

Pull Quotes for Reference - The primary results of this study are that (1)the proportion of drivers in a fatal motor vehicle crash who were marijuana-positive in Colorado was decreasing during the pre-marijuana commercialization period, but is now increasing, (2) similar changes are not seen in NMMS, (3) during the post-marijuana commercialization period, the increasing trend in the proportion of drivers in a fatal motor vehicle crash who were marijuana-positive is higher in Colorado compared to NMMS, and (4) no significant changes in the proportion of drivers in a fatal motor vehicle crash who were alcohol-impaired was seen in Colorado or in NMMS.

Notes - MEDICAL MARIJUANA - this is looking at medical marijuana commercialization in CO. This study would be STRONG if it were about legalization, but we do not have that data yet.

Country/State of data - Colorado

Author(s) - Miech et al.

Title - Trends in Use of Marijuana and Attitudes Toward Marijuana among Youth Before and After Decriminalization: The Case of California 2007-2013

Year - 2015 (Miech, Johnston, O'Malley, Bachman, & Schulenberg, 2015)

Journal - International Journal of Drug Policy

Study Type - Survey

Category - YOUTH

Systems Affected - Rates of use and Attitudes toward marijuana

Strength of Effect/ Direction of Effect - Strong - demonstrated significantly higher use rates among California 12th graders subsequent to marijuana decriminalization in 2010 compared to 12th graders in the rest of the country

Pull Quotes for Reference - The results of this study support decriminalization as a risk factor for increases in both marijuana acceptance and use among 12th graders. Following decriminalization both marijuana acceptance and use significantly increased among California 12th graders as compared to their peers in other states.

Notes - This study reverses the opinion provided in congressional testimony in 1980 by one of the authors and the PI of the MTF study (Lloyd Johnson)

Country/State of data - US

Author(s) - Anil A. Thomas, Lauren P. Wallner, Virginia P. Quinn, Jeffrey Slezak, Stephen K. Van Den Eeden, Gary W. Chien, and Steven J. Jacobsen

Title - Association between Cannabis Use and the Risk of Bladder Cancer: Results from the California Men's Health Study

Year - 2015 (Thomas, Wallner, Quinn, Slezak, & Van Den Eeden, Association between Cannabis Use and the Risk of Bladder Cancer: Results From the California Men's Health Study, 2015)

Journal - Urology

Study Type - prospective observational

Category - Cancer

Systems Affected - Cancer

Strength of Effect/ Direction of Effect - Medium - After adjusting for age, race or ethnicity, and body mass index, using tobacco only was associated with an increased risk of bladder cancer (hazard regression [HR], 1.52; 95% confidence interval [CI], 1.12-2.07), whereas cannabis use only was associated with a 45% reduction in bladder cancer incidence (HR, 0.55; 95% CI, 0.31-1.00). Using both cannabis and tobacco was associated with an HR of 1.28 (95% CI, 0.91-1.80).

Pull Quotes for Reference - In this multiethnic cohort of 82,050 men, we found that cannabis use alone was associated with a decreased risk of bladder cancer. Tobacco use alone was associated with an increased risk of bladder cancer.

Notes - NOTES: Interesting study, no dose response data at all, in fact conflicting. Findings are only marginally significant if at all, and they did not take into account when the men smoked marijuana.

Country/State of data - U.S.

Author(s) - Hall W

Title - What Has Research Over the Past Two Decades Revealed About the Adverse Health Effects of Recreational Cannabis Use?

Year - 2014 (Hall W. , What Has Research Over the Past Two Decades Revealed About the Adverse Health Effects of Recreational Cannabis Use?, 2014)

Journal - Addiction

Study Type - Review

Category - HEALTH

Systems Affected - Adverse Health Effects

Strength of Effect/ Direction of Effect - n/a

Pull Quotes for Reference - The epidemiological literature in the past 20 years shows that cannabis use increases the risk of accidents and can produce dependence, and that there are consistent associations between regular cannabis use and poor psychosocial outcomes and mental health in adulthood.

Notes - Solid summary, but the primary literature should be reviewed in order to critically assess the validity of studies that are relevant to the current undertaking.

Country/State of data - Unknown: Each of the studies referenced by the manuscript would need to be reviewed

Author(s) - Pacula & Lundberg

Title - Why Changes in Price Matter when Thinking About Marijuana Policy: A Review of the Literature on the Elasticity of Demand

Year - 2014 (Pacula & Lundberg, Why Changes in Price Matter When Thinking About Marijuana Policy: A Review of the Literature on the Elasticity of Demand, 2014)

Journal - Public Health Reviews

Study Type - Review

Category - Regulation

Systems Affected - Consumption

Strength of Effect/ Direction of Effect - Strong - examines the impact of laws, policies, and environmental factors (e.g., potency) on prevalence of marijuana use.

Pull Quotes for Reference - "Third, evidence presented here suggests that all aspects of marijuana use could change in response to this policy change, with more new initiates, more regular users, and people using for longer periods of time. Summary measures from initiation suggest that for every ten percent decline in the monetary price of marijuana, there will be an increase of three to five percent in new marijuana users prior to the age of 18, an increase of 2.5 percent in regular users, and an increase in the duration in which marijuana is used during adulthood. Absent more vigorous prevention efforts to counter these trends, the implication will be an expanding market, both in terms of the number of users and in the total quantity consumed by the market."

Notes - From RAND

Country/State of data - N/A

Casey Family Programs, Knowledge Management Unit

Rapid Response: Impacts of Recreational Marijuana Use on Caregiver Capacity and Youth Development

July 15, 2015

Vermont DCF Family Services Division Leaders and the Vermont Department of Health are conducting a Health Impact Assessment (HIA) and are interested in the potential impacts of legalization and regulation of recreational marijuana. The HIA process aims to assess scientific, peer-reviewed and evidence-based studies, if any, on the long-term impacts of recreational marijuana use on caregiver capacity and youth development. The requestor is interested in research regarding cognitive, behavioral and social impacts of recreational marijuana use. The links in this document were compiled between July 2 and July 14, 2015 and are not an exhaustive list or endorsement of any one approach. Instead, this Rapid Response provides information regarding potential impacts of recreational marijuana use on caregiver capacity and youth development – *Casey Family Programs Knowledge Management Unit*

Annotated Bibliography

Map: State Marijuana Laws

Governing the States and Localities. (2015). *State marijuana laws map*. Washington, DC: Author. Retrieved on July 13, 2015 from http://www.governing.com/gov-data/safety-justice/state-marijuana-laws-map-medical-recreational.html

This site features a map of states that have legalized medical marijuana, states that have legalized marijuana for recreational use and states that have no laws legalizing marijuana as of June 19, 2015. The following jurisdictions have legalized marijuana for recreational use: Alaska, Colorado, Oregon, Washington and the District of Columbia.

Legal Synopsis: Lessons from Tobacco Control for Marijuana Legislation

Cork, K. (2015). *Toking, smoking & public health: Lessons from tobacco control for marijuana regulation*. St. Paul, MN: Tobacco Control Legal Consortium. Retrieved on July 10, 2015 from http://publichealthlawcenter.org/sites/default/files/resources/tclc-synopsis-marijuana-tobacco-2015_0.pdf

This report presents an overview of regulatory issues related to medicinal and recreational uses of marijuana from a public health perspective. The report summarizes research on the impact of frequent marijuana use upon adults and youth. The report reviews states' marijuana laws and includes a checklist of tobacco control policies that could apply to marijuana regulation.

Fact Sheet: Adolescents and Marijuana

Alcohol and Drug Abuse Institute. (2014*). Learn about marijuana: Science-based information for the public*. Seattle, WA: University of Washington. Retrieved on July 7, 2015 from http://adai.uw.edu/marijuana/factsheets/adolescents.htm

This site includes a summary of impacts of marijuana use on youth development, including:

- Memory, attention and learning: Affect regulation, attention and ability to think clearly,
- School performance: Increased absenteeism and decreased performance
- Problematic behaviors: Lower incomes and greater welfare dependence, and
- Increased risk of mental health issues, including potential for depression and anxiety.

References include links to nine peer-reviewed articles and four state and national surveys.

