# Marijuana: The Facts



Marijuana is the most commonly used illegal drug in the U.S. and the world, and was a well-established medicine until it was federally criminalized in 1937. A majority of Americans believe marijuana should be legally regulated.

#### **Quick Facts**

- More than forty-five percent of American adults report that they have used marijuana.
- Marijuana has been consumed for at least 5,000 years and has a long history of traditional uses throughout Asia, Africa, Europe and the Americas.
- The marijuana plant contains more than 70 compounds, called cannabinoids, in its leaves and flowers.<sup>vi</sup> The most commonly known of these cannabinoids is tetrahydrocannabinol (THC), which is psychoactive. However, there are numerous non-psychoactive, yet highly therapeutic cannabinoids in marijuana as well.<sup>vii</sup>
- U.S. marijuana policy is unique among American criminal laws – no other law is enforced so widely and harshly, yet deemed unnecessary by such a substantial portion of the population.
- The price tag of marijuana prohibition is currently estimated at \$20 billion per year, including costs to law enforcement and lost potential tax revenue.

- Recent polls suggest that between 46% and 58% of the American population believe marijuana should be legally regulated, while support for allowing the medical use of marijuana is about 80%.
- Twenty-three states and Washington D.C. have approved the medical use of marijuana, 16 states and D.C. have decriminalized its use, and in 2012 Colorado and Washington voters made their states the first political jurisdictions anywhere in the world to legally regulate the production and distribution of marijuana.

#### Will legalizing marijuana lead to increased use?

# There is no evidence that implementing medical marijuana laws impacts the rate of adolescent use.

A common concern raised by people opposed to removing marijuana from the illicit market is the impact on teen marijuana use. Several recent reports have examined that question and found that, in the majority of medical marijuana states, youth used *decreased* after the medical marijuana law was passed. This has been attributed to a diminishing of the "forbidden fruit" effect, and decreased access as marijuana moved from the streets to inside licensed dispensaries.\*

A recent study sought to determine the effect of medical marijuana laws on adolescent marijuana use. The authors concluded, "Our results are not consistent with the hypothesis that the legalization of medical marijuana caused an increase in the use of marijuana and other substances among high school students. In fact, estimates from our preferred specification are small, consistently negative, and are never statistically distinguishable from zero. Using the 95 percent confidence interval around these estimates suggests that the impact of legalizing medical marijuana on the probability of marijuana use in the past 30 days is no larger than 0.8 percentage points, and the impact of legalization on the probability of frequent marijuana use in the past 30 days is no larger than 0.7 percentage points."xi

In addition to the impact on youth use, the decriminalization of marijuana has not been found to have an impact on adult use. xii A study conducted by the Institute of Medicine concluded, "In sum, there is little evidence that decriminalization of marijuana use necessarily leads to a substantial increase in marijuana use." xiii

#### Is marijuana a gateway drug?

# Most marijuana users never use any other illicit drug.

Marijuana is the most popular and easily accessible illegal drug in the United States today. Therefore, people who have used less accessible drugs such as heroin, cocaine and LSD, are likely to have also used marijuana. Most marijuana users never use any other illegal drug, and the vast majority of those who do try another drug never become addicted or go on to have associated problems. Indeed, for the large majority of people, marijuana is a terminus rather than a so-called gateway drug.xiv New evidence suggests that marijuana can function as an "exit drug" helping people reduce or eliminate their use of more harmful drugs by easing withdrawal symptoms.xv

## Are more people becoming dependent on marijuana?

# Rates of marijuana dependence have not increased over the past 10 years.

A landmark, Congressionally-mandated Institute of Medicine study found that fewer than 10 percent of those who try marijuana ever meet the clinical criteria for dependence, while 32 percent of tobacco users and 15 percent of alcohol users do.xvi As a result of treatment-instead-of-incarceration policies implemented over the past two decades to stem the skyrocketing U.S. prison population, marijuana treatment admissions referred by the criminal justice system rose from 48 percent in 1992 to 52 percent in 2011.xvii Just 45 percent of people who enter marijuana treatment meet the criteria for marijuana dependence. More than a third hadn't used marijuana in the 30 days prior to admission for treatment. Many people are "discovered" due to the smell of marijuana and forced to choose between jail and treatment. Treatment providers support drug courts because they ensure a steady stream of clients. Even with this increase in court-mandated marijuana treatment, only 1.1% of marijuana users 12 and older in 2011 went to treatment for it. Twice as many people were arrested for simple marijuana possession that year than entered treatment for marijuana dependence (750,000 vs. 333,578).xviii Increases in treatment access and emergency room visits related to marijuana use can be the result of the decriminalization of marijuana

consumers and the destigmatization of marijuana use. Both of these phenomena would result in consumers feeling more comfortable admitting use and seekig help related to their use.

## Does marijuana use have long-term cognitive effects?

## Marijuana does not cause long-term cognitive impairment in users that start after 21 years old.

The short-term effects of marijuana include immediate, temporary changes in thoughts, perceptions and information processing. The cognitive process most clearly affected by marijuana is short-term memory. In laboratory studies, subjects under the influence of marijuana have no trouble remembering things they learned previously. However, they temporarily display diminished capacity to learn and recall new information. This diminishment only lasts for the duration of the intoxication. There is no convincing evidence that heavy long-term marijuana use permanently impairs memory or other cognitive functions. xix A recent, large-scale, longitudinal study of adult marijuana users corroborates earlier findings that marijuana produces no long-term negative effects on cognition, stating, "The adverse impacts of cannabis use on cognitive functions either appear to be related to pre-existing factors or are reversible . . . even after potentially extended periods of use."xx However, it is not recommended that adolescents use marijuana unless under the care of a physician, as some research suggests potentially negative cognitive effects for adolescents who use marijuana. It is recommeded that individuals delay their marijuana use until adulthood.

