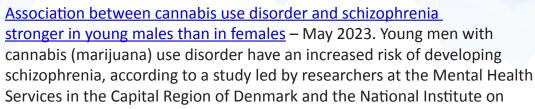
SUMMARY OF RESEARCH ARTICLES BY JOHNNY'S AMBASSADORS

Excerpted from johnnysambassadors.org/mental illness

IMPACT OF MARIJUANA ON MENTAL ILLNESS IN ADOLESCENTS

2023





Drug Abuse (NIDA) at the National Institutes of Health. The study analyzed detailed health records data spanning 5 decades and representing more than 6 million people in Denmark to estimate the fraction of schizophrenia cases that could be attributed to cannabis use disorder on the population level. Researchers found strong evidence of an association between cannabis use disorder and schizophrenia among men and women, though the association was much stronger among young men. Using statistical models, the study authors estimated that as many as 30% of cases of schizophrenia among men aged 21-30 might have been prevented by averting cannabis use disorder.

<u>Association between non-medical cannabis legalization and emergency department visits for cannabis-induced psychosis</u> – July 2023. The commercialization period was associated with an immediate increase in rates of ED visits for cannabis-induced psychosis

<u>Association Between Tobacco and Cannabis Use and the Age of Onset of Depression and Anxiety Symptoms Among Adolescents and Young Adults</u> – April 2023. The study's findings indicate that tobacco and cannabis use is directly linked to the early onset of depressive and anxiety symptoms among youth.

THE ASSOCIATION OF CANNABIS POTENCY WITH ADVERSE PSYCHIATRIC EFFECTS OF CANNABIS -

August 2023. The potency (THC content) of cannabis, both illicit and legal, has increased substantially over the past four decades, which may result in increased likelihood of developing adverse psychiatric effects. However, the evidence for the association between cannabis potency and adverse psychiatric effects is strong only for psychosis. The evidence for an association with cannabis use disorder, anxiety, or depression is inconsistent; most studies are of poor quality. Given the potential clinical and public health harms from the higher-potency cannabis now available, high-quality research studies are urgently needed.

<u>Cannabis Use Disorder and Subsequent Risk of Psychotic and Nonpsychotic Unipolar Depression and Bipolar Disorder</u> – May 2023. In this cohort study of 6,651,765 individuals in Demark, cannabis use disorder was associated with an increased risk of both psychotic and nonpsychotic unipolar depression

and bipolar disorder. The findings suggest that cannabis use disorder is independently associated with bipolar disorder and unipolar depression.

Is there a link between marijuana use and psychiatric disorders? April 2023 National Institute on Drug Abuse. "Marijuana can produce an acute psychotic reaction in non-schizophrenic people who use marijuana, especially at high doses. Recent research suggests that smoking high-potency marijuana every day could increase the chances of developing psychosis by nearly five times compared to people who have never used marijuana. The amount of drug used, the age at first use, and/or genetic vulnerability have all been shown to influence this relationship."

Nondisordered Cannabis Use Among US Adolescents – May 2023. A Columbia University study has found that teens who use cannabis recreationally are two to four times as likely to develop psychiatric disorders, such as depression and suicidality, than teens who don't use cannabis at all. In this cross-sectional study of 68, 263 adolescents, NDCU was approximately 4 times more common than cannabis use disorder (CUD). NDCU and CUD were both significantly associated with adverse psychosocial events in a stepwise gradient manner. These findings suggest that adolescents with NDCU or CUD had increased odds of adverse psychosocial events.

Prevalence of cannabis use disorder among individuals using medical cannabis at admission to inpatient treatment for substance use disorders – July 2023. High psychiatric comorbidities were present: 79% and 81% screened positive for an anxiety disorder, 60% and 61% screened positive for depression, and 66% and 57% screened positive for PTSD for the Medical-Only and Dual-Use inpatients, respectively."

Young men at highest risk of schizophrenia linked with cannabis use disorder – May 2023. Researchers found strong evidence of an association between cannabis use disorder and schizophrenia among men and women, though the association was much stronger among young men. Using statistical models, the study authors estimated that as many as 30% of cases of schizophrenia among men aged 21-30 might have been prevented by averting cannabis use disorder.

2022

<u>A Cannabinoid Hypothesis of Schizophrenia: Pathways to Psychosis</u> – The endocannabinoid system was reviewed. Evidence regarding the effect of delta 9-tetrahydrocannabinol (THC) on the brain was described. A connection between cannabis use and first-episode psychosis was explained.

A Panel Study of the Effect of Cannabis Use on Mental Health, Depression and Suicide in the 50 States – June 2022. COMMISSIONED BY JOHNNY'S AMBASSADORS and authored by the Drug-Free America Foundation. This research establishes a correlative link between monthly cannabis use among adolescents and young adults and self-reported major depressive events with both statistical significance and strong explanatory power. Additionally, positive correlation is shown between monthly cannabis use by young adults and the prevalence of self-reported severe mental illnesses and suicidal thoughts.

Adolescent cannabis use and later development of schizophrenia: An updated systematic review of longitudinal studies — January 2022. Both high- and low-frequency marijuana usage were associated with a significantly increased risk of schizophrenia. The frequency of use among high- and low-frequency users is similar in both, demonstrating statistically significant increased risk in developing schizophrenia.

Association of Cannabis Use-Related Predictor Variables and Self-Reported Psychotic Disorders: U.S. Adults, 2001-2002 and 2012-2013 — A study of 80,000 members of the general American population shows that those with cannabis use disorder during the previous year have a 2.5-fold increase in the rate of formally diagnosed schizophrenia-like psychotic disorder. Their findings on the association of cannabis use and self-reported psychosis adds to the growing literature that suggests there is a relationship between marijuana use and psychotic disorders.

<u>Association of cannabis potency with mental ill health and addiction: a systematic review</u> – July 2022. Overall, use of higher potency cannabis, relative to lower potency cannabis, was associated with an increased risk of psychosis and CUD.

Cannabis and Psychosis: Recent Epidemiological Findings Continuing the "Causality Debate"

– January 2022. In summary, much of the available evidence supports the criteria of strength, consistency, biological gradient, and temporality for cannabis causing psychosis. Furthermore, supporting specificity, while many substances are known to induce psychosis, the risk for conversion to schizophrenia is greatest with cannabis-induced psychosis. As noted earlier, there is robust experimental evidence from placebo-controlled studies that THC can induce transient psychotic symptoms. Lastly, some of the neurobiological markers of chronic cannabis exposure (e.g., P300, synaptic vesicle density) overlap with those seen in psychotic disorders, supporting biological plausibility and coherence.

Geographical variation in hospitalization for psychosis associated with cannabis use and cannabis legalization in the United States – January 2022. This is the first cross-sectional population-based study of hospital discharges that revealed there is geographic variation in hospitalizations for psychosis associated with cannabis use that was associated with implementation of cannabis legalization policies.

Gone to Pot: Examining the Association Between Cannabis Use and Medical/Psychiatric Disorders (Editorial) – February 2022. Multiple lines of evidence ranging from epidemiological studies (3-5) [both cross-sectional and within-subject studies (6)], human laboratory studies using delta-9 tetrahydrocannabinol, the main psychoactive constituent in cannabis (7, 8), and more recently, genetic studies (9, 10) suggest that cannabis use is a risk factor for the later development of psychosis.