Research on Marijuana Use During and After Pregnancy

National Institute on Drug Abuse. (2015). *Can marijuana use during and after pregnancy harm the baby?* Bethesda, MD: National Institutes of Health. Retrieved on July 9, 2015 from http://www.drugabuse.gov/publications/research-reports/marijuana/can-marijuana-use-during-pregnancy-harm-baby

This article, part of a series of research reports on marijuana, indicates that:

- Some babies born to women who used marijuana during their pregnancies respond differently to visual stimuli, tremble more, and have a high-pitched cry (which could indicate problems with neurological development),
- Children prenatally exposed to marijuana are more likely to show gaps in problem-solving skills, memory, and the ability to remain attentive, and
- More research is needed, however, to disentangle marijuana's specific effects from other environmental factors, including maternal nutrition, exposure to nurturing/neglect, and use of other substances by mothers

The authors recommend the following behavioral treatments that have shown promise:

Treatment	Additional Recognition and Research
Cognitive-Behavioral Therapy (CBT)	National Registry Review of CBT studies (18 PDFs) http://www.nrepp.samhsa.gov/CBT.aspx Principles of Drug Addiction Treatment: A Research-Based Guide (3rd Ed.): CBT and Alcohol, Marijuana, Cocaine, Methamphetamine and Nicotine http://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral
Contingency Management (CM)	Contingency Management Interventions/Motivational Incentives (Alcohol, Stimulants, Opioids, Marijuana, Nicotine http://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/evidence-based-approaches-to-drug-addiction-treatment/behavioral-0 Contingency Management in Substance Abuse Treatment (Article) http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3307900/
Motivational Enhancement Therapy (MET)	National Registry Description of MET http://www.nrepp.samhsa.gov/ViewIntervention.aspx?id=347 California Child Welfare Evidence-Based Clearinghouse http://www.cebc4cw.org/program/motivational-enhancement-therapy-and-cognitive-behavioral-therapy-5-sessions/

The article concludes with links to 62 references, which include peer-reviewed journal articles, federal technical assistance resources and presentations.

Press Release: Journal Article on Medical Marijuana Edible Products, Need for Oversight

Williams, S. (2015). Press release: Medical marijuana 'edibles' mostly mislabeled, study shows. Baltimore, MD: Johns Hopkins University. Retrieved on July 12, 2015 from http://www.hopkinsmedicine.org/news/media/releases/medical_marijuana_edibles_mostly_mislabeled_study_shows

This press release announces the publication of a new Johns Hopkins University study of edible marijuana products. Researchers cite the need for greater standardization in labeling and dosage of products marketed to medical and recreational marijuana consumers.

Examples of State Guidance

Frequently-Cited Court Precedents Regarding Marijuana and Child Removals

State of California. (2015). *California courts: Official reports public access web site.* Sacramento, CA: The California Judiciary. Retrieved on July 10, 2015 from http://www.lexisnexis.com/clients/CACourts/

This Official Reports Web of the California Judiciary site is intended to provide public access to California´s precedent setting appellate decisions. Two cases are frequently cited by marijuana reform supporters: one involves a mother's marijuana use and the other involves a father's marijuana use.

> Jennifer A. v. Superior Court, 117 Cal. App. 4th 1322 (Cal. App. 4th Dist. 2004). In this case, the appellate court overturned a lower court's ruling that a mother's "marijuana use, as shown by the record, means the children's return to the mother would create a substantial risk of detriment to the physical or emotional well-being of the children in light of the factors in this case militating in favor of their return… Further, no one offered testimony linking the mother's marijuana and alcohol use to her parenting judgment or skills."
>
> IN RE: Drake M., a Person Coming Under the Juvenile Court Law. Los Angeles County Department of Children and Family Services, Plaintiff and Respondent, v. Paul M., Defendant and Appellant. Cal. App. 2nd Dist. 2012). In this case, a trial court ruling was overturned because "the record showed that Drake was well cared for. DCFS reported that there was plenty of food in the home and the utilities were working. DCFS described the family's strengths including that Drake was healthy, that there was family support and that the father was employed… There was no evidence or even allegations of abuse in the home. DCFS failed to show that there was any link between father's usage of medical marijuana and any risk of serious physical harm or illness to Drake as there was no evidence that father had failed or was unable to provide Drake with adequate supervision or protection."

Evidence-Based Studies from Addiction Medicine

California Society of Addiction Medicine (CSAM). (2009*). Impact of marijuana on children and adolescents*. San Francisco, CA: Author. Retrieved on July 13, 2015 from http://csam-asam.org/sites/default/files/impact_of_marijuana_on_children_and_adolescents.pdf

This compilation of peer-reviewed medical research includes the following chapters with data, trend information and supporting scientific evidence on:

- Brain Development in Children and Adolescents
- Marijuana Addiction in Children and Adolescents
- Impact of Marijuana on Brain Function in Children and Adolescents
- The Impact of Marijuana on Brain Structure in Children and Adolescents
- Subtle Effects on Emotions and Reasoning Occur in all Marijuana Users

The compilation includes citations and abstracts of 47 different scientific studies: for each study, the authors summarize methods, outcomes achieved and replicability of results.

Colorado Website for Retail Marijuana Information

State of Colorado. (2014). *Official state of Colorado website for retail marijuana information & resources.* Denver, CO: Author. Retrieved on July 12, 2015 from https://sites.google.com/a/state.co.us/marijuana/

This site contains information regarding the use of recreational marijuana by adults 21 and over and includes links to research on the use of marijuana by youth. The site also has information for women who may smoke marijuana during pregnancy and potential impacts upon the fetus.

Illinois Fact Sheet: Marijuana

State of Illinois. (2014). *Fact sheet: Marijuana.* Springfield, IL: Department of Human Services. Retrieved on July 12, 2105 form http://www.dhs.state.il.us/OneNetLibrary/27897/documents/Brochures/4494.pdf

This fact sheet describes marijuana as "the most often used illegal drug in the United States. Marijuana in its smoked form has no commonly accepted medical use. However, the active chemical in marijuana is manufactured into a pill available by prescription. This prescription drug is used to treat the nausea and vomiting that occur with certain cancer treatments and to help AIDS patients eat more to keep up their weight."

Oregon Child Welfare Staff Tools: Foster Parent Medical Marijuana Use

State of Oregon. (2015). *Child welfare staff tools: Safety model frequently asked questions (FAQs)*. Salem, OR: Department of Human Services. Retrieved on July 10, 2015 from http://www.dhs.state.or.us/caf/safety_model/faq/cert_fp.html

Question: What about a foster parent who has a medical marijuana card?

Answer: In some very limited circumstances, an applicant with a medical marijuana card may be approved to be a certified caregiver. The assessment should consider the medical diagnosis requiring the use of medical marijuana and answers the following questions:

- Can the applicant with a medical condition who is using medical marijuana provide for the safety and child well-being?

- Where and how does the applicant use medical marijuana?
- What is the plan to ensure a child placed in the home would not have access to or be exposed to any second hand smoke?
- Does the applicant's physician have concerns about the applicant's ability to provide safety and well-being for the child?

Washington (Consulting Firm): Recreational Marijuana: A Guide for Local Governments.

Municipal Research and Services Center (MRSC). (2015). *Recreational marijuana: A guide for local governments*. Seattle, WA: Author. Retrieved on July 13, 2015 from http://mrsc.org/Home/Explore-Topics/Legal/Regulation/Recreational-Marijuana-A-Guide-for-Local-Governmen.aspx

The MRSC is a nonprofit organization supporting local governments in Washington State. This guide includes compilations of state regulations, basic information about implementation, regulatory documents, sample ordinances, and examples of signage and policies and procedures.

Works Cited

(n.d.).

Adda, J., McConnell, B., & Rasul, I. (2014). Crime and the Depenalization of Cannabis Possession: Evidence from a Policing Experiment. *Journal of Polictical Economy, Vol. 122, No. 5*.

Albertella, L., & Norberg, M. M. (2012). Mental Health Symptoms and their Relationship to Cannabis Use in Adolescents Attending Residential Treatment. *Journal of Psychoactive Drugs*.

Aldington, S., Harwood, M., Cox, B., Weatherall, M., & Beckert, L. e. (2008). Cannabis Use and Risk of Lung Cancer: A Case Control Study. *Eur Respir J. 2008 February; 31(2): 280-286*.

Aldington, S., Harwood, M., Cox, B., Weatherall, M., & Beckert, L. e. (2008). Cannabis Use and Risk of Lung cancer: A Case-control study. *European Respiratory Journal*.

Ammerman, S., Ryan, S., & Adelman, W. (2015). The Impact of Marijuana Policies on Youth: Clinical, Research, and Legal Update. *Pedicatrics*.

