**2021 SENATE HUMAN SERVICES** 

SB 2284

#### 2021 SENATE STANDING COMMITTEE MINUTES

#### **Human Services Committee**

Sakakawea Room, State Capitol

SB 2284 2/9/2021

A BILL for an Act to create and enact section 19-24.1-03.2 of the North Dakota Century Code, relating to administration of pediatric medical marijuana; and to amend and reenact subsection 30 of section 19-24.1-01 of the North Dakota Century Code, relating to the definition of pediatric medical marijuana.

**Madam Chair Lee** opened the hearing on SB 2284 at 11:02 a.m. Members present: Lee, K. Roers, Hogan, Anderson, Clemens, O. Larsen.

#### **Discussion Topics:**

- Brain development of minor children
- Availability of minor patient's medical marijuana products
- Adverse effects on pediatric medical marijuana patients

[11:03] Senator Mark Weber, District 22. Introduced SB 2284.

[11:07] Jason Wahl, Director, Division of Medical Marijuana, NDDoH. Provided testimony #5971 in opposition.

[11:19] Kurt Stembridge, Director Government Affairs, Greenwich Biosciences. Provided neutral testimony #5951.

[11:30] Alexa Johnson, District 16. Provided testimony #7018 in favor.

[11:39] Gail Pederson, Valley City Citizen. Provided written testimony #6044, #6045 in favor.

[11:48] Jody Vetter, Committee for Compassionate Care. Provided testimony #6113 in favor.

[11:52] Chris Nolden, District 7 Citizen. Provided testimony #6369 in favor.

[11:59] Jennifer Cabezas, District 24 Citizen. Provided testimony #6053 in favor.

[12:06] Courtney Koebele, Executive Director, North Dakota Medical Association. Provided testimony #5999 in opposition.

Additional written testimony: (2)

Sandy Smith, West Fargo Citizen. Provided written testimony #6028 in favor.

**Joan Connell, North Dakota Citizen.** Provided written testimony #6058 in opposition.

Senate Human Services Committee SB 2284 2/9/2021 Page 2

**Madam Chair Lee** closed the hearing on SB 2284 at 12:07 a.m.

Justin Velez, Committee Clerk



### Senate Bill 2284 Human Services Committee February 9, 2021, 10:30 a.m.

Good morning Chairwoman Lee and members of the Senate Human Services Committee. My name is Jason Wahl, Director of the Division of Medical Marijuana within the North Dakota Department of Health (NDDoH). I am here to oppose the changes in Senate Bill 2284 regarding the removal of the maximum concentration or amount of tetrahydrocannabinol (THC) for minor patients, adding dried leaves and flowers and concentrates to the types of usable marijuana available for minor patients, and requiring a designated caregiver be responsible for ensuring a medical marijuana product administered to a minor patient does not exceed 6% THC.

The NDDoH opposes the removal of the 6% THC maximum for minor patients. Providing access to higher THC amounts for individuals under the age of 19 presents serious concerns related to the brain development of minor patients. Research has supported this position. State law currently limits the amount of THC in products to 6%. THC is the cannabinoid in marijuana that provides the euphoria, or a "high." Allowing dried leaves and flowers and concentrate products to minors would significantly increase the THC percentage. Rather than a product with 6% THC or less, this change could provide access to concentrates with THC percentages in excess of 85%.

The NDDoH opposes the addition of a new section of law authorizing a designated caregiver to create a medical marijuana product or dilute a product to meet a requirement of it being no more than 6% THC. Only registered manufacturing facilities are currently authorized to create a medical marijuana product. Manufacturing facilities use specialized equipment following specific processes and procedures. The products are tested to ensure the products are safe. No testing requirements exist with a designated caregiver creating a product which puts minor patients at risk of consuming a product not fit for consumption as well as exceeding 6%.

This concludes my testimony. I am happy to answer any questions you may have.



#### Testimony SB 2284

February 8, 2021

Madame Chair Lee and Members of the Senate Human Services Committee,

#### **About Greenwich Biosciences**

Greenwich Biosciences is the US leader in the development and commercialization of prescription cannabinoid medicines to address serious medical conditions. Along with parent company GW Pharmaceuticals, we have been advancing cannabinoid science for more than two decades, with much of what is known about cannabinoids discovered by our researchers. In addition to lead product - EPIDIOLEX® (cannabidiol) oral solution, indicated for the treatment of seizures associated with three rare disorders - we have a robust pipeline of cannabinoid-derived therapies for serious illnesses (e.g., Rett syndrome, spasticity associated with multiple sclerosis and spinal cord injury, post-traumatic stress disorder, schizophrenia and autism spectrum disorders).

#### Concerns with ND Medical Marijuana Chapter

Currently, North Dakota's medical marijuana code contains definitions and provisions that could be applied to Epidiolex, potentially inhibiting its distribution to patients in need.

Nothing in North Dakota's underlying medical marijuana statute, Chapter 19-24.1, excepts an FDA-approved product from its coverage. Indeed, the law broadly defines a cannabinoid product intended for medical use: Under 94-24.1-01(24), "medical cannabinoid product' means a product intended for human consumption or use which contains cannabinoids," and includes cannabinoid solutions, capsules, transdermal patches and topicals.

Further, in a bill that recently passed the House, HB 1213, Section 1 states that a "cannabinoid solution" is a "solution consisting of a mixture created from cannabinoid concentrate and other ingredients" and that such a container may not exceed thirty milliliters. There is no exception in this provision for a prescription medication approved by the FDA, such as Epidiolex, which is dispensed in 100 milliliter vials. This provision would therefore potentially prohibit Epidiolex from being made available to patients in North Dakota. If so applied, patients would be denied a treatment that has been approved to treat serious and intractable seizures associated with three types of childhood-onset seizure conditions. Patient access to additional future FDA- approved cannabinoid medicines would also potentially be impacted.



As a result, the law imposes a number of restrictions and requirements on patients who have been prescribed FDA-approved cannabinoid products, which do not apply to patients using any other type of FDA-approved product. For example, only a patient with a specific "qualifying condition" may be certified to use a cannabinoid product, but an FDA-approved medicine may be approved for a condition not on that list. A person may not produce, process, dispense or use medical marijuana unless authorized by the state's medical marijuana law. However, a pharmaceutical product is likely to be manufactured outside of the state by an entity that is not licensed by the state and dispensed within the state by pharmacies, rather than by licensed dispensaries. Qualifying patients must become part of a patient registry and must annually pay for a registry identification card, but this requirement does not apply to patients using other types of FDA-approved products. In short, the state's medical marijuana is likely intended to apply to cannabis/cannabinoid products that have not been approved as prescription medications by the FDA, but the law inadvertently sweeps such FDA-approved products into its purview.

#### **Amendment Request to SB 2284**

Understanding this bill addresses pediatric medical marijuana and the medical marijuana statute, we would like to request what is hopefully seen as a friendly amendment. In order to ensure that physicians and pharmacies in North Dakota are not restricted in their ability to prescribe and dispense FDA-approved cannabinoid drugs to appropriate patients, and to ensure that such patients are not subject to burdens and limitations that other patients to whom non-cannabinoid FDA-approved medications have been prescribed, we would ask that the following amendment be included in SB 2844 and applied to the full medical marijuana statute:

"Nothing in this chapter shall apply to a drug approved by the Food and Drug Administration pursuant to section 505 of the federal Food, Drug and Cosmetic Act (21 U.S.C. § 301 et. Seq.)"

Thank you for your time and consideration.

Kurt Stembridge Regional Director Government Affairs Greenwich Biosciences Office 801-796-9646 kstembridge@greenwichbiosciences.com





# State of North Dakota Office of the Governor

Doug Burgum Governor Day Bug

# **Autism, Age 11**

Family worked to get autism on debilitating conditions list in 2019

Original-strength pediatric THC tincture provided therapeutic relief of Ronnie's autistic anxiety/self-injury/insomnia

Received original debilitating condition certification (card criteria) from physician employed by a health-care organization that publicly granted provider freedom to do so; Physician quit taking new pediatric cannabis patients after administration discovered her involvement

Family discovered that original pediatric tincture would soon be sold out; Other pediatric THC tincture contained 56% as much medicine, for same price (\$200/30 gram bottle)

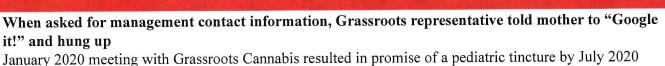
Family alerted ND Division of Medical Marijuana of impending pediatric tincture shortage in Sept. 2019

Division recommended contacting growers

Desperate correspondence begging for more
original-strength pediatric tincture sent to Pure
Dakota (Bismarck) manufacturing facility
No response from Pure Dakota

Desperate correspondence begging for pediatric tincture sent to Grassroots Cannabis (Fargo manufacturing facility)

Grassroots representative reached by phone, listened to mother's plea



Original tincture went out of stock

Price tag for a month's supply of available, low THC pediatric tincture for Ronnie rose to \$1,000

Family could no longer afford medical cannabis as Ronnie's primary medication

Ronnie forced to go on risperidone, an antipsychotic with serious side effect risks

Ronnie hospitalized after grand mal seizure in May 2020

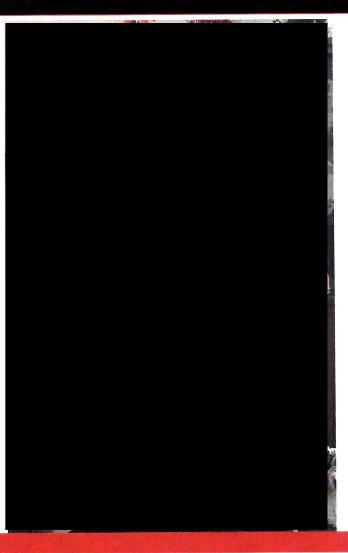
Essentia Health confiscated Ronnie's cannabis tincture after initially agreeing to his regular bedtime dose

Unmedicated insomnia sent Ronnie running and screaming through hospital halls

Essentia refused to return cannabis tincture unless Ronnie exited hospital

Cannabis tincture returned to Ronnie's designated caregiver after Ronnie (who had suffered first grand mal seizure just hours before) discharged into rainy parking lot at 3 am

-Grassroots failed to produce promised pediatric tincture by July 2020



# **Autism, Age 7**

Makes 12 hr round trip multiple times each year to see a provider who will certify her debilitating condition

Family worked to get autism on debilitating conditions list in 2019

Original-strength pediatric THC tincture proved very therapeutic for Miley's autistic anxiety/self-injury/insomnia

Family alerted Human Services Interim Committee (Nov. 17, 2019 meeting) of pediatric tincture shortage/unaffordability

No timely solutions offered

Family sent letters to both growers, asking for continued production of original strength pediatric tinctures

Received no response from Pure Dakota/Received empty promise for July 2020 pediatric tincture from Grassroots Cannabis

Family can no longer afford cannabis tincture for daytime use

"We can only afford to give Miley a bedtime dose of medical cannabis now. The \$200+ per bottle price forced us to put Miley on gabapentin, which carries risks of serious side-effects. Also, the North Dakota caregiver law makes it impossible for me to leave Miley for any amount of time. I am the only person who can handle her cannabis tincture."

# **Autism, Age 10**

Aggression and anxiety successfully being treated with cannabis ONLY (completely weaned off 3 pharmaceuticals within one year of starting cannabis treatment)

# Side effects while dependent on pharmaceuticals:

- 1) heart palpitations
- 2) tardive dyskenesia (involuntary facial movements)
- 3) rapid weight gain (+16 pounds in 8 months)

#### After medical cannabis:

- 1) heart palpitations stopped
- 2) tardive dyskenesia almost completely subsided
- 3) lost 11 pounds within 1 year

"Cannabis has been a miracle for us. But children deserve access to a broader variety of cannabis strains. The pediatric THC cap of 6% greatly limits medication variety. As Drasyn gets older, I know we will need to rotate strains. He is doing well, but starting to have more trouble in school. The pediatric cap doesn't protect our children from anything--it just forces us to buy more watered-down product. Additionally, the single caregiver limit puts incredible stress on me. I am the only person who can legally dose Drasyn. My own husband can't medicate him."

Testimony on SB 2284 Gail Pederson, SPRN, HN-BC

Thank you Chairwoman Lee and the Senate Human Services Committee for allowing me to speak today. Many thanks to Senators Weber and Poolman, and Representative Pyle for sponsoring this bill. I am here speaking for SB 2284, but I would like to offer an amendment to the proposed changes.