## What is the relationship between marijuana and cancer?

## Marijuana use is not associated with elevated cancer risk as shown in preclinical studies.

Several longitudinal studies have established that even long-term marijuana smoking is not associated with elevated cancer risk, including tobacco-related cancers or with colorectal, lung, melanoma, prostate, breast or cervix. A 2009 population-based case-control study found that moderate marijuana smoking over a 20-year period was associated with reduced risk of head and

neck cancer.xxi And a five-year-long population-based case-control study found even long-term heavy marijuana smoking was not associated with lung cancer or upper aerodigestive tract cancers.xxii In fact, some of the chemicals in marijuana, such as THC and especially CBD, have been found to induce tumor cell death and show potential as effective tools in treating cancer.xxiii Scientists who have conducted this type of research, such as UCLA's Donald Tashkin, hypothesize that the anti-oxidant properties of cannabis might override any cancer causing chemicals found in marijuana smoke, therefore protecting the body against the impact of smoking. xxiv Newer research indicates that marijuana has anti-cancer properties and could one day unlock new cancer treatments.xxv

Moreover, marijuana smoking is not associated with any other permanent lung harms, such as chronic obstructive pulmonary disorder (COPD), emphysema or reduced lung function – even after years of frequent use. xxvi

#### Does marijuana affect mental health?

## The majority of adults who use marijuana do not have adverse mental health issues.

Many opponents of medical marijuana make much of the purported link between marijuana use and mental illness. But there is simply no compelling evidence to support the claim that marijuana is a causal risk factor for developing a psychiatric disorder in otherwise healthy individuals.xxvii Most tellingly, population-level rates of schizophrenia or other psychiatric illnesses have remained flat even when marijuana use rates have increased. xxviii Emerging evidence indicates that patients who have tried marijuana may show significant improvements in symptoms and clinical outcomes (such as lower mortality rates xxix and better cognitive functioningxxx ) compared with those who have not. In fact, some of the unique chemicals in marijuana, such as cannabidiol (CBD), seem to have anti-psychotic properties.xxxi Researchers are investigating marijuana as a possible source of future schizophrenia treatments; until it is legalized, however, this research is significantly impeded.

Rates of mental illness have remained stable in light of changes in marijuana consumption levels. For example, when marijuana use rates have increased,

there have been no increases in schizophrenia diagnoses. XXXIII We do see these types of correlations, however for other behaviors that are connected. For example, rates of diabetes in the U.S. have increased as obesity rates have increased. This is not to say, however, that there is no relationship between psychoactive substances and mental functioning. Some effects of marijuana use can include feelings of panic, anxiety and paranoia. Such experiences can be frightening, but the effects are temporary.

Some psychoactive substances have been shown to improve mental health functioning and some do not. Recent research at the University Medical Center Utrecht in the Netherlands concluded that the endocannabinoid system is responsible for making chemicals that combat mental health conditions such as depression. Stimulating the endocannabinoid system via the use of cannabinoids found in the cannabis plant might hold promise as a treatment for depressions and other mental health conditions.xxxiii

Part of the reason that is it so difficult to detangle psychoactive substance use from mental health is age of onset. For most people, symptoms of mental disturbance occur in the late teens and early 20's. While it is impossible to predict who will develop a mental disturbance, there seem to be some ties to genetics and to behavioral cues in early childhood.

Those who have risk factors, such as a family history of mental health issues, should be cautious in their exposure to all substances that have any intoxicating effects. Unfortunately, in adolescence, teens are more likely to experiment with intoxicants and less likely to be open with their parents about their drug use and/or any symptoms of mental disturbance they may be experiencing. As a result, drug and alcohol use has usually already started by the time symptoms of mental illness become noticeable. This is why we see so many studies that confirm that most people diagnosed with severe mental illness have had a history of alcohol and drug use. The alcohol and drug use was not the cause of the mental illness, but rather a behavior that coincides with the undetected development of mental health symptoms. xxxiv In fact, research suggests that those with mental illness might be self-medicating with marijuana. One study demonstrated that psychotic symptoms predict later use of marijuana, suggesting that people might turn to the plant for help rather than become ill after use. However, it should be noted that studies of marijuana

as a "treatment" for certain mental health disorders are in preliminary phases, and there is no mental health condition for which marijuana is a standard of care treatment.

These findings have been replicated by myriad other studies, including a new study conducted by Harvard University researchers, which found that marijuana "is unlikely to be the cause of illness," even in people who may be genetically predisposed to schizophrenia or other psychotic disorders. The researchers concluded, "In summary, we conclude that cannabis does not cause psychosis by itself. In genetically vulnerable individuals, while cannabis may modify the illness onset, severity and outcome, there is no evidence from this study that it can cause the psychosis."xxxxv

Finally, available evidence indicates that medical marijuana laws may *reduce* rates of suicide among young adult males, who are most vulnerable to suicide.xxxvi

Encouraging an open dialogue with adolescents about their drug use and paying attention to their behavior during the teen years are better prevention tools toward the future development of mental illness than to simply blame marijuana.

#### How strong is today's marijuana?

# Marijuana regulation allows for a wider variety of THC levels in products.

Although marijuana potency has reportedly increased in recent decades, this is largely due to prohibition.xxxvii When access to a particular substance is sporadic, risky and limited, both consumers and producers are incentivized to use or sell higher potency material. We saw a similar trend during alcohol prohibition, when beer and cider were largely replaced by spirits and hard liquor, which was easier and more profitable to transport.xxxviii When access is regulated and controlled, like in medical marijuana states, we see a wider variety of potencies, including marijuana with virtually no traces of psychoactive THC but high in cannabidiol (CBD), which is highly therapeutic but not psychoactive.