Anderson, D. M., & Rees, D. I. (2014). The Legalization of Recreational Marijuana: How likely is the Worst-Case Scenario? *Journal of Policy Analysis and Management*.

Asbridge, M., Hayden, J. A., & Cartwright, J. L. (2012). Acute Cannabis Consumption and Motor Vehicle Collision Risk: Systematic Review of Observational Studies and Meta-analysis. *BMJ*.

Bachhuber, M. A., Saloner, B., Cunningham, C. O., & Barry, C. L. (2014). Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999 - 2010. *JAMA*.

Baggio, S., N'Goran, A. A., Deline, S., Studer, J., & Dupuis, M. e. (2014). Patterns of Cannabis Use and Prospective Associations with Health Issues Among Young Males. *Addiction*.

Batalla, A., J.A, C., Busatto, G., Guimaraes, F., Zuardi, A., & al., e. (2014). Neuroimaging Studies of Acute Effects of THC and CBD in Humans and Animals: A Systematic Review. *Current Pharmaceutical Design*.

Bechtold, J., Simpson, T., White, H. R., & Pardini, D. (2015). Chronic Adolescent Marijuana Use as a Risk Factor for Physical and Mental Health Problems in Young Adult Men. *Psychology of Addictive Behaviors*.

Beshay, M., Kaiser, H., Niedhart, D., Reymond, M. A., & Schmid, R. (2007). Emphysema and Secondary Pneumothorax in Young Adults Smoking Cannabis. *European Journal of Cardio-thoracic Surgery*.

Bhattacharyya, S., Mandal, S., Banerjee, S., Mandal, G. K., & Bhowmick, A. K. (2014). Cannabis Smoke Can Be A Major Risk Factor for Early-age Laryngeal Cancer - A Molecular Signaling-based Approach. *Tumor Biology*.

Biehl, J. R., & Burnham, E. L. (2015). Cannabis Smoking in 2015: A Concern for Lung Health? *Chest*.

Bitter, S. M., Adler, C. M., Eliassen, J. C., Weber, W. A., & Welge, J. A. (2014). Neurofunctional Changes in Adolescent Cannabis Users With and Without Bipolar Disorder. *Society for the Study of Addiction*.

Bossong, M. G., Jansma, J. M., van Hell, H. H., Jager, G., & Kahn, R. S. (2013). Default Mode Network in the Effects of D9-Tetrahydrocannabinol (THC) on Human Executive Function. *PLOS (Public Library of Science) One*.

Boydell, K. M., Willinsky, C., Baker, N., & Boydell, C. (2011). CANNABIS AND PSYCHOSIS AWARENESS PROJECT A Pan-Canadian Study of Youth Experiences. *Report*.

Brown, H. L., & Graves, C. R. (2013). Smoking and Marijuana Use in Pregnancy. *Clinical Obstetrics and Gynecology*.

Budney, A. (2014). Clinical Epidemiology, Characteristics, Services, and Outcomes for Youth with Cannabis Use Disorders: Status of the Problem and Expectations for the Future. *N/A*.

Callaghan, R. C., Allebeck, P., & Sidorchuk, A. (2013). Marijuana Use and Risk of Lung Cancer: A 40-year Cohort Study. *Cancer Causes and Control*.

Cerda, M., Wall, M., Keyes, K., Galea, S., & Hasin, D. (2012). Medical Marijuana Laws in 50 States: Investigating the Relationship Between State Legalization of Medical Marijuana and Marijuana Use, Abuse, and Dependence. *Drug and Alcohol Dependence*.

Chadwick, B., Miller, M. L., & Hurd, Y. L. (2013). Cannabis Use During Adolescent Development: Susceptibility To Psychiatric Illness. *Frontiers in Psychiatry*.

Choo, E. K., Benz, M., Zaller, N., Warren, O., Rising, K. L., & al., e. (2014). The Impact of State Medical Marijuana Legislation on Adolescent Marijuana Use. *Journal of Adolescent Health* .

Chu, Y.-W. L. (2014). The Effects of Medical Marijuana Laws on Illegal Marijuana Use. *Journal of Health Economics*.

Cobb-Clark, D. A., Kassenboehmer, S. C., Le, T., McVicar, D., & Zhang, R. (2013). "High"-School: The Relationship Between Early Marijuana Use and Educational Outcomes. *Institute for the Study of Labor (IZA) in Bonn - discussion paper*.

Cork, K. (2015). Toking, Smoking & Public Health: Lessons from Tobacco Control for Marijuana Regulation . *Tobacco Control Legal Consortium Report*.

Daling, J. R., Doody, D. R., Sun, X., Trabert, B., & Weiss, N. e. (2009). Association of Marijuana Use and the Incidence of Testicular Germ Cell Tumors. *Cancer*.

Damjanovi, A., Pantovi, M., Damjanovi, A., Dunji-Kosti, B., & Ivkovi, M. e. (2015). Cannabis and Psychosis Revisited. *Psychiatria Danubina*.

Danielsson, A.-K., Falkstedt, D., Hemmingsson, T., Allebeck, P., & Agardh, E. (n.d.). Cannabis Use Among Swedish Men in Adolescence and the Risk of Adverse Life Course Outcomes: Results From a 20 Year-follow-up Study.

David, A. L., Holloway, A., Thomasson, L., Syngelaki, A., & Nicolaides, K. e. (2014). A Case-Control Study of Maternal Periconceptual and Pregnancy Recreational Drug Use and Fetal Malformation Using Hair Analysis. *PLOS ONE*.

Day, N. L., Goldschmidt, L., & Thomas, C. A. (2006). Prenatal Marijuana Exposure Contributes to the Prediction of Marijuana Use at Age 14. *Addiction* .

Day, N. L., Goldschmidt, L., & Thomas, C. A. (2006). Prenatal Marijuana Exposure Contributes to the Prediction of Marijuana Use at Age 14. *Addiction*.

Degenhardt, L., Coffey, C., Romaniuk, H., Swift, W., & Carlin, J. B. (2012). The Persistence of the Association between Adolescent Cannabis Use and Common Mental Disorders into Young Adulthood. *Addiction*.

Donoghue, K., Doody, G. A., Murray, R. M., Jones, P. B., & Morgan, C. e. (2014). Cannabis Use, Gender and Age of Onset of Schizophrenia: Data from the ÆSOP Study. *Psychiatry Research215 (2014) 528-532*.

Donoghue, K., Doody, G., Murray, R., Jones, P. B., & Morgan, C. e. (2014). Cannabis Use and Age of Onset of Schizophrenia: Data from the AESOP Study. *Psychiatry Research*.

D'Souza, D. C., Sewell, R. A., & Ranganathan, M. (2007). Cannabis and Psychosis/Schizophrenia: Human Studies. *European Archives of Psychiatry and Clinical Neuroscience*.

Ehrenreich, H., Nahapetyan, L., Orpinas, P., & Song, X. (2004). Marijuana Use From Adolescence to Young Adulthood: Multiple Developmental Trajectories and Their Associated Outcomes. *Health Psychology*.

El Marroun, H., Tiemeier, H., Steegers, E., Roos-Hesselink, J., & Jaddoe, V. e. (2010). A Prospective Study on Intrauterine Cannabis Exposure and Fetal Blood Flow. *Early Human Development*.

Evans-Polce, R. J., Vasilenk, S. A., & Lanza, S. T. (2015). Changes in Gender and Racial/Ethnic Disparities in Rates of Cigarette Use, Regular Heavy Episodic Drinking, and Marijuana Use: Ages 14 to 32. *Addictive Behaviors 41 (2015) 218-222*.

Fergusson, D. M., Boden, J. M., & Horwood, L. J. (2015). Psychosocial Sequelae of Cannabis Use and Implications for Policy: Findings from the Christchurch Health and Development Study. *Social Psychiatry and Psychiatric Epidemiology*.

Fernandez-Artamend, S., Fernandez-Hermida, J. R., Secades-Villa, R., & Garcia-Portilla, P. (2011). Cannabis and Mental Health. *Actas Espanolas de Psiquiatria*.

Filbey, F. M., Aslan, S., Calhoun, V. D., Spence, J. S., & Damaraju, E. e. (2014). Long-term Effects of Marijuana Use on the Brain. *Proceedings of hte National Academy of Sciences of hte United States*.

Filbey, F. M., McQueeny, T., Kadamangudi, S., Brice, C., & Ketcherside, A. (2015). Combined Effects of Marijuana and Nicotine on Memory Performance and Hippocampal Volume. *Behavioral Brain Research*.