I am Gail Pederson from Valley City, District 24. I am a Special Practice Registered Nurse in Holistic Nursing, a nationally recognized Board Certified Holistic Nurse and a trained cannabis nurse. A lot has changed since I first spoke before this committee against SB 2344 in 2016. My knowledge of cannabis therapeutics, and I will refer to it as cannabis, has increased 100 fold. I am a member of the American Nurses Association, The Cannabis Nurses Network and The American Cannabis Nurses Association and I have over 40 hours of cannabis therapeutics education in the last 2 years. I have the extensive network of these organizations and medical professionals. We are researching, educating and solving problems with legislation and implementation of medical cannabis in our states and federally. As a SPRN, my scope of practice includes cannabis education and consultation. I have a continuing education program approved by the ND BON for 1.5 hrs CEU's, entitled "Cannabis 101: What Medical Professionals Need to Know" based on the National Counsel for State Boards of Nursing "Guidelines for the Nursing Care of Patients Who Use Marijuana.

I would like to enter an amendment to the bill proposed, with 2 changes. The amendment as rewritten is attached as another file. First, the 6% THC cap is irrelevant. It needs to go away completely. Cannabis is measured in mg/ml for our commercial solutions, whether it is a pediatrics or adult preparation. To establish dosing in a pediatrics cannabis patient, it is measured in mg/kg. That is it! It should make no difference in the dilution

rate. This is the same as with any medication we would give to a pediatrics patient.

This chart of dosing guidelines comes from a database called CannaKeys. It is a new resource that compiles research information from around the globe. 18 out of 20 studies have proven that cannabinoids have been proven effective for ASD. <a href="https://www.cannakeys.com">www.cannakeys.com</a>

### **THC Dosage Considerations**

THC micro dose: 0.1 mg to 0.4 mg (0.001 mg/kg to 0.005 mg/kg)

**THC low dose:** 0.5 mg to 5 mg (0.006mg/kg to 0.06mg/kg)

THC medium dose: 6 mg to 20 mg (0.08mg/kg to 0.27mg/kg)
THC high dose: 21 mg to 50+ mg (0.28mg/kg to 0.67mg/kg)

Formula for converting a set dose into mg/kg considerations: mg ÷ kg = mg/kg

(sample conversion calculated on a person weighing 75kg)

The 6% cap that is in place would actually create a stronger solution than what I have seen for adult medical use. The new "pediatrics solution" is a little over 3%. 1000mg of THC in 30ml is a little over 3%! This is stronger than the adult solutions. Now, this is a good thing, for the fact that it can be difficult for some children to take. It doesn't taste that great. The less volume the better. Even then, getting a child to take a cannabis product is a challenge. For the most part a child may not need that high a concentration.

The second part of the amendment is to allow caregivers to make their own solution out of flower/plant material. The difficulty is the definition of flower as a combustible product which is the current definition. This is not what caregivers wish to do and I have tried to define the changes proposed to reflect that.

Why should we allow parents to make their own product? Using

a child on the ASD, there is a lot that goes in to this reasoning. We were fortunate to acquire a video presentation by Dr. Bonni Goldstein in support of our children with autism and these changes. Clinical Endocannabinoid Deficiency is suggested in many conditions. The theory with an ASD child is their system disregulates instead of regulating vital brain functions because they do not make enough of these naturally occurring endocannabinoid molecules. Supplementation with a CBD/THC product can reduce behaviors and improve quality of life, greatly. CB1 receptors are mostly located in the brain and nervous system. The THC molecule fits almost perfectly, while the CBD molecule attaches to the side of this receptor. What happens when the dose is too low? Unlike a normal person's brain that may not have any response, the nonneurotypical brain reacts paradoxically, injurious behaviors increase, interactions with others retreat and there can be a regression of normal activities. For about 15% of these children, high THC doses are needed to overcome this. This is outlined on the circle graph here and handed out. I do want to point out that Dr Bonni Goldstein disputes the myth that cannabis causes a multitude of problems for teens in the video she made for this legislative session. Cannabis can repair brains!

Cost and quality is a big concern for the caregiver of an ASD child. The cannabis plant has hundreds of identifiable cannabinoids, terpenes, and flavinoids, each playing a role in interacting with our ECS. This is called the Entourage Effect. It is the synergistic action of all these parts together. That is why whole plant products are best for anyone. That is why parents need the choice to determine what cultivar works for their child. Terpenes are of particular importance to the success of a child using cannabis solutions. That is the essential oil of the cannabis plant. Terpenes may drive a successful treatment more than THC content. Our commercial products are made from a full spectrum oil (FSO) and diluted with a MCT oil. There are trace amounts of alcohol in the solutions according to the label. We do not have

access to the Certificate of Analysis of these products nor do we test for terpene profiles as many states do. Are the terpenes adequate to provide a quality solution? We do not know.

Allowing caregivers to find a chemovar that works without spending a lot of money is another factor in allowing plant material or concentrate to be used. I hate the thought of anyone buying a 1000mg bottle with no recourse for return and using up a portion of their monthly allotment for a product that may not work. That is another question this poses. That goes against the 4000mg monthly allotment. What if it doesn't work for that child. It can't be returned, Their allotment is not credited back. By allowing caregivers to make their own solutions with a small amount of flower they purchase can ensure that the terpene profile is correct and the product has a better chance of working. That the carrier oil used is more palatable or doesn't upset a digestive system. It is not too much to ask for our kids.

There are many factors which could prove detrimental to an ASD patient with current production, including the processing techniques and the carrier oil used. The quality of the product is also pertinent and there have been problems as outlined in other hearings. There are a lot of variables in pediatrics treatment, that allowing caregivers to manufacture their own solutions would solve. This is the first legislative cycle that we have had products. Changes need to be made. Removing the irrelevant 6% THC cap cleans the law up a little more. Allowing caregivers to use flower/plant material to find the plant that works best for their child should be a logical move when cannabis therapeutics is involved.

Thank you and I stand for questions.

#6045

#### 21.1000.01000

Sixty-seventh Legislative Assembly of North Dakota

Introduced by

15

16

Senators Weber, Poolman

Representative Pyle

#### SENATE BILL NO. 2284

- 1 A BILL for an Act to create and enact section 19-24.1-03.2 of the North Dakota Century
- 2 Code, relating to administration of pediatric medical marijuana; and to amend and
- 3 reenact subsection 30 of section 19-24.1-01 of the North Dakota Century Code, relating
- 4 to the definition of pediatric medical marijuana.

#### 5 BE IT ENACTED BY THE LEGISLATIVE ASSEMBLY OF NORTH DAKOTA:

- 6 **SECTION 1. AMENDMENT.** Subsection 30 of section 19-24.1-01 of the North Dakota 7
- 7 Century Code is amended and reenacted as follows:
- 8 30. "Pediatric medical marijuana" means a medical marijuana product containing
   9 cannabidiol/tetrahydrocannabinol, which may not contain a maximum
   10 concentration or amount of tetrahydrocannabinol of more than six percent
   11 or the dried leaves or flowers of the plant of the genus cannabis in a
   12 combustible delivery form. The term does not include a cannabinoid concentrate
   13 intended for inhalation or dried leaves and flowers used as a combustible
   14 product.
  - **SECTION 2.** Section 19-24.1-03.2 of the North Dakota Century Code is created and enacted as follows:
- 17 **19-24.1-03.2. Qualifying patients Minors.**
- 18 A designated caregiver may not administer to a registered qualifying patient who 19 is a minor a medical marijuana product exceeding a maximum concentration of 20 tetrahydrocannabinol of more than six percent. To comply with this section, 21 A designated caregiver may create a medical cannabis product using the dried 22 leaves or flowers of the plant of the genus cannabis in a combustible delivery 23 form or may dilute a medical cannabis product. The caregiver/minor patient is 24 not allowed to use a cannabinoid concentrate intended for inhalation or the 25 dried leaves/flower of the genus cannabis as a combustible product.

Madam Chair and committee, I encourage a dee pass for bill 2284 with the suggested amendments by Gail Peterson.

We should not dilute.

They need the full plant.

Dosage should be based on ml/mg per dose.

The age and weight different matters.

I know the health department disagrees, but I question what the department knows about cannabis?

Thank you

Jody Vetter

Committee for Compassionate Care

Chairwoman Lee; Senate Human Services Committee members;

My name is Chris Nolden.

I am a resident of Bismarck ND, District 7.

I am also a cardholder in the NDMMJP.

Even though I did have no intention of providing testimony; after listening to many of the testimonies provided, I felt very compelled to stand up and speak.

One of the reasons I felt compelled to speak, was to offer my sincere thanks and appreciation to Senator Weber, Senator Poolman, and Representative Pyle. I do believe the reasons this bill was brought forward, are very valid. I give them a lot of respect for sponsoring it.

Access to cannabis flower, is not only access to the most natural, unadulterated version of the medicine; it is also a "quality" check. Every cannabis product is made from cannabis leaves and flowers. Quality matters.

I also wanted to mention, that even though I hadn't fully reviewed Ms. Pederson's proposed amendment, that I do agree, the 6% THC cap on pediatric medicine is arbitrary, a detriment to pediatric patients, as well as the program, and should be removed.

Another reason I felt compelled to rise was; it seems to me at least, that you are often given misleading or non-factual information. These issues and problems are not new; they are not a few weeks, or even a couple months old.

I attended and testified, at the first annual program update the NDMMJP ever had, it was given at an interim Human Services meeting; with representatives from each chambers Human Services committees.

I brought up several concerns and issues on that day, one of the concerns I brought up was this very issue, pediatric medicine quality, and availability.

Until very recently, as far as I know, there has been little to no action taken.

This meeting was held November 7, 2019.

This picture was provided in another testimony, and the final reason for which I felt the need to speak.

I am on the far left, same suit, different tie and shoes with which I appeared in front of you on 2/9/2021, at the hearing for SB2284.

When I look at this picture, I feel the same shame, disappointment, distrust, and despair others mentioned in their testimonies.

I would like to sincerely thank you all, for allowing me to offer my spoken testimony.

I did my best to capture the reason why I was compelled to speak.

Even though there was no questions for me, I am open to trying to answer any questions you may have.



Jennifer Cabezas, Valley City. Testified to get autism on debilitating conditions list in 2019. jennifer.birdgirl@gmail.com



### Senate Human Services Committee SB 2284 February 9, 2021

Chair Lee and Committee Members, I am Courtney Koebele, the Executive Director of the North Dakota Medical Association. The North Dakota Medical Association is the professional membership organization for North Dakota physicians, residents, and medical students.

#### NDMA opposes SB 2284.

For pediatric medical marijuana use, NDMA believes in using the usual Food and Drug Administration (FDA) processes instead of "medical marijuana" laws. The FDA has a long track record of being sure that medicines are safe and effective and are dispensed and sold safely. This is particularly important in medication for children.

Marijuana is classified as a Schedule I drug by the US Drug Enforcement Agency (DEA), signifying the drug has a high potential for abuse, no accepted medical use, and there is a lack of accepted safety for use of the drug or substance under medical supervision. Cannabinoids, which are components of marijuana, have been proven to be effective in treating of specific conditions in adults including nausea, vomiting, and chronic pain conditions.

Youth are different from adults—and may react differently to marijuana. Though anecdotal accounts have shown that certain cannabinoids could benefit children with certain chronic debilitating diseases, there are no published studies on the effects on cannabinoids on the pediatric population.

NDMA urges a DO NOT PASS on SB 2284.

Thank you.

Courtney Koebele Executive Director North Dakota Medical Association TESTIMONY IN SUPPORT OF SENATE BILL 2284 relating to the administration and definition of pediatric medical marijuana.

Sandy Smith 165 23<sup>rd</sup> Ave E West Fargo, ND 58078 701-367-9855

Chairman Lee and Senate Human Services Committee Members, my name is Sandy Smith. I am the parent of a son with severe autism. I am testifying in favor of Senate Bill 2284 relating to the administration of pediatric medical marijuana; and relating to the definition of pediatric medical marijuana.

Our son was diagnosed with autism in 2002. He is now 18 years old and my husband and I are his legal guardians. Our son was doing very well after having received extensive therapy for much of his life. However, our lives changed on July 4, 2018 when he had his first grand mal seizure. We now think about our lives as "before seizures and after seizures." Our son was put on seizure medication which caused him to engage in very aggressive & dangerous behavior. We spent two years changing and adjusting medication only to see his behavior become even more aggressive and more dangerous. Our son is 6'1" and weighs 255 lbs. He is bigger than both me and my husband.

