E Duvall APRN, FNP-C, PMHNP-BC

SUBSTANCE USE UPDATE

WHAT'S HAPPENING NATIONALLY AND LOCALLY

OBJECTIVES

1. Provide training and technical assistance services to the substance use prevention field
2. Provide an overview of common trends within current geographic region of Missouri
3. Provide guidelines and resources for clinicians to assist those who have substance use disorder
4. Discuss medications used to treat substance abuse disorders

EXTRA EXTRA

- Over 115 million pills containing illicit fentanyl seized by law enforcement in 2023
-
- More than 321,000 U.S. children lost a parent to drug overdose from 2011 to 2021
- Law enforcement seizures of psilocybin mushrooms rose dramatically between 2017-2022
- Overdose deaths increased in pregnant and postpartum women from early 2018 to late 2021

NIH data all published in 2023


BLACKMON GETS SIX-YEAR, $108 MILLION CONTRACT

THE DENVER POST

Overdoses overwhelming

KEEPING THE DREAM ALIVE

WHAT'S HAPPENING

- **FENTANYL IS FINDING ITS WAY INTO THE HANDS OF MIDDLE SCHOOLERS. EXPERTS SAY NARCAN IN CLASSROOMS CAN HELP PREVENT DEATHS.**
- **NO LONGER 'JUST SAY NO.' NEW APPROACH TO DRUG ADDICTION OFFERS NUANCE.**
- More than 87,000 Americans died of drug overdoses over the 12-month period that ended in September (2022), according to preliminary federal data, eclipsing the toll from any year since the opioid epidemic began in the 1990s.
- The surge represents an increasingly urgent public health crisis, one that has drawn less attention and fewer resources while the nation has battled the coronavirus pandemic.

- NIH data all published in 2023

ONLY 1 IN 5 U.S. ADULTS WITH OPIOID USE DISORDER RECEIVED MEDICATIONS TO TREAT IT IN 2021

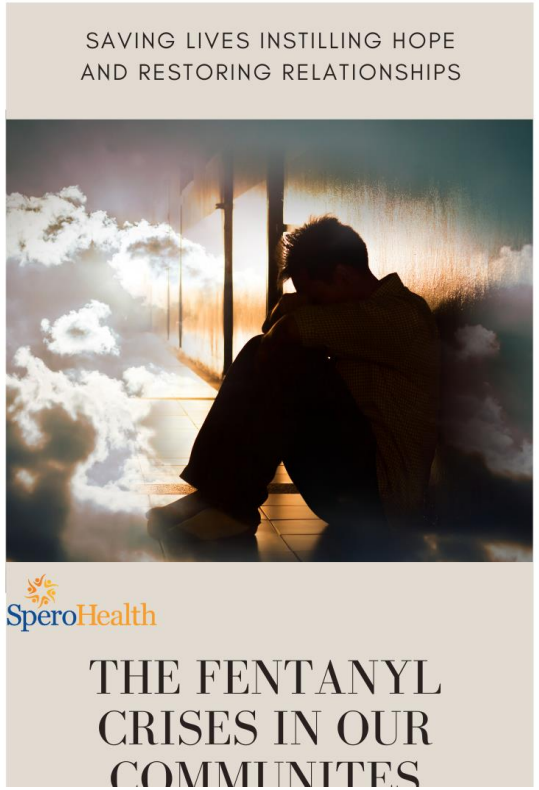
- In 2021, an estimated 2.5 million people aged 18 years or older in the U.S. had opioid use disorder in the past year, yet only 1 in 5 of them (22%) received medications to treat it.
- Substantially less likely to receive medication for opioid use disorder, including:
  - Black adults
  - Women
  - Those who were unemployed,
  - Those in nonmetropolitan areas

In 2021, nearly 107,000 people died of a drug overdose, with 75% of those deaths involving an opioid

National Institute on Drug Abuse (NIDA) (nih.gov)

MISSOURI DATA

- **Data points to a nearly 75% increase in overdoses in Missouri since 2019, and last year was the second consecutive year that fentanyl accounted for over two-thirds of overdoses in Missouri.**
- The drug is up to 50 times more powerful than heroin and far cheaper to produce. It can also be spliced into various drugs to make counterfeit pills that can be fatal.
- National Survey on Drug Use and Health. The new report finds that approximately 943,000 Missouri residents have a substance use disorder and 1,248,000 adults have a mental illness.
    - Fighting Fentanyl: The Federal Response to a Growing Crisis | 2022 Congressional Testimony from CDC



CDC UPDATE

- The preliminary data released Wednesday by the Centers for Disease Control and Prevention show a 29 percent rise in overdose deaths from October 2019 through September 2020 — the most recent data available — compared with the previous 12-month period. Illicitly manufactured fentanyl and other synthetic opioids were the primary drivers, although many fatal overdoses have also involved stimulant drugs, particularly methamphetamine.