Is Cannabis Use Increasing Schizophrenia? January 2022. The juxtaposition of 2 recent research reports should give us pause for concern. In September, the National Institute on Drug Abuse reported that cannabis use among college students reached 44% in 2020, a significant increase from 38% in 2015 and at its highest level since the 1980s. The cannabis currently available is more potent than that used in the past. This follows a July report from researchers in Denmark who claim that the increasing use of cannabis is a likely cause of increasing incidence of schizophrenia noted in that country over the past 2 decades. An increasing incidence of schizophrenia, or psychosis in general, has also been reported in England, Switzerland, and Canada, especially among young people. Since 19 US states have already legalized the recreational use of cannabis and other states are considering doing so, a possible relationship between cannabis use and increasing schizophrenia is potentially very important and needs to be confirmed.

<u>A Systematic Review and Recommendations of Cannabis use in Bipolar Disorder and Major Depressive Disorder</u> – June 2022. The data indicate that cannabis use is associated with worsened course and functioning of bipolar disorder and major depressive disorder.

2021

Applying the Bradford Hill Elements of Causation to Cannabis Use Causing Psychosis and Chronic Psychotic Disorders – June 2021. Epidemiologist Austin Bradford Hill recognized that no one type of study could fully address the causal relationship between an agent and an outcome in human populations. The analysis he developed to categorize the different types of research necessary to substantiate causation have withstood the test of time. Although not all key elements he defined can be applied to all types of outcomes, in the case of cannabis causing psychosis, their full application is possible. You will find in this article what is termed "elements of causation" and the studies that satisfy them. This is intended to be a living document, with edits from leading researchers incorporated as more relevant and up-to-date literature is made available.

Association of Cannabis Use–Related Predictor Variables and Self-Reported Psychotic Disorders: U.S. Adults, 2001–2002 and 2012–2013 – Oct. 2021. Data from the U.S. general population, especially more recent data, suggest associations between self-reported psychotic disorder and frequent nonmedical cannabis use and cannabis use disorder.

<u>Cannabinoid Pathway Linked to Psychiatric Disorders</u> – July 2021. Cannabis has an effect on humans because it mimics endocannabinoids, chemicals occurring naturally in the brain. Endocannabinoids are produced by an enzyme called diacylglycerol lipase alpha (DAGLA), which is concentrated in synapses. Endocannabinoids dampen synaptic strength, one reason for the calming effects of marijuana. Aberrant expression of ankyrin-G — either too much or too little — has been associated with disorders such as bipolar disorder, schizophrenia and autism.

<u>Cannabis psychosis: how super-powered skunk blew our minds</u> – Sept. 2021. Cannabis is far stronger than it used to be and psychosis rates are soaring. Megan Agnew meets former smokers — and the medics helping them to recover. Featuring Marti di Forti and Sir Robin Murray's cannabis clinic.

Cannabis use in adolescence and risk of psychosis: Are there factors that moderate this relationship? A systematic review and meta-analysis – February 2021. The following factors moderate the relationship between cannabis use and the risk of psychosis: age of onset of cannabis use, frequent cannabis use, exposure to childhood trauma, concurrent use of other substances and genetic factors. Conclusion: Adolescent cannabis use is associated with an increased risk for psychosis later in life. In addition, there are factors that moderate this relationship; therefore there is a need for research to assess the interaction between these factors, adolescent cannabis use and psychosis risk.

Cannabis users at 'much higher' risk of developing mental health issues – Oct. 1, 2021. Using primary care data drawn from the IQVIA Medical Research Database (IMRD-UK), the researchers found following the first recorded use of cannabis, patients were three times more likely to develop common mental health problems such as depression and anxiety. In addition, they were almost seven times more likely to develop severe mental illnesses such as psychosis or schizophrenia. The dataset included records from 787 GP practices around the UK gathered over a 23-year period between 1995 and 2018. The researchers were able to include data from 28,218 patients who had a recorded exposure to cannabis.

<u>Development Over Time of the Population-Attributable Risk Fraction for Cannabis Use Disorder in Schizophrenia in DENMARK</u> – July 2021. Has the population-attributable risk fraction for cannabis use

disorder in schizophrenia increased over time, as would be expected with increasing use and potency of cannabis? In this Danish nationwide, register-based cohort study, the population-attributable risk fraction for cannabis use disorder in schizophrenia increased from approximately 2% in the period to 1995 to approximately 6% to 8% since 2010. These findings may indicate that cannabis use disorders are associated with an increase in the proportion of cases of schizophrenia.

<u>Does Cannabis Cause Psychosis?</u> March 2021. As summarized in the <u>Table</u>, there are robust associations between cannabis use and psychosis risk, with evidence for a dose-response relationship, which supports the plausibility of a causal association. Comorbid cannabis use is highly prevalent in psychosis (especially FEP, with declining use over time), with strong evidence for an earlier age of onset of illness, as well as effects of psychopathology and cognition. In patients with psychosis, continued cannabis use is associated with antipsychotic nonadherence, illness relapse, and longer hospitalizations. These findings raise the possibility of a dose-response relationship between current cannabis use and transition to psychosis. Findings suggest that targeting cannabis use during the ultrahigh risk period may confer significant benefits on long-term outcomes.

<u>Does Marijuana Cause Schizophrenia?</u> by Dr. Erik Messamore – Feb. 2021. The risk of schizophrenia jumps by more than 300% among regular cannabis users. This is a well-established fact. Emerging scientific findings are more supportive of a causal relationship – that regular cannabis use actually drives the extra schizophrenia risk. The anandamide-depletion hypothesis can explain how regular cannabis makes schizophrenia more likely. Inflammation is a major contributor to psychosis. The brain's own cannabinoid substance, anandamide, rises during inflammation and is part of a natural anti-inflammatory response. Regular exposure to plant-derived cannabinoids reduces the brain's ability to produce its own cannabinoids This would make the frequent marijuana user more vulnerable to the effects of brain inflammation and thus more prone to develop a schizophrenia-like psychosis.

<u>Effects of Cannabis on Mental Health</u> – May 2021. Informational resources from the College of Psychiatrists of Ireland to raise awareness that cannabis is a harmful substance that can have considerable, negative effects on mental health.

<u>Is Marijuana Good for Depression?</u> by Dr. Erik Messamore – Jan. 2021. While studies have not shown evidence that marijuana is good for improving depression, it's important to also ask if marijuana can worsen depression symptoms. Several long-term mood surveys of marijuana users have built upon the conclusions of Moreau and Kotin, finding that 25% of marijuana users report depression as a side effect. These surveys show again that while users may experience short-term relief, depression symptoms continued or even got worse over time. For the average person, data shows that marijuana use is not good for depression, and it can actually get in the way of treatment and recovery.

<u>Large population-based survey finds that marijuana use is associated with psychotic disorders in the U.S. population</u> – Oct. 2021. Dr. Sharif Mohr stated "The results of this study provide further confirmation of what we already know—use of high-potency marijuana products drastically increases risk of developing psychotic disorders and schizophrenia. The increasing normalization of marijuana use, coupled with the growing availability of high-potency marijuana products throughout the country, will likely result in a large increase in mental illness at the population level."

<u>Risks and Benefits of Cannabis and Cannabinoids in Psychiatry</u> – Dec. 8, 2021. There are currently no psychiatric indications approved by the U.S. Food and Drug Administration (FDA) for cannabinoids, and there is limited evidence supporting the therapeutic use of cannabinoids for treatment of psychiatric disorders. To date, evidence supporting cannabinoid prescription beyond the FDA indications is

strongest for the management of pain and spasticity. As cannabinoids become more available, the need for an evidence base adequately evaluating their safety and efficacy is increasingly important. There is considerable evidence that cannabinoids have a potential for harm in vulnerable populations such as adolescents and those with psychotic disorders. The current evidence base is insufficient to support the prescription of cannabinoids for the treatment of psychiatric disorders.