We were literally afraid of our own son. I was afraid to be home with him by myself and I could not let anyone else be alone with him either. I was aware of others trying medical marijuana to help their children with aggressive behavior. We did some research and decided we would try it. Honestly, it came down to the decision of whether we were going to be able to keep him at home with us anymore. We started in September 2020. Medical marijuana has been life changing for us. Our sons' behavior has improved significantly. We are no longer afraid of him. Teachers, therapists and others that work with him are reporting significant changes in behavior and cooperation. He is happier, more engaging and his language has even increased slightly. He tolerates haircuts and shaving with no problems. Most importantly he has not hit anyone since got on a therapeutic dose in early October.

Medical marijuana has worked very well for our son but the cost of maintaining certification and the cost of purchasing product with the six percent maximum concentration or amount of THC limit is making it very difficult for us to continue giving this life changing "medicine" to our son.

- The cost of getting and maintaining certification. After determining that the doctors my son regularly sees could not certify him, we had to find an independent provider who would. The provider we found does not accept insurance and my sons' first appointment was \$470. He must be seen every 3 months and each of those visits is \$300. Since July 28th, our out-of-pocket expenses have been \$1,170 to get initial certification and maintain it for less than a year.
- My son is the size of an adult man and limiting him to the pediatric product is absurd. I have to force a large amount of coconut oil base down him in order for him to ingest enough of the active ingredient needed to calm him and reduce aggressive behavior.
- The pediatric product is becoming cost prohibitive. Again, because my son is the size of an adult man we have to purchase a large amount of the pediatric product. The regular price of a 30 ml bottle of tincture is \$150-\$200 per bottle and costs between \$1,050 to \$1,400 per month.

Medical marijuana has been very effective for our son and I urge you to recommend a do pass for SB 2284.

I sincerely thank you for your time today.

Thank you, Sandy Smith 701-367-9855 Senate Bill 2284- In Opposition Human Services Committee Sixty-seventh Legislative Assembly of North Dakota February 9, 2021

Dear Chairman Lee, Vice Chair Roers, and Senate Human Services Committee members, My name is Joan Connell. As a pharmacist-trained pediatrician and parent, I urge you to vote "DO NOT PASS" on SB 2284, which would amend current legislation on pediatric medical marijuana to make a combustible form available to children as well as leave it to the discretion of the caregiver to modify a marijuana product to contain up to 6% tetrahydrocannabinol (THC). Combustible marijuana damages lung tissue. The American Lung Association has published a document describing the many damaging effects of marijuana on the lungs <a href="https://www.lung.org/quit-smoking/smoking-facts/health-effects/marijuana-and-lung-health">https://www.lung.org/quit-smoking/smoking-facts/health-effects/marijuana-and-lung-health</a>. Imagine what the mechanisms of toxicity described in this publication will do to the growing and developing lungs of children. Just within the last few weeks, one of my pediatric asthmatic patients has required care in the emergency room due to an asthma attack resulting from smoking marijuana.

Expecting that caregivers of a medically complex child also become skilled pharmacists/chemists/mathematicians capable of diluting out products to "create" a medical marijuana product that does not exceed 6% THC is unreasonable, unrealistic, and unnecessary-as well as makes no sense, assuming that those requesting a change to this part of the legislation are concerned about the well-described adverse effects of exposure to potent THC products on a child's mind and body. I have included a link to the American Academy of Child and Adolescent Psychiatry's statement on use of medical marijuana in pediatric patients with autism spectrum disorder

https://www.aacap.org/AACAP/Policy Statements/2019/Use of Medical Marijuana in Childr en and Adolescents with Autism Spectrum Disorder for Core Autism S.aspx which advises against use of medical marijuana products due to current lack of scientific evidence of efficacy combined with the myriad of scientific evidence regarding damaging effects of this drug on the developing brain.

Finally, as a parent and pediatrician, I am sickened by history repeating itself. Here is a link to a document that describes the history of tobacco marketing <a href="https://stopswithme.com/history-tobacco-marketing-scary-story/">https://stopswithme.com/history-tobacco-marketing-scary-story/</a>. Big-Marijuana continues to dupe us by using the same playbook as the tobacco industry used decades ago. Have we learned nothing? I encourage you to take a look at this and consider what role you (want to) play in Big-Marijuana's game of normalizing and promoting utilization of an addictive drug that has adverse consequences on multiple organs of the body.

Thank you for considering my testimony. As always, I am available via this email address for any further questions/discussion.

#### 2021 SENATE STANDING COMMITTEE MINUTES

#### **Human Services Committee**

Sakakawea Room, State Capitol

SB 2284 2/10/2021

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**Madam Chair Lee** opened the discussion on SB at 11:11 a.m. Members present: Lee, K. Roers, Hogan, Anderson, Clemens, O. Larsen.

#### **Discussion Topics:**

- 6 milligram cannabinoid solution availability
- Fargo Psychiatric Clinic

[11:14] Lisa Feldner, Pure Dakota. Provided clarification to the committee on the availability of the 6 milligram cannabinoid solution.

Additional written testimony: (1)

Barb Stanton, PhD, LPCC, LMFT, Mental Health Therapist, Anne Carlsen Center – Fargo. Provided written neutral testimony #6193

Madam Chair Lee closed the discussion on SB at 11:20 a.m.

Justin Velez, Committee Clerk

Disclaimer: I can't promote medical interventions or give medical advice.

However, I can provide anecdotal information. We have families who have had great success with cannabis. The family needs to feel that they can be open and have an honest conversation with providers and the prescribers (pediatricians, psychiatrists, etc...) without fear of legal reprisals. Having medical professionals involved leads to a much better outcome than having families driven underground.

Thanks for reaching out and I'll check in to it more later. I'll get back to you.



Barb Stanton, PhD, LPCC, LMFT
Pronouns: she/her/hers
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#### 2021 SENATE STANDING COMMITTEE MINUTES

#### Human Services Committee Sakakawea Room, State Capitol

SB 2284 2/15/2021

Relating to the definition of pediatric medical marijuana.

**Senator Lee** opened the committee work at 2:51 PM. Present: **Senators Lee**, **Anderson**, **Clemens**, **Hogan**, **Larsen**, **Roers**.

#### **Discussion Topics:**

- Medical marijuana use for children
- Medical marijuana certification
- Impact of cannabis on the adolescent brain
- Legal percentages of THC dosages for children

Dr. Stefanie Hanisch, Child & Adolescent Psychiatrist, Fargo Sanford Health, testified orally online stating she doesn't believe there is enough medical scientific evidence to suggest medical marijuana for children.

Jason Wahl, Director Division of Medical Marijuana, ND Dept. of Health answered committee questions regarding percentages of THC dosages for pediatric use.

**Senator Lee** adjourned the hearing at 3:35 PM.

Rose Laning for Justin Velez, Committee Clerk

#### 2021 SENATE STANDING COMMITTEE MINUTES

#### **Human Services Committee**

Sakakawea Room, State Capitol

SB 2284 2/16/2021

A BILL for an Act to create and enact section 19-24.1-03.2 of the North Dakota Century Code, relating to administration of pediatric medical marijuana; and to amend and reenact subsection 30 of section 19-24.1-01 of the North Dakota Century Code, relating to the definition of pediatric medical marijuana.

**Madam Chair Lee** opened the discussion on SB 2284 at 11:08 a.m. Members present: Lee, K. Roers, Hogan, Anderson, Clemens, O. Larsen.

#### **Discussion Topics:**

Behavioral health services

Senator K. Roers moves DO NOT PASS.

**Senator Hogan** seconded.

Senators	Vote
Senator Judy Lee	Υ
Senator Kristin Roers	Υ
Senator Howard C. Anderson, Jr.	Υ
Senator David A. Clemens	Υ
Senator Kathy Hogan	Υ
Senator Oley Larsen	Absent

The motion passed 5-0-1.

Senator Lee will carry SB 2284.

Additional written testimony: (4)

Helen Shen, Science Writer. "Cannabis and the adolescent brain" (testimony #6667).

National Institute on Drug Abuse; National Institutes of Health; U.S. Department of Health and Human Services. "Marijuana Research Report" (testimony #6666).

**Doug Griffin, MD, Vice President, Sanford Clinic/Medical Center Fargo.** Opposition testimony #6620.

Barbara Stanton, PhD, LPCC, LMFT. Neutral testimony #6721.

Madam Chair Lee closed the discussion on SB 2284 at 11:14 a.m.

Justin Velez, Committee Clerk

#### REPORT OF STANDING COMMITTEE

Module ID: s\_stcomrep\_30\_006

Carrier: Lee

SB 2284: Human Services Committee (Sen. Lee, Chairman) recommends DO NOT PASS (5 YEAS, 0 NAYS, 1 ABSENT AND NOT VOTING). SB 2284 was placed on the Eleventh order on the calendar.

### Cannabis and the adolescent brain

With the use of legal marijuana proliferating, many want to understand the potential risks to teen users in particular. But thus far, definitive answers about the drug's effect on young brains have been hard to come by.

Helen Shen, Science Writer

For a developmental neuroscientist, Kuei Y. Tseng gets recruited to deliver a lot of talks to the public. Parents, educators, law enforcement, and teenagers all want Tseng to educate them about a hot-button issue: how cannabis affects the adolescent brain.

Tseng, based at the University of Illinois in Chicago, investigates how rats respond to THC (tetrahydrocannabinol), the main psychoactive ingredient in cannabis. He's found that exposure to THC or similar molecules during a specific window of adolescence delays maturation of the prefrontal cortex (PFC), a region involved in complex behaviors and decision making (1). The disruption alters how the area processes information when the animals are adults.

Audiences of parents and teachers tend to be alarmed by the long-lasting deficits, Tseng says. But when he speaks with teenagers, especially those already using cannabis, he gets a different response. "It's surprising, but they're not that worried." Youths often want to know how much cannabis they can consume without harming brain development; they press Tseng to extrapolate from rats the age at which it's "safe" for people to start using the drug. "They need to understand this is not black and white," says Tseng.

Nevertheless, some policymakers are already urging caution. In an advisory released August 29, the US Surgeon General went so far as to state that "until and unless more is known about the long-term impact, the safest choice for pregnant women and adolescents is not to use marijuana." At a luncheon in May, former US Food and Drug Administration (FDA) commissioner Scott Gottlieb said he had significant concerns about the "great natural experiment we're conducting in this country by making THC widely available," citing his fears about "the impact that this has on developing brains."

The question of safety for young users has taken on particular urgency in the United States, where, since 2012, 11 states and the District of Columbia have legalized the use of recreational marijuana by adults. Although it remains illegal for minors, the changing legal and commercial landscapes raise the possibility

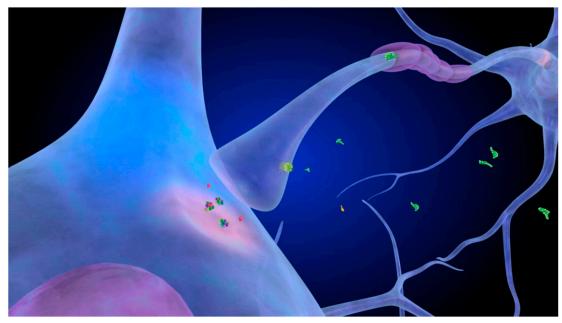


Most researchers stress that despite increasingly relaxed societal views toward marijuana, cannabis use—especially in adolescence—is not benign. Image credit: Shutterstock/Yarygin.

that cannabis products may also become more accessible and attractive to teens.

Despite such worries, definitive evidence remains elusive. Many observational studies have suggested that adolescent cannabis use may be linked to longterm harms, including cognitive impairment and increased risk of schizophrenia (2). But in almost every area that researchers have examined, results have been inconclusive regarding the precise nature and strength of these associations. In particular, there's little consensus as to whether cannabis directly causes long-term health harms in people, whether it's one of a number of risk factors, or whether it simply correlates with other root causes.