Fischer, B., Imtiaz, S., Rudzinski, K., & Rehm, J. (2015). Crude Estimates of Cannabis-Attributable Mortality and Morbidity in Canada - Implications for Public Health Focused Intervention Priorities. *Journal of Public Health Advances*.

Fonseca, B. M., Correia-da-Silva, G., Almada, M., A., C. M., & Teixeira, N. A. (2013). The Endocannabinoid System in the Postimplantation Period: A Role During Decidualization and Placentation. *International Journal of Endocrinology*.

Fontes, M. A., Bolla, K. I., Cunha, P. J., Almeida, P. P., & Jungerman, F. e. (2011). Cannabis Use Before Age 15 and Subsequent Executive Functioning. *British Journal of Psychiatry*.

Friese, B., & Grube, J. W. (2013). Legalization of Medical Marijuana and Marijuana Use among Youths. *Drugs: Education, Prevention, and Policy*.

Gates, P., Jaffe, A., & Copeland, J. (2014). Cannabis Smoking and Respiratory Health: Consideration of the Literature. *Respirology*.

Gilman, J. M., Kuster, J. K., Lee, S., Lee, M. J., & Kim, B. W. (2014). Cannabis Use is Quantitatively Associated with Nucleus Accumbens and Amygdale Abnormalities in Young Adult Recreational Users. *The Journal of Neuroscience*.

Goldschmidt, L., Richardson, G. A., Willford, J., & Day, N. L. (2008). Prenatal Marijuana Exposure and Intelligence Test Performance at Age 6. *J . AM. Acad. Child Adolesc. Psychiatry*.

Goldschmidt, L., Richardson, G. A., Willford, J., & Day, N. L. (2008). Prenatal Marijuana Exposure and Intelligence Test Performance at Age 6. *J. Am. Acad. Child Adolesc. Psychiatry*.

Gordon, A. J., Conley, J. W., & Gordon, J. M. (2013). Medical Consequences of Marijuana Use: A Review of Current Literature. *Current Psychiatry Reports*.

Gossong, M., Jansma, J. M., van Hell, H. H., Jager, G., & Kahn, R. e. (2013). Default Mode Network in the Effects of D9-Tetrahydrocannabinol (THC) on Human Executive Function.

Griffith-Lendering, M. F., Wigman, J. T., Prince van Leeuwen, A., Huijbregts, S. C., & Huizink, A. C. (2012). Cannabis Use and Vulnerability for Psychosis in Early Adolescence - A TRAILS Study. *Addiction*.

Haberstick, B. C., Young, S. E., Zeiger, J. S., Lessem, J. M., & Hewitt, J. K. (n.d.). Prevalence and Correlates of Alcohol and Cannabis Use Disorders in the United States: Results from the National Longitudinal Study of Adolescent Health. *Drug and Alcohol Dependence*.

Haberstick, B., Young, S. E., Zeiger, J. S., Lessem, J. M., & Hewitt, J. K. (2014). Pevalence and Correlates of Alcohol and Cannabis Use Disorders in the United States: Results from the National Longitudinal Study of Adolescent Health. *Drug and Alcohol Dependence*.

Hackman, D. G. (2015). Cannabis and Stroke Systematic Appraisal of Case Reports. *Stroke*.

Hall, W. (2014). What Has Research Over the Past Two Decades Revealed About the Adverse Health Effects of Recreational Cannabis Use? *Addiction*.

Hall, W., & Degenhardt, L. (2014). The Adverse Health Effects of Chronic Cannabis Use. *Drugh Tes. Analysis*.

Hall, W., & Weier, M. (2015). Assessing the Public Health Impacts of Legalizing Recreational Cannabis Use in the USA. *Clinical Pharmacology & Therapeutics*.

Hancox, R. J., Shin, H. H., Gray, A. R., Poulton, R., & Sears, M. R. (2015). Effects of Quitting Cannabis on Respiratory Symptoms. *European Respiratory Journal*.

Hartman, R. L., Brown, T. L., Milavetz, G., Spurgin, A., & Gorelick, D. A. (2015). Controlled Cannabis Vaporizer Administration: Blood and Plasma Cannabinoids with and without Alcohol. *Clinical Chemistry*.

Hartman, R., & Huestis, M. (2013). Cannabis Effects on Driving Skills. *Clinical Chemistry*.

Hasin, D. S., Wall, M., Keyes, K. M., Cerda, M., & Schulenberg, J. e. (2015). Medical Marijuana Laws and Adolescent Marijuana Use in the USA from 1991 to 2014: Results From Annual, Repeated Cross-sectional Surveys. *Lancet*.

Hayatbakhsh, M. R., Flenady, V. J., Gibbons, K. S., Kingsbury, A. M., & Hurrion, E. e. (2011). Birth Outcomes Associated with Cannabis Use Before and During Pregnancy. *Pediatric Research*.

Heron, J., Barker, E. D., Joinson, C., Lewis, G., & Hickman, M. e. (2013). Childhood Conduct Disorder Trajectories, Prior Risk Factors and Cannabis Use at Age 16: Birth Cohort Study. *Addiction*.

Hii, S. W., Tam, J. D., Thompson, B. R., & Haughton, M. T. (2008). Bullous Lung Disease Due to Marijuana. *Respirology*.

Hill, K. P. (2015). Medical Marijuana for Treatment of Chronic Pain and Other Medical and Psychiatric Problems . *JAMA*.

Hill, M., & Reed, K. (2013). Pregnancy, Breast-Feeding, and Marijuana: A Review Article. *Obstetrical and Gynecological Survey*.

Huizink, A. (2014). Prenatal Cannabis Exposure and Infant Outcomes: Overview of Studies. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*.

Huizink, A. (2014). Prenatal Cannabis Exposure and Infant Outcomes: Overview of Studies. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*.

Hutchinson, D., Silins, E., Mattick, R. P., Patton, G. C., & Fergusson, D. M. (2015). How Can Data Harmonisation Benefit Mental Health Research? An Example of the Cannabis Cohorts Research Consortium. *Australia & New Zealand Journal of Psychiatry*.

Jacobus, J., Squeglia, L. M., Sorg, S. F., Nguyen-Louie, T., & Tapert, S. F. (2014). Cortical Thickness and Neurocognition in Adolescent Marijuana and Alcohol Users Following 28 Days of Monitored Abstinence. *Journal of Studies on Alcohol and Drugs*.

Joshi, M., Joshi, A., & Bartter, T. (2014). Marijuana and Lung Diseases. *Curren Opinion in Pulmonary Medicine*.

Jouanjus, E., Lapeyre-Mestre, M., & Micallef, J. (2014). Cannabis Use: Signal of Increasing Risk of Serious Cardiovascular Disorders. *Journal of the American Heart Association*.

Jouanjus, E., Leymarie, F., Tubery, M., & Lapeyri-Mestre, M. (2010). Cannabis-related Hospitalizations: Unexpected Serious Events Identified Through Hospital Databases. *British Journal of Clinical Pharmacology*.

Jutras-Aswad, D., DiNieri, J. A., Harkany, T., & Hurd, Y. L. (2009). Neurobiological Consequences of Maternal Cannabis on Human Fetal Development and its Neuropsychiatric Outcome. *European Archives of Psychiatry and Clinical Neuroscience*.

Jutras-Aswad, D., DiNieri, J. A., Harkany, T., & Hurd, Y. L. (2009). Neurobiological Consequences of Maternal Cannabis on Human Fetal Development and Its Neuropsychiatric Outcome. *European Archives of Psychiatry and Clinical Neuroscience*.

Keith, D. R., Hart, C., McNeil, M. P., Silver, R., & Goodwin, R. (2015). Frequent Marijuana Use, Binge Drinking & Mental Health Problems Amoung Undergraduates. *The American Journal on Addictions*.

Kelly, E., & Rasul, I. (2014). Policing Cannabis and Drug-Related Hospital Admissions: Evidence from Administrative Records. *Journal of Public Economics*.

Kempker, J. A., Honig, E. G., & Martin, G. S. (2015). The Effects of Marijuana Exposure on Expiratory Airflow. *Annals of the American Thoracic Society*.

Kuepper, R., van Os, J., Lieb, R., Wittchen, H.-U., Höfler, M., & Henquet, C. (2013). Continued Cannabis Use and Risk of Incidence and Persistence of Psychotic Symptoms: 10 Year Follow-up Cohort Study. *British Medical Journal*.

