Marijuana and Public Health: The Evidence for Health Protection in Colorado

March 7, 2014

Agenda

8:30am-9:00am  Registration

9:00am-10:50am  Moderator: Tim Byers MD, MPH
Marijuana 101: Amanda Reiman PhD, MSW
Marijuana & Cancer: Daniel Bowles MD
Marijuana, Heart & Lung Diseases: David Goff MD, PhD
Marijuana & Mental Health: Paula Riggs MD
Marijuana & Drug Dependency: Christian Thurstone MD

10:50am-11:15am  Break

11:15am-12:20pm  Moderator: Art Way JD
Marijuana, Pregnancy & Breast Feeding: Laura Borgelt PharmD, FCCP, BCPS
Marijuana and Traffic Safety: Ashley Brooks-Russell PhD, MPH
Avoiding Unintentional Marijuana Exposure: George Sam Wang MD, FAAP

12:20pm-1:00pm  Lunch

1:00pm-2:10pm  Moderator: Chris Urbina MD, MPH
Issues Around Marijuana & Public Health in the State of Washington: Mary Segawa MS
Marijuana Issues in Colorado: Larry Wolk MD, MSPH
Marijuana Issues in Colorado: Local Public Health: Summer Laws MPH

2:10pm-2:30pm  Break

2:30pm-4:00pm  Moderator: Tim Byers MD, MPH
Panel Discussion & Audience Questions

Recordings, speaker presentations, and the annotated bibliography will be available on http://publichealthpractice.org/ following the Symposium.
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Featured Speaker Bios

Laura Borgelt, PharmD, FCCP, BCPS

Dr. Laura Borgelt is an Associate Professor at the University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences and School of Medicine. Her teaching, practice, and research focus on patient safety and women’s health. She served on the Committee for Consumer Safety and Social Issues for the regulation of marijuana in Colorado (Amendment 64) and the stakeholder and rulemaking working groups for Labeling, Packaging, Product Safety and Marketing, and Mandatory Testing and Random Sampling. She has extensive knowledge of marijuana pharmacology, pharmacokinetics, pharmacodynamics, therapeutic effectiveness, and potential risks.

Daniel Bowles, MD

Dr. Bowles is a medical oncologist at the University of Colorado Hospital and the Denver VA Medical Center. He is an Assistant Professor of Medicine at the University of Colorado School of Medicine. His main research interests are in drug development for head and neck, lung, and prostate cancers, and the role of cannabinoids in cancer and cancer care. Dr. Bowles previously served as the oncology representative for the State of Colorado’s Medical Marijuana Advisory Committee.

Ashley Brooks-Russell, PhD, MPH

Ashley Brooks-Russell, PhD, MPH, is an assistant professor at the Colorado School of Public Health and a member of the Pediatric Injury Prevention, Education and Research Program. She completed her doctoral training in Health Behavior at the University of North Carolina at Chapel Hill and completed a postdoctoral fellow at the Prevention Research Branch at the National Institute of Child Health and Human Development. Her research focuses on adolescent injury prevention, particularly in the areas of violence and suicide prevention, and promoting safe driving.
Tim Byers, MD, MPH

Dr. Byers is a Professor of Epidemiology and Associate Dean at the Colorado School of Public Health. He has previously served as the Deputy Director and Interim Director of the University of Colorado Comprehensive Cancer Center, where he is now the Associate Director for Cancer Prevention and Control. He is also the Director of the Center for Public Health Practice at the Colorado School of Public Health, where he is developing trainings and programs to improve the effectiveness of public health systems. He is an expert in the role of early detection, diet, and nutrition in the prevention of cancer.

David Calvin Goff Jr., MD, PhD

David C. Goff, Jr., M.D., Ph.D., is Dean and Professor of Epidemiology in the Colorado School of Public Health. His research interests include the epidemiology and prevention of heart disease and stroke with a focus on issues related to high blood pressure, diabetes, and dyslipidemia. He has served in a variety of leadership roles in multiple NIH-, CDC-, and AHA-funded studies and committees. He is currently the Chair of the Council on Epidemiology and Prevention for the American Heart Association.

