#### 1. Is marijuana addictive for teens?

Yes, 17% of those who began their use in adolescence become addicted, and up to about 50% of those who become daily users end up with addiction: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4827335/pdf/nihms762992.pdf Obvious withdrawal symptoms are experienced when heavy users cease their habit: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146100/ How long the most obvious symptoms of withdrawal last can be found here: https://pubmed.ncbi.nlm.nih.gov/15514394/ The risk of persisting marijuana use is greater if the product is high in THC concentration: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6991277/ To understand the how many teens this may affect, in 2019, 22% were using at least monthly by the time they reached 12th grade: http://www.monitoringthefuture.org/pubs/monographs/mtf-vol1\_2019.pdf And 6.4% were using daily: https://www.drugabuse.gov/sites/default/files/nida\_mtfinfographic2019\_fullgraphic.pdf In the U.S., dependence on marijuana has increased more than dependence on any other drug: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2797098/pdf/ascp-04-1-4.pdf

## 2. What is the difference between a habit and an addiction?

A sign that a habit has morphed into an addiction is to see continued usage despite the occurrence of life-altering negative consequences. To quote Dr. George Koob, head of the National Institute on Alcohol Abuse and Alcoholism "A healthy brain rewards healthy behaviors—like exercising, eating, or bonding with loved ones. It does this by switching on brain circuits that make you feel wonderful, which then motivates you to repeat those behaviors......But when you're becoming addicted to a substance, that normal hardwiring of helpful brain processes can begin to work against you. Drugs or alcohol can hijack the pleasure/reward circuits in your brain and hook you into wanting more and more. Addiction can also send your emotional danger-sensing circuits into overdrive, making you feel anxious and stressed when you're not using the drugs or alcohol. At this stage, people often use drugs or alcohol to keep from feeling bad rather than for their pleasurable effects." https://newsinhealth.nih.gov/sites/nihNIH/files/2015/October/NIHNiHOct2015.pdf

## 3. How can marijuana be addictive and a gateway drug at the same time?

This can happen because the pathways to addiction with different drugs share common features: <u>http://accurateclinic.com/wp-content/uploads/2016/01/The-Addictive-Brain-All-Roads-Lead-to-Dopamine-2012.pdf</u>

The common mechanism via dopamine is also the case for the effect of THC: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5123717/pdf/emss-70462.pdf</u>

When marijuana can no longer excite the common pathway as the drug's receptors become desensitized, the user switches to a new drug. The addiction to marijuana is no longer satisfying. Research has confirmed that marijuana acts as a gateway drug for many users: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3552239/pdf/nihms388189.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3552239/pdf/nihms388189.pdf</a>

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4291295/pdf/nihms-618789.pdf https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5537531/pdf/jech-2016-208503.pdf

#### 4. What are some of the ways in which marijuana influences adolescent brain development?

The best studies are those that follow the same individuals over time (longitudinal), so they know the baseline starting point for each person.

For microstructural effects on white matter in the brain: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4691379/pdf/main.pdf For effects on brain connectivity: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5963818/pdf/bhw015.pdf The superior frontal gyrus is thought to be important for higher cognitive functions and working memory: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6670783/pdf/fpsyt-10-00514.pdf For the science on IQ decrements: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3479587/pdf/pnas.201206820.pdf https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5963818/pdf/bhw015.pdf and cognitive impairment: https://ajp.psychiatryonline.org/doi/pdf/10.1176/appi.ajp.2018.18020202 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6821511/pdf/44-6-414.pdf

#### 5. At what age can the brain be considered fully mature?

The late twenties: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6623097/pdf/zns10937.pdf

# 6. What are some of the psychological symptoms that adolescents might try to treat with marijuana, and does it help (e.g. anxiety, depression, ADHD)?

The ability of a drug to transiently exert an effect that causes a person to essentially forget about negative symptoms they are experiencing is important to distinguish from the drug's long-lasting impact.

As a case in point, it is commonly thought that using marijuana reduces anxiety by making you more relaxed. While that can be a short-term effect, the long-term impact can be quite the opposite: anxiety or outright panic becomes worse, almost uniformly during intervals between uses (withdrawal effects):

https://pubmed.ncbi.nlm.nih.gov/12943018/ and in many individuals, even while using: https://pubmed.ncbi.nlm.nih.gov/17314727/ https://www.sciencedirect.com/science/article/abs/pii/S037687169601277X?via%3Dihub as confirmed by administering THC in the clinic: https://pubmed.ncbi.nlm.nih.gov/6285406/

Marijuana use has been shown to double the risk for depression in a rigorous study of twins: <u>https://pubmed.ncbi.nlm.nih.gov/28750823/</u>