While THC is virtually non-toxic to healthy cells or organs, and is incapable of causing a fatal overdose, marijuana's health impact is wide ranging and depends

on the way marijuana is ingested, as well as the specific constituents in the marijuana. Health effects of marijuana are related to the route, dose, frequency and duration of marijuana use. Currently, doctors may legally prescribe Marinol, an FDA-approved pill that contains 100 percent THC – but, critically, lacks other therapeutic, non-psychoactive compounds found in marijuana. The Food and Drug Administration found THC to be safe and effective for the treatment of nausea, vomiting and wasting diseases. When consumers encounter strong varieties of marijuana, they adjust their use accordingly and smoke less. XI

### Is it true that marijuana has medicinal properties?

Marijuana has been proven helpful for treating the symptoms of a variety of medical conditions. The body's endocannabinoid system may explain why.

For many seriously ill people, medical marijuana is the only medicine that relieves their pain and suffering, or treats symptoms of their medical condition, without debilitating side effects. Marijuana's medicinal benefits are incontrovertible, now proven by decades of peerreviewed, controlled studies published in highly respected medical journals. \*\(^{\mathbf{I}}\) Marijuana has been shown to alleviate symptoms of wide range of debilitating medical conditions including cancer, \*\(^{\mathbf{I}}\) HIV/AIDS, \*\(^{\mathbf{I}}\) multiple sclerosis, \*\(^{\mathbf{I}}\) Alzheimer's Disease, \*\(^{\mathbf{I}}\) post-traumatic stress disorder (PTSD), \*\(^{\mathbf{I}}\) epilepsy, \*\(^{\mathbf{I}}\) Crohn's Disease, \*\(^{\mathbf{I}}\) and glaucoma, \*\(^{\mathbf{I}}\) and is often an effective alternative to narcotic painkillers.\(^{\mathbf{I}}\)

Evidence of marijuana's efficacy in treating severe and intractable pain is particularly impressive. Researchers at the University of California conducted a decade of randomized, double-blind, placebo-controlled clinical trials on the medical utility of inhaled marijuana, concluding that marijuana should be a "first line treatment" for patients with painful neuropathy, who often do not respond to other available treatments. Ii

Marijuana has been shown to be effective in reducing the nausea induced by cancer chemotherapy, stimulating appetite in AIDS patients, and reducing intraocular pressure in people with glaucoma. Iii There is also appreciable evidence that marijuana reduces muscle spasticity in patients with neurological disorders. Iiii Marijuana has also been shown to help with mental health conditions, particularly PTSD. Iiv In 2013, both Maine and Oregon added PTSD to the list

of conditions that qualifies for medical marijuana. A synthetic capsule is available by prescription, but it is not as effective as smoked marijuana for many patients. <sup>IV</sup>

Our bodies contain a regulatory framework called the endocannabinoid system. This system is responsible for maintaining balance or homeostasis in the body. Some scientists theorize that a deficiency in the endocannabinoid system may contribute to certain diseases, such as Crohn's disease, which may explain why the introduction of phyto-cannabinoids (from the marijuana plant) help alleviate the symptoms of these conditions. Vi

Although an overwhelming majority of Americans support medical marijuana, the federal government continues to impede state medical marijuana laws. Marijuana prohibition has also thwarted research within the United States to uncover the best and most effective uses for marijuana as a medicine, making efforts to reform medical marijuana laws particularly difficult.

Learn more about medical marijuana. [6]

Does marijuana impair driving the way alcohol does?

#### Marijuana's effects on driving are subtle but real.

At some doses, marijuana affects perception and psychomotor performance - changes that could impair driving ability. Ivii However, in actual driving studies, marijuana produces little or no car-handling impairment – consistently less than produced by moderate doses of alcohol and many legal medications. Iviii In contrast to alcohol, which tends to increase risky driving practices, marijuana tends to make subjects more cautious. iix Surveys of fatally injured drivers show that when THC is detected in the blood, alcohol is almost always detected as well. Ix For some individuals, marijuana may play a role in bad driving, yet the overall rate of highway accidents appears not to be significantly affected by marijuana's widespread use in society. Ixi Frequent marijuana consumers, moreover, appear to develop a tolerance to marijuana's impairing effects. |Xii However, while the impairing effects of marijuana vary across users, no safe amount of marijuana use or intoxication level has been established. As a result of marijuana's

criminalization, harm reduction options that exist for alcohol consumption – such as designated driver education, alternate transportation from drinking establishments, and easily accessible information about how alcohol dosage effects one's physical and mental functioning – are not available for marijuana use. If marijuana were legally controlled and regulated, public education about using marijuana safely could be provided. Finally, available evidence indicates that medical marijuana laws do not increase – and in fact may *decrease* – traffic fatalities. Julii

How many people are getting arrested for marijuana every year?

Roughly 750,000 people are arrested for marijuana each year, the vast majority of them for simple possession, with racial minorities over-represented.

Approximately 750,000 people were arrested for marijuana law violations in 2012 according to the Federal Bureau of Investigation's annual Uniform Crime Report – comprising about half (48 percent) of all drug arrests in the United States; that's one marijuana arrest every 42 seconds. A decade ago, marijuana arrests comprised just 44 percent of all drug arrests. Approximately 42 percent of all drug arrests nationwide are for marijuana possession. Of total arrests for marijuana law violations, more than 87 percent were for simple possession, not sale or manufacture. There are more arrests for marijuana possession every year than for all violent crimes combined. Ixiv

A marijuana arrest is no small matter. Most people are handcuffed, placed in a police car, taken to a police station, fingerprinted and photographed, held in jail for 24 hours or more, and then arraigned before a judge. The arrest creates a permanent criminal record that can easily be found on the internet by employers, landlords, schools, credit agencies and banks. The collateral sanctions of a marijuana possession arrest can include loss of employment, financial aid, housing and child custody. Ixv

The criminalization of marijuana in the early 20<sup>th</sup> century was not based on any scientific assessment of its risks – but rather racial prejudice and politics. The first anti-marijuana laws, in the Midwest and the Southwest during the 1910s and 20s, were directed at

Mexican migrants and Mexican Americans. Artists and performers – especially black jazz musicians – were common targets. [kvi] Today, Latino and black communities are still subject to wildly disproportionate marijuana enforcement practices, even though these groups are no more likely than whites to use or sell marijuana.

