

Status of Cannabinoid Products and Potential Benefits and Risks of Marijuana Use

The information presented is compiled from several referenced sources regarding the observed and potential risks and benefits of marijuana use on the health and welfare of individuals and society.

Available Cannabinoid Products

Medication	Comments	Reference
Dronabinol (Marinol)	Active ingredient is a synthetic delta -9-tetrahydrocannabinol (THC) which is the found naturally in Cannabis sativa L (Marijuana). Given in capsule form and used to treat; nausea and vomiting associated with chemotherapy, loss of appetite and weight loss due to HIV/AIDS. This drug was approved by the FDA in 1985.	http://www.fda.gov/ohrms/dockets/dockets/05n0479/05N-0479-emc0004-04.pdf
Nabilone (Cesamet)	Active ingredient is a synthetic delta -9-tetrahydrocannabinol (THC) which is the found naturally in Cannabis sativa L (Marijuana). Given in capsule form for nausea and vomiting associated with chemotherapy. This drug was approved by the FDA in 1985.	http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/018677s011lbl.pdf
Sativex	Active ingredient is a cannabinoid combination of tetrahydrocannabinol (THC) and cannabidiol (CBD) given as an oromucosal spray for the treatment of neuropathic pain often associated with cancer, spasticity, overactive bladder, and other symptoms of multiple sclerosis. This drug will potentially be approved by the FDA in 2016.	http://www.gwpharm.com/sativex.aspx https://en.wikipedia.org/wiki/Nabiximols

Epidiolex	<p>Epilepsy is one of the most common neurological disorders in children. According to Russ in the February 2012 edition of Pediatrics, there is a point prevalence of 6.3 per 1000 children currently diagnosed with epilepsy or 466,000 childhood patients in the United States and 765,000 patients in Europe. Specialists estimate that up to 20% of these cases like children with Dravet’s and Lennox Gastaut syndromes, show pharmacoresistance to current treatment (i.e., seizures that persist, despite accurate diagnosis and carefully monitored treatment with multiple antiepileptic drugs) and are deemed “medically intractable.” Furthermore, it is recognized that many of those that do find relief often suffer side effects severe enough with their current medication that an alternative or adjunct is often sought. In total, therefore, the size of the intractable pediatric epilepsy population is 93,200 patients in the United States and 153,000 in Europe.*</p> <p>Epidiolex is a cannabinoid, cannabidiol. It does not possess the psychogenic effects of THC, but seems to be useful in treating intractable seizures.</p> <p>The FDA has approved “fast-track” status for Epidiolex.</p> <p>A phase three trial reported on June 27, 2016, demonstrated a monthly drop seizures of 44 percent (Epidiolex group)</p>	<p>* http://www.gwpharm.com/epidiolex.aspx</p> <p>**https://globenewswire.com/news-release/2016/06/27/851481/0/en/GW-Pharmaceuticals-Announces</p>
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	compared with a reduction of 22 percent in patients receiving placebo, and the difference between treatments was statistically significant (p=0.0135).**	
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Potential Benefits

Condition	Comments	Reference
Chronic pain Spasticity	Moderate quality of evidence	<i>Cannabinoids for Medical Use: A Systematic Review and Meta-analysis</i> , JAMA, PF Whiting, et al, 2015; 313(24):2456-2473. doi:10.1001/jama.2015.6358 . Study group – University Hospitals, Bristol, United Kingdom.
Nausea and vomiting due to chemotherapy Weight gain in HIV Sleep disorders Tourette syndrome	Low quality of evidence	<i>Cannabinoids for Medical Use: A Systematic Review and Meta-analysis</i> , JAMA, PF Whiting, et al, 2015;313(24):2456-2473. doi:10.1001/jama.2015.6358 . Study group – University Hospitals, Bristol, United Kingdom.
Obesity Addiction Inflammatory conditions	Promise lies in purified ingredients or synthetic compounds with more selectivity and less adverse effects. NIH research focuses on THC (tetrahydrocannabinol), CBD (cannabidiol), and other compounds that alter the function of the endocannabinoid system.	<i>Marijuana: What Science Tells Us</i> , National Institutes of Drug Abuse presentation by Jack B Stein PhD, Director, Office of Science Policy and Communications, November 17, 2015.
Certain seizure disorders	Dravet and Lennox Gastaut syndromes. Epidiolex CBD (cannabidiol) given to patients from 2- 55 years old (doses ranged from 10-20 mg /kg/day), saw a 44% reduction in monthly seizures versus 22% in the	<i>GW Pharmaceutical Investor Conference Call 2016</i> , GW Pharma Jumps as Cannabis Drug Treats Severe Epilepsy, http://www.investors.com/news/technology/gw-pharma-jumps-as-cannabis-drug-treats-severe-epilepsy/