Ultimately, most researchers stress that, despite increasingly relaxed societal views toward the drug, cannabis use—especially in adolescence—is not benign. Many say that public health messaging should encourage teens to abstain from cannabis use as long as possible. A host of unanswered questions remain: What specific harms can individual users expect if they



THC (green, right and center) can bind to endocannabinoid receptors (yellow-green bundle, center) on the surface of certain neurons and affect their activity, including the neurons' release of GABA (magenta, left), which then regulates the activity of other types of neurons. Image credit: National Institute on Drug Abuse.

start using in adolescence? Are only certain people susceptible to potential ill effects? Is there a threshold age, or degree of cannabis use, that is safe or safer? Is cannabis-related damage reversible over time?

"We still don't have a handle on how THC affects the adolescent brain. There's a lot of evidence pointing toward negative outcomes, but more research needs to be done," says neuroscientist Jodi Gilman at Harvard Medical School in Boston, MA. "The policy is ahead of the science."

Many researchers are looking toward an ambitious initiative, now getting underway at the National Institutes of Health (NIH) in Bethesda, MD, to help bridge that gap. Touted as the largest long-term US study of brain development and child health, the project will collect a wealth of information—genetics, brain imaging, cognitive tests, daily habits, and more—on nearly 12,000 children, and aims to follow them into early adulthood over the next decade. "It's got so much potential to give us so much insight into the developing brain," says cognitive neuroscientist Catherine Orr at the Swinburne University of Technology in Melbourne, Australia. In the meantime, researchers are trying to make sense of the existing data and push the research forward—despite practical limitations on investigating the effects of marijuana in teens.

#### **Revealing Rat Data**

Many observational studies in humans imply a link between teen marijuana use and poor outcomes but are clouded by several potential confounding variables, such as socioeconomic circumstances or family mental health history. To better understand how cannabis affects the brain itself, some researchers have turned to controlled drug experiments that, for ethical and scientific reasons, can only be done in animals. What

researchers really want to know is whether adolescent THC exposure could cause outsized neurobiological harms

During adolescence, the brain undergoes major remodeling, especially in the PFC—one of the last brain regions to fully mature. In humans, this area is involved with high-level functions such as making decisions, controlling impulses, maintaining attention, planning, and working toward goals. The PFC also plays a role in defining our personalities and helps us understand and respond appropriately to social situations (2).

The adolescent PFC is a hotbed of synaptic reorganization. Excess neuronal connections are eliminated; other connections are stabilized. At the same time, many neurotransmitter systems are turning up or down production of signaling chemicals and adjusting the distribution of receptors for those molecules in different brain regions. Both of these processes are thought to facilitate efficient neural communication and help the brain transition from an immature to an adult state (3). All of this activity has led to the theory that the adolescent brain could be especially vulnerable to insults such as stress or drugs (4).

THC could be disruptive because it binds to the CB1 receptor, which is designed to respond to naturally occurring endocannabinoids (named for their chemical similarity to compounds in cannabis). Endocannabinoids play many roles, including regulating stress, fear, anxiety, mood, appetite, and pain (5–8). In the fetal brain, endocannabinoids modulate several developmental processes, and growing evidence suggests that they have a similar function in adolescence as well, influencing brain maturation (2, 5).

Supporting this idea, Tiziana Rubino at the University of Insubria in Varese, Italy, and her colleagues reported

in 2015 that THC exposure in adolescent female rats disrupted the maturation of multiple neurotransmitter systems in the PFC. In adulthood, PFC neurons in these animals were less adept at rapidly adjusting their connection strengths—a key process in learning and memory. When faced with a maze-learning task, the rats performed worse than control animals (9).

And some of THC's effects on brain development may be limited to specific windows of vulnerability, Tseng has found. Giving rats a THC-like synthetic cannabinoid during early and mid-adolescence—but not late adolescence or adulthood-interfered with GABA (gamma-aminobutyric acid), a major inhibitory neurotransmitter, in the adult rat PFC. (Based on neurodevelopmental stages, the equivalent cutoff age would be about 16 or 17 years in humans, says Tseng.) As a result, the adult PFC failed to develop certain patterns of electrical activity typical of the mature brain, suggesting delayed brain development (1). "There are a lot of psychiatric disorders that happen when the brain is transitioning to maturation," says Tseng. "Somehow, exposure to cannabinoids makes that window of maturation much longer than normal and might increase susceptibility to the onset of psychiatric disorders happening."

At Western University in London, Canada, neuroscientist Steven Laviolette's group has also found that exposing adolescent rats to THC impairs GABA signaling in the PFC when the animals become adults. This disinhibition of the PFC also leads to overactivity in dopamine neurons in a brain region involved in motivation and reward processing (10). Similar features have been observed in the brains of people with schizophrenia, notes Laviolette.

"Clearly there's something unique about the adolescent brain that makes it specifically sensitive to THC," says Laviolette. There may also be genetic variations that make some teens more sensitive than others to these effects. But the precise mechanisms that underlie both aspects of susceptibility are still unknown. "That's the next big thing to figure out," he says.

#### **Cause and Effect Conundrum**

Although animal studies like these have revealed several potential mechanisms by which cannabis might do harm, it's hard to determine what this means for human teens. Increased risk of psychiatric disorders is a major concern, with schizophrenia having attracted the most attention and controversy. In double-blind, placebo-controlled studies, intravenous doses of pure THC have induced temporary symptoms resembling some aspects of schizophrenia (11, 12). But researchers are still trying to establish whether cannabis use, especially in adolescence, could lead to full-blown schizophrenia in the long run.

In a landmark 1987 study, researchers reported a link between cannabis use and schizophrenia risk among more than 45,000 Swedish military conscripts who were examined at the time of conscription around age 19 and again 15 years later. Those who had used cannabis more than 50 times before conscription were six times more likely to be diagnosed with

schizophrenia by the 15-year mark. The association was weaker, though still present, after controlling for factors such as adverse childhood conditions and diagnosis of other psychiatric disorders at the time of conscription (13).

In the decades that followed, several studies yielded similar associations. In one oft-cited 2002 study, psychiatrist Robin Murray at King's College London and his colleagues analyzed data from roughly 760 New Zealanders who had been followed since birth in the 1970s as part of a larger project, called the Dunedin Study. They found that starting cannabis use by age 15 was associated with a fourfold elevated risk of developing schizophrenia by age 26, whereas starting closer to age 18 carried only a small, nonsignificant increase in risk (14).

Heated debates linger over how to interpret such observations. "Most people would agree there's clearly a relationship that exists between cannabis use and schizophrenia," says neuropharmacologist Matthew Hill of the Hotchkiss Brain Institute at the University of Calgary. "I think it's the directionality of that relationship that's contentious."

# "Clearly there's something unique about the adolescent brain that makes it specifically sensitive to THC."

-Steven Laviolette

Theories abound, but the available data are inconclusive, leaving researchers to argue about whether cannabis can directly cause schizophrenia (Murray believes it can, especially with heavy use), or primarily triggers or accelerates schizophrenia in a subset of people already predisposed to developing the disorder. Many researchers favor the latter theory, which, according to Hill, could help explain why rates of cannabis consumption in the Western world have increased dramatically since the 1960s but rates of schizophrenia (often cited to be around 1% or less) have not changed much over time (15, 16).

It's also possible that other factors contribute to the observed correlations. For example, some research suggests that people already predisposed to schizophrenia are more prone to use cannabis. In a sample of more than 2,000 healthy adults, one study found that those with gene variants linked to increased schizophrenia risk were more likely to use cannabis, and to use more of it than others. "This is not to say that there is no causal relationship between use of cannabis and risk of schizophrenia," the authors concluded. "But it does establish that at least part of the association may be due to a causal relationship in the opposite direction" (17).

Complicating matters, the neurobiological mechanisms behind schizophrenia itself are not well understood, and a number of other factors—including family life, smoking and alcohol use, educational experience, and more—can influence mental health outcomes. "As long as you're studying humans, there's always going to be the problem of real life,"

Shen

says Orr. "Each person is unique and accumulates circumstances before the study and during the study."

#### **Cognitive Clues**

Among many parents, educators, and policymakers, cognitive impairment, not mental illness, is the biggest concern. But once again, observational research has not provided definitive answers about whether cognitive changes associated with cannabis use are temporary, or at some point might become irreversible.

"There have been a couple studies that have gotten a lot of headlines that have not replicated well," says Hill. "I don't think there's any compelling evidence that moderate levels of use are going to produce long-lasting cognitive deficits."

In 2012, one high-profile study used the Dunedin Study data to compare people's intelligence quotient (IQ) between ages 7 and 13 (before cannabis use) and at age 38, and assess their drug use at various ages. Regular users of cannabis saw IQ declines between childhood and adulthood, whereas nonusers did not (18). A persistent cannabis dependence was associated with a loss of up to six IQ points on average, with deficits especially pronounced in those who became dependent before age 18. However, in 2018, the same research group concluded that cannabis use was not the cause of IQ declines during adolescence, even in dependent users, based on tracking a cohort of

"I don't think there's any compelling evidence that moderate levels of use are going to produce long-lasting cognitive deficits."

-Matthew Hill

twins in England and Wales from age 5 to 18. Instead, they found that "family background factors" likely explained why the adolescent cannabis users performed worse on IQ tests (19).

In the short term, research led by neuropsychologist Randi Schuster at Massachusetts General Hospital in Boston has found that certain cannabis-related cognitive losses may be reversible. Among regular users aged 16 to 25, those who cut out cannabis for four weeks saw improvements in verbal memory—especially during the first week (20). "We don't know how long it would take for them to reach—or if they would reach—the level of a nonuser," says Gilman, one of the study's authors. "But we found that continued use is worse than stopping."

Different methods are likely at the root of some of the mixed results. Studies often sample different age groups, or people with varying levels of drug use, and examine them for different durations, ranging from weeks to decades (21). As in the case of schizophrenia, the bulk of the human research is observational, yielding correlations but not proving causation. However, randomized controlled trials, the gold standard for resolving many types of biomedical questions in humans, are limited by ethical

requirements that make it difficult to experimentally administer cannabis to teens.

Many researchers view the NIH's new large-scale prospective study as the next best thing. Besides schizophrenia and cognition, the Adolescent Brain Cognitive Development (ABCD) study could potentially clarify the role of adolescent cannabis use in other conditions, such as addiction or mood disorders.

#### **Clearing the Haze**

Interest in all these questions has intensified in recent years. As more states legalize marijuana for adults, some worry that young people will have greater access to and appetite for the drug. But it may be too soon to tell. A handful of early surveys in different states where recreational marijuana use was legalized, often using different sampling methods, have reached differing conclusions about whether youths perceive marijuana as less harmful, or are using it at higher rates after legalization (22-24). In November, a study of Colorado, Washington, Alaska, and Oregon found no changes in the rates of adolescent marijuana use after legalization, but did observe a slight rise in rates of cannabis use disorder among teens-though investigators couldn't rule out the influence of factors other than legalization, such as higher potency (25).

Despite lingering uncertainties, Nora Volkow, director of the National Institute on Drug Abuse in Bethesda, MD, says that there is enough information to be concerned. "The problem with marijuana is that we have data right now that go in all directions. What we're doing is building a study to answer the question of whether use of marijuana in adolescence affects the structure and function of the human brain, and whether it actually leads to cognitive or psychotic disruption," she says, adding, "There's urgency to establish this."

The ABCD study (26) completed enrollment in 2018, recruiting nearly 12,000 children aged 9 or 10, and will follow the children through roughly age 20. Researchers at 21 institutions around the United States have already collected the baseline brain images, genetic information, and neuropsychological, behavioral, and many other health measures. Over time, the project aims to characterize normal adolescent brain and cognitive development and tease apart multiple factors that can influence those processes, such as screen time, sports injuries, and—importantly—substance use.

By starting at a relatively young age and taking a diverse demographic, geographic, and socioeconomic sample, researchers intend to capture detailed information on circumstances that precede substance use and could influence risks (27). And by including 2,100 people who are either twins or triplets, they plan to compare many cannabis-using and nonusing siblings, to isolate the effects of genetic and family factors. Such comparisons could also help reveal whether some youths are more predisposed than others to use cannabis or are more vulnerable to its effects on the brain.

It will be years before the ABCD study finishes, and even then it's unlikely to settle all of the current questions and debates, as some researchers note. Although few researchers dismiss the potential for cannabis to harm the developing teenage brain,

much remains unknown. Many see the project's size, duration, and depth as a big step toward understanding important particulars. Such studies, says Gilman, "will go a long way to clearing things up."