With respect to Attention Deficit Hyperactivity Disorder (ADHD), this may be the sole example of a well-studied behavioral disorder which generally precedes marijuana use, not vice versa. It is widely acknowledged that ADHD makes substance use of all kinds more likely: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4120046/pdf/nihms592423.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4120046/pdf/nihms592423.pdf</a> and that the gateway model of drug use is accelerated in those with ADHD: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4180292/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4180292/</a>

It is worth noting that the stimulant drugs used to treat ADHD may play a role in susceptibility to substance abuse *if treatment is commenced in the teens* (rather than earlier) as discussed in this review article ("initiation of stimulant medication (methylphenidate in particular) for ADHD during adolescence may have negative consequences with respect to later SUD"): <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4864167/pdf/nihms774724.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4864167/pdf/nihms774724.pdf</a>

Although rigorous studies of marijuana's impact on ADHD symptoms are difficult to find in the literature, it has been reported that marijuana-using youth and young adults with ADHD exhibit more severe symptoms:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3390681/

#### 7. Is it true that marijuana triggers transient psychotic episodes?

Yes. Even with the low strength pot common in the last century, 15% of users reported psychotic episodes: <u>https://www.sciencedirect.com/science/article/abs/pii/S037687169601277X?via%3Dihub</u>

But the proof would have to await studies in the clinic, where it was found that administration of a moderate dose of pure THC would elicit transient psychotic symptoms in study subjects: <u>https://www.nature.com/articles/1300496.pdf</u> <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3055738/pdf/npp2010222a.pdf</u> <u>https://jamanetwork.com/journals/jamapsychiatry/fullarticle/1107444</u> <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4332941/pdf/sbu098.pdf</u>

## 8. Is there also a link to chronic psychosis (schizophrenia) in adolescent use?

Yes, and not just in adolescents. For a long while, the psychiatric community was unsure of the causal basis for the connection, because studying cause and effect is a complicated endeavor. It was important to find out if there was a greater effect at higher dose, which would indicate causality, and such a relationship was confirmed:

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(87)92620-1/fulltext https://www.ncbi.nlm.nih.gov/pmc/articles/PMC135493/pdf/1212.pdf https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3877688/pdf/nihms534094.pdf https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(14)00117-5/fulltext https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4988731/

Another element of the causal connection was to determine which came first, the marijuana use or the psychosis:

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC539839/pdf/bmj33000011.pdf https://www.cambridge.org/core/services/aop-cambridge-

core/content/view/D5CAA12A5F424146DABB9C6A6AB4CB56/S0007125017000526a.pdf/adolescen t cannabis use baseline prodromal symptoms and the risk of psychosis.pdf Those at the forefront of such studies were eventually convinced that the association was causal: <a href="https://www.researchgate.net/publication/323899315">https://www.researchgate.net/publication/323899315</a> Cannabis and psychosis What do we kno w and what should we do

The consensus is that use of marijuana with a THC content over 10% increases the risk of a psychotic disorder by 4 to 5-fold: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4988731/</u> <u>https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(14)00117-5/fulltext</u>

# 9. How does marijuana compare to other drugs that are associated with psychosis (LSD, cocaine, amphetamine, methamphetamine, PCP)?

Marijuana is more likely to lead to chronic psychosis than any other drug studied. About half of those who experience a marijuana-induced psychotic break will eventually develop a schizophrenia spectrum disorder:

https://www.psychiatrist.com/jcp/article/Pages/2013/v74n01/v74n0115.aspx https://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2017.17020223?rfr\_dat=cr\_pub%3Dpub med&url\_ver=Z39.88-2003&rfr\_id=ori%3Arid%3Acrossref.org&journalCode=ajp

#### 10. Does marijuana use lead to suicidal tendencies in some adolescents?

Yes. Two independent studies came up with a very similar elevation in risk (nearly 7-fold): <u>https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(14)70307-4/fulltext</u> <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4219077/pdf/wps0013-0322.pdf</u>

Part of the risk for suicide may be exerted through the mental disorders that marijuana triggers (as referenced previously), particularly psychotic disorders and depression: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4197787/pdf/cjp-2014-vol59-october-531-538.pdf</u>

However, there is also evidence that marijuana's effect can be more immediate from a recent study illustrating the likelihood of suicidal thoughts increased on the days when an adolescent uses marijuana:

https://www.sciencedirect.com/science/article/abs/pii/S0165178118323321?via%3Dihub