Large, M., Sharma, S., Compton, M. T., Slade, T., & Nielssen, O. (2011). Cannabis Use and Earlier Onset of Psychosis. *ARCH GEN PSYCHIATRY/VOL68 (NO. 6) (JAMA Psychiatry)*.

Lev-Rana, S., Imtiaza, S., Taylord, B., Shieldd, K., & Rehmd, J. e. (2012). Gender Differences in Health-related Quality of Life Amoung Cannabis Users: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug and Alcohol Dependence*.

Light, M. K., Orens, A., Lewandowski, B., & Pickton, T. (2014). Market Size and Demand for Marijuana in Colorado. *State Report*.

Lisdahl, K. M., Wright, N. E., Medina-Kirchner, C., Maple, K. E., & Shollenbarger, S. (2014). Considering Cannabis: The Effects of Regular Cannabis Use on Neuro-cognition in Adolescents and Young Adults. *Current Addiction Reports*.

Lorenzetti, V., Solowij, N., Fornito, A., Lubman, D. I., & Yucel, M. (2014). The Association between REgular Cannabis Exposure and Alterations of Human Brain Morphology: An Updated Review of hte Literature. *Current Pharmaceutical Design*.

Lubman, D. I., Cheetham, A., & Yucel, M. (2014). Cannabis and Adolescent Brain Development. *Pharmacology and Therapeutics*.

Lynne-Landsman, S. D., Livingston, M., & Wagenaar, A. C. (2013). Effects of Medical Marijuana Laws on Adolescent Marijuana Use. *American Journal of Public Health*.

Manrique-Garcia, E., Zammit, S., Dalman, C., Hemmingsson, T., & Andreasson, S. e. (2011). Cannabis, Schizophrenia and other non-affective Psychoses: 35 Years of Follow-up of a Population-Based Cohort. *Psychological Medicine*.

Marie, O., & Zolitz, U. (n.d.). "High" Achievers? Cannabis Access and Academic Performance. *Centre for Economic Performance*.

Marie, O., & Zolitz, U. (2015). "High" Achievers? Cannabis Access and Academic Performance. *Centre for Economic Performance; London School of Economics and Political Science*.

Marrouna, H. E., Hudziak, J. J., Tiemeier, H., Creemersa, H., Steegers, E. A., & al, e. (2011). Intrauterine Cannabis Exposure Leads to More Aggressive Behavior and Attention Problems in 18-month old Girls. *Drug and Alcohol Dependence 118 (2011) 470-474*.

McGrath, J., Welham, J., Scott, J., Varghese, D., & Degenhardt, L. e. (2010). Association Between Cannabis Use and Psychosis-Related Outcomes Using sibling Pair Analysis in a Cohort of Young Adults. *Archives of General Psychiatry*.

McLaren, J., Swift, W., Dillon, P., & Allsop, S. (2008). Cannabis Potency and Contamination: A Review of the Literature. *Addiction*.

Mehmedic, Z., Chandra, S., Slade, D., Denham, H., & Foster, S. e. (2010). Potency Trends of Δ9-THC and Other Cannabinoids in Confiscated Cannabis Preparations from 1993 - 2008. *Journal of Forensic Sciences*.

Mehra, R., Moore, B. A., Crothers, K., Tetrault, J., & Fiellin, D. A. (2006). The Association Between Marijuana Smoking and Lung Cancer. *Archives of Internal Medicine*.

Meier, M. H., Caspi, A., Ambler, A., Harrington, H., & Hout, R. e. (2012). Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife. *Psychological and Cognitive Sciences*.

Michaels, T. I., & Novakovic, V. (2015). Can Cannabis Cause Psychosis? *Clinical Neuropharmacology*.

Middlekauff, H. R., Park, J., & Moheimani, R. S. (2014). Adverse Effects of Cigarette and Non-cigarette Smoke Exposure on the Autonomic Nervous System. *Journal of the American College of Cardiology*.

Miech, R. A., Johnston, L., O'Malley, P. M., Bachman, J. G., & Schulenberg, J. e. (2015). Trends in Use of Marijuana and Attitudes toward Marijuana Amoung Youth Before and After Decriminalization: The Case of California 2007-2013. *International Journal of Drug Policy*.

Moffitt, T. E., Meier, M. H., Caspi, A., & Poulton, R. (2013). Reply to Rogeberg and Daly: No Evidence that SES Status or Personality Differences Confound the Association Between Cannabis Use and IQ Decline. *Preceedings of the National Academy of Sciences*.

Monte, A. A., Zane, R. D., & Heard, K. J. (2014). The Implications of Marijuana Legalization in Colorado. *JAMA*.

Moore, T. H., Zammit, S., Lingford-Hughes, A., Barnes, T. R., & Jones, P. B. (2007). Cannabis Use and Risk of psychotic of affective mental health outcomes: a systematic review. *Lancet*.

Niemi-Pynttari, J. A., Sund, R., Putkonen, H., Worma, H., & Wahlbeck, K. e. (2013). Substance-Induced Psychoses Converting into Schizophrenia: A Register-Based Study of 18,478 Finnish Inpatient Cases . *Journal of Clinical Psychiatry*.

Nutt, D. J., King, L. A., & Phillips, L. D. (2010). Drug Harms in the UK: A Multi-criteria Decision Analysis. *Lancet*.

Omayma, A., & Anthony, J. C. (2015). Cannabis Smoking and Diabetes Mellitus (Results from Meta-Analysis with Eight Independent Replication Samples). *Epidemiology*.

Onders, B., Casavant, M. J., Spiller, H. A., Chounthirath, T., & Smith, G. A. (2015). Marijuana Exposure Amoung Children Younger Than Six Years in the United States. *Clinical Pediatrics*.

Owen, K. P., Sutter, M. E., & Albertson, T. E. (2014). Marijuana: Respiratory Tract Effects. *Clinical Review of Allergy and Immunology*.

Pacula, L., & Sevigny, E. L. (2014). Marijuana Liberalization Policies: We Can't Learn Much From Policy Still in Motion. *Journal of Policy Analysis and Management*.

Pacula, R. L., & Lundberg, R. (2014). Why Changes in Price Matter When Thinking About Marijuana Policy: A Review of the Literature on the Elasticity of Demand. *Public Health Reviews*.

Pacula, R. L., & Sevigny, E. L. (2014). Natural Experiments in a Complex and Dynamic Environment: The Need for a Measured Assessment of the Evidence. *Journal of Policy Analysis and Management*.

Pacula, R. L., Powell, D., Heaton, P., & Sevigny, E. L. (2014). Assessing the Effects of Medical Marijuana Laws on Marijuana Use: The Devil is in the Details. *Journal of Policy Analysis and Management*.

Palamar, J. J., Fenstermaker, M., Kamboukos, D., Ompad, D. C., & Cleland, C. M. (2014). Adverse Psycosocial Outcomes Associated with Drug Use Among US High School Seniors: A comparison of Alcohol and Marijuana. *The American Journal of Drug and Alcohol Abuse*.

Palamar, J., Fenstermaker, M., Kamboukos, D., Ompad, D., & Cleland, C. e. (2014). Adverse Psychosocial Outcomes Associated with Drug Use Among US High School Seniors: a Comparisons of Alcohol and Marijuana. *AM J Drug Alcohol Abuse*.

Porath, A. J., & Fried, P. A. (2005). Effects of Prenatal Cigarette and Marijuana Exposure on Drug Use Among Offspring. *Neurotoxology and Teratology*.

Radhakrishnan, R., Wilkinson, S., & D'Souza, D. C. (2014). Gone to Pot - A Review of the Association Between Cannabis and Psychosis. *Frontiers in Psychiatry*.

Radhakrishnanm, R., Wilkinson, S. T., & D'Souza, D. C. (2014). Gone to Pot - A Review of hte Association between Cannabis and Psychosis. *Frontiers in Psychiatry*.

Renard, J., Krebs, M.-O., LePen, G., & Jay, T. M. (2014). Long-term Consequences of Adolescent Cannabinoid Exposure in Adult Psychopathology. *Frontiers in Neourscience*.

Ribal, J., Valle, M., Sampedros, F., Rodriguez-Pujadas, A., & Martinez Horta, S. e. (2015). Telling True from False: Cannabis Users Show Increased Susceptibility to false Memories. *Molecular Psychiatry*.

Romano, E., & Pollini, R. A. (2013). Patterns of Drug Use in Fatal Crashes. *Addiction* .