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#### **Research Report**

Revised July 2020

# Marijuana Research Report

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### Marijuana Research Report

Explores the latest research on marijuana, including the scope of marijuana use in the U.S., health consequences, its effects on everyday activities, and available treatments.

### Letter From the Director



Photo by NIDA

Changes in marijuana policies across states legalizing marijuana for medical and/or recreational use suggest that marijuana is gaining greater acceptance in our society. Thus, it is particularly important for people to understand what is known about both the adverse health effects and the potential therapeutic benefits linked to marijuana.

Because marijuana impairs short-term memory and judgment and distorts perception, it can impair performance in school or at work and make it dangerous to drive. It also affects brain systems that are still maturing through young adulthood, so regular use by teens may have negative and long-lasting effects on their cognitive development, putting them at a competitive disadvantage and possibly interfering with their well-being in other ways. Also, contrary to popular belief, marijuana can be addictive, and its use during adolescence may make other forms of problem use or addiction more likely.

Whether smoking or otherwise consuming marijuana has therapeutic benefits that outweigh its health risks is still an open question that science has not resolved. Although many states now permit dispensing marijuana for medicinal purposes and there is mounting anecdotal evidence for the

efficacy of marijuana-derived compounds, the U.S. Food and Drug Administration has not approved "medical marijuana." However, safe medicines based on cannabinoid chemicals derived from the marijuana plant have been available for decades and more are being developed.

This Research Report is intended as a useful summary of what the most up-to-date science has to say about marijuana and its effects on those who use it at any age.

#### Nora D. Volkow, M.D.

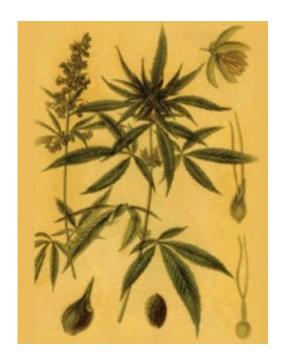
Director

National Institute on Drug Abuse

#### See Also:

 Message from the NIDA Director - Marijuana's Lasting Effects on the Brain, (Archives) (March 2013)

# What is marijuana?



Marijuana—also called *weed, herb, pot, grass, bud, ganja, Mary Jane*, and a vast number of other slang terms—is a greenish-gray mixture of the dried flowers of *Cannabis sativa*. Some people smoke marijuana in hand-rolled cigarettes called *joints*; in pipes, water pipes (sometimes called *bongs*), or in *blunts* (marijuana rolled in cigar wraps). Marijuana can also be used to brew tea and, particularly when it is sold or consumed for medicinal purposes, is frequently mixed into foods (*edibles*) such as brownies, cookies, or candies. Vaporizers are also increasingly used to consume marijuana. Stronger forms of marijuana include sinsemilla (from specially tended female plants) and concentrated resins containing high doses of marijuana's active ingredients, including honeylike *hash oil*, waxy *budder*, and hard amberlike *shatter*. These resins are increasingly popular among those who use them both recreationally and medically.

The main *psychoactive*(mind-altering) chemical in marijuana, responsible for most of the intoxicating effects that people seek, is *delta-9-tetrahydrocannabinol* (THC). The chemical is found in resin produced by the leaves and buds primarily of the female cannabis plant. The plant also contains more than 500 other chemicals, including more than 100 compounds that are chemically related to THC, called *cannabinoids*.<sup>2</sup>

# What is the scope of marijuana use in the United States?

Marijuana is the most commonly used psychotropic drug in the United States, after alcohol. In 2018, more than 11.8 million young adults reported marijuana use in the past year.  $^3$  Its use is more prevalent among men than women.  $^4$ 

Marijuana use is widespread among adolescents and young adults. According to the Monitoring the Future survey—an annual survey of drug use and attitudes among the Nation's middle and high school students—most measures of marijuana use by 8<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup> graders peaked in the mid-to-late 1990s and then began a period of gradual decline through the mid-2000s before levelling off. However, in 2019, there was a significant increase in daily use in the younger grades. In addition, teens' perceptions of the risks of marijuana use have steadily declined over the past decade. In 2019, 11.8% of 8th graders reported marijuana use in the past year and 6.6% in the past month (current use). Among 10<sup>th</sup> graders, 28.8% had used marijuana in the past year and 18.4% in the past month.

Rates of use among 12<sup>th</sup> graders were higher still: 35.7% had used marijuana during the year prior to the survey and 22.3% used in the past month; 6.4% said they used marijuana daily or near-daily.<sup>5</sup> With the growing popularity of vaping devices, teens have started vaping THC (the ingredient in marijuana that produces the high), with nearly 4% of 12<sup>th</sup> graders saying they vape THC daily.<sup>5</sup>

Medical emergencies possibly related to marijuana use have also increased. The Drug Abuse Warning Network (DAWN), a system for monitoring the health impact of drugs, estimated that in 2011, there were nearly 456,000 drug-related emergency department visits in the United States in which marijuana use was mentioned in the medical record (a 21% increase over 2009). About two-thirds of patients were male and 13% were between the ages of 12 and 17. It is unknown whether this increase is due to increased use, increased *potency* of marijuana (amount of THC it contains), or other factors. It should be noted, however, that mentions of marijuana in medical records do not necessarily indicate that these emergencies were directly related to marijuana intoxication.

# What are marijuana's effects?

When marijuana is smoked, THC and other chemicals in the plant pass from the lungs into the bloodstream, which rapidly carries them throughout the body to the brain. The person begins to experience effects almost immediately (see "<a href="How does marijuana produce its effects?">How does marijuana produce its effects?</a>"). Many people experience a pleasant euphoria and sense of relaxation. Other common effects, which may vary dramatically among different people, include heightened sensory perception (e.g., brighter colors), laughter, altered perception of time, and increased appetite.

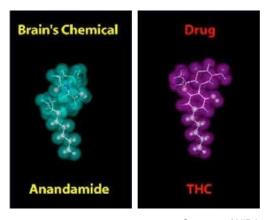
If marijuana is consumed in foods or beverages, these effects are somewhat delayed—usually appearing after 30 minutes to 1 hour—because the drug must first pass through the digestive system. Eating or drinking marijuana delivers significantly less THC into the bloodstream than smoking an equivalent amount of the plant. Because of the delayed effects, people may inadvertently consume more THC than they intend to.

Pleasant experiences with marijuana are by no means universal. Instead of relaxation and euphoria, some people experience anxiety, fear, distrust, or panic. These effects are more common when a person takes too much, the marijuana has an unexpectedly high potency, or the person is

inexperienced. People who have taken large doses of marijuana may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity. These unpleasant but temporary reactions are distinct from longer-lasting psychotic disorders, such as schizophrenia, that may be associated with the use of marijuana in vulnerable individuals. (See " Is there a link between marijuana use and psychiatric disorders?")

Although detectable amounts of THC may remain in the body for days or even weeks after use, the noticeable effects of smoked marijuana generally last from 1 to 3 hours, and those of marijuana consumed in food or drink may last for many hours.

## How does marijuana produce its effects?



Courtesy of NIDA

THC's chemical structure is similar to the brain chemical anandamide.

Similarity in structure allows drugs to be recognized by the body and to alter normal brain communication.

THC's chemical structure is similar to the brain chemical *anandamide*. Similarity in structure allows the body to recognize THC and to alter normal brain communication.

Endogenous cannabinoids such as anandamide (see figure) function as neurotransmitters because

they send chemical messages between nerve cells (*neurons*) throughout the nervous system. They affect brain areas that influence pleasure, memory, thinking, concentration, movement, coordination, and sensory and time perception. Because of this similarity, THC is able to attach to molecules called *cannabinoid receptors* on neurons in these brain areas and activate them, disrupting various mental and physical functions and causing the effects described earlier. The neural communication network that uses these cannabinoid neurotransmitters, known as the *endocannabinoid system*, plays a critical role in the nervous system's normal functioning, so interfering with it can have profound effects.

For example, THC is able to alter the functioning of the hippocampus (see "Marijuana, Memory, and the Hippocampus") and orbitofrontal cortex, brain areas that enable a person to form new memories and shift his or her attentional focus. As a result, using marijuana causes impaired thinking and interferes with a person's ability to learn and perform complicated tasks. THC also disrupts functioning of the cerebellum and basal ganglia, brain areas that regulate balance, posture, coordination, and reaction time. This is the reason people who have used marijuana may not be able to drive safely (see "Does marijuana use affect driving?") and may have problems playing sports or engaging in other physical activities.

People who have taken large doses of the drug may experience an acute psychosis, which includes hallucinations, delusions, and a loss of the sense of personal identity.

THC, acting through cannabinoid receptors, also activates the brain's reward system, which includes regions that govern the response to healthy pleasurable behaviors such as sex and eating. Like most other drugs that people misuse, THC stimulates neurons in the reward system to release the signaling chemical *dopamine* at levels higher than typically observed in response to natural stimuli. This flood of dopamine contributes to the pleasurable "high" that those who use recreational marijuana seek.

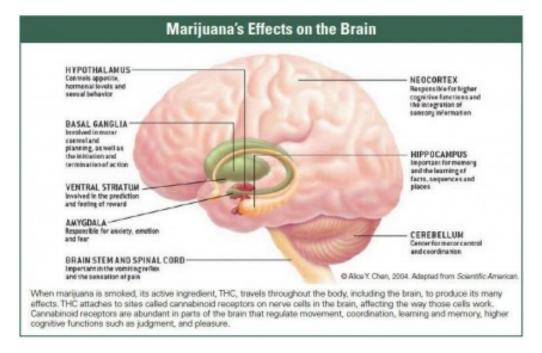


Diagram showing different parts of the brain and describing marijuana's effects on the brain

# Does marijuana use affect driving?



Photo by ©iStock.com/MadCircles

Marijuana significantly impairs judgment, motor coordination, and reaction time, and studies have found a direct relationship between blood THC concentration and impaired driving ability. 7–9

Marijuana is the illicit drug most frequently found in the blood of drivers who have been involved in vehicle crashes, including fatal ones. Two large European studies found that drivers with THC in their blood were roughly twice as likely to be culpable for a fatal crash than drivers who had not used drugs or alcohol. However, the role played by marijuana in crashes is often unclear because it can be detected in body fluids for days or even weeks after intoxication and because people frequently combine it with alcohol. Those involved in vehicle crashes with THC in their blood, particularly higher levels, are three to seven times more likely to be responsible for the incident than drivers who had not used drugs or alcohol. The risk associated with marijuana in combination with alcohol appears to be greater than that for either drug by itself.

Several meta-analyses of multiple studies found that the risk of being involved in a crash significantly increased after marijuana use —in a few cases, the risk doubled or more than doubled. However, a large case-control study conducted by the National Highway Traffic Safety Administration found no significant increased crash risk attributable to cannabis after controlling for drivers' age, gender, race, and presence of alcohol.

# Is marijuana addictive?

Marijuana use can lead to the development of problem use, known as a marijuana use disorder, which takes the form of addiction in severe cases. Recent data suggest that 30% of those who use marijuana may have some degree of marijuana use disorder. People who begin using marijuana before the age of 18 are four to seven times more likely to develop a marijuana use disorder than adults.

Marijuana use disorders are often associated with *dependence*—in which a person feels withdrawal symptoms when not taking the drug. People who use marijuana frequently often report irritability, mood and sleep difficulties, decreased appetite, cravings, restlessness, and/or various forms of physical discomfort that peak within the first week after quitting and last up to 2 weeks. Marijuana dependence occurs when the brain adapts to large amounts of the drug by reducing production of and sensitivity to its own endocannabinoid neurotransmitters.

Marijuana use disorder becomes addiction when the person cannot stop using the drug even though it

interferes with many aspects of his or her life. Estimates of the number of people addicted to marijuana are controversial, in part because epidemiological studies of substance use often use dependence as a proxy for addiction even though it is possible to be dependent without being addicted. Those studies suggest that 9% of people who use marijuana will become dependent on it, rising to about 17% in those who start using in their teens. 26,27

In 2015, about 4.0 million people in the United States met the diagnostic criteria for a marijuana use disorder; <sup>3</sup> 138,000 voluntarily sought treatment for their marijuana use. <sup>28</sup>

### **Rising Potency**

Marijuana potency, as detected in confiscated samples, has steadily increased over the past few decades. In the early 1990s, the average THC content in confiscated marijuana samples was less than 4%.2 In 2018, it was more than 15%.29 Marijuana concentrates can have much higher levels of THC (see Marijuana Concentrates DrugFacts). The increasing potency of marijuana, combined with the use of high-THC concentrates, raises concerns that the consequences of marijuana use today could be worse than in the past, particularly among those who are new to marijuana use and in young people, whose brains are still developing (see "What are marijuana's long-term effects on the brain?").