According to a 2012 ACLU report, black people are 3.7 times more likely to be arrested for marijuana possession than white people despite comparable usage rates. Furthermore, in counties with the worst disparities, blacks were as much as 30 times more likely to be arrested. |xvii

States spent an estimated \$3.61 billion enforcing marijuana possession laws in 2010 alone. New York and California combined spent over \$1 billion. |xviii

<sup>&</sup>lt;sup>i</sup> Substance Abuse and Mental Health Services Administration, "Results from the 2012 National Survey on Drug Use and Health," (Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013), Tables 1.1A and 1.1B.

<sup>&</sup>lt;sup>ii</sup> United Nations Office on Drugs and Crime, "World Drug Report 2013," (UNODC, 2013).

iii Richard J. Bonnie and Charles H. Whitebread, *Marijuana Conviction: A History of Marijuana Prohibition in the United States* (1999); David F Musto, "Opium, cocaine and marijuana in American history," *Scientific American* 265, no. 1 (1991).

<sup>&</sup>lt;sup>iv</sup> Substance Abuse and Mental Health Services Administration, "Results from the 2012 National Survey on Drug Use and Health," Tables 1.28B.

<sup>&</sup>lt;sup>v</sup> Sunil K Aggarwal et al., "Medicinal Use of cannabis in the United States: Historical perspectives, current trends, and future directions," *Journal of opioid management* 5, no. 3 (2009); Ethan Russo, "History of cannabis and its preparations in saga, science, and sobriquet," *Chem Biodivers* 4, no. 8 (2007); Ethan B Russo et al., "Phytochemical and genetic analyses of ancient cannabis from Central Asia," *Journal of experimental botany* 59, no. 15 (2008).

<sup>&</sup>lt;sup>vi</sup> M. A. Elsohly and D. Slade, "Chemical constituents of marijuana: the complex mixture of natural cannabinoids," *Life Sci* 78, no. 5 (2005); Y. Shoyama et al., "Structure and function of 1-tetrahydrocannabinolic acid (THCA) synthase, the enzyme controlling the psychoactivity of Cannabis sativa," *J Mol Biol* 423, no. 1 (2012).

vii Z. Fišar, "Phytocannabinoids and endocannabinoids," *Current Drug Abuse Reviews* 2, no. 1 (2009); Ethan B. Russo, "Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects," *British Journal of Pharmacology* 163, no. 7 (2011); F. Grotenhermen and K. Muller-Vahl, "The therapeutic potential of cannabis and cannabinoids," *Dtsch Arztebl Int* 109, no. 29-30 (2012).
viii Matt Sledge, "Marijuana Prohibition Now Costs The Government \$20 Billion A Year: Economist," *Huffington Post* 2013. Citing; Jeffrey A Miron and Katherine Waldock, *The Budgetary Impact of Ending Drug Prohibition* (Cato Institute, 2010).

Art Swift, "For First Time, Americans Favor Legalizing Marijuana: Support surged 10 percentage points in past year, to 58%," *Gallup*, October 22 2013; Pew Research Center, "Majority Now Supports Legalizing Marijuana," *Pew Research Center* 2013; CNN/Time Magazine, (2002); CNN/ORC International Survey, (2014).

\* Sarah D. Lynne-Landsman, Melvin D. Livingston, and Alexander C. Wagenaar, "Effects of State Medical Marijuana Laws on Adolescent Marijuana Use," *American Journal of Public Health* 103, no. 8 (2013); S. Harper, E. C. Strumpf, and J. S. Kaufman, "Do medical marijuana laws increase marijuana use? Replication study and extension," *Ann Epidemiol* 22, no. 3 (2012); Karen O'Keefe and Mitch Earleywine, "MARIJUANA USE BY YOUNG PEOPLE: The Impact of State Medical Marijuana Laws," (Marijuana Policy Project, 2011).

xi D Mark Anderson, Benjamin Hansen, and Daniel Rees, "Medical marijuana laws and teen marijuana use," *Available at SSRN 2067431* (2012).

xii xii Robin Room, Cannabis policy: moving beyond stalemate (Oxford University Press, USA, 2010); Eric W Single, "The impact of marijuana decriminalization: an update," Journal of public health policy (1989); Clifford F. Thies and Charles A. Register, "Decriminalization of marijuana and the demand for alcohol, marijuana and cocaine," The Social Science Journal 30, no. 4 (1993); Jonathan P Caulkins et al., Marijuana Legalization: What Everyone Needs to Know (Oxford: Oxford University Press, 2012); Sarah D. Lynne-Landsman, Melvin D. Livingston, and Alexander C. Wagenaar, "Effects of State Medical Marijuana Laws on Adolescent Marijuana Use; Caitlin Elizabeth Hughes and Alex Stevens, "What Can We Learn From The Portuguese Decriminalization of Illicit Drugs?," British Journal of Criminology 50, no. 6 (2010). xiii Janet Elizabeth Joy, Stanley J Watson, and John A Benson, Marijuana and medicine: assessing the science base