Rooke, S. E., Norberg, M. M., Copeland, J., & Swift, W. (2013). Health Outcomes Associated with Long-Term Regular Cannabis and Tobacco Smoking. *Addictive Behaviors*.

Salomonsen-Sautela, Min, S.-J., Sakaia, J. T., & Thurstonea, C. H. (2014). Trends in Fatal Motor Vehicle Crashes before and after Marijuana Commercialization in Colorado. *Drug and Alcohol Dependence*.

Smith, A. M., Longo, C. A., Fried, P. A., Hogan, M. J., & Cameron, I. (2010). Effects of Marijuana on Visuospatial Working Memory: An MRI Study in Young Adults. *Psychopharmacology (2010) 210:429-438*.

Smith, M. J., Cobia, D. J., Wang, L., Alpert, K. I., & Cronenwett, W. J. (2013). Cannabis-Related Working Memory Deficits and Associated Subcortical. *Schizophrenia Bulletin vol. 40 no. 2 pp. 287-299, 2014*.

Sonon, K. E., Richardson, G. A., Cornelius, J. R., Kim, K. H., & Day, N. L. (2015). Prenatal Marijuana Exposure Predicts Marijuana Use in Young Adulthood. *Neurotoxicology and Teratology*.

Sonon, K. E., Richardson, G. A., Cornelius, J. R., Kim, K. H., & Day, N. L. (2015). Prenatal Marijuana Exposure Predicts Marijuana Use in Young Adulthood. *Neurotoxicology and Teratology*.

Stefanis, N. C., Dragovic, M., Power, B. D., Jablensky, A., & Castle, D. e. (2013). Age at Initiation of Cannabis Use Predicts Age at Onset of Psychosis: The 7 to 8 Year Trend. *Schizophrenia Bulletin*.

Stinson, F. S., Ruan, W. J., Pickering, R., & Grant, B. F. (2006). Cannabis Use Disorders in the USA: Prevalence, Correlates and Co-morbidity. *Psychological Medicine*.

Tan, W. C., Lo, C., Jong, A., Xing, L., & FitzGerald, M. J. (2009). Marijuana and Chronic Obstructive Lung Disease: A Population-based Study. *Canadian Medical Association Journal* .

Tashkin, D. (2013). Effects of Marijuana Smoking on the Lung. *Ann Am Thorac Soc 10(3):239-247*.

Thomas, A. A., Wallner, L. P., Quinn, V. P., Slezak, J., & Van Den Eeden, S. K. (2015). Association between Cannabis Use and the Risk of Bladder Cancer: Results From the California Men's Health Study. *Urology*.

Thomas, A. A., Wallner, L. P., Quinn, V. P., Slezak, J., & Van Den Eeden, S. K. (2015). Association Between Cannabis Use and the Risk of Bladder Cancer: Results from the California Men's Health Study. *Oncology*.

Thomas, G., Kloner, R. A., & Rezkalla, S. (2014). Adverse Cardiovascular, Cerebrovascular, and Peripheral Effects of Marijuana Inhalation: What Cardiologists Need to Know. *The American Journal of Cardiology*.

van der Pol, P., Liebregts, N., de Graaf, R., Have, M. T., & Korf, D. J. (2013). Mental Health Differences Between Frequent Cannabis Users With and Without Dependence and the General Population. *Addiction*.

van Gastel, W., MacCabe, J. H., Schubart, C. D., van Otterdijk, E., & Kahn, R. S. (2014). Cannabis Use is a Better Indicator of Poor Mental Health in Women than in Men: A Cross-Sectional Study in Young Adutls from the General Population. *Community Mental Health J (2014) 50:823-830*.

van Gastel, W., Tempelaar, W., Bun, C., Schubart, C. D., & Kahn, R. S. (2013). Cannabis Use as an Indicator of Risk for Mental Health Problems in adolescents: A Population-based Study at Secondary Schools. *Psychological Medicine*.

van Gelder, M. M., Reefhuis, J., Caton, A. R., Werler, M. M., & Druschel, C. M. (2010). Characteristics of Pregnant Illicit Drug Users and Associations between Cannabis Use and Perinatal Outcome in a Population-based Study. *Drug and Alcohol Dependence*.

Van Os, J., Bak, M., Hanssen, M., Bijl, R. V., & de Graaf, R. e. (2002). Cannabis Use and Psychosis: A longitudinal Population-based Study. *American Journal of Epidemiology*.

van Ours, J., & Williams, J. (2012). The Effects of Cannabis Use on Physical and Mental Health. *Journal of Health Economics*.

van Ours, J., & Williams, J. (2014). Cannabis Use and its Effects on Health, Education and Labor Market Success.

Vinkersa, C. H., Van Gastela, W. A., Schubarta, C. D., Van Eijka, K. R., Luykxz, J. J., & al., e. (2013). The Effect of Childhood Maltreatment and Cannabis Use on Adult Psychotic Sysmptoms is Modified by the COMT VAL158 Met Polymorphism. *Schizophrenia Research 150 (2013) 303-311*.

Volkow, N. D., Baler, R. D., Compton, W. M., & Weiss, S. R. (2014). Adverse Health Effects of Marijuana Use. *New England Journal of Medicine*.

Warner, T. D., Roussos-Ross, D., & Behnke, M. (2014). It's Not Your Mother's Marijuana: Effects on Maternal-Fetal Health and the Developing Child. *Clinics of Perinatology*.

Washburn, I. J., & Capaldi, D. M. (2015). Heterogeneity in Men's Marijuana Use in the 20s: Adolescent Antecedents and Consequences in the 30s. *Development and Psychopathology*.

Williams, J., & Skeels, C. L. (2006). The Impact of Cannabis and Cigarette Use on Health. *Department of Economics, University of Melbourne, Research Paper Number 969*.

Wilson, F. A., Stimpson, J. P., & Pagán, J. A. (2014). Fatal Crashes from Drivers Testing Positive for Drugs in the U.S., 1993-2010. *Public Health Reports*.

Wittchen, H.-U., Frohlich, C., Behrendt, S., Gunther, A., & Rehm, J. e. (2007). Cannabis Use and Cannabis Use Disorders and their Relationship to Mental Disorders: A 10-year Prospective-longitudinal Community Study in Adolescents. *Drug and Alcohol Dependence*.

Yucel, M., Solowij, N., Respondek, C., Whittle, S., & Fornito, A. e. (2008). Regional Brain Abnormalities Associated with Long-term Heavy Cannabis Use. *Archives of General Psychiatry*.

Zalesky, A., Solowij, N., Yücel, M., Lubman, D., & Takagi, M. e. (2012). Effect of Long-Term Cannabis Use on Axonal Fiber Connectivity. *Brain* .

20 Flaws in Study Finding No Health Problems in Adult Males Who Were "Chronic" Marijuana Users as Teens, Young Adults

A new study has caused quite a stir among would-be marijuana cognoscenti because it contradicts major research about the impact of marijuana on physical and mental health. The neuroscientist, Bertha K. Madras of Harvard Medical School looked briefly at the study. Dr. Madras served as Deputy Director for Demand Reduction in the White House Office of National Drug Control Policy from 2006 to 2008 . . . She writes:

A recent manuscript by Bechtold et al[1], describes a longitudinal assessment of a population of marijuana users which were subsequently divided into four user groups: (1)non-users to low use (46%, n=177; (2) limited to adolescent use (11%, n=43); (3) late initiation and increasing (21%, n=81); (4) early onset with chronic use (22%, n=85). Marijuana use was monitored from adolescence (age 15) into young adulthood (age 26). Study authors then asked the subjects, now at an average age of 35.8 years, to report their health status, *ten years after the last determination of marijuana use*. Subjects self-reported no differences in physical or mental health problems at age 36. The authors concluded that regardless of quantity and duration of marijuana use, or race, these four groups did not differ significantly in terms of their physical and mental health problems. They also claim that this is a definitive study because of its longitudinal structure and superiority over other published reports on long term health consequences of marijuana.

A critical evaluation of the validity of the findings and sweeping conclusions is essential, lest they are interpreted inappropriately. A perusal of the study and the authors' stated caveats in the manuscript reveal significant weaknesses, using an unrepresentative, archaic population, inadequate sample size, inadequate methodologies to assess mental health and physical problems, (self-reports, evaluation of psychiatric status without considering "spectrum" nature of psychiatric conditions, and absence of addiction evaluation. The

findings conflict with other better designed longitudinal studies that assess long term consequences of marijuana use of early age of initiation of marijuana.