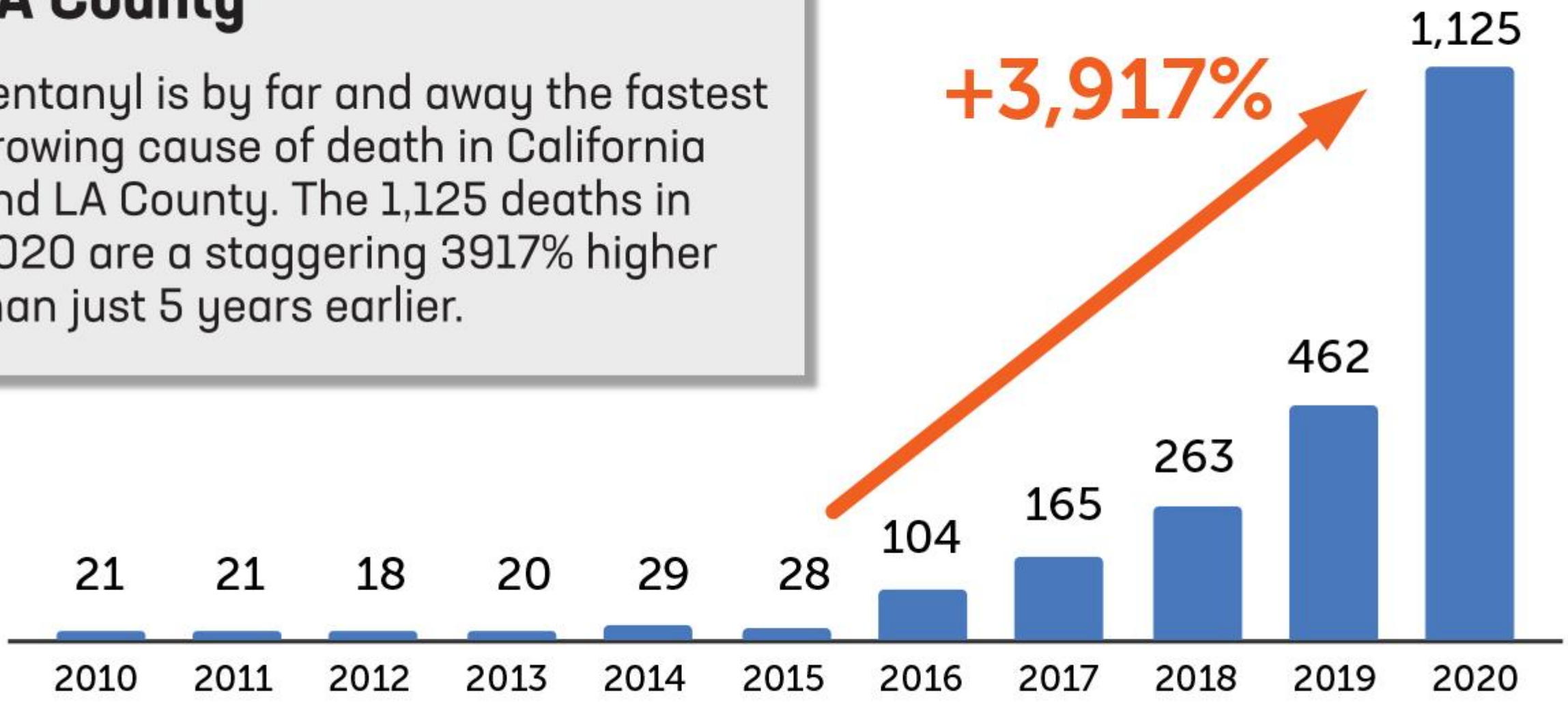
- Fighting Fentanyl: The Federal Response to a Growing Crisis | 2022 Congressional Testimony from CDC

WHO IS IT AFFECTING NOW

- And unlike in the early years of the opioid epidemic, when deaths were largely among white Americans in rural and suburban areas, the current crisis is affecting Black Americans disproportionately.
- “The highest increase in mortality from opioids, predominantly driven by fentanyl, is now among Black Americans,” Dr. Nora Volkow, the director of the National Institute on Drug Abuse, said at a national addiction conference last week. “And when you look at mortality from methamphetamine, it’s chilling to realize that the risk of dying from methamphetamine overdose is 12-fold higher among American Indians and Alaskan Natives than other groups.”
- Dr. Volkow added that more deaths than ever involved drug combinations, typically of fentanyl or heroin with stimulants.

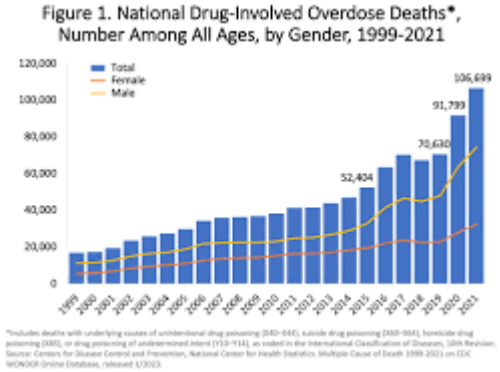
Fentanyl Overdose Deaths in LA County

Fentanyl is by far and away the fastest growing cause of death in California and LA County. The 1,125 deaths in 2020 are a staggering 3917% higher than just 5 years earlier.

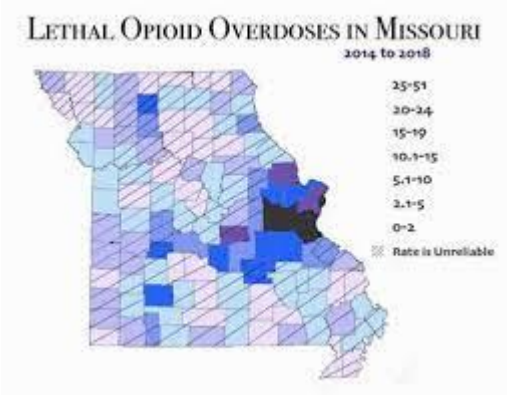


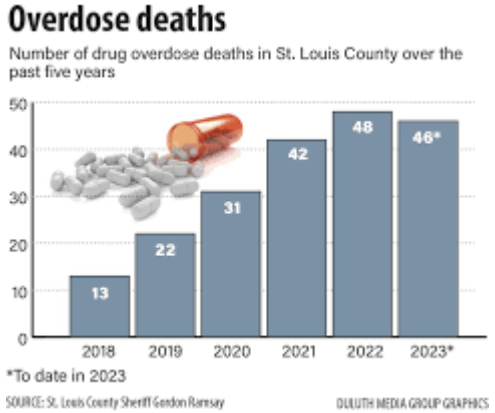
Source: L.A. County Coroner

WHAT'S HAPPENING NATIONAL VS LOCALLY?



WHAT'S HAPPENING LOCALLY?





- **Three Springfield Men Sentenced for Conspiracy to Distribute Nearly 38 Kilos of Fentanyl**
- Tuesday, October 17, 2023

- GREENE-supplementary-data.pdf (mo.gov)

GREENE COUNTY MO

- In 2020, Missouri saw 1,386 drug overdose deaths, 142 of which were in the DHSS Southwest Region. This represents in 21% increase statewide and 15% increase in Southwest Missouri compared to 2019. Approximately ¾ of these deaths involved opioids – an increase statewide by 30%.
- Revive is an app designed to prevent overdose deaths. Get step-by-step rescue instructions to follow on what to do when you or someone you're with is experiencing an opioid overdose.
- The app also features information about where to access naloxone in Greene County, Good Samaritan laws, information about treatment and recovery services and more.
-

- Substance Use | Springfield, MO - Official Website (springfieldmo.gov)

OPIOID – all natural, synthetic, and semi-synthetic chemicals that interact with opioid receptors in the body and brain to relieve the feelings of pain and reduce pain signals;

opioids include but are not limited to heroine, fentanyl, morphine, oxycodone, and codeine;

the term opiate refers to natural opiates (opium) or those derived from opium

Alcohol Use Disorder (AUD) → alcoholism, alcohol dependence, alcohol abuse

Opioid Use Disorder (OUD) → opioid dependence, opioid addiction, opioid abuse

Substance Use Disorder (SUD) – umbrella term to include substances under AUD and OUD

BUPRENORPHINE

- Buprenorphine is a synthetic opioid developed in the late 1960s and is used to treat pain and opioid use disorders (OUDs).
- This drug is a synthetic analog of thebaine—an alkaloid compound derived from the poppy flower.
- Buprenorphine is categorized as a Schedule III drug, which means it has a moderate-to-low potential for physical dependence or a high potential for psychological dependence.
- **FDA-Approved Indications:**

  Buprenorphine is approved by the U.S. Food and Drug Administration (FDA) to treat acute and chronic pain and opioid dependence.