In Colorado, the THC positive toxicology screens in youth aged 15-19 have consistently increased over the past several years (while such data was being collected by the Colorado Department of Health), such that it became the leading drug found in suicide victims of that age range (32% were positive by 2017, about 1.5-fold higher than the average monthly use rate for that age group in Colorado):

https://cohealthviz.dphe.state.co.us/t/HSEBPublic/views/CoVDRS\_12\_1\_17/Story1?:embed=y&:sho wAppBanner=false&:showShareOptions=true&:display\_count=no&:showVizHome=no#4

Colorado has experienced an overall year-to-year increase in teen suicides: <u>https://www.cpr.org/2019/09/17/the-rate-of-teen-suicide-in-colorado-increased-by-58-percent-in-</u><u>3-years-making-it-the-cause-of-1-in-5-adolescent-deaths/</u> Although the rate of teen use has not increased that much in Colorado, the potency of what is used by youth in states with legalized marijuana has increased markedly: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5534375/pdf/nihms880035.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5534375/pdf/nihms880035.pdf</a>

# 11. Does having schizophrenia in your genetics mean that you would have manifested the disorder anyway?

No one is predestined to develop schizophrenia based on their genetics. Even if you have an identical twin who develops schizophrenia, only about half the time will the other twin develop schizophrenia as well. Environmental factors, like marijuana, can make the difference between leading a normal life and not.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC335617/pdf/pnas00677-0218.pdf

For clinical studies showing that THC can cause psychotic symptoms in people with no family history, see: <a href="https://www.nature.com/articles/1300496.pdf">https://www.nature.com/articles/1300496.pdf</a> <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3055738/pdf/npp2010222a.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3055738/pdf/npp2010222a.pdf</a> <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4332941/pdf/sbu098.pdf">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3055738/pdf/npp2010222a.pdf</a>

In Denmark, they found that for those who experienced psychosis from marijuana, a family history of psychosis did not determine who progressed to developing schizophrenia; very many became schizophrenic from marijuana without having a family history: http://archpsyc.ama-assn.org/cgi/reprint/65/11/1269

#### 12. Is there an age where it is MORE risky to develop mental illness, such as 13 or 15?

In the case of bipolar disorder, an early age of onset is more commonly seen in those with a family history of the disease:

https://pubmed.ncbi.nlm.nih.gov/16449477/

and, those early onset cases have been reported to be more severe than adult onset cases: <u>https://pubmed.ncbi.nlm.nih.gov/19931918/</u>

However, for schizophrenia, original findings of a worse prognosis when the diagnosis occurs as early as thirteen years of age:

https://pubmed.ncbi.nlm.nih.gov/25792697/

have now been challenged by a much larger and more recent study, showing that early onset schizophrenia does *not* carry a worse prognosis:

https://www.sciencedirect.com/science/article/abs/pii/S0920996420301559

For drug-induced mental illness, while there is some data showing use of marijuana at those young ages is more likely to lead to chronic mental illness because the brain is still developing, this does not mean it is safe to begin use after the teenage years. A recent study in Europe demonstrated that frequency of use, no matter what the age when use began, was the most significant risk factor for a psychotic break:

https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(14)00117-5/fulltext

Irrespective of the age when a marijuana-induced psychotic break occurs, ceasing use is crucial to improving the odds of recovery (about 50% can recover):

https://www.thelancet.com/journals/lanpsy/article/PIIS2215-0366(15)00363-6/fulltext https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3080669/pdf/sbp126.pdf

## 13. What would you say to parents who say that it's "just marijuana," or "kids will be kids," or "at least they're not doing hard drugs."?

I would say that marijuana containing THC is one of the most dangerous drugs for mental health out there, a true wolf in sheep's clothing. Even if it does not lead to the use of other drugs, it is bad enough all by itself.

More in-depth reviews of the literature on these topics can be found in the following book chapters:

Miller CL. The Impact of Marijuana on Mental Health, in: Contemporary Health Issues on Marijuana (K.Winters and K. Sabet, eds.) Oxford University Press, 2018. <u>https://global.oup.com/academic/product/contemporary-health-issues-on-marijuana-</u> <u>9780190263072?q=Contemporary%20Health%20Issues%20on%20Marijuana&lang=en&cc=us</u>

Miller CL, Jackson MC, Sabet K. Marijuana and Suicide: Case-control Studies, Population Data, and Potential Neurochemical Mechanisms, in: Cannabis in Medicine, An Evidence Based Approach (K Finn, ed.) Springer Press, in press:

https://www.springer.com/fr/book/9783030459673?gclid=EAIaIQobChMIrp\_0wfjR6QIVSY2FCh1xfA-ZEAEYASABEgJuX\_D\_BwE#aboutAuthors