Summer Laws, MPH

Summer Laws is the Public Health Improvement Coordinator at Boulder County Public Health, where she oversees community strategic planning and implementation processes to improve population health. She came to Boulder County Public Health from the Northwest Colorado Visiting Nurses Association, where she coordinated a local contract with the Regional Care Collaborative Organization. Her area of focus throughout her career has been health equity and has coordinated community teams to advocate for services and programs to address health disparities and the social determinants of health.
Amanda Reiman, PhD, MSW

Amanda Reiman is the California policy manager for the Drug Policy Alliance. Based in San Francisco, Reiman leads DPA’s marijuana reform work in California. She has conducted numerous studies on medical marijuana dispensaries, patients and the use of marijuana as a treatment for addiction. She served as the first chairwoman of the Medical Cannabis Commission for the City of Berkeley, currently serves on the Cannabis Regulatory Commission for the city of Oakland, and has consulted with various cities, states and countries on the development of marijuana policy. Reiman is currently a lecturer in the School of Social Welfare at the University of California-Berkeley, where she teaches Drug and Alcohol Policy, Substance Abuse Treatment, and Sexuality and Social Work.

Paula Riggs, MD

Dr. Paula Riggs is Professor and Director of the Division of Substance Dependence in the Department of Psychiatry at the University of Colorado School of Medicine. She is nationally known for her clinical research in adolescents with co-occurring psychiatric and substance use disorders. She has developed a research-based integrated mental health and substance treatment known as Encompass: Integrated Treatment for Adolescents and Young Adults that is now being nationally disseminated. Dr. Riggs’ current research efforts are focused on implementing a briefer school-based adaptation of Encompass in Denver area high schools.

Mary Segawa, MS

Mary Segawa came to the WA State Liquor Control Board in January, 2010, as the Alcohol Awareness Program Manager. Her position has now expanded to include marijuana outreach and education, emphasizing prevention of underage use. Her previous experience includes community-based work at TOGETHER!, a county-wide non-profit agency focused on preventing youth substance abuse and violence, where she was Executive Director from 2003-2009.
Christian Thurstone, MD

Christian Thurstone, M.D., is a board-certified addiction psychiatrist, general psychiatrist and child/adolescent psychiatrist. He is an associate professor of psychiatry at the University of Colorado Anschutz Medical Campus and the medical director of an adolescent/young adult substance treatment program at Denver Health. His research focuses on treating marijuana addiction.

Chris Urbina, MD, MPH

A native of Pueblo, Colorado, Christopher Urbina is a public and environmental health advocate. He is the past Director of Denver Public Health and of the Colorado Department of Public Health and Environment, where he was active in the development of the new adult use recommendations for marijuana serving as the co-chair of subcommittee on health and safety. He attended Stanford University for his undergraduate degree and the University Of Colorado School Of Medicine. He did his family practice residency at the University of New Mexico and his MPH at Johns Hopkins. He is board certified in family medicine and preventive medicine.

George Sam Wang, MD, FAAP

Dr. Wang attended University of Notre Dame for undergraduate degree in biology, and New York Medical College for medical school. He completed his general pediatric residency and pediatric emergency medicine fellowship at Children’s Hospital Colorado, and then his medical toxicology fellowship at Rocky Mountain Poison and Drug Center at Denver Health. He is currently an assistant professor of pediatrics at Children’s Hospital Colorado, where he practices Pediatric Emergency Medicine and Medical Toxicology, and is also on faculty at the Rocky Mountain Poison and Drug Center.
Art Way, JD

Art Way is Colorado senior drug policy manager for the Drug Policy Alliance, based in Denver. Art is a graduate of Florida Coastal School of Law, where he was appalled at the gap between our theoretical constitutional liberties and what he witnessed growing up during the escalation of the drug war in the 1980s. A belief in the ills of mass incarceration and drug war policies fuel Art's desire to manage DPA's efforts in Colorado. This effort primarily includes minimizing the role of the criminal justice system in addressing drug-related issues.

Larry Wolk, MD, MSPH

Since Sept. 16, 2013 Larry Wolk has been the Executive Director and Chief Medical Officer for the Colorado Department of Public Health and Environment. Prior to this position, he served as Chief Executive Officer of CORHIO, Colorado’s nonprofit, state-designated health information exchange organization. Dr. Wolk is a practicing physician, and held leadership positions at a variety of health care organizations. He is the founder and executive director of Rocky Mountain Youth Clinics, one of Colorado’s largest safety-net clinics, and served nearly five years as President and Chief Operating Officer at Correctional Healthcare Companies, a national organization with more than 2,500 employees. Dr. Wolk has also served as the senior medical director for both Blue Cross/Blue Shield of Colorado and Prudential Healthcare of Colorado, and held regional and national roles as senior health care executive at CIGNA.
Annotated bibliography of research on marijuana and health

Assembled by the Colorado School of Public Health
as background for the Marijuana and Public Health Symposium on March 7, 2014.

This is a selective bibliography intended as a primer on the scientific evidence relating marijuana and health. This listing favors the more recent research and evidence-based reviews over individual studies. The annotated summaries were written by Tim Byers. This bibliography can also be found online at http://publichealthpractice.org.