  Agonist substitution treatment—a method for addressing addiction by substituting a more potent full agonist opioid, such as heroin, with a less potent opioid, such as buprenorphine or methadone.

Buprenorphine - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- **Indications (additional):**
- For the management of opioid-dependent patients with a contraindication to methadone.
- Methadone facilities and healthcare providers are currently unavailable, and there exists a waitlist exceeding 3 months for enrollment in a methadone clinic.
- For patients dependent on opioids who are intolerant to or have experienced treatment failure with methadone.
- Buprenorphine may also be beneficial for individuals with a brief history of opioid dependence and/or lower requirements for opioid agonists.

- Buprenorphine - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- **Mechanism of Action**
- Buprenorphine is a partial agonist at the mu receptor, which means it partially activates mu-opiate receptors.
- Buprenorphine also acts as a weak kappa receptor antagonist and delta receptor agonist.
- Buprenorphine is a potent analgesic acting on the central nervous system (CNS), which possesses a distinctive quality with its partial agonism at the mu receptor.

  The mu-1 receptor is responsible for analgesia and dependence.

  The mu-2 receptor is vital for euphoria, dependence, respiratory depression, miosis, decreased digestive tract motility/constipation

  Mu-3 receptor causes vasodilation. Kappa receptors (KOR) bind to dynorphin A and B (Prodynorphin as the precursor). They provide analgesia, diuresis, and dysphoria.

- This unique characteristic imparts several notable properties, including the plateauing of its analgesic effects at higher doses.

  - Physiology, Opioid Receptor - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- Buprenorphine exhibits ceiling effects on respiratory depression, signifying its safety superiority over methadone in the context of agonist substitution treatment for addiction.
- ***Buprenorphine exhibits high-affinity binding to the mu-opioid receptors and slow-dissociation kinetics***. In this way, it differs from other full-opioid agonists such as morphine and fentanyl, which results in milder and less uncomfortable withdrawal symptoms for the patient.
- (11) Mechanism of Action of a Partial Opioid Agonist - YouTube

BUPRENORPHINE

- ***Buprenorphine is a partial opioid agonist, meaning that it binds to those same opioid receptors but activates them less strongly than full agonists do.***
- Like methadone, it can reduce cravings and withdrawal symptoms in a person with an opioid use disorder without producing euphoria, and patients tend to tolerate it well.
- A partial agonist is a drug that interacts with a receptor but produces less than the maximal effect
- A partial agonist produces less than full agonist effects and is by definition less efficacious than a full agonist.
- Buprenorphine for Opioid Use Disorder (youtube.com)

Physiology, Opioid Receptor - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- Research has found buprenorphine to be similarly effective as methadone for treating opioid use disorders, ***as long as it is given at a sufficient dose and for sufficient duration***.
- The U.S. Food and Drug Administration (FDA) approved buprenorphine in 2002, making it the first medication eligible to be prescribed by certified physicians.
- Additionally, the Comprehensive Addiction and Recovery Act (CARA), which was signed into law in July 2016, temporarily expands eligibility to prescribe buprenorphine-based drugs for medication-assisted treatment (MAT)

- Physiology, Opioid Receptor - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- **GOAL:** Buprenorphine substitute treatment enables patients to focus on therapy rather than enduring uncomfortable withdrawals. The drug proves to be an effective choice for addressing opioid dependence by diminishing cravings and enhancing the overall quality of life during addiction treatment. By mitigating many distressing symptoms associated with opioid withdrawal, this approach facilitates the development of treatment plans that patients are more likely to adhere to, thereby reducing both morbidity and mortality rates.
- **Federal Regulations for Buprenorphine Prescribing:**
- Sublingual buprenorphine preparations are beneficial in the treatment of opioid dependence, including substances such as heroin, oxycodone, hydrocodone, and morphine. The utilization of buprenorphine as a replacement in opioid dependence management is subject to strict regulations and rigorous monitoring.
    - Physiology, Opioid Receptor - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- **Pharmacokinetics**
- Absorption: When administered orally, buprenorphine experiences poor bioavailability due to the first-pass effect, where the liver and intestine extensively metabolize the drug. **The preferred route of administration is sublingual, as it ensures rapid absorption and circumvents the first-pass effect.** Placing the tablet under the tongue results in a slow onset of action, with the peak effect occurring approximately 3 to 4 hours after administration.
- Distribution: Buprenorphine is highly lipophilic; therefore, it is extensively distributed and rapidly penetrates the blood-brain barrier. Buprenorphine is approximately 96% protein-bound.
- Metabolism: Buprenorphine undergoes metabolism by cytochrome CYP3A4 enzymes after it enters the body and forms an active metabolite.

- Physiology, Opioid Receptor - StatPearls - NCBI Bookshelf (nih.gov)

BUPRENORPHINE

- The average half-life of buprenorphine is approximately 38 hours, which ranges from 25 to 70 hours after sublingual administration. Substances that strongly inhibit the CYP3A4 enzyme can elevate buprenorphine levels, while inducers of this enzyme may lead to decreased levels.
- Excretion: Most of the drug and its metabolite are eliminated through fecal excretion, with less than 20% excreted by the kidneys. Due to its slow onset of action and extended duration, buprenorphine proves effective in the treatment of opioid dependence.
- Once stabilized on a daily dose, prescribing buprenorphine on alternate days may be considered.
- Urine toxicology tests for patients taking buprenorphine often measure norbuprenorphine levels, which are highly concentrated in urine. This helps confirm patients are not manipulating tests by adding buprenorphine directly.