2020

An Open Letter to Anyone Struggling with Addiction – 2020. The symptoms of addiction can be ugly; they often involve activities like cheating, disrupting, lying, stealing and other egregious acts. That's because addicts will do anything to get out of the pain they are in. The addict brain has an appetite for destruction and is fueled more by chaos than harmony. In other words, it's hard for addicts to feel okay. And it's not easy to feel compassion for someone who's leaving shrapnel in their wake. But the more you can understand that the addict is in pain and just trying to get out of it, the easier it can be to deal with the recklessness and chaos that comes with it.

Are we any closer to identifying a causal relationship between cannabis and psychosis? – August 2020. This review provides the reader with an update on developments in research relating to cannabis psychosis. For over four decades researchers and clinicians have focused on the relationship between exposure to cannabis and the emergence of psychotic symptoms.

As marijuana-induced psychosis rises, parents say treatment for young people hard to find – Jan. 2020. A Substance Abuse and Mental Health Services Administration survey found in 2018 there were 3,752 substance abuse treatment programs in the nation that served adolescents. That's about 25% of the number available for adults as federal data shows marijuana use soaring among high school students. Lori Robinson is the founder of Moms Strong, a group that works to educate people on the connection between marijuana, mental illness and suicide. She tells her story in this article of her son, Shane, who died by suicide in 2012 after two hospitalizations for psychosis in 2009 and 2011. She calls the treatment he received "horrendous." Her story is proof that awareness still lags.

Association Between Cannabis Use and Schizophrenia: Causative or Curative? A Systematic Review

– July 2020. Cannabis and schizophrenia/psychosis have a close relationship. We have evidence suggesting that cannabis use, primarily THC in cannabis, in genetically predisposed or at-risk populations, leads to earlier diagnosis of psychosis/schizophrenia. This tells us that THC in cannabis has a small causative effect on schizophrenia. THC in cannabis also makes schizophrenia and psychosis symptoms worse and causes more relapses and hospitalizations. Neuroimaging studies show the detrimental effect of cannabis on brain morphology, especially adolescent brains. Recent trials in therapeutic CBD use are showing its alleviating effect on positive symptoms of schizophrenia and its opposing effect on THC, which warrants further research.

Association of High-Potency Cannabis Use With Mental Health and Substance Use in Adolescence — May 2020. Globally, cannabis is the most commonly used internationally regulated drug, and policy on its use is becoming more liberal worldwide. The primary psychoactive component of cannabis is $\Delta 9$ -tetrahydrocannabinol (THC). The potency (concentration of THC) may be an important factor in the association between cannabis use and mental health. Experimental studies indicate that THC intoxication is dose dependent, with higher doses causing greater memory impairment and transient psychotic-like symptoms. Policy liberalization has been accompanied by proliferation of high-potency

cannabis in legal markets, and THC concentrations have increased in markets where cannabis remains illegal.

Cannabis / Marijuana (and other street drugs) Have Been Linked to Significant Increases in a Person's Risk for Schizophrenia – Schizophrenia.com summary updated 2020. Use of street drugs (including LSD, methamphetamine, marijuana/hash/cannabis) have been linked with significantly increased probability of developing schizophrenia. This link has been documented in over 30 different scientific studies (studies done mostly in the UK, Australia and Sweden) over the past 20 years. In one example, a study interviewed 50,000 members of the Swedish Army about their drug consumption and followed up with them later in life. Those who were heavy consumers of cannabis at age 18 were over 600% more likely to be diagnosed with schizophrenia over the next 15 years than those did not take it. Experts estimate that between 8% and 13% of all schizophrenia cases are linked to marijuana / cannabis use during teen years.

<u>Cannabis Probably Does Cause Schizophrenia</u> – 2020. Without a doubt, some portion of the link between earlier-life cannabis use and later-life schizophrenia risk comes from the acceleration of symptoms in those predestined to express them. However, there is a really good case to be made for the likelihood that regular cannabis use can cause schizophrenia-like illness de novo. In other words, regular cannabis use across a population probably does increase the number of schizophrenia cases above the natural background. We should make sure people know this.

Cannabis use among U.S. adolescents in the era of marijuana legalization – Feb. 2020.

Decriminalization, medicalization, and legalization of cannabis use by a majority of U.S. states over the past 25 years have dramatically shifted societal perceptions and use patterns among Americans. How marijuana policy changes have affected population-wide health of U.S. youth and what the downstream public health implications of marijuana legalization are topics of significant debate. Cannabis remains the most commonly used federally illicit psychoactive drug by U.S. adolescents and is the main drug for which U.S. youth present for substance use treatment. Converging evidence indicates that adolescent-onset cannabis exposure is associated with short- and possibly long-term impairments in cognition, worse academic/vocational outcomes, and increased prevalence of psychotic, mood, and addictive disorders.

Cannabis Use Disorder: no accepted medical purpose and a high potential for abuse – Jun. 2020. It should be stressed that continuous and/or heavy use of cannabis can increase the risk of intoxication or withdrawal requiring medical attention, and long term complications which may be irreversible. With the expansion of evidence-based uses, it is important to separate the abuse of marijuana from use with a thorough history taking. Differences in state regulations governing medical indications for cannabis should be considered. And providers should not forget that Medical Marijuana is a not product of the tightly regulated and scientifically back pharmaceutical industry – it is a product produced by growing operations without similar oversight and indicated for conditions mostly not based on rigorous medical or scientific evidence required for products they prescribe, as opposed to a permitted use.

<u>Causality of marijuana and schizophrenia video</u> – Feb. 2020. Cannabis is not necessarily the most dangerous drug, but cannabis has one of the largest gaps between actual level of harm and perceived level harm by the public. One of the biggest dangers of cannabis use is the development of psychotic thinking. Patients with cannabis-induced psychosis often don't see a connection between cannabis use and their psychotic state and often will continue to using and repeat the cycle of cannabis use and

psychosis. After a period of time, the brain can't always bounce back. According to research, 34 % of patients with cannabis-induced psychosis convert to having schizophrenia or another psychotic illness, which do not need the presence of actively using substances. Cannabis beats all other drugs in terms of its conversion rate.

Co-occurrence across time and space of drug- and cannabinoid- exposure and adverse mental health outcomes in the National Survey of Drug Use and Health — Dec 2020. Our interpretation of these results is that all four of the adverse mental health outcomes mapped geotemporospatially by SAMHSA are linked upon formal geospatial analysis with the use of all four of the addictive drugs for which data was available. On testing of single domains of variables against serious mental illness only the drug group was significant, whilst median household income and racial profiling were not. After adjustment for the usual battery of ethnic, drug use and socioeconomic covariates, terms including cannabis were significantly linked with all four domains of mental ill-health from a high level of statistical significance, implying that the widespread deployment of cannabis and cannabinoids for primarily commercial motivations is likely to carry with it major negative mental health implications for the future.

<u>Even One THC Hit Carries Risk for Inducing Psychosis</u> – March 2020. The psychoactive components of cannabis were linked to new-onset psychotic symptoms even at low doses, according to a systematic review and meta-analysis. Across nine studies involving 196 healthy young adults, tetrahydrocannabinol (THC) was associated with significantly increased total symptom severity on the Brief Psychiatric Rating Scale compared with placebo.

Heavy Pot Use Linked to Mental Problems Even After Quitting – May 2020. Marijuana dependence goes hand in hand with poor mental health, and problems may persist long after stopping the drug, according to Canadian researchers. Nearly half of people who have been or are now dependent on pot have some form of mental illness or dependence on another substance, according to a report this month in the journal Advances in Preventative Medicine. That compares with 8% of people with no history of pot dependence have mental illness or another drug or alcohol addiction. Lead author Esme Fuller-Thomson said the study doesn't answer which came first, marijuana dependence or mental illness, nor does it prove heavy pot use causes mental problems, but it does show a strong link.