General reviews of marijuana and health

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

   
   This is an excellent non-systematic review written by Dr. Laura Borgelt from the Skaggs School of Pharmacy at the Anschutz Medical Campus. Although this review focuses on medical marijuana, it is an excellent summary of cannabis pharmacology and toxicology, including a summary of evidence on potential adverse health effects.

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

   
   This systematic review of all studies linking mortality to cannabis use was based on 19 studies. The data presentation and discussion are not particularly enlightened. They concluded mostly that evidence was inconclusive except for death from traffic crashes, and that better long-term cohort studies are needed.

   
   Although this review is principally focused on medical marijuana, it presents a thoughtful summary of the challenges in interpreting research on marijuana, so it is good background reading.

   
   This is a general review of adverse health effects associated with chronic use. Although this paper is not very systematically written and is inferior to the other general reviews in terms of its scientific quality, it is included here because it is succint and recent.
Marijuana and cancer

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

   From this review of 19 studies on this question, there is not a pattern suggesting marijuana causes lung cancer, but studies do show increased inflammation of bronchial mucosa, so there is a biologic basis for concern.

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

   The pooled analysis of 1,921 oropharyngeal cancer cases, 356 tongue cancer cases, and 7,639 controls found a 24% higher risk for oropharyngeal cancer, but no increased risk (actually 53% lower risk) for tongue cancer. After adjusting for potential human papilloma virus infection (a major risk factor for oropharyngeal cancer) the association with marijuana disappeared. Although this is interpreted by the authors as evidence that cannabinoids may be both pro-carcinogenic and anti-carcinogenic, it is probably best regarded as evidence that any association between cannabis use and increased risk of cancers in the mouth would be quite small.
Marijuana and heart diseases

   This is a very technical and dense article that explains the functioning of the endocannabinoid system, which has complex regulatory functions in various parts of the body, including the brain and circulatory system. Although this is a very technical review, it does help in understanding the various neurologic and physiologic effects of cannabis as reviewed in other papers.

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

   This is another review of the physiology of the endocannabinoid system, explaining its effects on blood pressure, glucose metabolism, lipid metabolism, and immune function from the perspective of the documented effects from randomized controlled trials using rimonabant, a cannabinoid receptor antagonist. This drug has multiple beneficial effects, including on weight loss, blood pressure, insulin sensitivity, and lipids, but it has not been approved for use because of a high rate of neurologic side effects (nausea and dizziness).

   This is only an average-quality review, not very systematic in approach, but included here as a general review since it is recent.

   This is a single cohort study of about 3900 survivors of an MI who were followed for 18 years for mortality. There were 22 deaths among the 109 who reported using marijuana at some time during the year before their MI. This was a rate of death that was 29% higher than among who did not report marijuana use, though it was not a statistically significant increase.

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

   
   This review addresses the question of co-occurrence of strokes and marijuana use, whether this is a causal connection or only coincidental. This paper reviews 59 case reports in the medical literature in which strokes occurred following marijuana use. As cases are reported only when they are unusual, it is important to note that this series is young, with an average age of 33. There is some evidence that a condition similar to Reversible Cerebral Vasoconstriction Syndrome (RCVS) may be induced by cannabis and may account for some of these strokes. The author concludes that the co-occurrence of strokes and cannabis use reflects a causal connection between the two caused by reversible cerebral narrowing, but the scientific evidence supporting causality is not clear-cut. See also their subsequent response to a critical letter in *Stroke*, 44:e57.

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

Marijuana and lung diseases

   
   This is a good review. They conclude that despite short-term benefits of cannabis smoking for bronchial dilation, there are potential long-term adverse effects tied to increased inflammation. Chronic marijuana smokers have about a 2-fold increased risk for chronic cough, and bronchial biopsies show clear evidence for increased inflammation. To date no convincing adverse effects have been seen for chronic obstructive pulmonary disease (COPD) or lung cancer, but there are biologic bases for concern for those conditions.

   
   There are short-term benefits of cannabis smoking for bronchial dilation, but potential long-term adverse effects from increased inflammation. It is hard to separate the effects of cannabinoids from the many other constituents of inhaled smoke. There does not seem to be a link between marijuana use and risk for COPD. The review concludes by stating that harm to the lungs is substantially greater from tobacco than from marijuana.

   
   This is a single cohort study, but one that was very well done and quite recent. They measured pulmonary function in the CARDIA cohort of about 5000 men over 20 years. There was no association between marijuana smoking and declines in lung function, though the expected declines were clearly seen with tobacco smoking.