xiv J. C. Anthony, "Steppingstone and gateway ideas: a discussion of origins, research challenges, and promising lines of research for the future," Drug Alcohol Depend 123 Suppl 1(2012); L. Degenhardt et al., "Evaluating the drug use "gateway" theory using cross-national data: consistency and associations of the order of initiation of drug use among participants in the WHO World Mental Health Surveys, ibid.108, no. 1-2 (2010); David M Fergusson, Joseph M Boden, and L John Horwood, "Cannabis use and other illicit drug use: testing the cannabis gateway hypothesis," Addiction 101, no. 4 (2006); Wayne D Hall and Michael Lynskey, "Is cannabis a gateway drug? Testing hypotheses about the relationship between cannabis use and the use of other illicit drugs," Drug and alcohol review 24, no. 1 (2005); Tristan Kirby and Adam E. Barry, "Alcohol as a Gateway Drug: A Study of US 12th Graders," Journal of School Health 82, no. 8 (2012); Andrew R Morral, Daniel F McCaffrey, and Susan M Paddock, "Reassessing the marijuana gateway effect," Addiction 97, no. 12 (2002); C. J. Rebellon and K. Van Gundy, "Can Social Psychological Delinquency Theory Explain the Link between Marijuana and other Illicit Drug Use? A Longitudinal Analysis of the Gateway Hypothesis.' Journal of Drug Issues 36, no. 3 (2006); Ralph E. Tarter et al., "Does the "gateway" sequence increase prediction of cannabis use disorder development beyond deviant socialization? Implications for prevention practice and policy," Drug and Alcohol Dependence 123, Supplement 1, no. 0 (2012); Karen Van Gundy and Cesar J. Rebellon, "A Lifecourse Perspective on the "Gateway Hypothesis", " J Health Soc Behav 51, no. 3 (2010); F. A. Wagner and J. C. Anthony, "Into the world of illegal drug use: exposure opportunity and

other mechanisms linking the use of alcohol, tobacco, marijuana, and cocaine," Am J Epidemiol 155, no. 10 (2002). xv Philippe Lucas et al., "Cannabis as a substitute for alcohol and other drugs: A dispensary-based survey of substitution effect in Canadian medical cannabis patients," Addiction Research & Theory 21, no. 5 (2013); A. Reiman, "Cannabis as a substitute for alcohol and other drugs," Harm Reduct J 6(2009); R. Swartz, "Medical marijuana users in substance abuse treatment," ibid.7(2010); Helen Nunberg et al., "An Analysis of Applicants Presenting to a Medical Marijuana Specialty Practice in California," Journal of Drug Policy Analysis 4, no. 1 (2011); Jillian L. Scavone et al., "Impact of Cannabis Use during Stabilization on Methadone Maintenance Treatment," The American Journal on Addictions 22, no. 4 (2013); W. N. Raby et al., "Intermittent marijuana use is associated with improved retention in naltrexone treatment for opiate-dependence," Am J Addict 18, no. 4 (2009).

xvi Janet Elizabeth Joy, Stanley J Watson, and John A Benson, *Marijuana and medicine: assessing the science base* (Washington, DC: Institute of Medicine, National Academies Press, 1999).

xvii Substance Abuse and Mental Health Services Administration Center for Behavioral Health Statistics and Quality, "Treatment Episode Data Set (TEDS): 2001-2011. National Admissions to Substance Abuse Treatment Services," (Rockville, MD: Substance Abuse and Mental Health Services Administration, 2013).

xviii Ibid; Federal Bureau of Investigation, "Crime in the United States, 2011," (Washington, DC: U.S. Department of Justice, Federal Bureau of Investigation, 2012).

xix Sunita Bava et al., "Longitudinal changes in white matter integrity among adolescent substance users," Alcoholism, Clinical and Experimental Research 37 Suppl 1(2013); J. Jacobus et al., "White Matter Integrity Pre- and Post Marijuana and Alcohol Initiation in Adolescence," *Brain Sci* 3, no. 1 (2013); S. Bava and S. F. Tapert, "Adolescent brain development and the risk for alcohol and other drug problems," Neuropsychol Rev 20, no. 4 (2010); J. Jacobus et al., "White matter integrity in adolescents with histories of marijuana use and binge drinking," Neurotoxicol Teratol 31, no. 6 (2009); O. Rogeberg, "Correlations between cannabis use and IQ change in the Dunedin cohort are consistent with confounding from socioeconomic status," Proc Natl Acad Sci USA 10.1073/pnas.1215678110(2013); L. M. Squeglia, J. Jacobus, and S. F. Tapert, "The influence of substance use on adolescent brain development," Clin EEG Neurosci 40, no. 1 (2009); Lynn E DeLisi et al., "A preliminary DTI study showing no brain structural change associated with adolescent cannabis use," Harm Reduct J 3, no. 1 (2006); L. Iversen, "Long-term effects of exposure to cannabis," Curr Opin Pharmacol 5, no. 1 (2005).

\*\* Robert J. Tait, Andrew Mackinnon, and Helen Christensen, "Cannabis use and cognitive function: 8-year trajectory in a young adult cohort," *Addiction* 106, no. 12 (2011).

\*\*\*Caihua Liang et al., "A Population-Based Case-Control Study of Marijuana Use and Head and Neck Squamous Cell Carcinoma," *Cancer Prevention Research* 2, no. 8 (2009).

\*\*\*Mia Hashibe et al., "Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study," *Cancer Epidemiology Biomarkers* & *Prevention* 15, no. 10 (2006).

xxiii P. Pacher, "Towards the use of non-psychoactive cannabinoids for prostate cancer," *Br J Pharmacol* 168, no. 1 (2013); M. Guzman, "Cannabinoids: potential anticancer agents," *Nat Rev Cancer* 3, no. 10 (2003); S. Pisanti et al., "The endocannabinoid signaling system in cancer," *Trends* 

Pharmacol Sci 34, no. 5 (2013); Guillermo Velasco, Cristina Sánchez, and Manuel Guzmán, "Towards the use of cannabinoids as antitumour agents," Nature Reviews Cancer 12, no. 6 (2012); Mar Salazar et al., "Cannabinoid action induces autophagy-mediated cell death through stimulation of ER stress in human glioma cells," The Journal of Clinical Investigation 119, no. 5 (2009).

xxiv Marc Kaufman, "Study Finds No Cancer-Marijuana Connection," *Washington Post*, Friday, May 26 2006; Mia Hashibe et al., "Marijuana use and the risk of lung and upper aerodigestive tract cancers: results of a population-based case-control study."