Management of Psychosis in the Context of Cannabis Use: Beyond the Chicken or the Egg Question – June 2020. Cannabis use is not the only factor that increases the risk of psychosis. Most heavy cannabis users will never develop the disorder, which stems from multiple factors such as genetic, trauma, immigration, birth complications, and others. That being said, multiple studies have associated cannabis use with a greater risk of developing a psychotic disorder like schizophrenia, more so when use is frequent and if products used contain high THC levels.

Marijuana & Mental Health – Smart Approaches to Marijuana – 2020. As commercialization increases in legalized states, false advertising of marijuana products as being "natural" and "healthier than alcohol and tobacco" have greatly decreased the perceived risk of harm related to marijuana use. The main psychoactive ingredient in marijuana, THC, has now been observed to cause many different types of mental and physiological health problems— especially in children and youth. Marijuana use directly affects the brain — specifically the parts of the brain responsible for memory, learning, attention and reaction time. These effects can last up to 28 days after abstinence from use. Science confirms that the adolescent brain — particularly the part of the brain that regulates planning for complex cognitive behavior, personality expression, decision making and social behavior — is not fully

developed until the early to mid-20s. Developing brains are especially susceptible to all of the negative effects of marijuana and other drug use.

Marijuana, but not alcohol, use frequency associated with greater loneliness, psychological distress, and less flourishing among young adults — Nov. 2020. Greater frequency of marijuana use was associated with higher levels of loneliness, higher levels of psychological distress, and lower levels of flourishing, with the greatest difference observed for daily marijuana users compared to non-users. However, these indicators of well-being did not significantly differ by levels of alcohol use frequency. Study findings suggest that frequent users of marijuana, but not alcohol, may experience more loneliness, more psychological distress, and less flourishing. Intervention approaches for frequent marijuana users may be warranted to reduce impacts of loneliness and psychological distress and improve overall well-being.

Mental Health and Substance Use Disorders — Apr. 2020. For people under the age of 18, the term "Serious Emotional Disturbance" refers to a diagnosable mental, behavioral, or emotional disorder in the past year, which resulted in functional impairment that substantially interferes with or limits the child's role or functioning in family, school, or community activities. Substance use disorders occur when the recurrent use of alcohol and/or drugs causes clinically significant impairment, including health problems, disability, and failure to meet major responsibilities at work, school, or home. The coexistence of both a mental health and a substance use disorder is referred to as co-occurring disorders. The National Institute for Mental Health's Mental Health Information page has information about specific conditions and disorders as well as their symptoms.

New Approach to Lessen Negative Symptoms in Schizophrenia is Based on Brain Circuit Discovery

– Jan. 2020. Negative symptoms in schizophrenia and schizophrenia spectrum disorders impact a variety of cognitive processes that result in a flattening of emotional expression, diminished motivation, behavioral rigidity, and difficulty experiencing pleasure. They are distinguished from positive symptoms, which refer to patients' altered relationship with reality, including experiences such as hallucinations, delusions, and paranoia. While positive symptoms can be diminished through the administration of antipsychotic medicines, there are no pharmaceutical treatments to address negative symptoms. Other forms of therapy have shown promise, including various methods of cognitive training, but they are not widely used at this time.

Novel Insights on Cannabis and Psychosis – July 2020. Moore and colleagues performed a systematic review of 35 studies of cannabis use and risk of psychotic mental health outcomes. They found that individuals who had used cannabis had a significant, 1.4-fold increased risk of any psychotic outcomes, independent of potential confounding and transient intoxication effects. Findings also provided evidence for a dose-response effect, with even greater, 2.1-fold risk in individuals who used cannabis most frequently. More recently, Marconi and colleagues performed a meta-analysis of 10 studies, including 66,810 individuals, which investigated the association between the degree of cannabis consumption and risk of psychosis. In all individual studies, higher levels of cannabis use were associated with increased risk of psychosis.

<u>Our very long story: marijuana is addictive</u> – Feb. 2020. A mom, whose son was addicted to cannabis as a teen, shares her thoughts: "We fell for many of the myths perpetuated by the pro-cannabis community. We believed that it was harmless, because "everyone his age is using it." We didn't know about the new high potency THC available today. We didn't know that is was affecting the pruning

of synapses of developing brains, and that it was THE number one environmental factor triggering schizophrenia. We didn't know that it was addictive. Commercialization of cannabis is normalizing its use, and its use is contributing to the anxiety and depression and increased suicide rates of our son's generation. We wanted to believe our friends and the press. Education about the risks of using cannabis and the testing of safety limits are crucial for the health of our next generation."

Persistent Cannabis Use Among Young Adults with Early Psychosis Receiving Coordinated Specialty Care in the United States — Marino, May 2020. Persistent cannabis use among young adults with first episode psychosis (FEP), even those receiving early intervention services, has been associated with poor outcomes. In the United States (US), Coordinated Specialty Care (CSC) has been shown to be more effective at reducing symptoms, improving quality of life and increasing involvement in work or school, compared to typical care for FEP. This study suggests that cannabis use is common among young adults enrolled in a CSC program in the US and that persistent cannabis users may have worse outcomes while reducing cannabis use may improve outcomes. These findings highlight the potential impact of secondary prevention in this population through reduction in cannabis use.

<u>Single joint linked with temporary psychiatric symptoms, review finds</u> – Mar. 2020. A review of existing research published Tuesday found that a single dose of the main psychoactive ingredient (THC) in cannabis — equal to one joint — in otherwise healthy people, can temporarily induce psychiatric symptoms, including those associated with schizophrenia. People who use cannabis recreationally should continue to be careful when using the drug because of the potential harms to mental health which can be associated with the drug.

The Marijuana Market As An "Essential Service" Threatens Everyone – Apr. 2020. It is ironic, when confronted with a disease that destroys respiratory function, that states such as Michigan, Nevada, Colorado and California support the continued consumption of high-potency (THC-laden) marijuana plants and concentrates as an "essential" activity, even though the product is consumed by smoking, vaping, or butane-fueled combustion, often multiple times a day. Moreover, the decisions often rely on states using a double standard for what counts as a "necessary medicine." When confronted with proposals to dispense some drugs with the potential to protect against COVID-19 infection, public health officials warn that there have not been adequate demonstrations of effectiveness against the virus by the high standards of clinical trials. Yet this reasonable scientific standard is simply thrown out when the drug in question is marijuana. In fact, access to raw marijuana is being fostered despite the absence of any convincing clinical trial outcomes showing safety or effectiveness of its use for any medical condition, sufficient for it to become a prescribe-able, FDA-approved medication.

The perils of recreational marijuana use: relationships with mental health among emergency department patients – June 2020. Participants who used marijuana more frequently reported more days of anxiety. Among participants with mental health conditions, most began using marijuana before the onset of the mental health conditions. Earlier age of starting to use marijuana was correlated with higher number of years of anxiety or tension in lifetime. Perceived effects of marijuana use on mental health were variable. Most participants stated that marijuana improved their mental health, and some reported that marijuana did not improve their mental health.

THINK YOUR TEEN'S POT SMOKING IS NO BIGGIE? STUDIES SHOW IT CAN TRIGGER PSYCHOSIS – Amen Clinic May 2020. A wealth of research shows that cannabis not only harms the teenage brain, but findings also suggest that regular use of marijuana is associated with a higher risk of psychosis. The risk is even greater in people who start smoking at a young age.