- Physiology, Opioid Receptor - StatPearls - NCBI Bookshelf (nih.gov)

SUBUTEX VS SUBOXONE (CONTROLLED SCHEDULE III)

SUBUTEX

- Straight buprenorphine
  - Buprenorphine prevents withdrawal symptoms from and reduces cravings for opiate drugs like heroine, cocaine, and prescription pain killers
- Prescribed during pregnancy/nursing, have severe liver disease, or a documented naloxone allergy
- Second choice by prescribers because still can be abused by injecting intravenously in order to obtain the high

SUBOXONE

- Combination of buprenorphine and naloxone
  - Naloxone was later combined with buprenorphine to deter abuse of the medication by blocking the effect of opioids
- Always prescribe first unless patient is pregnant/nursing or has documented severe side effects
- If injected, patient will immediately go into precipitated withdrawal which can be distressing

- Sublocade – monthly injectable buprenorphine- will be offered at a future date (training on clinic staff is needed)
- Vivitrol – monthly injectable naltrexone
- Zubsolv, Belbuca, Bunavail – other oral buprenorphine

PRESCRIBING

- Any SUD medications will be written as a 1-28 day supply
- Patients are to use one main pharmacy; this will NOT be negotiable from provider standpoint
- Use of the Prescription Drug Monitoring Program (PDMP)

COMPLIANCE

- Patients may not crush, inject, or shave medication
- Dose changes are not permitted without consulting the provider
- Patients must agree to safe storage and no sharing
- Use of alcohol or other substances will be discouraged and addressed
    - Opioids | National Institute on Drug Abuse (NIDA) (nih.gov)

CHALLENGES

- Because maintenance medications (methadone and buprenorphine) are themselves opioids and are able to produce euphoria in people who are not dependent on opioids, many people have assumed that this form of treatment just substitutes a new substance use disorder for an old one. This belief has unfortunately hindered the adoption of these effective treatments.

Daily Sublingual Buprenorphine Dose*	BRIXADI Weekly	BRIXADI Monthly
≤6 mg	8 mg	-
8-10 mg	16 mg	64 mg

FASTER APPROACH FOR STARTING EXTENDED-RELEASE NALTREXONE TO TREAT OPIOID USE DISORDER SHOWN EFFECTIVE

- Naltrexone

- **May Treat:** Alcohol use disorder · Relapse to opioid dependence
- **Brand Names:** Revia · Depade · Trexan (naltrexone HCl), Vivitrol
- Naltrexone is a prescription medication used to treat alcohol use disorder (AUD) and opioid use disorder (OUD) to reduce cravings and help control physiological dependence. Naltrexone works by blocking the effects of alcohol and opioid medications, preventing the euphoria and intoxication (the “buzz”) these substances cause, and it also helps reduce the urge or cravings to use alcohol or opioids.
- Naltrexone is an opioid antagonist. Its mechanism of action (MOA) is blocking the mu opioid receptor.
- This medicine also modifies how the hypothalamus, pituitary gland, and adrenal gland (hypothalamic-pituitary-adrenal axis, HPA axis) interact to suppress the amount of alcohol consumed.

VIVITROL

- Vivitrol is a long-acting injectable form of naltrexone, which is a medication used to treat two substance use disorders - opioid use disorder and alcohol use disorder (alcoholism).
- Vivitrol is used as part of a treatment program.
- It helps prevent people with alcohol or opioid dependence from feeling like they need to use these substances.
- Vivitrol is an opioid antagonist, which works by blocking mu opioid receptors.
- It also suppresses the amount of alcohol you feel like drinking by changing how your hypothalamus, pituitary gland and adrenal gland work together.
- Vivitrol blocks the intoxication and euphoria or 'high' that alcohol and opioids cause. It also blocks the pain relief that opioids provide.

VIVITROL

Sudden opioid withdrawal:

- Anyone who receives a Vivitrol injection must not use any type of opioid (must be opioid-free) including street drugs, prescription pain medicines, cough, cold, or diarrhea medicines that contain opioids, or opioid dependence treatments, buprenorphine or methadone, for at least 7 to 14 days before starting treatment with this medication.
- Using opioids in the 7 to 14 days before you start receiving Vivitrol may cause you to suddenly have symptoms of opioid withdrawal when you get your injection.
- Sudden opioid withdrawal can be severe, and you may need to go to the hospital.
- You must be opioid-free before receiving Vivitrol unless your healthcare provider decides that you don't need to go through detox first. Instead, your doctor may decide to give your injection in a medical facility that can treat you for sudden opioid withdrawal.

VIVITROL

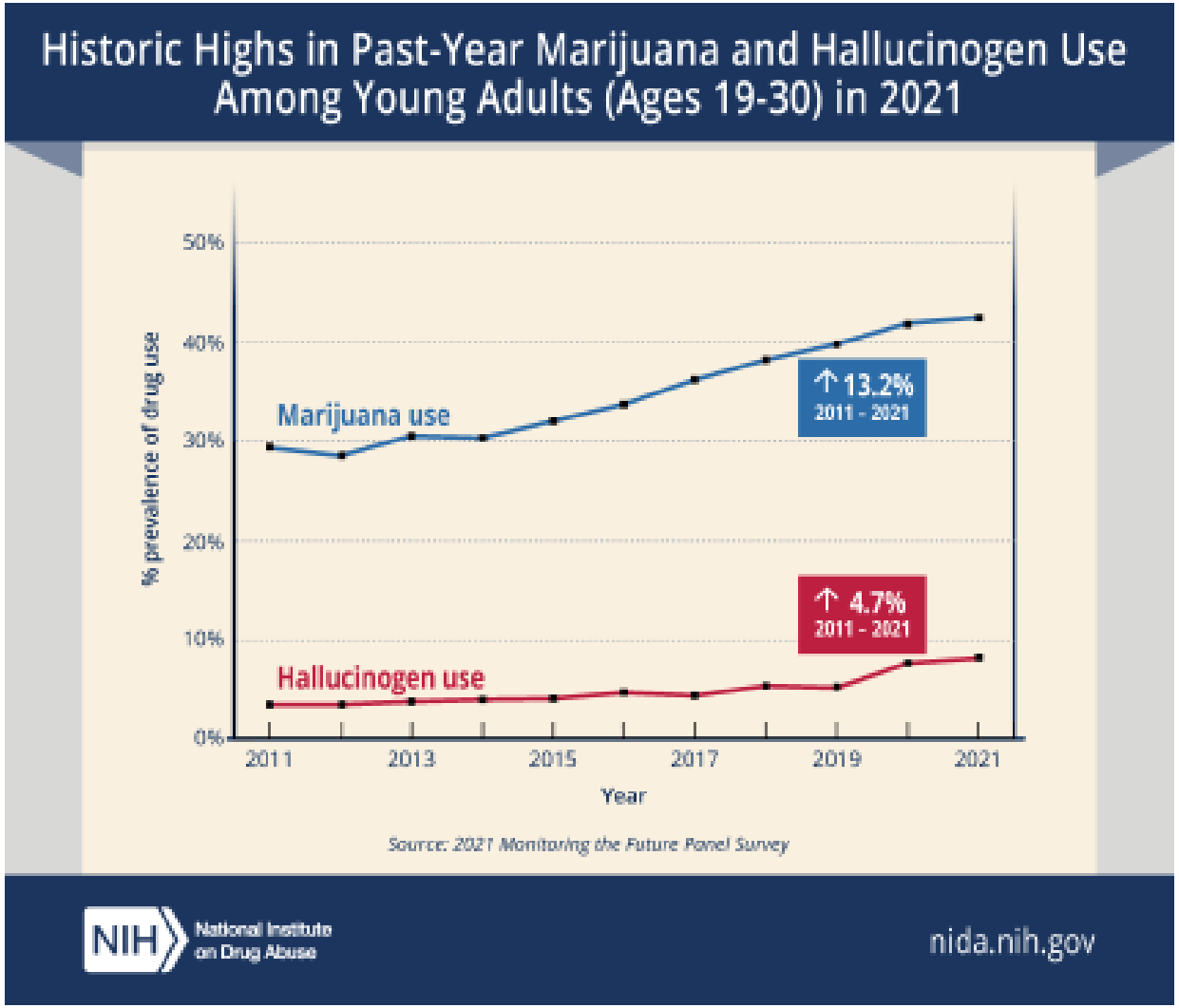
What do I need to know before giving Vivitrol?