	placebo group.	
Reduced risk of diabetes	Study of 39,695 past and current marijuana users	<i>Decreased Prevalence of Diabetes in Marijuana Users: Cross-sectional Data from the National Health and Nutrition Examination Survey (NHANES) III</i> , Rajavashishth TB, 2012, British Medical Journal Open, 2, e000494 http://bmjopen.bmj.com/content/2/1/e000494.full .

Potential Risks

Condition	Comments	Reference
Respiratory system		
Respiratory problems (chronic bronchitis, cough, phlegm production, wheezing, and abnormal breath sounds)	The effect was noted even in non-tobacco users	<i>Respiratory Effects of Marijuana and Tobacco Use in a U.S. Sample</i> Moore BA, 2005, Journal of General Internal Medicine, 20, 33-37, http://onlinelibrary.wiley.com/doi/10.1111/j.1525-1497.2004.40081.x/full .
Cardiovascular system		
Elevated cardiovascular risk factors (fasting glucose and insulin, triglycerides, systolic and diastolic blood pressure)	Based on a 30-day dose-dependent relationship	<i>Emerging Issues for Our Nation's Health: the Intersection of Marijuana and Cardiometabolic Disease Risk</i> , Vidot DC, 2015, Drug and Alcohol Dependence, 146, e11, https://www.researchgate.net/publication/259958415_Emerging_Issues_for_our_Nation's_Health_The_Intersection_of_Marijuana_Use_and_Cardiometabolic_Disease_Risk
Adverse effects on breathing and heart rate		<i>What is Marijuana?</i> , 2015, National Institute on Drug Abuse, https://www.drugabuse.gov/publications/drugfacts/marijuana .
Brain and mental health		
Psychosis risk	Particularly early onset psychosis and schizophrenia in	<i>Cannabis Use in Young People: The Risk of Schizophrenia</i> ,

	<p>adults and adolescents.</p> <p>Marijuana use increases the risk of schizophrenia for people with specific genotypes (AKT1rs2494732)*</p> <p>One study demonstrated that marijuana users were not significantly different in terms of their physical and mental health problems assessed in their mid-30's, and marijuana users did not vary from non-users in developing later health problems via race.**</p>	<p>Casadio P, Neuroscience and Biobehavioral Reviews, 2011, 35, 1779-1787, https://www.researchgate.net/publication/51086876_Cannabis_use_in_young_people_The_risk_for_schizophrenia.</p> <p><i>A Systematic Review of the Evidence for Medical Marijuana in Psychiatric Indications.</i> Wilkinson ST, The Journal of Clinical Psychiatry. 77: 1050-64. PMID 27561138, DOI: 10.4088/JCP.15r10036.</p> <p><i>Cannabis as a Risk Factor for Psychosis: Systematic Review,</i> Semple DM, Journal of Psychopharmacology, 2005, 19, 187-194, http://www.mh-hannover.de/fileadmin/klinken/linische_psychologie/downloads/te st22/beispiel_review.pdf.</p> <p>* <i>Marijuana: What Science Tells Us,</i> National Institutes of Drug Abuse presentation by Jack B Stein PhD, Director, Office of Science Policy and Communications, November 17, 2015, referenced Di Forti et al, Biological Psychiatry, 2012.</p> <p>** <i>Chronic Adolescent Marijuana Use as a Risk Factor for Physical and Mental Health Problems in Young Adult Men,</i> Bechtold J, 2015, Psychology of Addictive Behaviors online publication, http://www.antonioacasella.eu/arc_hila/Bechtold_Pardini_2015.pdf</p>
<p>Prodromal psychosis symptoms (paranoia,</p>		<p><i>Cannabis Use and Vulnerability for Psychosis in Early Adolescence,</i></p>