<u>Trump Takes a Stand for the Mentally III</u> – Feb. 2020. Hundreds of thousands of Americans with serious mental illness sleep in jails, shelters and prisons on any given night. Fewer than 40,000 are in state psychiatric hospitals. This is largely due to a federal policy, the Institutions for Mental Disease Exclusion, which created a financial incentive for states to kick the mentally ill out of hospitals. The White House's new budget proposes easing the exclusion. It's the most important thing federal government could do to improve care for the seriously mentally ill.

Users of High-Potency Cannabis Four Times More Likely to Report Associated Problems – Science Daily May 2020. People who use cannabis are more likely to report mental health problems than those who don't use cannabis, but reducing the potency and regularity of their cannabis use may be effective for lessening likelihood of harms from use. In countries where cannabis is sold legally, limiting the availability of high-potency cannabis may reduce the number of individuals who develop cannabis use disorders, prevent cannabis use escalating to a regular behavior, and reduce impacts on mental health. In countries like the UK, where we are not able to limit the availability of high-potency cannabis, we should make sure there is good treatment and support for those who develop problems from cannabis use. What to Do If You Suspect Your Teen Has a Mental Illness Apr. 2020. Mental health issues are usually very treatable. And a problem doesn't mean your teen is "crazy." Instead, it means your teen needs medical attention. Similar to the way some teens develop physical health problems, like asthma or acne, others develop mental health problems, like obsessive-compulsive disorder or bipolar disorder. Stay calm, but take action. Rather than spend months worrying about a potential problem, commit to finding out if your teen could benefit from treatment.

Will Legalization and Commercialization of Cannabis Use Increase the Incidence and Prevalence of Psychosis? Murray & Hall, April 2020. There is a worldwide trend toward liberalizing cannabis policy and commercializing its sale. Uruguay legalized recreational cannabis in 2013, as did Canada in 2018, as well as 10 US states. Other countries have decriminalized the drug. In Holland, cannabis can be bought in designated cafes, and in Portugal, the police refer those who regularly use cannabis for counseling. Psychiatrists have played a prominent role in the debate over the health consequences of legalization in many countries, especially in the UK, but the public debate in the US has been notable for the absence of input from psychiatrists.

2019

Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood – Feb. 2019. Longitudinal and prospective studies, assessing cannabis use in adolescents younger than 18 years (at least 1 assessment point) and then ascertaining development of depression in young adulthood (age 18 to 32 years) were selected, and odds ratios (OR) adjusted for the presence of baseline depression and/or anxiety and/or suicidality were extracted. The studies assessing cannabis use and depression at different points from adolescence to young adulthood and reporting the corresponding OR were included. In the studies selected, depression was diagnosed according to the third or fourth editions of Diagnostic and Statistical Manual of Mental Disorders or by using scales with predetermined cut-off points.

<u>Before Maryland Legalizes Marijuana, It Should Consider This: Pot is Linked to Psychosis</u> – Miller April 2019. Before Maryland legalizes marijuana it should consider this: Pot is linked to psychosis. There is evidence that heavy pot use, prolonged length of exposure and age at the beginning of exposure may all be risk factors in triggering a first episode of psychosis. Where mental illness — especially

schizophrenia — already exists, the report concludes, heavy and prolonged pot use may make symptoms worse.

Cannabis and Psychosis: Are We any Closer to Understanding the Relationship? Jun. 2019. It is sometimes difficult for individuals to distinguish between cannabis and tobacco dependence particularly when they are used in combination. So even when someone has psychosis thought to have been associated with cannabis use, they can struggle to abstain from cannabis. Little evidence exists as to how this group can be encouraged and supported to abstain from cannabis use with the aim of reducing the impact of psychosis on their lives. There is the opportunity to learn from those with psychosis who have successfully reduced or abstained completely from using cannabis.

<u>Cannabis and Psychosis Through the Lens of DSM-5</u> – Nov. 2019. In the present review we examine cannabis/psychosis associations as they pertain to Cannabis Intoxication, Cannabis-Induced Psychotic Disorder, and Schizophrenia. This allows for an understanding of the cannabis and psychosis association along something approaching a continuum. Cannabis intoxication becomes Cannabis-Induced Psychotic Disorder once certain severity and duration criteria are met and Cannabis-Induced Psychotic Disorder is heavily associated with future schizophrenia diagnoses.

Cannabis-related psychosis, addiction, ER visits: For young users, marijuana can be a dangerous game

– Dec. 2019. The National Institute on Drug Abuse cites research that suggests between 9% and 30% of people who use marijuana may develop use disorder, and the risk increases the younger someone starts using. Individuals who begin using cannabis before age 18 are four to seven times more likely than adults to develop marijuana use disorder. And the likelihood is that more young people will be impacted; two studies published earlier this month in the Journal of the American Medical Association found that more teenagers are vaping cannabis than ever before.

<u>Daily Marijuana Use and Highly Potent Weed Linked To Psychosis</u> – Mar. 2019. The study found that those who used pot daily were three times more likely to have a psychotic episode compared with someone who never used the drug. Those who started using cannabis at 15 or younger had a slightly more elevated risk than those who started using in later years. Use of high-potency weed almost doubled the odds of having psychosis compared with someone who had never smoked weed. And for those who used high-potency pot on a daily basis, the risk of psychosis was even greater — four times greater than those who had never used.

Even a Little Marijuana May Change Teen Brain, Study Finds – January 2019. We need to carefully balance enquiry into cannabis and schizophrenia between neurophysiology and the social aspects of cannabis psychosis. Attention and research funding leans towards the biological hypothesis at the expense of the cultural. As cannabis use and the development of psychosis are both influenced by social as well as biological factors, it is important that we keep pursuing a balanced blend of enquiry. Dose and frequency of cannabis use continue to be reliable indicators in the risk of developing psychosis. As an increasing number of American states allow access to cannabis for recreational or medicinal purposes, this presents a large naturalistic experiment involving these populations, it will be some years before we can judge the impact of these regulatory changes on health and incidence and prevalence of psychosis in particular.

<u>Grey Matter Volume Differences Associated with Extremely Low Levels of Cannabis Use in</u>
<u>Adolescence</u> – March 2019. Almost 35% of American 10th graders have reported using cannabis and

existing research suggests that initiation of cannabis use in adolescence is associated with long-term neurocognitive effects. We understand very little about the earliest effects of cannabis use, however, because most research is conducted in adults with a heavy pattern of lifetime use. This study presents evidence suggesting structural brain and cognitive effects of just one or two instances of cannabis use in adolescence. Converging evidence suggests a role for the endocannabinoid system in these effects. This research is particularly timely as the legal status of cannabis is changing in many jurisdictions and the perceived risk by youth associated with smoking cannabis has declined in recent years.

Is Marijuana Linked to Psychosis, Schizophrenia? It's Contentious, but Doctors, Feds Say Yes – Dec. 2019. More research and stricter regulation would improve both the quality and the fact-based promotion of cannabis. The information would help legislators better determine if the benefits of legalization outweigh the risks. Many marijuana users are familiar with the possibility that smoking cannabis can cause paranoia, and paranoia is a textbook definition of an episode of psychosis, along with hallucinations and a distorted sense of reality. One of the biggest problem is that people think THC is a panacea cure for conditions, and they use an exorbitant amount of it despite a lack of research to back it.

<u>Legalized Cannabis in Colorado Emergency Departments: A Cautionary Review of Negative Health and Safety Effects</u> – Jul. 2019. ED visits and hospitalizations with marijuana-related billing codes have increased following legalization. Mental illness represents a concerningly large number of marijuana-related visits. Between 2000 and 2015, hospitalization rates increased 116% from 274 to 593 per 100,000 hospitalizations. For primary diagnosis categories, the prevalence of mental illness was five-fold higher for ED visits and nine-fold higher for hospital admissions for patients with marijuana-related billing codes compared to those without. This data compared diagnostic categories between patients with a marijuana-related diagnostic code and those without.