- have liver problems
- use or abuse street (illegal) drugs
- have hemophilia or other bleeding problems
- have kidney problems
- have any other medical conditions

SO HERE WE ARE……

MARIJUANA AND HALLUCINOGEN USE AMONG YOUNG ADULTS REACHED ALL TIME-HIGH IN 2021

MARIJUANA AND HALLUCINOGEN USE AMONG YOUNG ADULTS REACHED ALL TIME-HIGH IN 2021 | NATIONAL INSTITUTE ON DRUG ABUSE (NIDA) (NIH.GOV)



WHERE IS MARIJUANA LEGAL?

- 2012 Colorado legalized marijuana.
- Recreational marijuana is legal in 19 states, Washington, D.C., and Guam since 2012.
- Opponents say marijuana poses a public health and safety risk.
- Some are morally against legalization.
- Proponents argue that it is not as dangerous as alcohol.
- evidence that it has therapeutic benefits, such as stress and pain relief?
- Advocates also see it as a moneymaker for states and a necessary social justice initiative.

STATES WHERE MARIJUANA IS LEGAL

Colorado	Washington	Alaska	Oregon	Washington, D.C.	California
Maine	Massachusetts	Nevada	Michigan	Vermont	Guam
Illinois	Arizona	Montana	New Jersey	South Dakota	New York
Virginia	New Mexico	Connecticut			

MARIJUANA

- **Marijuana Use:** Past-year, past-month, and daily marijuana use (use on 20 or more occasions in the past 30 days) reached the highest levels ever recorded since these trends were first monitored in 1988. The proportion of young adults who reported past-year marijuana use reached 43% in 2021, a significant increase from 34% five years ago (2016) and 29% 10 years ago (2011). Marijuana use in the past month was reported by 29% of young adults in 2021, compared to 21% in 2016 and 17% in 2011. Daily marijuana use also significantly increased during these time periods, reported by 11% of young adults in 2021, compared to 8% in 2016 and 6% in 2011.

FEDERAL VS STATE LAW

- The problem is that under the Supremacy Clause of the U.S. Constitution, federal law trumps state law.

  Therefore, the federal government wins any conflicts of laws.

  As such, state recreational marijuana structures and commercial operations remain in an uneasy legal position.
- Not selling to minors, not crossing state lines, and not allowing criminal enterprises to engage with the licensed marijuana business are all restrictions under state marijuana laws.
- If all state laws are followed, the federal government is choosing to look the other way.

- https://www.pharmacytoday.org/article/S1042-0991(20)30965-8/fulltext

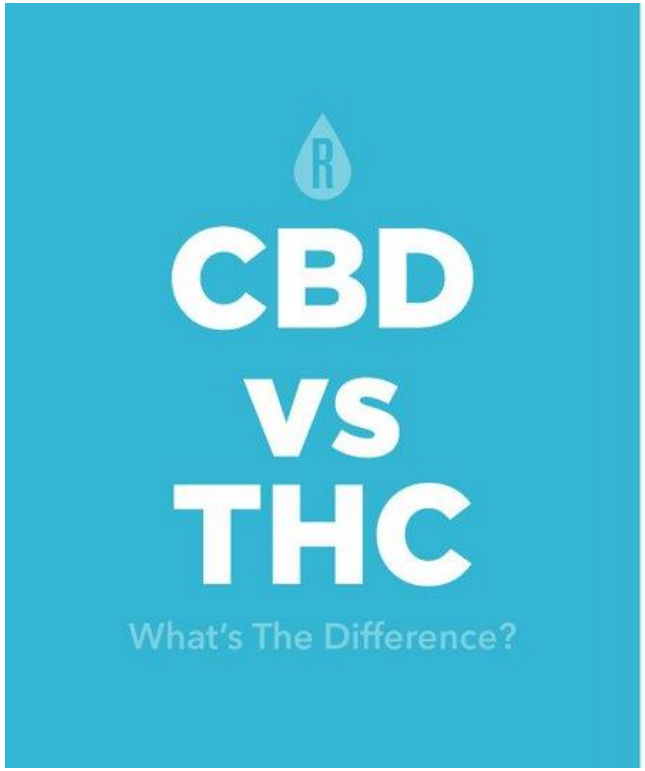
HISTORY OF CANNABIS

- Dates back to 1500 BC
- 19th century; documented use for tetanus and seizures disorder
- It was available as a licensed medicine in the United States for about a century before the American Medical Association removed it from the 12th edition of the *U.S. Pharmacopeia* (IOM, 1999).
- In 1985, pharmaceutical companies received approval to begin developing tetrahydrocannabinol (THC) preparations
- Dronabinol and nabilone started being looked at for therapeutic use
- As a result, cannabinoids were reintroduced into the armamentarium of willing health care providers (Grotenhermen and Müller-Vahl, 2012).

https://www.pharmacytoday.org/article/S1042-0991(20)30965-8/fulltext


CBD
Low THC (<0.3%)
108-120 days growth cycle
Non-psychoactive
Adaptable growing
Clothing, body care
THC
High THC (5-35%)
60-90 days growth cycle
Psychoactive
Carefully growing
Medical and recreational uses

CANNABIS


CBD
VS
THC
What's The Difference?