Researchers do not yet know the full extent of the consequences when the body and brain (especially the developing brain) are exposed to high concentrations of THC or whether the recent increases in emergency department visits by people testing positive for marijuana are related to rising potency. The extent to which people adjust for increased potency by using less or by smoking it differently is also unknown. Recent studies suggest that experienced people may adjust the amount they smoke and how much they inhale based on the believed strength of the marijuana they are using, but they are not able to fully compensate for variations in potency. 30,31

What are marijuana's long-term effects on the brain?

Substantial evidence from animal research and a growing number of studies in humans indicate that marijuana exposure during development can cause long-term or possibly permanent adverse changes in the brain. Rats exposed to THC before birth, soon after birth, or during adolescence show notable problems with specific learning and memory tasks later in life. Cognitive impairments in adult rats exposed to THC during adolescence are associated with structural and functional changes in the hippocampus. Studies in rats also show that adolescent exposure to THC is associated with an altered reward system, increasing the likelihood that an animal will self-administer other drugs (e.g., heroin) when given an opportunity (see "Is marijuana a gateway drug?").

Imaging studies of marijuana's impact on brain structure in humans have shown conflicting results. Some studies suggest regular marijuana use in adolescence is associated with altered connectivity and reduced volume of specific brain regions involved in a broad range of executive functions such as memory, learning, and impulse control compared to people who do not use.  $\frac{38,39}{}$  Other studies have not found significant structural differences between the brains of people who do and do not use the drug.  $\frac{40}{}$ 

Several studies, including two large longitudinal studies, suggest that marijuana use can cause functional impairment in cognitive abilities but that the degree and/or duration of the impairment depends on the age when a person began using and how much and how long he or she used.<sup>41</sup>

Among nearly 4,000 young adults in the Coronary Artery Risk Development in Young Adults study tracked over a 25-year period until mid-adulthood, cumulative lifetime exposure to marijuana was associated with lower scores on a test of verbal memory but did not affect other cognitive abilities such as processing speed or executive function. The effect was sizeable and significant even after eliminating those involved with current use and after adjusting for confounding factors such as demographic factors, other drug and alcohol use, and other psychiatric conditions such as depression. 42

Some studies have also linked marijuana use to declines in IQ, especially when use starts in adolescence and leads to persistent cannabis use disorder into adulthood. However, not all of the studies on the link between marijuana and IQ have reached the same conclusion, and it is difficult to prove that marijuana causes a decline in IQ when there are multiple factors that can influence the results of such studies, such as genetics, family environment, age of first use, frequency of use, having a cannabis use disorder, duration of use, and duration of the study. Key research in this area to date is described below.

A large longitudinal study in New Zealand found that persistent marijuana use disorder with frequent use starting in adolescence was associated with a loss of an average of 6 or up to 8 IQ points measured in mid-adulthood. Those who used marijuana heavily as teenagers and quit using as adults did not recover the lost IQ points. People who only began using marijuana heavily in adulthood did not lose IQ points. Two shorter-duration prospective longitudinal twin studies found that youth who used marijuana showed significant declines in verbal ability (equivalent to 4 IQ points) and general knowledge between the preteen years (ages 9 to 12, before use) and late adolescence/early adulthood (ages 17 to 20); however those who went on to use marijuana at older ages already had lower scores on these measures at the start of the study, before they started using the drug. Also, no predictable difference was found between twins when one used marijuana and one did not. 44

More research will be needed to answer definitively whether marijuana use causes long-term IQ losses and whether factors that weren't measured in the prior research, such as the increasing amounts of THC in cannabis and the emergence of new cannabis products, are relevant.

Also, the ability to draw definitive conclusions about marijuana's long-term impact on the human brain from past studies is often limited by the fact that study participants use multiple substances, and there is often limited data about the participants' health or mental functioning prior to the study. Over the next decade, the National Institutes of Health is funding the Adolescent Brain Cognitive Development (ABCD) study—a major longitudinal study that will track a large sample of young Americans from late childhood (before first use of drugs) to early adulthood. The study will use neuroimaging and other advanced tools to clarify precisely how and to what extent marijuana and other substances, alone and in combination, affect adolescent brain development.

#### Marijuana, Memory, and the Hippocampus

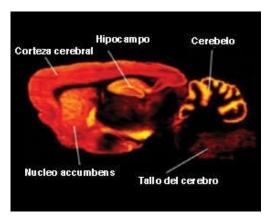


Image by NIDA

Distribution of cannabinoid receptors in the rat brain. Brain image reveals high levels (shown in orange and yellow) of cannabinoid receptors in many areas, including the cortex, hippocampus, cerebellum, and nucleus accumbens (ventral striatum).

Memory impairment from marijuana use occurs because THC alters how the hippocampus, a brain area responsible for memory formation, processes information. Most of the evidence supporting this assertion comes from animal studies. For example, rats exposed to THC *in utero*, soon after birth, or during adolescence, show notable problems with specific learning/memory tasks later in life. Moreover, cognitive impairment in adult rats is associated with structural and functional changes in the hippocampus from THC exposure during adolescence.

As people age, they lose neurons in the hippocampus, which decreases their ability to learn new information. Chronic THC exposure may hasten age-related loss of hippocampal neurons. In one study, rats exposed to THC every day for 8 months (approximately 30% of their lifespan) showed a level of nerve cell loss at 11 to 12 months of age that equaled that of unexposed animals twice their age.

# Is marijuana a gateway drug?

Some research suggests that marijuana use is likely to precede use of other licit and illicit substances<sup>45</sup>

and the development of addiction to other substances. For instance, a study using longitudinal data from the National Epidemiological Study of Alcohol Use and Related Disorders found that adults who reported marijuana use during the first wave of the survey were more likely than adults who did not use marijuana to develop an alcohol use disorder within 3 years; people who used marijuana and already had an alcohol use disorder at the outset were at greater risk of their alcohol use disorder worsening. Marijuana use is also linked to other substance use disorders including nicotine addiction.

Early exposure to cannabinoids in adolescent rodents decreases the reactivity of brain dopamine reward centers later in adulthood. To the extent that these findings generalize to humans, this could help explain the increased vulnerability for addiction to other substances of misuse later in life that most epidemiological studies have reported for people who begin marijuana use early in life. It is also consistent with animal experiments showing THC's ability to "prime" the brain for enhanced responses to other drugs. For example, rats previously administered THC show heightened behavioral response not only when further exposed to THC but also when exposed to other drugs such as morphine—a phenomenon called *cross-sensitization*.

These findings are consistent with the idea of marijuana as a "gateway drug." However, the majority of people who use marijuana do not go on to use other, "harder" substances. Also, cross-sensitization is not unique to marijuana. Alcohol and nicotine also prime the brain for a heightened response to other drugs<sup>51</sup> and are, like marijuana, also typically used before a person progresses to other, more harmful substances.

It is important to note that other factors besides biological mechanisms, such as a person's social environment, are also critical in a person's risk for drug use. An alternative to the gateway-drug hypothesis is that people who are more vulnerable to drug-taking are simply more likely to start with readily available substances such as marijuana, tobacco, or alcohol, and their subsequent social interactions with others who use drugs increases their chances of trying other drugs. Further research is needed to explore this question.

How does marijuana use affect school, work, and social life?



Image by @iStock.com/AntonioGuillem

Research has shown that marijuana's negative effects on attention, memory, and learning can last for days or weeks after the acute effects of the drug wear off, depending on the person's history with the drug. <sup>52</sup> Consequently, someone who smokes marijuana daily may be functioning at a reduced intellectual level most or all of the time. Considerable evidence suggests that students who smoke marijuana have poorer educational outcomes than their nonsmoking peers. For example, a review of 48 relevant studies found marijuana use to be associated with reduced educational attainment (i.e., reduced chances of graduating). <sup>53</sup> A recent analysis using data from three large studies in Australia and New Zealand found that adolescents who used marijuana regularly were significantly less likely than their non-using peers to finish high school or obtain a degree. They also had a much higher chance of developing dependence, using other drugs, and attempting suicide. <sup>54</sup> Several studies have also linked heavy marijuana use to lower income, greater welfare dependence, unemployment, criminal behavior, and lower life satisfaction. <sup>55,56</sup>

To what degree marijuana use is directly causal in these associations remains an open question requiring further research. It is possible that other factors independently predispose people to both marijuana use and various negative life outcomes such as school dropout. That said, people report a perceived influence of their marijuana use on poor outcomes on a variety of life satisfaction and achievement measures. One study, for example, compared people involved with current and former long-term, heavy use of marijuana with a control group who reported smoking marijuana at least once in their lives but not more than 50 times. All participants had similar education and income backgrounds, but significant differences were found in their educational attainment: Fewer of those

who engaged in heavy cannabis use completed college, and more had yearly household incomes of less than \$30,000. When asked how marijuana affected their cognitive abilities, career achievements, social lives, and physical and mental health, the majority of those who used heavily reported that marijuana had negative effects in all these areas of their lives.

Studies have also suggested specific links between marijuana use and adverse consequences in the workplace, such as increased risk for injury or accidents.  $^{59}$  One study among postal workers found that employees who tested positive for marijuana on a pre-employment urine drug test had 55% more industrial accidents, 85% more injuries, and 75% greater absenteeism compared with those who tested negative for marijuana use.  $^{60}$ 

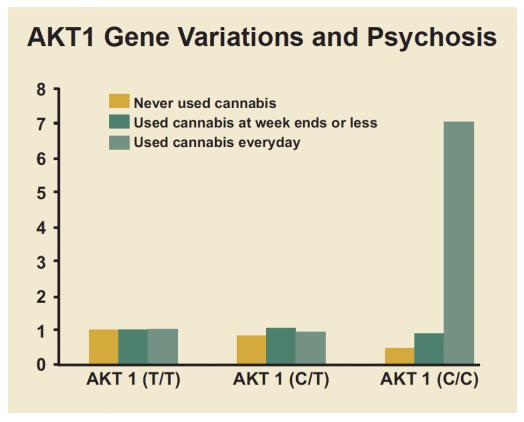
# Is there a link between marijuana use and psychiatric disorders?

Several studies have linked marijuana use to increased risk for psychiatric disorders, including psychosis (schizophrenia), depression, anxiety, and substance use disorders, but whether and to what extent it actually causes these conditions is not always easy to determine. 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 genetic vulnerability have all been shown to influence this relationship. The strongest evidence to date concerns links between marijuana use and psychiatric disorders in those with a preexisting genetic or other vulnerability.

Research using longitudinal data from the National Epidemiological Survey on Alcohol and Related Conditions examined associations between marijuana use, mood and anxiety disorders, and substance use disorders. After adjusting for various confounding factors, no association between marijuana use and mood and anxiety disorders was found. The only significant associations were increased risk of alcohol use disorders, nicotine dependence, marijuana use disorder, and other drug use disorders. 62

Recent research (see "AKT1 Gene Variations and Psychosis") has found that people who use marijuana and carry a specific variant of the AKT1 gene, which codes for an enzyme that affects

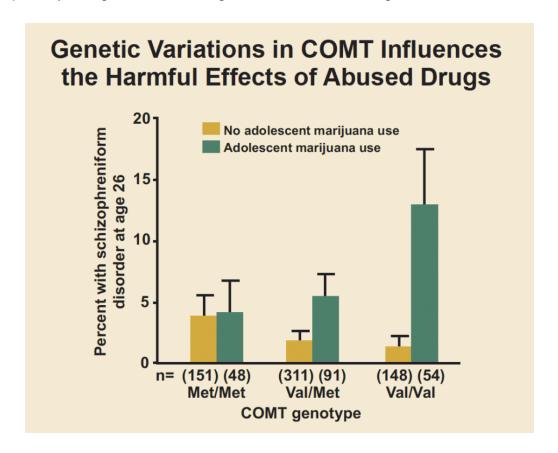
dopamine signaling in the *striatum*, are at increased risk of developing psychosis. The striatum is an area of the brain that becomes activated and flooded with dopamine when certain stimuli are present. One study found that the risk of psychosis among those with this variant was seven times higher for those who used marijuana daily compared with those who used it infrequently or used none at all.  $\frac{63}{2}$ 



Source: Di Forti et al. Biol Psychiatry. 2012.