Psychotic disorders hospitalizations associated with cannabis abuse or dependence: A nationwide big data analysis — October 2019. The number of hospitalizations with a primary diagnosis of PD and schizophrenia associated with CU rose 29.4 times during the study period, from 20 to 588 hospitalizations yearly (2000 and 2015, respectively) with a total of 3,233 hospitalizations and an average episode cost of €3,500. Male patients represented 89.8% of all episodes, and the mean/median age at discharge were 30.66/29.00 years, respectively. From all hospitalizations with a primary diagnosis of PD or schizophrenia, the ones with a secondary diagnosis of CU rose from 0.87% in 2000 to 10.60% in 2015. Conclusions: The increase on secondary diagnosis coding and the change on cannabis patterns of consumption in Portuguese population with an increasing frequency of moderate/high dosage cannabis consumers may explain the rise on PD hospitalizations.

Teen marijuana vaping is on the rise, a new report says, threatening to 'undo years of progress' – Dec. 2019. The increased use by teens of marijuana, especially by vaping, which can more than double the potency, comes during what Volkow called young people's "period of greatest vulnerability" of brain development. One student reports that alcohol is much harder for underage teens to get than pot, which people are getting far more excited about and accepting of. High schooler know that alcohol makes you feel good but causes serious harm to your body over time, gives you hangovers, and can kill you at large consumption. Nearly no one knows about the risks of psychosis associated with marijuana. Teenagers tend to think they will get all the feel goods of alcohol and the calm without any of the negative after effects of alcohol.

Tell Your Children: Marijuana, Mental Illness, and Violence – Jan. 2019. Advocates for people with mental illness do not like discussing the link between schizophrenia and crime. They fear it will stigmatize people with the disease. Most people with mental illness are not violent, but wishing away the link can't make it disappear. In truth, psychosis is a shockingly high risk factor for violence. The best analysis came in a 2009 paper in PLOS Medicine by Dr. Seena Fazel, an Oxford University psychiatrist and epidemiologist. Drawing on earlier studies, the paper found that people with schizophrenia are five times as likely to commit violent crimes as healthy people, and almost 20 times as likely to commit homicide.

The Contribution of Cannabis Use to Variation in the Incidence of Psychotic Disorder Across Europe (EU-GEI): a Multicentre Case-Control Study – Marta Di Forti, The Lancet, May 2019. Frequency of use and type of cannabis used were combined to generate a single-measure of frequency plus type of use because these two measures had the highest ORs. Adjusted logistic regression indicated that daily use of high-potency cannabis carried more than a four-times increase in the risk of psychotic disorder compared with never having used cannabis; the odds were lower for those who used low-potency cannabis daily. Transition of Substance-Induced, Brief, and Atypical Psychoses to Schizophrenia: A Systematic Review and Meta-analysis – Oct. 2019. Substance-induced psychoses are common and serious conditions. They are associated with a substantial risk for transition to schizophrenia. The risk of transition to schizophrenia is particularly increased following cannabis-induced psychosis, which should be responded to with assertive attempts at engagement, assessment, and care.

2018

Acute Mental Health Symptoms in Adolescent Marijuana Users -Dec. 2018. The association between marijuana use during adolescence and poor adult outcomes has been well documented, and there is a strong association between its use and the development of mental health problems and psychotic disorders. 6 Marijuana use is also associated with psychotic symptoms related to intoxication. The association between these phenomena is poorly understood. Experiencing acute psychotic symptoms while using marijuana may be a marker of risk for developing a psychotic disorder in the future.

Adolescent cannabis use, baseline prodromal symptoms and the risk of psychosis – Jan. 2018. Adolescent cannabis use is associated with increased risk of psychosis even after adjustment for baseline prodromal symptoms, parental psychosis and other substance use (in as little as 5 times using). Current evidence indicates that early-onset cannabis use predates the onset of psychosis, especially among those with pre-existing vulnerability and heavier cannabis use. Cannabis-use disorder has been associated with greater psychosis conversion, independently of other forms of substance use.

Association of Cannabis Use With Adolescent Psychotic Symptoms — August 2018. An annual survey of 3,720 adolescents obtained self-reports of past-year cannabis use and psychotic symptoms over four years, from age 13 to 16. The findings demonstrated a clear association of cannabis use frequency with increased psychotic symptoms, and not vice versa. Cannabis use in any given year was found to predict an increase in psychotic symptoms a year later, and not the other way around.

Association of Substance Use Disorders With Conversion From Schizotypal Disorder to Schizophrenia – June 2018. In this Danish nationwide, register-based cohort study that identified 2539 participants with incident schizotypal disorder, any substance use disorder was associated with conversion to

schizophrenia at a rate of 33.1%; for cannabis use disorders, the conversion rate was 58.2%. Results were statistically significant after controlling for confounders.

<u>Can Drugs Cause Schizophrenia?</u> – May 2018. This is a Joe Rogan interview on marijuana-related psychosis. Marijuana can trigger psychosis and schizophrenia. This is especially a danger for individuals pre-disposed to schizophrenia because of age, family history, etc. Suggestions in this video are given for ways to regulate the drug-use. <u>Cannabis and Psychosis – what do we know and what should we do?</u> Robin Murray – 2018. Cannabis is used by approximately 200 million people across the world. The current trend to popularize its medicinal properties, real and imagined, and to decriminalize or legalize it in many countries, is likely to be followed by greater use. However, cannabis is not as safe as was once thought. Just as longitudinal studies of tobacco smokers versus non-smokers nailed the link between cigarettes and lung cancer, so similar prospective studies have shown that heavy cannabis use carries with it an increased risk of psychosis.

Cannabis consumption and psychosis or schizophrenia development – Nov. 18, 2018. Cannabis consumption appeared to be significantly associated with positive symptoms of psychosis, even after adjusting for the use of other drugs, depressive symptoms, gender and education; negative symptoms were also associated with the frequency of use of cannabis. Additionally, a great difference was described between patients who had initiated consumption before and after the age of 15 years, for both symptoms, positive and negative (Stefanis et al., 2004). The authors concluded that cannabis contributes to the expression of psychosis, particularly the exposure to cannabis at early ages, such as consumption onset during adolescence, and increases the risk of experiencing positive and negative symptoms of psychosis (Stefanis et al., 2004).

Genetic vulnerability to schizophrenia is associated with cannabis use patterns during adolescence – Sept. 2018. Our findings support a relation between genetic risk to schizophrenia and prospective cannabis use patterns during adolescence. In contrast, no relation between alcohol and smoking was established.

GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal influence of schizophrenia – April 2018. Cannabis is a widely used psychoactive substance, and its use is associated with various adverse mental health outcomes, including psychosis and schizophrenia1–3. Successful prevention and intervention efforts aimed at reducing cannabis use, misuse and related outcomes require a better understanding of why some people use cannabis whereas others do not. Lifetime cannabis use, defined as any use of cannabis during lifetime, is a heritable trait: a meta-analysis of twin studies4 estimated the heritability to be approximately 45%. Twin studies have shown there is substantial overlap in the genetic factors influencing cannabis use and those underlying problematic cannabis use (abuse or dependence).