Hemp
• Higher CBD
• Traces of THC < 0.3%
• Medicinal Uses
• Various Industrial Uses
• Food
Marijuana
• Higher THC
• Recreational Uses
• Medicinal Uses
Cannabidiol (CBD) and Delta-9 tetrahydrocannabinol (THC), both active in marijuana, have different and sometimes opposite effects.
CBD no high
non-psychoactive
Widely Known Benefits
• Anxiety
• Cramps
• Migraine/Headache
• Inflammation
• Arthritis
• Seizures +much more
CBD does not directly bind with the CB1 receptor, instead CBD interacts with other receptors and pathways in the body which explains specific and non-psychoactive relieved health benefits.
THC gets you high
psychoactive
Widely Known Benefits
• Nausea
• Appetite
• Sleep
• Glaucoma
• Muscle Spasms
• Pain Relief +much more
THC directly binds to CB1 receptors in the body, which are predominantly found in the brain and nervous sysytem. The CB1 receptor activation is therefore responsible for the "High" from cannabis.

CANNABIS USE: WHAT PROVIDERS NEED TO KNOW

- To date, the FDA has not approved a marketing application for cannabis for the treatment of any disease or condition.
- The agency has, however, approved one cannabis-derived drug product:
- Epidiolex (cannabidiol), and three synthetic cannabis-related drug products:

  Marinol (dronabinol), Syndros (dronabinol), and Cesamet (nabilone).
- These approved drug products are only available with a prescription from a licensed healthcare provider. Importantly, the FDA has not approved any other cannabis, cannabis-derived, or cannabidiol (CBD) products currently available on the market.

- https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process

CANNABIS USE: WHAT PROVIDERS NEED TO KNOW

At the federal level: Cannabis remains classified as a Schedule I substance under the Controlled Substances Act

Schedule I substances are considered to have a high potential for dependency and no accepted medical use, making distribution of cannabis a federal offense

https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process

CANNABIS USE: WHAT PROVIDERS NEED TO KNOW

Schedule I, banned substances
Federally illegal to possess, obtain, or distribute without proper license.
Schedule I substances are thought to have a high potential for abuse and dependence and no medicinal qualities
Synthetic cannabinoids are often used illicitly (eg, Spice, K2, Kronic, and Purple Haze)
https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process

The Cannabis and Cannabinoids Knowledge Assessment Survey (CCKAS) was conducted in January 2020

The questionnaire generated 556 responses

Fairly equal distribution across five specialties (roughly 20% each): Neurology, physiatry/pain medicine, family medicine/general practice, internal medicine, and pediatrics.

Approximately half (52%) of the respondents reported practicing in an office setting.

17% said they were a part of a university/academic-based practice

15% were hospital-based.

The mean age of the respondents was 53, and they reported being in practice for an average of 21 years.

https://www.neurologyreviews-digital.com/neurologyreviews/nord_march_2020/MobilePagedArticle.action?articleId=1566841#articleId1566841

NEUROLOGY REVIEW

Half of your peers are under the mistaken impression that tetrahydrocannabinol (THC) has been clinically proven as safe

Many providers remain confused about THC and cannabidiol (CBD) pharmacology and potential mechanisms of action, the formulations of cannabinoids that are FDA approved, and the conditions under which hemp and products derived from it are descheduled.

Majority of respondents report that they are self-educating in an effort to keep current.

Sixty percent of respondents are self educating, while 20% have no training at all.

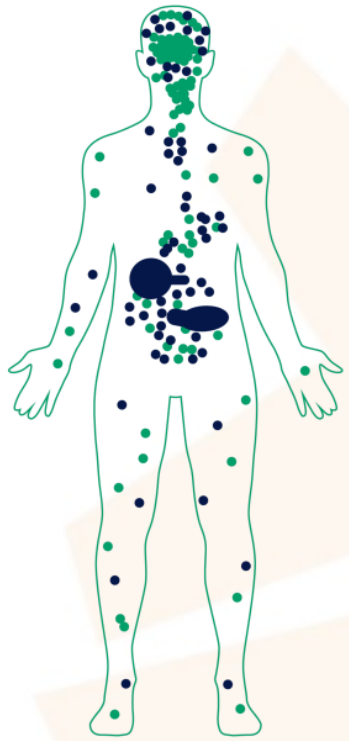
When it comes to the endocannabinoid system specifically, 40% report no training at all, while 40% are self educating.

https://www.neurologyreviews-digital.com/neurologyreviews/nord_march_2020/MobilePagedArticle.action?articleId=1566841#articleId1566841

Cannabinoid Receptors: CB1 and CB2

CB1

- Primarily found in the brain and CNS, and to a lesser extent in other tissues such as lung, muscle, and gut
- Responsible for euphoric effects, anti-anxiety, neurotransmitter suppression (decreased excitation/reduced inhibition)



CB2

- Mostly in peripheral organs, especially cells associated with the immune system (eg, spleen, tonsils)
- Anti-oxidant, anti-inflammatory, immunosuppressive/activating effects

CNS = central nervous system.

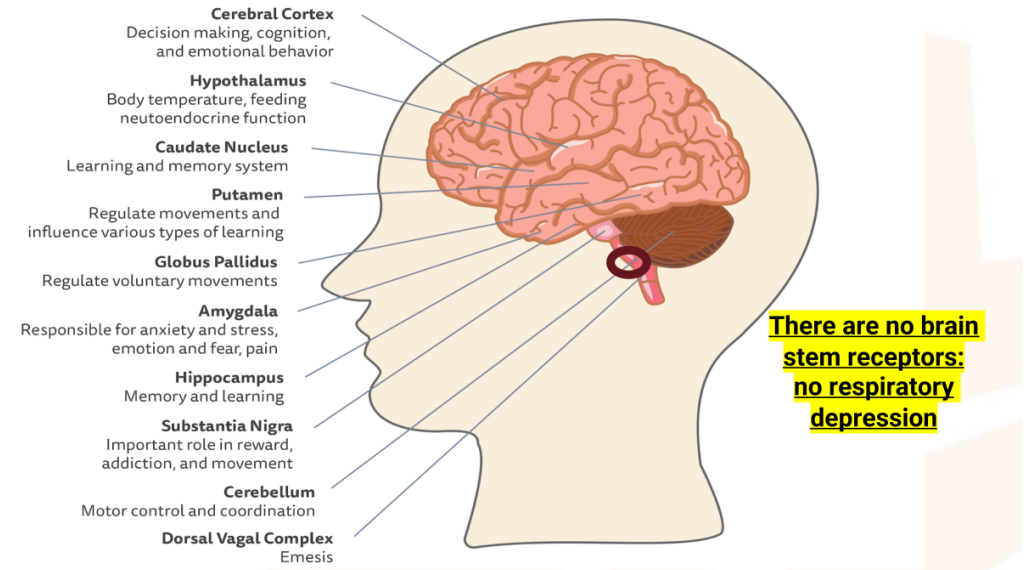
Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. 2013. Accessed July 21, 2021. www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/marihuana/med/infoprof-eng.pdf