This type of study would not approach or fulfill rigorous criteria for longitudinal research, as exemplified by the 2014 NIDA funding opportunity with similar goals (*see final paragraph*). The questionable conclusions may be compromised by the following perceived shortcomings of the study.

Population Problems

1. **The sample size was too small to detect a marijuana effect on psychotic disorders or on other health conditions.** NIDA recommends a sample size of 10,000 to detect differences (see last paragraph). About 50% of the subjects – age 14 - were selected on the basis that they has high scores on anti-social behaviors (conduct problems) and the rest from other adolescents, but we don't know whether the drop-out rate from the study was equally represented by both categories. There is strong and accumulating evidence that marijuana use is associated with psychosis, with earlier age of onset of schizophrenia, and with worsening of psychotic and schizophrenic symptoms. A number of these association studies were performed on thousands of people, not on less than 400. There is also increased reporting of cardiovascular complications related to marijuana and the extreme seriousness of this (death rate of 25.6%). Marijuana is a possible risk factor for cardiovascular disease in young adults[6]. There is also mounting evidence of a temporal association between marijuana use and serious adverse events, including heart attacks, sudden cardiac death, disease of heart muscle, stroke, transient ischemic attack, and marijuana-induced arteritis.[7] Pulmonary symptoms attributable to marijuana use, even after less intense use, include chronic bronchitis, daily cough, phlegm production (four quality manuscripts document these findings).
   ***Think about this**:* The prevalence of schizophrenia is 1 in 100. If you only sample 86 subjects in the riskiest group, "early onset chronic users" category, it is unlikely that you will detect a significant increase in psychosis or schizophrenia. Another example: a recent study found the incidence of serious cardiac effects of marijuana in 1.8% of heavy users. Serious cardiac effects would be hard to detect in the small sample size of early onset chronic users, especially if self-reporting.

2. **By including subjects who chose to use marijuana, the study does not have a non-marijuana using population to compare outcomes.** The study reports that the amount of marijuana used during adolescence and early adulthood has no effect on the occurrence of a range of health problems**.**
   This about this: Compared to what population? Compared to the other groups? Are the group sizes large enough to detect differences? The study has no group that controls for the general, representative population, a non marijuana using population. Other studies have shown differences in outcome measures between youth who choose not to use, those who use occasionally, and heavy users.

3. **The populations and use patterns investigated in this study are anachronistic and conceivably irrelevant for 2015. The study, initiated in 1987-1988, recruited a majority of users that did not fall into the heavy use range (daily or near daily use).** The majority of subjects used marijuana during the 1990's.
   Think about this: The most serious health outcomes associated with marijuana use are in populations of heavy (daily or near daily use), including addiction. Currently, marijuana access has risen rapidly as its legal status changes, its perception of harm has plummeted among youth, and the perception that it is a medicine to be used safely and daily has risen. Daily use of high potency marijuana among adolescents and young adults is near or at its highest level in nearly three decades. The population in this study may be irrelevant because of these 21st century factors that have altered use patterns and perception of harm; these could influence not only self-reporting of effects, but the magnitude of effects.

4. **The population is not representative of the general population: (a) the prevalence of concussions (27.7%) is inordinately high. (b) death by gunfire is inordinately high.** No explanations are offered for the abnormally high concussion rate or death by gunfire rate in the population examined. Does this population have a higher than average rate of cognitive impairment? Were concussions associated with marijuana use?
   Think about this: The overall rate of traumatic brain injury (concussions) presenting in emergency departments in the United States (recent CDC statistics) is 19 per 100,000 persons, and for males in this age group it is about 470 per 100,000 persons (or 4.7 for each 1,000 persons), according to recent CDC statistics. A concussion rate of 27% of this population (270 per 1000 persons), is about 60 times higher than the general population within this age range. Also, rigorous research criteria would exclude subjects with traumatic brain injury because of the potential for cognitive impairment. The high death rates due to gunfire are anomalous if compared to the general population statistics.

5. **Self reported medical health problems, on the basis of race, differ from population statistics.** According to CD statistics in 2010, the prevalence of diseases in the general population among African American adults compared to white adults is quite different than in this study: Diabetes, CDC = 1.6:1; in this study = 4:0. Chronic kidney disease, CDC = 1.14:1, in this study = 0:0.6. Sexually transmitted diseases, CDC = 4:1; in this study = 0.45.
   Think about this: The health problems self-reported by the African-Americans and white subjects may or may not be accurate, but they differ markedly from the CDC data on prevalence. The differences may reflect the unusual populations of this study. Nonetheless, they highlight the need for recruiting sufficiently large numbers of subjects to be representative of the population as a whole.

Methodological Problems: Outcome measures

6. **The core outcomes are mental and physical health and whether marijuana affected health. All findings are self-reported, a highly inadequate method because of potential bias and recall errors.** The authors did not investigate medical records, did not confirm marijuana and other drug use with biometric tests, did not interrogate contacts, and did not inquire about sequence of use of other drugs.
   ***Think about this*:** more than 75% of people harboring a substance use disorder (SUD), based on objective DSM-IV criteria (Diagnostic and Statistical Manual-IV), do not think they have a SUD and do not seek treatment[2]. To rely solely on self-reporting of mental or physical health problems with a questionnaire, raises doubts about the overall study design and conclusions. Another example: Fifty percent of men who die of heart disease had no obvious symptoms. A diagnosis of diabetes is made by biometric testing,

7. **There is no evidence that subjects reported health outcomes based on their medical records. Authors did not question whether study participants had visited a physician during the past year, past five years or ten years since the last contact. Confirmation of medical conditions by a medical record would strengthen the conclusions.** The core outcomes of this study are mental and physical health. Knowing whether the mental and physical health of subjects in this study had been objectively diagnosed by a physician or specialist (psychiatrist) is critical. The fact that the medical record is unknown represents a significant weakness in assuming the accuracy subjects' self-reports.
   Think about this: a number of the recent mass murderers who killed people in public places and who were designated as harboring a psychotic disorder after their actions, had no or limited contact with psychiatrists prior to their violent deeds and went untreated. It is possible that all subjects had annual checkups for the past 20 years, but unless this information is provided, along with objective measures, one cannot assume that self-reports are accurate.

8. **Mental and physical diagnoses were based on questionnaires, not on biometric testing or long term assessment (mental health diagnosis requires long term evaluation).** The diagnosis of psychosis, mood disorders, anxiety disorders, high blood pressure or other medical problems does not rely solely on a person's response to oral or written questionnaires or impressions of their own health. Definitive diagnosis for a mental health problem requires systematic questioning, and over a significant period of time to determine whether symptoms persist. Moreover, mental health problems including addiction, occur along a continuum of mild to severe. It is not possible to determine whether scores were generated that reflect this continuum, or whether authors arbitrarily selected a cut-off point and rated the presence or absence of symptoms as having a diagnosis or not.
   ***Think about this**:* It is simple to detect one's own asthma or headache but, for many mental health and medical conditions, self-diagnosis may be inaccurate. Can one

know whether high blood pressure, or diabetes, exist unless measured objectively? Can one know if an early stage of cancer is present unless it is diagnosed by imaging or by biopsy? Can one know if an asymptomatic heart disease conditions is present, unless an ECG is performed? Do most people self-diagnose a serious mental illness and seek help?

Methodological problems: Marijuana use

9. **The investigators divided marijuana users over time into four groups, using model fit statistics. The chart showing marijuana use over time for these four groups provides no error bars indicating whether these groups are significantly different at each age during the study.**
   Think about this: One would assume the groups were different, based on the four-group solution that was selected on the basis of model fit statistics, substantive interpretation, face validity of classes, parsimony, and consistency of findings with prior research. But, it would be helpful if error bars representing standard deviations at each age were included to assure the reader that the subjective criteria (interpretation, face validity of classes, parsimony, consistency of findings with prior research were transparently clear from the error bars. References given for prior research would further validate for this criterion.

10. **Some data of marijuana use component are missing: 46% of the subjects had voids is data.** 46% of people did not report marijuana use at various times during the 10 years of survey. This partial set of data is problematic, even though authors claim missing data was from people similar to those who yielded full data sets.
    Think about this*:* If a segment of data are not available, does it invalidate or skew the chart showing trends of the four groups? Authors should provide reasons for these data gaps.