The Problem with the Current High Potency THC Marijuana from the Perspective of an Addiction Psychiatrist – December 2018. If states continue to commercialize marijuana as has been done in Colorado we are destined to see many more people requiring treatment for addiction, depression, anxiety, suicidal ideation, and psychosis. We need to continually educate every one of the risks and increase prevention efforts to prevent children and adolescents from initiating marijuana use. This should include a strong ban on any advertising that appears to be directed toward youth – for all drugs including marijuana, tobacco, and alcohol. States will need to commit to increased funding for and availability of treatment options. The strongest recommendation would be to initiate regulations to

limit the concentration of THC. Ideally this would be to less than 10% as there is no good research on concentrations greater than this for any medical condition and there is significant literature on the negative effects of high potency THC.

2017 and later

Adolescent brain maturation, the endogenous cannabinoid system and the neurobiology of cannabis-induced schizophrenia — February 2010. Etiology: cannabis hampers the protective action of the endogenous cannabinoid system during a vulnerable period: adolescence. Pathogenesis: lack of a protective system during sensitive periods of brain maturation of specific areas within the prefrontal cortex causes a disturbed neurotransmitter release (glutamate/GABA), affecting the strengthening and pruning process of synapses and dendrites. Pathology: misshapen local cortical neurocircuitries within the prefrontal cortex due to mistakenly connected or lacking neural connections. Pathophysiology: disturbed control (excitation and inhibition) of cortical and subcortical neural networks by the affected circuitries in the prefrontal cortex. Symptoms: disturbed neurotransmission in the projection areas of the affected prefrontal cortical areas, e.g. overactive dopamine in the striatum, or hypoactive dopamine in the prefrontal cortex.

Association of Cannabis Use with Hospital Admission and Antipsychotic Treatment Failure in First Episode Psychosis: an Observational Study – Patel, Oct. 2016. Our findings suggest that patients with a history of cannabis use recorded at presentation to an early intervention service were more likely to be admitted to hospital, to require compulsory admission to hospital, and to spend longer in hospital in the 5 years following presentation. We demonstrated an association between cannabis use and the number of different antipsychotics prescribed during the follow-up period (a proxy marker for treatment failure). Finally, the association between cannabis use and the number of unique antipsychotics was found to mediate the increased risk of subsequent hospitalization, particularly with respect to number of days spent in hospital.

A Synopsis of the Numerous Studies Supporting an Causal Relationship between Marijuana

Use and The Chronic Psychotic Disorder Schizophrenia – 2015. The psychotomimetic effects
of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis.

Neuropsychopharmacology. Δ-9-THC (1) produced schizophrenia-like positive and negative symptoms;
(2) altered perception;(3) increased anxiety; (4) produced euphoria; (5) disrupted immediate and delayed word recall, sparing recognition recall; (6) impaired performance on tests of distractibility, verbal fluency, and working memory (7) did not impair orientation; (8) increased plasma cortisol.

These data indicate that D-9-THC produces a broad range of transient symptoms, behaviors, and cognitive deficits in healthy individuals that resemble some aspects of endogenous psychoses."

Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia — March 2012. Shows how breeding the CBD out of marijuana has contributed to the development of psychotic symptoms and schizophrenia, because cannabidiol does not activate cannabinoid receptors but moderately inhibits the degradation of the endocannabinoid anandamide. Furthermore, enhanced anandamide signaling led to a lower transition rate from initial prodromal states into frank psychosis as well as postponed transition. The reduction in anandamide due to a downregulation from THC binding to the CB1 receptor could be to blame for psychosis.

<u>Cannabis and first-episode psychosis: different long-term outcomes depending on continued or discontinued use</u> – May 2011. Those who don't quit cannabis have a worse course of repeated

psychotic episodes and are less likely to recover. Cannabis has a deleterious effect, but stopping use after the first psychotic episode contributes to a clear improvement in outcome. The positive effects of stopping cannabis use can be seen more clearly in the long term.

<u>Cannabis and schizophrenia</u>. A <u>longitudinal study of Swedish conscripts</u> – Dec. 1987. The association between level of cannabis consumption and development of schizophrenia during a 15-year follow-up was studied in a cohort of 45,570 Swedish conscripts. The relative risk for schizophrenia among high consumers of cannabis (use on more than fifty occasions) was 6.0 (95% confidence interval 4.0-8.9) compared with non-users. Persistence of the association after allowance for other psychiatric illness and social background indicated that cannabis is an independent risk factor for schizophrenia.

<u>Cannabis-Induced Psychosis: A Review</u> – July 2017. Cannabis is the most widely used illicit drug in the United States, and trends show increasing use in the general population. As cannabis consumption rises, there has been significant emerging evidence for cannabis-related risks to health. Numerous lines of evidence suggest a correlation between cannabis consumption and a variety of psychiatric conditions, including cannabis-induced psychosis (CIP). While it can be difficult to differentiate CIP from other psychoses, CIP holds distinguishing characteristics, which may aid in its diagnosis. Given the increasing push toward cannabis legalization, assessing CIP and employing timely treatments is critical. Specifically in youth, there is a direct relationship between cannabis use and its risks. The lack of knowledge surrounding its detrimental effects, combined with misunderstandings related to its therapeutic effects, has potential for catastrophic results.

Cannabis-induced psychosis associated with high potency "wax dabs" - April 2016. With mounting evidence that the risk of cannabis-induced psychosis may be related to both dose and potency of tetrahydrocannabinol (THC), increasing reports of psychosis associated with cannabinoids containing greater amounts of THC are anticipated. We report two cases of emergent psychosis after using a concentrated THC extract known as cannabis "wax," "oil," or "dabs" raising serious concerns about its psychotic liability. Although "dabbing" with cannabis wax is becoming increasingly popular in the US for both recreational and "medicinal" intentions, our cases raise serious concerns about its psychotic liability and highlight the importance of understanding this risk by physicians recommending cannabinoids for purported medicinal purposes. Cannabis users are 5.2 times as likely to develop Schizophrenia – Nov. 2016. Our findings confirm the association between abuse of cannabis and schizophrenia found in previous studies. However, we found an association between almost any type of substance abuse and the risk of developing schizophrenia, with alcohol abuse as the most surprising result, as there has not been much evidence of this before. I believe our findings opens up for many interesting studies regarding the association between alcohol abuse and schizophrenia. Alcohol is one of the substances most used in the world, however I believe it has not been thoroughly examined in the association with psychosis. We are currently looking at parental substance abuse and the offspring's risk of developing schizophrenia later in life.

Continued versus discontinued cannabis use in patients with psychosis: a systematic review and metaanalysis – March 2016. Continued cannabis use after onset of psychosis predicts adverse outcome, including higher relapse rates, longer hospital admissions, and more severe positive symptoms than for individuals who discontinue cannabis use and those who are non-users. These findings point to reductions in cannabis use as a crucial interventional target to improve outcome in patients with psychosis. <u>Familial Predisposition for Psychiatric Disorder</u> – Nov. 2008. Whether cannabis-induced psychosis is a distinct clinical entity is unclear. The existing knowledge base does not enable a firm hypothesis about the validity of the diagnosis. One way of investigating this subject is to evaluate data on familial predisposition to psychiatric disorders, and this was the purpose of the present study. First, we investigated whether cannabis-induced psychosis can be differentiated from schizophrenia on the basis of a history of psychiatric disorder in first-degree relatives. Second, we evaluated the absolute risk of having a diagnosis of schizophrenia spectrum disorder after treatment of a cannabis-induced psychosis subdivided by familial predisposition to psychiatric disorders.