xxv P. Pacher, "Towards the use of non-psychoactive cannabinoids for prostate cancer; M. Guzman, "Cannabinoids: potential anticancer agents; S. Pisanti et al., "The endocannabinoid signaling system in cancer; Guillermo Velasco, Cristina Sánchez, and Manuel Guzmán, "Towards the use of cannabinoids as antitumour agents; María Salazar et al., "Cannabinoid action induces autophagy-mediated cell death through stimulation of ER stress in human glioma cells," Journal of Clinical Investigation 119, no. 5 (2009). xxvi Donald P. Tashkin, "Effects of Marijuana Smoking on the Lung," Annals of the American Thoracic Society 10, no. 3 (2013); M. J. Pletcher et al., "Association between marijuana exposure and pulmonary function over 20 years," JAMA 307, no. 2 (2012); S. Aldington et al., "Effects of cannabis on pulmonary structure, function and symptoms," Thorax 62, no. 12 (2007); Mark A. Ware, "Cannabis and the Lung: No More Smoking Gun?," Annals of the American Thoracic Society 10, no. 3 (2013).

xxviii S. H. Gage, S. Zammit, and M. Hickman, "Stronger evidence is needed before accepting that cannabis plays an important role in the aetiology of schizophrenia in the population," *F1000 Med Rep* 5(2013). xxviii M. Frisher et al., "Assessing the impact of cannabis use

M. Frisher et al., "Assessing the impact of cannabis use on trends in diagnosed schizophrenia in the United Kingdom from 1996 to 2005," *Schizophr Res* 113, no. 2-3 (2009); S. H. Gage, S. Zammit, and M. Hickman, "Stronger evidence is needed before accepting that cannabis plays an important role in the aetiology of schizophrenia in the population."

xxix M. M. Koola et al., "Alcohol and cannabis use and mortality in people with schizophrenia and related psychotic disorders," *J Psychiatr Res* 46, no. 8 (2012).

xxx M. Yucel et al., "The impact of cannabis use on cognitive functioning in patients with schizophrenia: a meta-analysis of existing findings and new data in a first-episode sample," Schizophr Bull 38, no. 2 (2012).

xxxi A. W. Zuardi et al., "Cannabidiol, a Cannabis sativa constituent, as an antipsychotic drug," Braz J Med Biol Res 39, no. 4 (2006); A. W. Zuardi, "Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action," Rev Bras Psiguiatr 30, no. 3 (2008); A. W. Zuardi et al., "Cannabidiol for the treatment of psychosis in Parkinson's disease," J Psychopharmacol 23, no. 8 (2009); A. W. Zuardi et al., "A critical review of the antipsychotic effects of cannabidiol: 30 years of a translational investigation," Curr Pharm Des 18, no. 32 (2012); R. Levin et al., "Antipsychotic profile of cannabidiol and rimonabant in an animal model of emotional context processing in schizophrenia," ibid; A. R. Schier et al., "Cannabidiol, a Cannabis sativa constituent, as an anxiolytic drug," Rev Bras Psiquiatr 34 Suppl 1(2012). xxxii M. Frisher et al., "Assessing the impact of cannabis use on trends in diagnosed schizophrenia in the United Kingdom from 1996 to 2005; S. H. Gage, S. Zammit, and M. Hickman, "Stronger evidence is needed before accepting that cannabis plays an important role in the aetiology of schizophrenia in the population.'

xoxiii A. W. Zuardi et al., "Cannabidiol, a Cannabis sativa constituent, as an antipsychotic drug; A. W. Zuardi, "Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action; A. W. Zuardi et al., "Cannabidiol for the treatment of psychosis in Parkinson's disease; A. W. Zuardi et al., "A critical review of the antipsychotic effects of cannabidiol: 30 years of a translational investigation; R. Levin et al., "Antipsychotic profile of cannabidiol and rimonabant in an animal model of emotional context processing in schizophrenia," ibid; A. R. Schier et al., "Cannabidiol, a Cannabis sativa constituent, as an anxiolytic drug."

xxxiv S. H. Gage, S. Zammit, and M. Hickman, "Stronger evidence is needed before accepting that cannabis plays an important role in the aetiology of schizophrenia in the population."

population."

XXXX A. C. Proal et al., "A controlled family study of cannabis users with and without psychosis," *Schizophr Res* 10.1016/j.schres.2013.11.014(2013).

xxxii D. Mark Anderson, Daniel I. Rees, and Joseph J. Sabia, "Medical Marijuana Laws and Suicides by Gender and Age," *American Journal of Public Health* 10.2105/AJPH.2013.301612(2014).

xxxxvii James Richard Burgdorf, Beau Kilmer, and Rosalie Liccardo Pacula, "Heterogeneity in the composition of marijuana seized in California," *Drug and Alcohol Dependence* 117, no. 1 (2011); Jennifer McLaren et al., "Cannabis potency and contamination: a review of the literature," *Addiction* 103, no. 7 (2008); E. L. Sevigny, "Is today's marijuana more potent simply because it's fresher?," *Drug Test Anal* 5, no. 1 (2013); Dan Werb et al., "The temporal relationship between drug supply indicators: an audit of international government surveillance systems," *BMJ Open* 3, no. 9 (2013).

xxxviii Harry G. Levine and Craig Reinarman, "From Prohibition to Regulation: Lessons from Alcohol Policy for Drug Policy," The Milbank Quarterly 69, no. 3 (1991).

xxxix G. T. Carter et al., "Cannabis in palliative medicine: improving care and reducing opioid-related morbidity," *Am J Hosp Palliat Care* 28, no. 5 (2011).

xl D. J. Korf, A. Benschop, and M. Wouters, "Differential responses to cannabis potency: a typology of users based on self-reported consumption behaviour," *Int J Drug Policy* 18, no. 3 (2007); Peggy Pol et al., "Validation of self-reported cannabis dose and potency: an ecological study," *Addiction* 108, no. 10 (2013).