Whether adolescent marijuana use can contribute to developing psychosis later in adulthood appears to depend on whether a person already has a genetically based vulnerability to the disorder. The AKT1 gene governs an enzyme that affects brain signaling involving the neurotransmitter dopamine. Altered dopamine signaling is known to be involved in schizophrenia. AKT1 can take one of three forms in a specific region of the gene implicated in susceptibility to schizophrenia: T/T, C/T, and C/C. Those who use marijuana daily (green bars) with the C/C variant have a seven times higher risk of developing psychosis than those who use it infrequently or use none at all. The risk for psychosis among those with the T/T variant was unaffected by whether they used marijuana.

Another study found an increased risk of psychosis among adults who had used marijuana in adolescence and also carried a specific variant of the gene for *catechol-O-methyltransferase* (COMT), an enzyme that degrades neurotransmitters such as dopamine and norepinephrine (see "Genetic Variations in COMT Influences the Harmful Effects of Abused Drugs"). Marijuana use has also been shown to worsen the course of illness in patients who already have schizophrenia. As mentioned previously, marijuana can produce an acute psychotic reaction in non-schizophrenic people who use marijuana, especially at high doses, although this fades as the drug wears off.



The influence of adolescent marijuana use on adult psychosis is affected by genetic variables. This figure shows that variations in a gene can affect the likelihood of developing psychosis in adulthood following exposure to cannabis in adolescence. The COMT gene governs an enzyme that breaks down dopamine, a brain chemical involved in schizophrenia. It comes in two forms: "Met" and "Val." Individuals with one or two copies of the Val variant have a higher risk of developing schizophrenic-type disorders if they used cannabis during adolescence (dark bars). Those with only the Met variant were unaffected by cannabis use.

Inconsistent and modest associations have been reported between marijuana use and suicidal thoughts and attempted suicide among teens. Marijuana has also been associated with an *amotivational syndrome*, defined as a diminished or absent drive to engage in typically rewarding activities. Because of the role of the endocannabinoid system in regulating mood and reward, it has been hypothesized that brain changes resulting from early use of marijuana may underlie these associations, but more research is needed to verify that such links exist and better understand them.

## Adverse Consequences of Marijuana Use

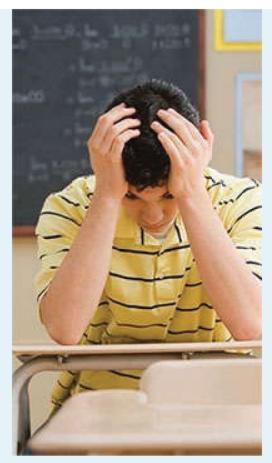


Photo by ©getttyimages.com/Fuse

#### Acute (present during intoxication)

- Impaired short-term memory
- Impaired attention, judgment, and other cognitive functions
- Impaired coordination and balance
- Increased heart rate
- Anxiety, paranoia
- Psychosis (uncommon)

Persistent (lasting longer than intoxication, but may not be permanent)

■ Impaired learning and coordination

Sleep problems

#### Long-term (cumulative effects of repeated use)

- Potential for marijuana addiction
- Impairments in learning and memory with potential loss of IQ\*
- Increased risk of chronic cough, bronchitis
- Increased risk of other drug and alcohol use disorders
- Increased risk of schizophrenia in people with genetic vulnerability\*\*

\*Loss of IQ among individuals with persistent marijuana use disorder who began using heavily during adolescence

\*\*These are often reported co-occurring symptoms/disorders with chronic marijuana use. However, research has not yet determined whether marijuana is causal or just associated with these mental problems.

# What are marijuana's effects on lung health?

Like tobacco smoke, marijuana smoke is an irritant to the throat and lungs and can cause a heavy cough during use. It also contains levels of volatile chemicals and tar that are similar to tobacco smoke, raising concerns about risk for cancer and lung disease. 67

Marijuana smoking is associated with large airway inflammation, increased airway resistance, and lung hyperinflation, and those who smoke marijuana regularly report more symptoms of chronic bronchitis than those who do not smoke. One study found that people who frequently smoke marijuana had more outpatient medical visits for respiratory problems than those who do not smoke. Some case studies have suggested that, because of THC's immune-suppressing effects, smoking marijuana might increase susceptibility to lung infections, such as pneumonia, in people with immune deficiencies; however, a large AIDS cohort study did not confirm such an association.  $\frac{67}{2}$  Smoking

marijuana may also reduce the respiratory system's immune response, increasing the likelihood of the person acquiring respiratory infections, including pneumonia.  $\frac{68}{100}$  Animal and human studies have not found that marijuana increases risk for emphysema.  $\frac{67}{100}$ 

#### Reports of Deaths Related to Vaping Marijuana

The Food and Drug Administration has <u>alerted</u> the public to hundreds of reports of serious lung illnesses associated with vaping, including several deaths. They are working with the <u>Centers for Disease Control and Prevention (CDC)</u> to investigate the cause of these illnesses. Many of the suspect products tested by the states or federal health officials have been identified as vaping products containing THC, the main psychotropic ingredient in marijuana. Some of the patients reported a mixture of THC and nicotine; and some reported vaping nicotine alone. No one substance has been identified in all of the samples tested, and it is unclear if the illnesses are related to one single compound. Until more details are known, FDA officials have warned people not to use any vaping products bought on the street, and they warn against modifying any products purchased in stores. They are also asking people and health professionals to <u>report</u> any adverse effects. The CDC has posted an information page for consumers.

Whether smoking marijuana causes lung cancer, as cigarette smoking does, remains an open question. Marijuana smoke contains carcinogenic combustion products, including about 50% more benzoprene and 75% more benzanthracene (and more phenols, vinyl chlorides, nitrosamines, reactive oxygen species) than cigarette smoke. Because of how it is typically smoked (deeper inhale, held for longer), marijuana smoking leads to four times the deposition of tar compared to cigarette smoking. However, while a few small, uncontrolled studies have suggested that heavy, regular marijuana smoking could increase risk for respiratory cancers, well-designed population studies have failed to find an increased risk of lung cancer associated with marijuana use.

One complexity in comparing the lung-health risks of marijuana and tobacco concerns the very different ways the two substances are used. While people who smoke marijuana often inhale more deeply and hold the smoke in their lungs for a longer duration than is typical with cigarettes, marijuana's effects last longer, so people who use marijuana may smoke less frequently than those

who smoke cigarettes.

Additionally, the fact that many people use both marijuana and tobacco makes determining marijuana's precise contribution to lung cancer risk, if any, difficult to establish. Cell culture and animal studies have also suggested THC and CBD may have antitumor effects, and this has been proposed as one reason why stronger expected associations are not seen between marijuana use and lung cancer, but more research is needed on this question. 67

# What are marijuana's effects on other aspects of physical health?

Within a few minutes after inhaling marijuana smoke, a person's heart rate speeds up, the breathing passages relax and become enlarged, and blood vessels in the eyes expand, making the eyes look bloodshot. The heart rate—normally 70 to 80 beats per minute—may increase by 20 to 50 beats per minute or may even double in some cases. Taking other drugs with marijuana can amplify this effect.

Limited evidence suggests that a person's risk of heart attack during the first hour after smoking marijuana is nearly five times his or her usual risk. This observation could be partly explained by marijuana raising blood pressure (in some cases) and heart rate and reducing the blood's capacity to carry oxygen. Marijuana may also cause *orthostatic hypotension* (head rush or dizziness on standing up), possibly raising danger from fainting and falls. Tolerance to some cardiovascular effects often develops with repeated exposure. These health effects need to be examined more closely, particularly given the increasing use of "medical marijuana" by people with health issues and older adults who may have increased baseline vulnerability due to age-related cardiovascular risk factors (see "Is marijuana safe and effective as medicine?").

A few studies have shown a clear link between marijuana use in adolescence and increased risk for an aggressive form of testicular cancer (nonseminomatous testicular germ cell tumor) that predominantly strikes young adult males. The early onset of testicular cancers compared to lung and most other cancers indicates that, whatever the nature of marijuana's contribution, it may accumulate over just a few years of use.

Studies have shown that in rare cases, chronic use of marijuana can lead to Cannabinoid Hyperemesis Syndrome—a condition marked by recurrent bouts of severe nausea, vomiting, and dehydration. This syndrome has been found to occur in persons under 50 years of age and with a long history of marijuana use. Cannabinoid Hyperemesis Syndrome can lead sufferers to make frequent trips to the emergency room, but may be resolved when a person stops using marijuana.

### Is marijuana safe and effective as medicine?

The potential medicinal properties of marijuana and its components have been the subject of research and heated debate for decades. THC itself has proven medical benefits in particular formulations. The U.S. Food and Drug Administration (FDA) has approved THC-based medications, dronabinol (Marinol and nabilone (Cesamet<sup>®</sup>), prescribed in pill form for the treatment of nausea in patients undergoing cancer chemotherapy and to stimulate appetite in patients with wasting syndrome due to AIDS.

In addition, several other marijuana-based medications have been approved or are undergoing clinical trials. Nabiximols (Sativex<sup>®</sup>), a mouth spray that is currently available in the United Kingdom, Canada, and several European countries for treating the spasticity and neuropathic pain that may accompany multiple sclerosis, combines THC with another chemical found in marijuana called cannabidiol (CBD).

The FDA also approved a CBD-based liquid medication called Epidiolex<sup>®</sup> for the treatment of two forms of severe childhood epilepsy, Dravet syndrome and Lennox-Gastaut syndrome. It's being delivered to patients in a reliable dosage form and through a reproducible route of delivery to ensure that patients derive the anticipated benefits. CBD does not have the rewarding properties of THC.

Researchers generally consider medications like these, which use purified chemicals derived from or

based on those in the marijuana plant, to be more promising therapeutically than use of the whole marijuana plant or its crude extracts. Development of drugs from botanicals such as the marijuana plant poses numerous challenges. Botanicals may contain hundreds of unknown, active chemicals, and it can be difficult to develop a product with accurate and consistent doses of these chemicals. Use of marijuana as medicine also poses other problems such as the adverse health effects of smoking and THC-induced cognitive impairment. Nevertheless, a growing number of states have legalized dispensing of marijuana or its extracts to people with a range of medical conditions.

An additional concern with "medical marijuana" is that little is known about the long-term impact of its use by people with health- and/or age-related vulnerabilities—such as older adults or people with cancer, AIDS, cardiovascular disease, multiple sclerosis, or other neurodegenerative diseases. Further research will be needed to determine whether people whose health has been compromised by disease or its treatment (e.g., chemotherapy) are at greater risk for adverse health outcomes from marijuana use.

#### Medical Marijuana Laws and Prescription Opioid Use Outcomes

A new study underscores the need for additional research on the effect of medical marijuana laws on opioid overdose deaths and cautions against drawing a causal connection between the two. Early research suggested that there may be a relationship between the availability of medical marijuana and opioid analgesic overdose mortality. In particular, a NIDA-funded study published in 2014 found that from 1999 to 2010, states with medical cannabis laws experienced slower rates of increase in opioid analgesic overdose death rates compared to states without such laws. <sup>78</sup>

A 2019 analysis, also funded by NIDA, re-examined this relationship using data through 2017. Similar to the findings reported previously, this research team found that opioid overdose mortality rates between 1999-2010 in states allowing medical marijuana use were 21% lower than expected. When the analysis was extended through 2017, however, they found that the trend reversed, such that states with medical cannabis laws experienced an overdose death rate 22.7% higher than expected. The investigators uncovered no evidence that either broader cannabis laws (those allowing recreational use) or more restrictive laws (those only permitting

the use of marijuana with low tetrahydrocannabinol concentrations) were associated with changes in opioid overdose mortality rates.

These data, therefore, do not support the interpretation that access to cannabis reduces opioid overdose. Indeed, the authors note that neither study provides evidence of a causal relationship between marijuana access and opioid overdose deaths. Rather, they suggest that the associations are likely due to factors the researchers did not measure, and they caution against drawing conclusions on an individual level from ecological (population-level) data. Research is still needed on the potential medical benefits of cannabis or cannabinoids.