<u>Psychotic Symptoms</u> – 2011. 40% of people develop symptoms of psychosis after administration of THC in the clinic. <u>Link between Adolescent Pot Smoking and Psychosis Strengthens</u> – Oct. 2017. "There is no doubt," concludes Robin Murray, a professor of psychiatry at King's College London, that cannabis use in young people increases the risk of developing schizophrenia as an adult. Speaking at the Berlin conference, Murray—one of the first scientists to research pot's link to the disorder—cited 10 studies that found a significant risk of young cannabis users developing psychosis. He also mentioned three other studies that identified a clear trend but had a sample size that was too small to reach statistical significance. "The more [cannabis] you take—and the higher the potency—the greater the risk," he contends, warning this makes the increasingly potent new strains of marijuana especially concerning.

Long lasting effects of chronic heavy cannabis abuse – Jun. 2017. The existence of hallucinations, delusions, and organic brain dysfunction in heavy cannabis users seems to be associated with cannabinoid levels in hair. The continuation of persistent symptoms 3 months after the discontinuation of cannabis abuse, was a remarkable finding. Scientific significance: We provide evidence that chronic and heavy cannabis abuse results in long-lasting brain dysfunction in all users and in long-lasting schizophrenia-like psychotic symptoms in more than half of all users. These findings suggest a reevaluation of the current classification of cannabis as a "soft narcotic" which erroneously, therefore, is typically considered harmless.

Marijuana Addictive Disorders: DSM-5 Substance-Related Disorders – Journal of Addiction Research & Therapy – Jan. 2017. Cannabis is most commonly smoked via a variety of methods including pipes, water pipes, cigarettes (joints or reefers) or, more recently, in the paper of hallowed out cigars (blunts) [3,4]. Cannabis is also sometimes ingested orally, typically by mixing into food. More recently, devices have been developed in which cannabis is vaporized. Individuals with cannabis use disorder may use cannabis throughout the day over a period of months or years and, thus, may spend many hours a day under the influence. Cannabis use affects work with repeated absences or increased risk working around dangerous situations. Arguments with spouses and other interpersonal relationship difficulties along with legal, medical, and mental health problems arise with cannabis use.

Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis – Feb. 2016. the heavier the marijuana use, and the more potent the product, the more likely a psychotic outcome like schizophrenia. The meta-analysis provides the most accurate estimate of the effect size of cannabis use as a risk factor for psychosis using all the available published data. In addition, it measures a dose-response relationship between the level of use and the risk for psychosis. Thus, for public policy, apart from prevention programs targeting cannabis use in general, harm minimization approaches aiming at dose reduction or later onset of use are also relevant in the prevention and treatment of psychosis.

Proportion of Patients in South London with First-Episode Psychosis Attributable to Use of High Potency Cannabis: a Case-Control Study — Lancet Feb. 2015. Our findings show the importance of raising public awareness of the risk associated with use of high-potency cannabis (panel), especially when such varieties of cannabis are becoming more available. The worldwide trend of liberalization of the legal constraints on the use of cannabis further emphasizes the urgent need to develop public education to inform young people about the risks of high-potency cannabis.

Rates and Predictors of Conversion to Schizophrenia or Bipolar Disorder Following Substance-Induced Psychosis – Nov. 2017. Overall, 32.2% (95% CI=29.7–34.9) of patients with a substance-induced psychosis converted to either bipolar or schizophrenia-spectrum disorders. The highest conversion rate was found for cannabis-induced psychosis, with 47.4% (95% CI=42.7–52.3) converting to either schizophrenia or bipolar disorder.

Risks of Increasingly potent Cannabis: The joint effects of potency and frequency – 2017. A number of studies have determined an association between Cannabis use and brain changes involving structures governing memory and emotional processing, including reduced volume of the hippocampus, temporal cortex, insula, and orbitofrontal cortex. Although many of these changes appear to be doserelated, some morphologic changes have been reported among young recreational users without Cannabis dependence. This has resulted in an understandable concern about the effects of Cannabis on the brains of young people with limited exposure; however, it is not yet clear to what extent detected brain changes are pathological and reflect functional deficits. Similar to any drug, the effects of THC and its psychiatric sequelae can be expected to increase with dosage. To date, much of the information about psychiatric risks has been based on studies of low- and moderate potency Cannabis rather than the much higher potency Cannabis products, such as hyper-concentrated "wax dabs," that are available today.

<u>Schizophrenia – latest research from the Brain and Behavior Foundation</u>. Some statistics to note are that 3.5 million adults (1.1%) of the US Adult population live with schizophrenia. More than 21 million people worldwide are affected by schizophrenia. This website is a link to many articles and information on Schizophrenia and the latest research from the Brain and Behavior Foundation.

<u>Seize the Awkward – talking to your friend about mental health</u>. This website offers tools from conversation guides to tips that can help you help those in need. Their message is: 'Don't be afraid to shatter the silence and seize the awkward.' Having a conversation about mental health might be uncomfortable, but it can make all the difference. You don't need to be an expert to recognize when someone needs outside help – if you can tell a friend isn't doing well, they might need a greater network of support. In times of uncertainty, connecting with friends and family can really help in managing feelings of fear and anxiety, and be good for your health.

<u>Significant link between cannabis use and onset of mania symptoms</u> – Feb. 2015. Our review suggests that cannabis use is a major clinical problem occurring early in the evolving course of bipolar disorder. More research is needed to consider specific pathways from cannabis use to mania and how these may be effected by genetic vulnerability and environmental risk factors. Cannabis is the most prevalent drug used by the under-18s and during this critical period of development services should be especially aware of and responsive to the problems that cannabis use can cause for adolescent populations.

<u>Substance-Induced Psychoses Converting Into Schizophrenia: A Register-Based Study of 18,478 Finnish Inpatient Cases</u> – 2013. Eight-year cumulative risk to receive a schizophrenia spectrum diagnosis was 46% (95% CI, 35%-57%) for persons with a diagnosis of cannabis-induced psychosis and 30% (95% CI, 14%-46%) for those with an amphetamine-induced psychosis. Meaning, between LSD and cannabis, it is cannabis that is the recreational drug most likely to result in conversion to a permanent psychotic disorder (schizophrenia spectrum disorder) that won't go away after use is stopped.

The Maturing Brain and Schizophrenia – Dec. 2005. To date, much of the discussion around teenagers has focused on why so many change from adorable children into sometimes moody pre-adults. But the latest research has focused on defining normal and tracking the changes that may trigger mental illnesses or strip the defenses of a mind already vulnerable to psychiatric disease. The key is to figure out who is vulnerable in time to change the course of brain development and head off the disease or reduce the devastation caused by mental illnesses. There is no question that the brains of people with schizophrenia and bipolar disorder look and work differently from those of their healthy peers. And those changes probably start earlier than most people suspect. It now seems that some people may be genetically predisposed to develop illness, but the defect does not become apparent until the brain matures. Stress, drugs, and other brain traumas are also known to trigger schizophrenia in people who are genetically predisposed to the disorder.

The psychotomimetic effects of intravenous delta-9-tetrahydrocannabinol in healthy individuals: implications for psychosis – Aug. 2004. Recent advances in the understanding of brain cannabinoid receptor function have renewed interest in the association between cannabinoid compounds and psychosis. In a 3-day, double-blind, randomized, and counterbalanced study, the behavioral, cognitive, and endocrine effects of 0, 2.5, and 5 mg intravenous delta-9-tetrahydrocannabinol (Delta-9-THC) were characterized in 22 healthy individuals, who had been exposed to cannabis but had never been diagnosed with a cannabis abuse disorder. These data indicate that Delta-9-THC produces a broad range of transient symptoms, behaviors, and cognitive deficits in healthy individuals that resemble some aspects of endogenous psychoses. These data warrant further study of whether brain cannabinoid receptor function contributes to the pathophysiology of psychotic disorders.