etc.) in adolescents		Griffith-Lenderling MF, <i>Addiction</i> , 108, 733-740, http://onlinelibrary.wiley.com/doi/10.1111/add.12050/abstract .
Decreased life satisfaction		https://www.drugabuse.gov/publications/drugfacts/marijuana .
Decreased mental and physical health		
Increased relationship problems		
Decline in verbal memory in middle age		<i>Long-term Marijuana Use and Cognitive Impairment in Middle Age</i> , Wayne Hall, PhD ^{1,2} ; Michael Lynskey, PhD: <i>JAMA Intern Med</i> . 2016;176(3):362-363. doi:10.1001/jamainternmed.2015.7850 , bit.ly/1m8hQ2K
Potential association with adolescent depression	<p>Depressed teens are twice as likely to use marijuana and other illicit drugs.</p> <p>Depressed teens are more than twice as likely as peers to abuse or become dependent on marijuana.</p> <p>Marijuana use can worsen depression and lead to more serious mental illness such as schizophrenia, anxiety, and even suicide.</p> <p>Teens who smoke marijuana at least once a month are three times more likely to have suicidal thoughts than non-users.</p> <p>The percentage of depressed teens is equal to the percentage of depressed adults, but depressed teens are more likely than depressed adults to use marijuana than other drugs.</p> <p>The association between</p>	<p><i>Teen Marijuana Use Worsens Depression: An Analysis of Recent Data Shows Self-medication Could Actually Make Things Worse</i>, Office of National Drug Control Policy, May, 2008, https://www.ncjrs.gov/ondcppubs/publications/pdf/marij_mental_health.pdf.</p> <p>*Not part of the above report.</p>

	marijuana use and depression is not shown in all studies.*	
Structural differences in the brain	Early (starting at < 18 years old) long term cannabis use associated with decreased brain axonal fiber connectivity.	<i>Marijuana: What Science Tells Us</i> , National Institutes of Drug Abuse presentation by Jack B Stein PhD, Director, Office of Science Policy and Communications, November 17, 2015, referenced Zalesky, Brain, 2012.
Education		
Adverse educational impacts	More frequent marijuana use is associated with a decreased likelihood of high school completion and degree attainment. Persistent marijuana users show a significant IQ drop between childhood and midlife.*	<i>Marijuana: What Science Tells Us</i> , National Institutes of Drug Abuse presentation by Jack B Stein PhD, Director, Office of Science Policy and Communications, November 17, 2015, referenced <i>Young Adult Sequelae of Adolescent Cannabis Use: An Integrative Analysis</i> , Silins E et al, the Lancet Psychiatry, 2014, http://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(14)70307-4/abstract . * <i>Marijuana: What Science Tells Us</i> , National Institutes of Drug Abuse presentation by Jack B Stein PhD, Director, Office of Science Policy and Communications, November 17, 2015, referenced Meier MH et al, PNAS Early Edition, 2012, <i>Persistent Cannabis Users Show Neuropsychological Decline from Childhood to Midlife</i> , http://www.pnas.org/content/109/40/E2657.abstract .
Other substance abuse data		
Association with other drug use	Similar to alcohol and tobacco use, marijuana use increases the likelihood of other drug use	<i>Marijuana: What Science Tells Us</i> , National Institutes of Drug Abuse presentation by Jack B Stein PhD,

	(sedatives, hallucinogens, cocaine and other stimulants, and opioids).	Director, Office of Science Policy and Communications, November 17, 2015, referenced Lynsky MT et al. JAMA, 289, pp 427-433, 2003, <i>Escalation of Drug Use in Early-onset Cannabis Users vs Co-twin Controls</i> , https://www.ncbi.nlm.nih.gov/pubmed/12533121 .
Cannabis withdrawal syndrome	Symptoms are most intense during the 1 st week post withdrawal but can persist for one month. Criteria of the cannabis withdrawal syndrome must include at least two of the following; irritability, restlessness, anxiety, depression, aggressiveness, loss of appetite, sleep disturbance, and at least one physical symptom; pain, shivering, sweating, elevated body temperature, chills.	<i>The Health and Social Effects of Nonmedical Cannabis Use</i> , World Health Organization, 2016, http://www.who.int/substance_abuse/publications/cannabis_report/en/ .
Increased addiction and abuse of marijuana	8*-10% of marijuana users meet the definition of addiction and 30% of users abuse the drug. Addiction is significantly higher when usage begins during adolescence (16% for marijuana).	<i>Marijuana: What Science Tells Us</i> , National Institutes of Drug Abuse presentation by Jack B Stein PhD, Director, Office of Science Policy and Communications, November 17, 2015, referenced Anthony JC, 1994, <i>Comparative Epidemiology of Dependence on Tobacco, Alcohol, Controlled Substances, and Inhalants: Basic Findings from the National Comorbidity Survey</i> , Anthony JC, Warner LA, Kessler RC (1994): <i>Experimental and Clinical Psychopharmacology</i> 2:244-268, https://www.erowid.org/references/refs_view.php?ID=1278 . * <i>From First Drug Use to Drug Dependence: Developmental</i>