xii See e.g., Igor Grant et al., "Medical marijuana: clearing away the smoke," Open Neurology Journal 6(2012): 18-25; Arno Hazekamp and Franjo Grotenhermen, "Review on clinical studies with cannabis and cannabinoids 2005-2009," Cannabinoids 5, no. special (2010); M. Ben Amar, "Cannabinoids in medicine: A review of their therapeutic potential," J Ethnopharmacol 105, no. 1-2 (2006); F. Grotenhermen and K. Muller-Vahl, "The therapeutic potential of cannabis and cannabinoids."

xiii Gil Bar-Sela et al., "The medical necessity for medicinal cannabis: prospective, observational study evaluating the treatment in cancer patients on supportive or palliative care," Evidence-Based Complementary and Alternative Medicine 2013(2013); Suzanne Johannigman and Valerie Eschiti, "Medical Use of Marijuana in Palliative Care," Clinical Journal of Oncology Nursing 17, no. 4 (2013).

National Type 1 (Cannabis in painful HIV-associated sensory neuropathy: a randomized placebo-controlled trial," Neurology 68, no. 7 (2007); Ronald J Ellis et al., "Smoked medicinal cannabis for neuropathic pain in HIV: a randomized, crossover clinical trial,"

Neuropsychopharmacology 34, no. 3 (2008); Elizabeth E

Lutge, Andy Gray, and Nandi Siegfried, "The medical use of cannabis for reducing morbidity and mortality in patients with HIV/AIDS," *status and date: New, published in,* no. 4 (2013); P. K. Riggs et al., "A pilot study of the effects of cannabis on appetite hormones in HIV-infected adult men," *Brain Res* 1431(2012)

xiiv Jody Corey-Bloom et al., "Smoked cannabis for spasticity in multiple sclerosis: a randomized, placebo-controlled trial," *Canadian Medical Association Journal* 184, no. 10 (2012). xiv A. W. Zuardi, "Cannabidiol: from an inactive cannabinoid to a drug with wide spectrum of action; N. M. Kogan and R. Mechoulam, "Cannabinoids in health and disease," *Dialogues Clin Neurosci* 9, no. 4 (2007).

xivi Torsten Passie et al., "Mittigation of post-traumatic stress symptoms by Cannabis resin: A review of the clinical and neurobiological evidence," *Drug Testing and Analysis* 4, no. 7-8 (2012); A. Neumeister et al., "Elevated brain cannabinoid CB receptor availability in post-traumatic stress disorder: a positron emission tomography study," *Mol Psychiatry* 10.1038/mp.2013.61(2013); George A. Fraser, "The Use of a Synthetic Cannabinoid in the Management of Treatment-Resistant Nightmares in Posttraumatic Stress Disorder (PTSD)," *CNS Neuroscience & Therapeutics* 15, no. 1 (2009). xivii Brenda E Porter and Catherine Jacobson, "Report of a parent survey of cannabidiol-enriched cannabis use in pediatric treatment-resistant epilepsy," *Epilepsy & Behavior* 29, no. 3 (2013).

Response in Patients with Crohn's Disease: a Prospective Placebo-Controlled Study," *Clinical Gastroenterology and Hepatology* 11, no. 10 (2013).

xlix N. M. Kogan and R. Mechoulam, "Cannabinoids in health and disease."

<sup>1</sup> D. I. Abrams et al., "Cannabinoid-opioid interaction in chronic pain," *Clin Pharmacol Ther* 90, no. 6 (2011); Philippe Lucas et al., "Cannabis as a substitute for alcohol and other drugs: A dispensary-based survey of substitution effect in Canadian medical cannabis patients."

<sup>II</sup> California Center for Medicinal Cannabis Research, *Report to the Legislature & Governor of the State of California* (2010); B. Wilsey et al., "Low-dose vaporized cannabis significantly improves neuropathic pain," *J Pain* 14, no. 2 (2013).

Janet Elizabeth Joy, Stanley J Watson, and John A Benson, Marijuana and medicine: assessing the science base. Jody Corey-Bloom et al., "Smoked cannabis for spasticity in multiple sclerosis: a randomized, placebo-controlled trial.' iv Torsten Passie et al., "Mitigation of post-traumatic stress symptoms by Cannabis resin: A review of the clinical and neurobiological evidence; A. Neumeister et al., "Elevated brain cannabinoid CB receptor availability in post-traumatic stress disorder: a positron emission tomography study: George A. Fraser, "The Use of a Synthetic Cannabinoid in the Management of Treatment-Resistant Nightmares in Posttraumatic Stress Disorder (PTSD)." See also, Mordechai Mashiah, "Medical Cannabis as Treatment for Chronic Combat PTSD: Promising Results in an Open Pilot Study" (Abarbanel Mental Hospital, Israel presented at Patients out of Time Conference, Tucson (2012),

Arno Hazekamp et al., "The medicinal use of cannabis and cannabinoids—An international cross-sectional survey on administration forms," *Journal of psychoactive drugs* 45, no. 3 (2013).

<sup>№</sup> V. Di Marzo, "The endocannabinoid system: its general strategy of action, tools for its pharmacological manipulation and potential therapeutic exploitation," *Pharmacol Res* 60, no. 2 (2009); P. G. Fine and M. J. Rosenfeld, "The