CANNABIS: WHAT PROVIDERS NEED TO KNOW

CB1 Receptor Distribution

CB1

CB1 is most abundant receptor in the brain



There are no brain stem receptors: no respiratory depression

Mackie K. *Handb Exp Pharmacol.* 2005;(168):299-325.

CANNABIS USE: WHAT PROVIDERS NEED TO KNOW

Phytocannabinoids (CBD/THC)

Most well-studied cannabinoids:

- Delta-9-tetrahydrocannabinol (THC)
- Cannabidiol (CBD)

HOWEVER, THERE ARE >100 OTHER CANNABINOIDS

Ratio and concentration of THC and CBD produce both the health benefits and side effects

- Different cannabis varieties have different THC:CBD ratios
- THC:CBD ratio is dependent on species genetics, environmental growing conditions, and selection /processing of female buds

THC, CBD, and other compounds in cannabis may work synergistically:

THE ENTOURAGE EFFECT

Entourage Effect: Medicinal value of the **WHOLE** plant → it is the combination of the various cannabinoids (eg, THC, CBD, CBG, CBN, etc.) in conjunction with the aromatic terpenes that gives patients relief for a broad constellation of symptoms (eg, pain, anxiety, insomnia, inflammation, GI distress, etc.)

Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the cannabinoids. 2013. Accessed July 21, 2021. www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/marihuana/med/infoprof-eng.pdf

- **CANNABIS**

- *Cannabis sativa L.* is a plant that contains over 80 different naturally occurring compounds called “cannabinoids”
- Two well-known cannabinoids:
  - **Cannabidiol (CBD)**
  - **Tetrahydrocannabinol (THC)**
- Plants are grown to produce varying concentrations of cannabinoids – **THC** or **CBD**
- These plant variations are called cultivars

- **Cannabis-derived compounds**

- Compounds occurring naturally in the plant – like **CBD** and **THC**
- These compounds are extracted directly from the plant
- Can be used to manufacture drug products
- Example: highly-purified CBD extracted from the plant
  - https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process

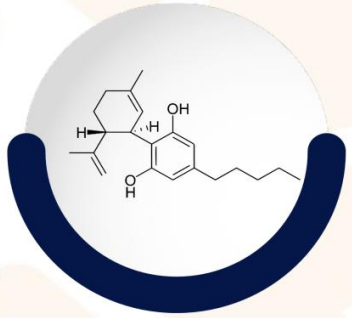
ANY APPROVAL?

- FDA has approved Epidiolex, which contains a purified form of the drug substance cannabidiol (CBD) for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome.
- For those 2 years of age and older.
- FDA has concluded that CBD product is safe and effective for its intended use

CANNABIS USE: WHAT PROVIDERS NEED TO KNOW

CBD
(Cannabidiol)

- Minimal psychoactive (impairing) effects
- Does not fit directly into CB1/CB2 receptors (negative allosteric modulator of CB1) but has indirect effects on ECS
  - Works on regulatory enzymes in endocannabinoid system (↑eCBs) via reuptake inhibition
- Can work synergistically and/or antagonize psychoactive effects of THC
- May have more medicinal applications than THC:
  - Anti-inflammatory
  - Anti-emetic
  - Anti-convulsant
  - Anxiolytic
  - Analgesic
  - Anti-psychotic



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Cannabis: The Plant

Genus: *Cannabis*
Family: Cannabaceae
Main species: *C. Sativa, C. Indica*

	C. Sativa	*C. Indica*
Plant Morphology	• Taller, less dense • Longer, more narrow leaves	• Shorter, bushier • Shorter, wider leaves

Purported Effects	• "Head high"
	  • Alertness
	  • Uplifting, euphoric
	  • ↑ creativity
	  • ↑ energy
		• "Body high"
		  • Deep relaxation
		  • Sleep aid
		  • Appetite stimulant
		  • Pain relief

Best Suited for	Daytime use	Nighttime use

Atakan Z. *Ther Adv Psychopharmacol*. 2012;2(6):241-254.


MY JOINTS ARE STIFF.
IT'S BECAUSE YOU'RE ROLLING THEM TOO TIGHT.
STAHLER. 5/25
©2016 Jeff Stahler/Dist. by Universal UClick for UFS

SHOULD I TAKE BOTH?

CANNABIDIOL (CBD)

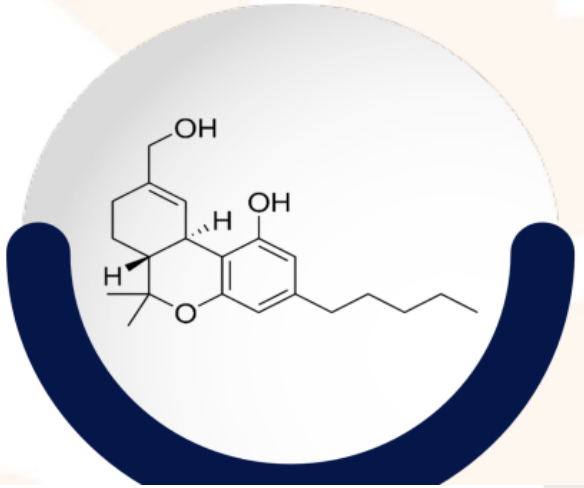
- CBD is well tolerated, even in large doses
- Any side effects that occur with CBD use are likely the result of drug-to-drug interactions between CBD and other medications
- CBD is metabolized through the CYP450 Pathway (3A4 & 2C19)

TETRAHYDROCANNABINOL (THC)