		<p><i>Periods of Risk for Dependence upon Marijuana, Cocaine, and Alcohol</i>, Fernando A Wagner ScD and James C Anthony Ph.D, Neuropsychopharmacology (2002) 26 479-488.10.1038/S0893-133X(01)00367-0, http://www.nature.com/npp/journal/v26/n4/full/1395810a.html.</p>
Healthcare systems		
<p>Increased emergency department visits and hospital admissions related to marijuana use</p>	<p>Colorado emergency department visit per year related to marijuana increased from 14,148 in 2013 to 18,255 in 2014.</p> <p>Colorado hospitalizations related to marijuana use increased progressively from 2011 to 2014:</p> <ul style="list-style-type: none"> • 6,305 (2011) • 6,715 (2012) • 8,272 (2013) • 11,439 (2014) 	<p><i>Rocky Mountain High Intensity Drug Trafficking Area, The Legalization of Marijuana in Colorado, The Impact</i>, Volume 4, September, 2016. www.rmhidta.org.</p>
<p>Childhood overdose/poisonings/emergency department visits</p>	<p>In the last few years, Colorado has seen a dramatic increase in the number of marijuana overdoses in children who ingest marijuana edibles. 268% increase in marijuana poisoning exposures between 2006-2009 and 2010-2013</p>	<p><i>The Implications of Medical Marijuana Legalization in Colorado</i>, JAMA.2015;313(3):241-242.doi:1001/jama.2014.17057, http://www.ktvz.com/news/bend/c-o-hospitals-see-dramatic-spike-in-pot-related-illnesses/69167250</p> <p><i>Pediatric Marijuana Exposures in a Medical Marijuana State</i>, JAMA. 2015;313(3):241-242. doi:10.1001/jama.2014.17057 http://jamanetwork.com/journals/jama/article-abstract/2022370</p> <p><i>The Legalization of Marijuana in Colorado: The Impact</i>, http://www.rmhidta.org.html/August%202014%20Legalization%20of</p>

		%20MJ%20in%20Colorado%20the%20Impact.pdf.
Child development		
Adverse fetal/childhood development	Prenatal marijuana use is associated with short and long term adverse development in the areas of neurobehavior, cognition and achievement. In utero exposure is associated with impaired attention, learning and memory, impulsivity, behavioral problems, higher likelihood of using cannabis as an adult.*	<i>Prenatal Substance Abuse: Short and Long-term Effects on the Exposed Fetus</i> , Pediatrics, 2013, 131: pp e1016, https://www.ncbi.nlm.nih.gov/pubmed/23439891/ . *The Health and Social Effects of Nonmedical Cannabis Use, World Health Organization, 2016.

Short term adverse effects

Condition	Comments	Reference
Dizziness	Methods used; Meta-analysis of 28 studies, administration methods included oral capsules, oromucosal spray, vaporization, smoking, and intramuscular injections.	<i>Cannabinoids for Medical Use: A Systematic Review and Meta-analysis</i> , JAMA, PF Whiting, et al, 2015;313(24):2456-2473.doi:10.1001/jama.2015.6358. Study group – University Hospitals, Bristol, United Kingdom, https://www.ncbi.nlm.nih.gov/pubmed/26103030 .
Dry mouth		
Nausea		
Fatigue		
Somnolence		
Euphoria		
Vomiting		
Disorientation		
Drowsiness		
Confusion		
Loss of balance		
Hallucinations		

Other societal Impacts

Impact	Comments	Reference
Increased traffic fatalities	100% increase in traffic fatalities in Colorado involving marijuana three years after medical marijuana legalization	http://www.rmhidta.org.html/August%202014%20Legalization%20of%20MJ%20in%20Colorado%20the%20Impact.pdf .
Diversion of marijuana by parcel	1080% increase in mailing marijuana outside of Colorado	
Deaths reported due to erratic behavior while under the influence of marijuana	Discusses the dangers and risks associated with erratic behavior due to the drug. In the three cases mentioned, all three committed suicide.	Third Death in Colorado Linked to Marijuana Edibles, http://www.foodsafetynews.com/2015/03/third-death-in-colorado-linked-to-edible-marijuana/#.VzXx1WMwesM .