endocannabinoid system, cannabinoids, and pain," Rambam Maimonides Med J 4, no. 4 (2013); D. J. Hermanson and L. J. Marnett, "Cannabinoids, endocannabinoids, and cancer," Cancer Metastasis Rev 30, no. 3-4 (2011); A. A. Izzo et al., "Non-psychotropic plant cannabinoids: new therapeutic opportunities from an ancient herb," Trends Pharmacol Sci 30, no. 10 (2009); D. Koethe, C. Hoyer, and F. M. Leweke, "The endocannabinoid system as a target for modelling psychosis," Psychopharmacology (Berl) 206, no. 4 (2009); S. Maione, B. Costa, and V. Di Marzo, "Endocannabinoids: A unique opportunity to develop multitarget analgesics," Pain 10.1016/j.pain.2013.03.023(2013); E. M. Marco et al., "Endocannabinoid system and psychiatry: in search of a neurobiological basis for detrimental and potential therapeutic effects," Front Behav Neurosci 5(2011); A. Saito et al., "Endocannabinoid system: potential novel targets for treatment of schizophrenia," Neurobiol Dis 53(2013); H. Ujike and Y. Morita, "New perspectives in the studies on endocannabinoid and cannabis: cannabinoid receptors and schizophrenia," J Pharmacol Sci 96, no. 4 (2004); E. Zamberletti, T. Rubino, and D. Parolaro, "The endocannabinoid system and schizophrenia: integration of evidence," Curr Pharm Des 18, no. 32 (2012); M. Alhouayek and G. G. Muccioli, "The endocannabinoid system in inflammatory bowel diseases: from pathophysiology to therapeutic opportunity," Trends Mol Med 18, no. 10 (2012); Timna Naftali et al., "Cannabis Induces a Clinical Response in Patients with Crohn's Disease: a Prospective Placebo-Controlled Study."

<sup>Ivii</sup> P. Armentano, "Cannabis and psychomotor performance: a rational review of the evidence and implications for public policy," *Drug Test Anal* 5, no. 1 (2013); J. G. Ramaekers et al., "Dose related risk of motor vehicle crashes after cannabis use," *Drug and Alcohol Dependence* 73, no. 2 (2004); Johannes G Ramaekers et al., "Dose related risk of motor vehicle crashes after cannabis use: an update," in *Drugs*, *Driving and Traffic Safety* (Springer, 2009).

wiii R. Elvik, "Risk of road accident associated with the use of drugs: A systematic review and meta-analysis of evidence from epidemiological studies," *Accid Anal Prev* 60(2013); P. Armentano, "Cannabis and psychomotor performance: a rational review of the evidence and implications for public policy; S. Blows et al., "Marijuana use and car crash injury," *Addiction* 100, no. 5 (2005).

i<sup>ix</sup> R. A. Sewell, J. Poling, and M. Sofuoglu, "The effect of cannabis compared with alcohol on driving," *Am J Addict* 18, no. 3 (2009); A. Ronen et al., "Effects of THC on driving performance, physiological state and subjective feelings relative to alcohol," *Accid Anal Prev* 40, no. 3 (2008); Annick Ménétrey et al., "Assessment of Driving Capability Through the Use of Clinical and Psychomotor Tests in Relation to Blood Cannabinoids Levels Following Oral Administration of 20 mg Dronabinol or of a Cannabis Decoction Made with 20 or 60 mg Δ9-THC," *Journal of Analytical Toxicology* 29, no. 5 (2005).

k J. Ahlner, A. Holmgren, and A. W. Jones, "Prevalence of alcohol and other drugs and the concentrations in blood of drivers killed in road traffic crashes in Sweden," *Scand J Public Health* 10.1177/1403494813510792(2013). 

□ P. Armentano, "Cannabis and psychomotor performance: a rational review of the evidence and implications for public policy; D. M. Schwope et al., "Psychomotor performance, subjective and physiological effects and whole blood Delta(9)-tetrahydrocannabinol concentrations in heavy, chronic cannabis smokers following acute smoked cannabis," *J Anal Toxicol* 36, no. 6 (2012); Guohua Li, Joanne E. Brady, and Qixuan Chen, "Drug use and fatal motor vehicle crashes: A

case-control study," Accident Analysis & Prevention 60, no. 0

(2013).  $^{\mbox{\tiny lxii}}$  Stefan W Toennes et al., "Comparison of cannabinoid pharmacokinetic properties in occasional and heavy users smoking a marijuana or placebo joint," Journal of analytical toxicology 32, no. 7 (2008); Stefan W Toennes et al., "Pharmacokinetic Properties of Δ9-Tetrahydrocannabinol in Oral Fluid of Occasional and Chronic Users," Journal of analytical toxicology 34, no. 4 (2010); Eef L Theunissen et al., "Neurophysiological functioning of occasional and heavy cannabis users during THC intoxication," Psychopharmacology 220, no. 2 (2012); Johannes G Ramaekers et al., "Tolerance and cross-tolerance to neurocognitive effects of THC and alcohol in heavy cannabis users," ibid.214(2011).

D. Mark Anderson, Benjamin Hansen, and Daniel I. Rees, "Medical Marijuana Laws, Traffic Fatalities, and Alcohol Consumption," Journal of Law and Economics 56, no. 2

(2013).

biv Federal Bureau of Investigation, "Crime in the United

10 (2013).

DC: U.S. Department of Justine 10 (2013). States, 2012," (Washington, DC: U.S. Department of Justice, 2013).

by Babe Howell, "Broken Lives from Broken Windows: The Hidden Costs of Aggressive Order-Maintenance Policing," New York University Review of Law & Social Change 33(2009); Richard Glen Boire, Life Sentences: Collateral Sanctions Associated with Marijuana Offenses (Center for Cognitive Liberty & Ethics, 2007); Robert C Boruchowitz, Malia N Brink, and Maureen Dimino, Minor Crimes, Massive Waste: The Terrible Toll of America's Broken Misdemeanor Courts (National Association of Criminal Defense Lawyers. 2009); American Civil Liberties Union, "The War on Marijuana in Black and White," (2013).

lxvi Richard J. Bonnie and Charles H. Whitebread, Marijuana Conviction: A History of Marijuana Prohibition in the United States; David F Musto, "Opium, cocaine and marijuana in American history; David F Musto, THE AMERICAN DISEASE: ORIGINS OF NARCOTICS CONTROL (Oxford University Press, 1999).

Ixvii American Civil Liberties Union, "The War on Marijuana in Black and White."

lxviii Ibid.