   
   This is the most recent narrative review of research on the effects of marijuana smoking on the lung. It makes the same points covered by Lee et al.
Marijuana and mental health

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

   
   This analysis reviews 43 studies, including 8 in adolescents. This very complex article shows several studies have found structural brain changes related to chronic cannabis use, especially in areas of the brain that are rich in cannabinoid receptor like the hippocampus.

   
   This review is not particularly systematic in style, but it does cover the question of brain development. Although it is quite technical on the endocannabinoid system, it documents the reasons for concern that because the adolescent brain is still in active development, drugs such as cannabinoids that alter development of brain signaling pathways and structures, and could thereby have adverse effects on brain development.

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

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

   
   This is a systematic review based on 14 cohort studies relating marijuana use to the onset of depression. There was a 17% increased risk for depression onset among all uses. Among heavy users (defined as a cannabis use disorder or use at least weekly) risk was increased by 62%. There were no differences noted by age.

   
   This is a general review summarizing the associations between cannabis use in adolescence and various mental health disorders.

   Military conscripts who had used cannabis ten or more times by 18 years of age were 2-3 times more likely to later be diagnosed with schizophrenia than those who had not.


   This meta-analysis of longitudinal studies reported a pooled estimate of 40% increased risk of psychotic symptoms or psychotic disorders in those who had ever used cannabis.


   Among about 3200 Australian children followed longitudinally, those who used marijuana in adolescence were 3.4 times more likely to have anxiety disorders.


   Among a cohort of 3800 adults in the Netherlands, risk for depression and anxiety was increased by 60% among marijuana users.

**Marijuana and drug dependency**


   Although cannabis is not addictive it can induce dependency. This is a review of the definition and treatment of cannabis use disorder. Estimates are that about 1% of US adults meet the definition of cannabis dependence in the previous year. There are not any medications shown to be helpful for treatment, but brief cognitive behavioral therapy seems to help.


   This is a very technical review that largely covers animal model systems and brain neurochemistry. Although this evidence is not easily applicable to human clinical behavior, it is a good basic science summary of the neurologic effects of cannabinoids that are relevant to dependency and withdrawal.


   This review included 49 studies. Overall, effects of interventions for preventing marijuana use were characterized as “trivial to small”. Programs that were more universal and more multi-modal were superior to more focused programs. The review criticized much of the research as difficult to evaluate, but concluded that there is not yet any compelling evidence that marijuana prevention programs have any substantial effects.
Marijuana and pregnancy, breast feeding

   This is a non-systematic review of various issues tied to cannabis exposures in utero or during lactation. There is no compelling evidence suggesting cannabis causes birth defects or that it is associated with poor birth outcomes, but cannabis does easily cross the placental barrier and is excreted in milk, so there is reason to believe that cannabis may interfere with brain development of the fetus and/or the infant.

   This review presents detailed information about three prospective longitudinal studies on prenatal cannabis exposure, including the Generation R study. Preclinical studies and potential mechanisms for marijuana’s effects are also described.

   Among 655 children examined at age 3 those who had been exposed in utero to marijuana tested lower on the Stanford-Binet test of intelligence.

   This follow-up examinatin of the cohort above (reference 3) found that at age 10 the children who had been exposed to marijuana in utero had intelligence tests that were not different from children unexposed, but they had more of a tendency to have hyperactivity disorders.

   This is a meta-analysis of 5 studies done at that time showing considerable heterogeneity in findings. The overall relative risk for low birthweight with marijuana use in pregnancy was 1.09 (not statistically significant). The conclusion was that the overall evidence is inconclusive.

   This is a cohort of about 12,000 women, about 5% of whom reported cannabis use before and/or during pregnancy. Cannabis use in pregnancy was associated with lower birth weights, but that relationship was largely confounded by other factors. The adjusted difference in birth weights was 90 grams (not a statistically significant difference in that study).

   This is a review of three prospective studies. Cannabis use early in pregnancy resulted in reduced fetal growth, but there is not a consistent pattern of adverse neurological or cognitive outcomes in the early period of life.
   At 12 years of age, children who were exposed to cannabis did not differ on full-scale intelligence quotient (IQ) scores from those not exposed, but there were small differences in higher cognitive processes (eg, perceptual organization and planning).

Marijuana and traffic safety

There have been three recent systematic reviews of cannabis and motor vehicle crashes:

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

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

   This metanalysis is based on 10 studies, concluding a 2-fold increased risk for motor vehicle accidents after marijuana use.

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

Avoiding unintentional marijuana exposures

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

   This is an analysis of national data from poison control centers, showing that although unintentional marijuana ingestion is uncommon, it has increased more in states that have legalized medical marijuana than in states that have not over time.