11. **Marijuana use was not questioned at the end of the study (age 36 years)** Strong longitudinal studies have shown that early onset and heavy use of marijuana has long term adverse effects on educational achievement, employment, welfare dependency, use of other illicit drugs and psychotic symptoms, I.Q. reduction[3-5]. This study provides marijuana use rates until age 26, measures life outcomes at age 36 but doesn't ask subjects whether they used at age 36. Most users apparently were not consuming daily or nearly daily and three of the four groups had largely stopped using by the age of 26. Why was marijuana use not measured at the end of the study?
    Think about this*:* It is critical to know whether the people using marijuana from age 15 -26 years, were still using at age 36, at the time the health measures were interrogated.
    Think about this: If you are studying whether marijuana has interfered with the mental and physical health of subjects in a study at the present time, it is logical to

interrogate whether they are currently using, or stopped. If they stopped 10 years before, then long term consequences may be less likely.

12. **Marijuana potency was far lower** (1980's to 1990's) during the period of marijuana consumption of this population. This conceivably affects outcomes and consequences.

13. **Quantity, frequency, potency of marijuana use is a critical measure.** The main outcome measure was the number of times marijuana was used during the year. The number of times used each day of use, the potency, was not interrogated during each annual survey.

Methodological problems: Other outcomes not measured

14. **Addiction (cannabis use disorder) was not interrogated.** This is among the most significant of the adverse effects of marijuana and is related to age of onset, quantity and frequency of use and closely linked to other life outcomes.
***Think about this*:** addiction is among the most prominent effects of chronic marijuana use, and yet the study does not address it.

15. **Life outcomes were not measured (employment, educational achievement) at the end of the study.** Other strong longitudinal studies have interrogated life outcomes and concluded that marijuana has adverse long term effects on employment and educational achievements, other social consequences, as a function of age of onset and quantity used[3-5].
Think about this: When an individual is using marijuana very frequently for a number of years, are they more or less likely to maintain a job, complete high school or college, be on welfare? Longitudinal studies indicate that heavy continuous marijuana use leads to lower socioeconomic status and achievements (e.g. college education) than infrequent or no use.

16. **Cognitive testing was not performed.** Cognitive impairment is one of the hallmarks of acute and possibly long term marijuana use. It is also associated with other adverse life outcomes.
Think about this: If you were designing a study to learn whether an intoxicant, known to interfere with learning, memory, executive function, has adverse effects, would you omit testing from learning and memory evaluations from the study?

17. **Many health problems (e.g. cancer, high blood pressure, heart attacks, strokes) arise later than the average age of the subjects (mid-30's) at the end point.** The health questionnaire was filled out by marijuana users in their mid-30's, an age at which most significant health problems are not yet manifest (e.g. cancer, high blood pressure, heart attacks, strokes).

18. **No questions were asked about acute effects: intoxication, accidents, emergency department mentions, accidents.** For example, a recent European study collected Emergency Department data from 14 European centers for six months to determine acute toxicity of marijuana. Of the sample, 356 (16.2 %) involved marijuana alone or together with other drugs/alcohol and 1.6 % with marijuana alone. Of the 35 non-fatal lone marijuana presentations, the most commonly reported features were agitation/aggression (22.9 %), psychosis (20.0 %), anxiety (20.0 %) and vomiting (17.1 %). There was one fatality due to prolonged cardiac arrest, with no other drugs detected.[6]
Think about this: Acute marijuana toxicity can lead to emergencies requiring medical attention. Omitting this from the questionnaire does not achieve a comprehensive view of medical consequences of marijuana.

Citations and Comparison with other Studies

19. **Authors omit mention of important recent longitudinal studies that show the opposite of their findings.** Other carefully controlled and longitudinal studies have shown that early age of onset of marijuana use is associated with a number of mental and physical consequences, including addiction, cognitive deficits, mental health problems, educational, employment outcomes and others. Examples 3, 4 are not mentioned, others are dismissed with a list of weaknesses, even though the current study contains significant weaknesses.

20. **The authors attempt to support their conclusions by dismissing well designed reports by others.** In the introduction, they do not discuss severe limitations of their own study: (e.g. the majority of their subjects were infrequent users, whereas daily use of high potency marijuana is currently at its highest level in 30 years of surveys; weaknesses of self-reported medical and psychiatric conditions, and others as stated above). Instead, the introduction is a curious critique, entitled ***Limitations in Prior Research.*** In it they conclude that "prior research has produced mixed findings regarding the associations between chronic marijuana use and indicators of physical and mental health, …and that individuals who begin using marijuana frequently during early adolescence and those who use at high frequencies throughout adolescence and young adulthood tend to develop more health problems (i.e., psychotic symptoms, respiratory problems) than infrequent/nonusers, *in contradistinction to their own findings.*

Think about what is wrong with their critique*:* (1) they claim this study is among a "handful of studies that have been able to prospectively delineate subgroups of individuals with varying developmental patterns of marijuana use from adolescence into young adulthood". The strength of the present study was to document marijuana use, but not in depth, annually for the decade of life encompassing adolescence and early adulthood. Yet, other research has interrogated key variables, age of onset,

frequency and quantity of marijuana use, some in prospective, longitudinal studies, others in cross-sectional studies. The medical record at the study's inception is of limited value because it is neither comprehensive nor independently verified. The initial assessment of 15 year old boys was inadequate and was not followed by a longitudinal assessment, except for marijuana use. The 10 year hiatus in data collection is a weakness. Self-reports of mental and physical health are inappropriate.

(2) They claim that "few longitudinal studies have examined whether young men who exhibit early and chronic developmental patterns of marijuana use are more likely to exhibit both physical and mental health problems in their mid-30s". Unfortunately, this study does not answer this question because of the low quality of the outcome measures, with no marijuana use patterns recorded for 10 years, with the only medical and mental health records being ones reported by mothers of the subjects around age 15, and by the subjects themselves at ~ age 36.

(3) They claim that "Many studies have failed to control for important confounding factors, such as health problems that predated the onset of regular marijuana use and co-occurring use of tobacco, alcohol, and hard drugs". Yet, the documented and age-appropriate deficits associated with marijuana use, in-depth psychiatric status, cognitive impairment, declining academic performance, school drop-out rates, accidents, and others, were not interrogated in this survey. High blood pressure, heart disease, strokes, kidney disease, Type II diabetes, cancer, sexually transmitted infection, psychotic disorders are rare in 15 year old boys, whereas asthma, allergies, headaches can occur and fluctuate throughout life.

(4) The claim that "few studies have examined whether chronic marijuana use differentially affects physical and psychological health outcomes across racial groups", is inaccurate.

Limited references

1. Bechtold, J., Simpson, T., White, H. R., & Pardini, D. Chronic Adolescent Marijuana Use as a Risk Factor for Physical and Mental Health Problems in Young Adult Men Online First Publication, August 3, 2015. http://dx.doi.org/10.1037/adb0000103 *Psychology of Addictive Behaviors*.
2. Substance Abuse and Mental Health Services Administration, *Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-48, HHS* Publication No. (SMA) 14-4863. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2014.
3. Fergusson DM, Boden JM, Horwood LJ. Psychosocial sequelae of cannabis use and implications for policy: findings from the Christchurch Health and Development Study. Soc Psychiatry Psychiatr Epidemiol. 2015 May 26. [Epub ahead of print]

4. Fergusson DM, Boden JM. Cannabis use and later life outcomes. Addiction. 2008 Jun;103(6):969-76; discussion 977-8.
5. Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RS, McDonald K, Ward A, Poulton R, Moffitt TE. Persistent cannabis users show neuropsychological decline from childhood to midlife. Proc Natl Acad Sci *U S A.* 2012 Oct 2;109(40):E2657-64.
6. Dines AM, Wood DM, Galicia M, Yates CM, Heyerdahl F, Hovda KE, Giraudon I, Sedefov R; Euro-DEN Research Group, Dargan PI. Presentations to the Emergency Department Following Cannabis use-a Multi-Centre Case Series from Ten European Countries. J Med Toxicol. 2015 Feb 5. [Epub ahead of print]
7. Jouanjus E, Lapeyre-Mestre M, Micallef J; French Association of the Regional Abuse and Dependence Monitoring Centres (CEIP-A) Working Group on Cannabis Complications*. Cannabis use: signal of increasing risk of serious cardiovascular disorders. J Am Heart Assoc. 2014 Apr 23;3(2):e000638. doi:10.1161/JAHA.113.000638.
8. Thomas G, Kloner RA, Rezkalla S. Adverse cardiovascular, cerebrovascular, and peripheral vascular effects of marijuana inhalation: what cardiologists need to know. Am J Cardiol. 2014 Jan 1;113(1):187-90.