# What are the effects of secondhand exposure to marijuana smoke?

People often ask about the possible psychoactive effect of exposure to secondhand marijuana smoke and whether a person who has inhaled secondhand marijuana smoke could fail a drug test. Researchers measured the amount of THC in the blood of people who do not smoke marijuana and had spent 3 hours in a well-ventilated space with people casually smoking marijuana; THC was present in the blood of the nonsmoking participants, but the amount was well below the level needed to fail a drug test. Another study that varied the levels of ventilation and the potency of the marijuana found that some nonsmoking participants exposed for an hour to high-THC marijuana (11.3% THC concentration) in an unventilated room showed positive urine assays in the hours directly following exposure study showed that nonsmoking people in a confined space with people smoking high-THC marijuana reported mild subjective effects of the drug—a "contact high"—and displayed mild impairments on performance in motor tasks.

The known health risks of secondhand exposure to cigarette smoke—to the heart or lungs, for instance—raise questions about whether secondhand exposure to marijuana smoke poses similar health risks. At this point, very little research on this question has been conducted. A 2016 study in rats found that secondhand exposure to marijuana smoke affected a measure of blood vessel function as much as secondhand tobacco smoke, and the effects lasted longer. One minute of exposure to secondhand marijuana smoke impaired flow-mediated dilation (the extent to which arteries enlarge in

response to increased blood flow) of the femoral artery that lasted for at least 90 minutes; impairment from 1 minute of secondhand tobacco exposure was recovered within 30 minutes. The effects of marijuana smoke were independent of THC concentration; i.e., when THC was removed, the impairment was still present. This research has not yet been conducted with human subjects, but the toxins and tar levels known to be present in marijuana smoke (see "What are marijuana's effects on lung health?") raise concerns about exposure among vulnerable populations, such as children and people with asthma.

# Can marijuana use during and after pregnancy harm the baby?



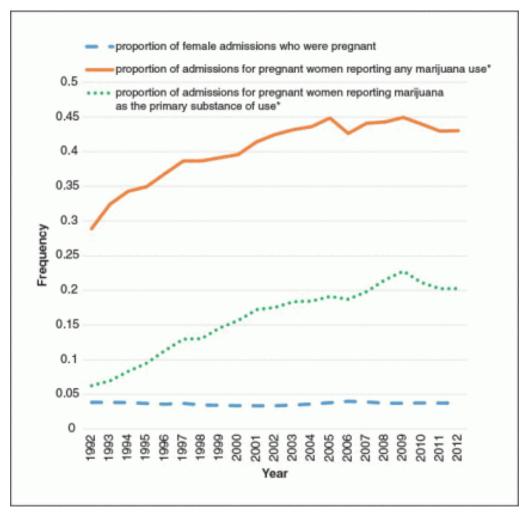
Photo by ©Thinkstock.com/Creatas Images

More research is needed on how marijuana use during pregnancy could impact the health and development of infants, given changing policies about access to marijuana, as well as significant

increases over the last decade in the number of pregnant women seeking substance use disorder treatment for marijuana use.83 One study found that about 20% of pregnant women 24-years-old and younger screened positive for marijuana. However, this study also found that women were about twice as likely to screen positive for marijuana use via a drug test than they state in self-reported measures. This suggests that self-reported rates of marijuana use in pregnant females may not be an accurate measure of marijuana use.84 Additionally, in one study of dispensaries, nonmedical personnel at marijuana dispensaries were recommending marijuana to pregnant women for nausea, but medical experts warn against it.

There is no human research connecting marijuana use to the chance of miscarriage, <sup>85,86</sup> although animal studies indicate that the risk for miscarriage increases if marijuana is used early in pregnancy. <sup>87</sup>

Some associations have been found between marijuana use during pregnancy and future developmental and hyperactivity disorders in children. Evidence is mixed as to whether marijuana use by pregnant women is associated with low birth weight or premature birth, although long-term use may elevate these risks. Research has shown that pregnant women who use marijuana have a 2.3 times greater risk of stillbirth. Given the potential of marijuana to negatively impact the developing brain, the American College of Obstetricians and Gynecologists recommends that obstetrician-gynecologists counsel women against using marijuana while trying to get pregnant, during pregnancy, and while they are breastfeeding. It is important to note that despite the growing popularity of using marijuana in vaping devices, the Food and Drug Administration recommends that pregnant women should not use any vaping product, regardless of the substance.



Source: Martin et al., 2015

Recent Trends in Treatment Admissions for Marijuana Use During Pregnancy

Some women report using marijuana to treat severe nausea associated with their pregnancy; <sup>99,100</sup> however, there is no research confirming that this is a safe practice, and it is generally not recommended. Women considering using medical marijuana while pregnant should not do so without checking with their health care providers. Animal studies have shown that moderate concentrations of THC, when administered to mothers while pregnant or nursing, could have long-lasting effects on the child, including increasing stress responsivity and abnormal patterns of social interactions. <sup>101</sup> Animal studies also show learning deficits in prenatally exposed individuals. <sup>33,102</sup>

Human research has shown that some babies born to women who used marijuana during their

pregnancies display altered responses to visual stimuli, increased trembling, and a high-pitched cry, which could indicate problems with neurological development. In school, marijuana-exposed children are more likely to show gaps in problem-solving skills, memory, and the ability to remain attentive. More research is needed, however, to disentangle marijuana-specific effects from those of other environmental factors that could be associated with a mother's marijuana use, such as an impoverished home environment or the mother's use of other drugs. Prenatal marijuana exposure is also associated with an increased likelihood of a person using marijuana as a young adult, even when other factors that influence drug use are considered. More information on marijuana use during pregnancy can be found in the NIDA's <u>Substance Use in Women Research Report</u>.

Very little is known about marijuana use and breastfeeding. One study suggests that moderate amounts of THC find their way into breast milk when a nursing mother uses marijuana. Some evidence shows that exposure to THC through breast milk in the first month of life could result in decreased motor development at 1 year of age. There have been no studies to determine if exposure to THC during nursing is linked to effects later in the child's life. With regular use, THC can accumulate in human breast milk to high concentrations. Because a baby's brain is still forming, THC consumed in breast milk could affect brain development. Given all these uncertainties, nursing mothers are discouraged from using marijuana. New mothers using medical marijuana should be vigilant about coordinating care between the doctor recommending their marijuana use and the pediatrician caring for their baby.

### Available Treatments for Marijuana Use Disorders

Marijuana use disorders appear to be very similar to other substance use disorders, although the long-term clinical outcomes may be less severe. On average, adults seeking treatment for marijuana use disorders have used marijuana nearly every day for more than 10 years and have attempted to quit more than six times. People with marijuana use disorders, especially adolescents, often also suffer from other psychiatric disorders (comorbidity). They may also use or be addicted to other substances, such as cocaine or alcohol. Available studies indicate that effectively treating the mental health disorder with standard treatments involving medications and behavioral therapies may help reduce marijuana use, particularly among those involved with heavy use and those with more chronic

mental disorders. The following behavioral treatments have shown promise:

- Cognitive-behavioral therapy: A form of psychotherapy that teaches people strategies to identify and correct problematic behaviors in order to enhance self-control, stop drug use, and address a range of other problems that often co-occur with them.
- **Contingency management**: A therapeutic management approach based on frequent monitoring of the target behavior and the provision (or removal) of tangible, positive rewards when the target behavior occurs (or does not).
- **Motivational enhancement therapy**: A systematic form of intervention designed to produce rapid, internally motivated change; the therapy does not attempt to treat the person, but rather mobilize his or her own internal resources for change and engagement in treatment.

Currently, the FDA has not approved any medications for the treatment of marijuana use disorder, but research is active in this area. Because sleep problems feature prominently in marijuana withdrawal, some studies are examining the effectiveness of medications that aid in sleep. Medications that have shown promise in early studies or small clinical trials include the sleep aid zolpidem (Ambien<sup>®</sup>), an anti-anxiety/anti-stress medication called buspirone (BuSpar<sup>®</sup>), and an anti-epileptic drug called gabapentin (Horizant<sup>®</sup>, Neurontin<sup>®</sup>) that may improve sleep and, possibly, executive function. Other agents being studied include the nutritional supplement N-acetylcysteine and chemicals called FAAH inhibitors, which may reduce withdrawal by inhibiting the breakdown of the body's own cannabinoids. Future directions include the study of substances called *allosteric modulators* that interact with cannabinoid receptors to inhibit THC's rewarding effects.

# Where can I get further information about marijuana?

To learn more about marijuana and other drugs, visit the NIDA website at <u>drugabuse.gov</u> or contact the DrugPubs Research Dissemination Center at 877-NIDA-NIH (877-643-2644; TTY/TDD: 240-645-0228).

#### The NIDA website includes:

information about drugs and related health consequences

- NIDA publications, news, and events
- resources for health care professionals
- funding information (including program announcements and deadlines)
- international activities
- links to related websites (access to websites of many other organizations in the field)
- information in Spanish (en español)

#### NIDA websites and webpages

- drugabuse.gov
- teens.drugabuse.gov
- easyread.drugabuse.gov
- drugabuse.gov/drugs-abuse/marijuana
- drugabuse.gov/related-topics/hivaids
- researchstudies.drugabuse.gov
- irp.drugabuse.gov

### For physician information

■ NIDAMED: <u>drugabuse.gov/nidamed</u>

#### Other websites

Information about marijuana is also available through the following websites:

- Substance Abuse and Mental Health Services Administration (SAMHSA)
- Drug Enforcement Administration (DEA)
- Monitoring the Future
- Partnership for Drug-Free Kids

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#6620

#### Dear Senator Judy Lee,

I am writing to urge you to give a DO NOT PASS recommendation to SB 2284 regarding allowing the home mixture of dried leave forms of cannabis for the treatment of pediatric and adolescent conditions including autism. I am a family physician with more than 30 years in practice, and now have the pleasure of serving in the capacity of Vice President, Medical Officer of Sanford Health in Fargo. This has given me a very close perspective to understanding the challenges that patients and families face in caring for these challenging conditions. It is very emotionally and physically taxing and parents will do almost anything to help their children. This is understandable yet we should not let this lead to unsafe and unproven therapies. Furthermore, my current role gives me a window into the situation with behavioral health hospitals, medical floors, and jails filled with increasingly more patients with serious mental health issues such as schizophrenia, which use of cannabis has been shown to increase the risk for. I offer the following arguments.

- 1. Medical cannabis has very little research to support its use in autism
- 2. Exposing young lungs to inhaled cannabis is very dangerous
- 3. It is very complex to mix dried leaves to a certain concentration, and to expect parents to do this safely and potentially exposing patients (children) to the risk of dangerous toxicity is a poor idea
- 4. Reported adverse events include irritability, decreased appetite, and restlessness
- 5. Finally, the increased risk for developing very serious psychiatric issues in the future exists with any use of cannabis.

Thanks you for your consideration. I would be happy to talk further about this if that would be helpful.

#### Doug Griffin, MD

Vice President, Medical Officer Sanford Clinic/Medical Center Fargo Office-(701)-234-6160 Mobile- (320)-491-9161 douglas.griffin@sanfordhealth.org Senator Lee,

Sorry for the late reply. I wanted to follow up on the bill regarding pediatric use of medical marijuana for children on the spectrum.

I appreciate the concerns, especially regarding the uncertainty of long term effects. However, many of the children I work with are taking powerful psychotropic medications that we don't know what the long term effects are either. Many children are prescribed these medications "off label" meaning that they are not FDA approved for children. The atypical antipsychotics that are frequently prescribed for children with behavioral issues, even the one that is FDA approved for children, can have significant side effects. I've seen children develop tardive dyskinesia, diabetes, have liver and kidney damage, experience cognitive delays, etc. from prescribed medications. The issues with prescription medications are rarely discussed.

Many parents are using CBD products for their children. They report great effectiveness.

I believe that we have to be open to all possible treatments that can help children. I fully believe in providing options to parents who are educated by their prescribers so that they can make an informed choice. As with any medication, follow up is critical.

I work with several adults on the spectrum who are prescribed medical marijuana with great success. They are able to function more successfully without the side effects of the psychotropic medications. (Sandy Smith was correct in her testimony about the significant costs that limit some people from accessing this valuable treatment option.)

I found this article that you may find interesting. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7000154/

Again, I can't recommend or promote the use of any medications or over the counter products. But, I did want to share my thoughts and experiences.

Please let me know if you have further questions.

(And I like the new version of SB 2089.) Thank you!

Barb

Barbara Stanton, PhD, LPCC, LMFT