- THC binds with the cannabinoid 1 (CB1) receptors in the brain
- It produces a high or sense of euphoria

THC
(9-Tetrahydrocannabinol)

- Principle psychoactive compound in plant
- Agonizes CB1 and weak to moderate effects on CB2
- Medical applications/effects:
  - Anti-inflammatory
  - Anti-emetic
  - Sedative
  - Anxiolytic/Anxiogenic
  - Analgesic
  - Appetite Stimulating



Health Canada. Information for Health Care Professionals: Cannabis (marihuana, marijuana) and the

CANNABIS: WHAT PROVIDERS NEED TO KNOW

Inhalation of THC

- Diffusion into alveolar capillaries and then enters in the bloodstream
- Maximal onset occurs at **10–30 minutes** and last **2–3 hours**
- Metabolism occurs in the lung, liver, brain
- Rapid dose delivery
- Bioavailability factors (breath holding, duration, depth of inhalation) ~20%
- Highest abuse potential

Sharma P, et al. *Iran J Psychiatry*. 2012;7(4):149-156.

CANNABIS: WHAT PROVIDERS NEED TO KNOW

Ingestion of THC

- Metabolized in the liver and turned into 11-hydroxy THC via CYP450 (CYP3A4, CYP2C9, CYP2C19), CBD undergoes conversion to 7-OH CBD, 6OH-CBD
- Activated prior to ingestion by heating (decarboxylation)
- Increase in sedation or euphoria
- Variables to consider (high intra/inter-patient variability)
  - Other food ingested/gastric contents
  - Individual variation in metabolism rates
  - Frequency of use
- Onset can be anywhere from 30 minutes to 2 hours and can last 5–8 hours
- Extensive liver metabolism reduces bioavailability ~13%

Sharma P, et al. *Iran J Psychiatry*. 2012;7(4):149-156.

I HAVE GOOGLED AND IT IS TOTALY SAFE

CBD SIDE EFFECTS

- CBD’s side effects may include:
- appetite changes
- fatigue
- weight loss
- dizziness
- diarrhea
- These side effects are part of the compound’s psychoactive properties.

THC SIDE EFFECTS

- THC causes temporary side effects, such as:
- increased heart rate
- coordination problems
- dry mouth
- red eyes
- slower reaction times
- memory loss
- Anxiety
- Hyperemesis

- Cannabinoids like THC and CBD are stored in the body's fat
- Cannabinoids can show up on drug tests for several days or weeks after you use them
- Not every drug test will be able to detect CBD, but CBD-sensitive tests are available
- Most standard drug tests will look for chemicals related to THC

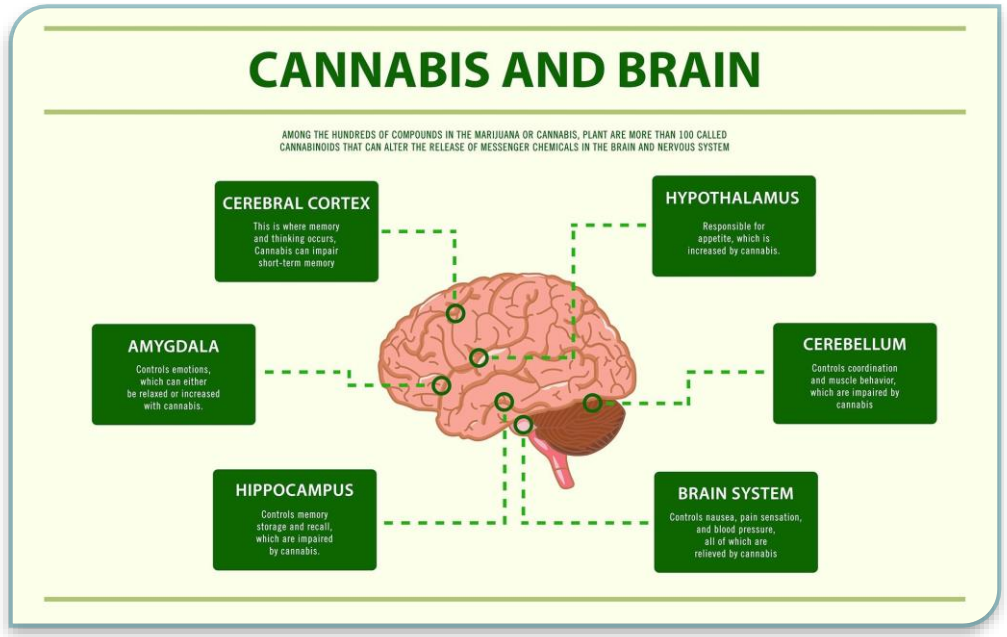
  THC or marijuana use might show up on a screening.

https://www.healthline.com/health/cbd-vs-thc#drug-testing

MARIJUANA AND TEENS

- 38% of high school students report having used marijuana in their life
- Research shows that marijuana can have affect on the developing brain in adolescents; concerns increase with regular or heavy use (regular and heavy use have no defined definition). What information we have on use is self disclosed
- **Decline in school performance.** Students who smoke marijuana may get lower grades
  more likely to drop out of high school than their peers who do not use
- **Increased risk of mental health issues.** Marijuana use has been linked to a range of mental health problems in teens:
  Depression or anxiety
  Psychosis has also been seen in teens at higher risk like those with a family history
  Largest age group for growth of moderate THC use: 11-14 years old.
  Not gender specific
- **Potential for addiction.** Research shows that about 1 in 6 teens who repeatedly use marijuana can become addicted
- Evidence is linking marijuana as the gateway for other substance use disorders
- The earlier the exposure to marijuana, the earlier to "harder" substance use and alcohol
  - https://www.cdc.gov/marijuana/factsheets/teens.htm

I FEEL GREAT ON MARIJUANA, I AM NOT IMPAIRED



- **Impaired driving.** Driving while impaired by any substance, including marijuana, is dangerous.
- Marijuana negatively affects skills required for safe driving:
  - Delayed reaction time
  - Coordination
  - Concentration

https://www.cdc.gov/marijuana/factsheets/teens.htm

TOXICOLOGY OF CANNABIODS?

- No fatal overdoses are reports
- CBD tolerated >100mg
- THC Toxidrome:

  Tachycardia

  Anxiety

  Paranoia

  Hallucinations

  Hyperemesis

  Shortness of breath

NEUROLOGY REVIEW

- 13% said, incorrectly, that clinical trials have proven that THC and CBD work better when used together

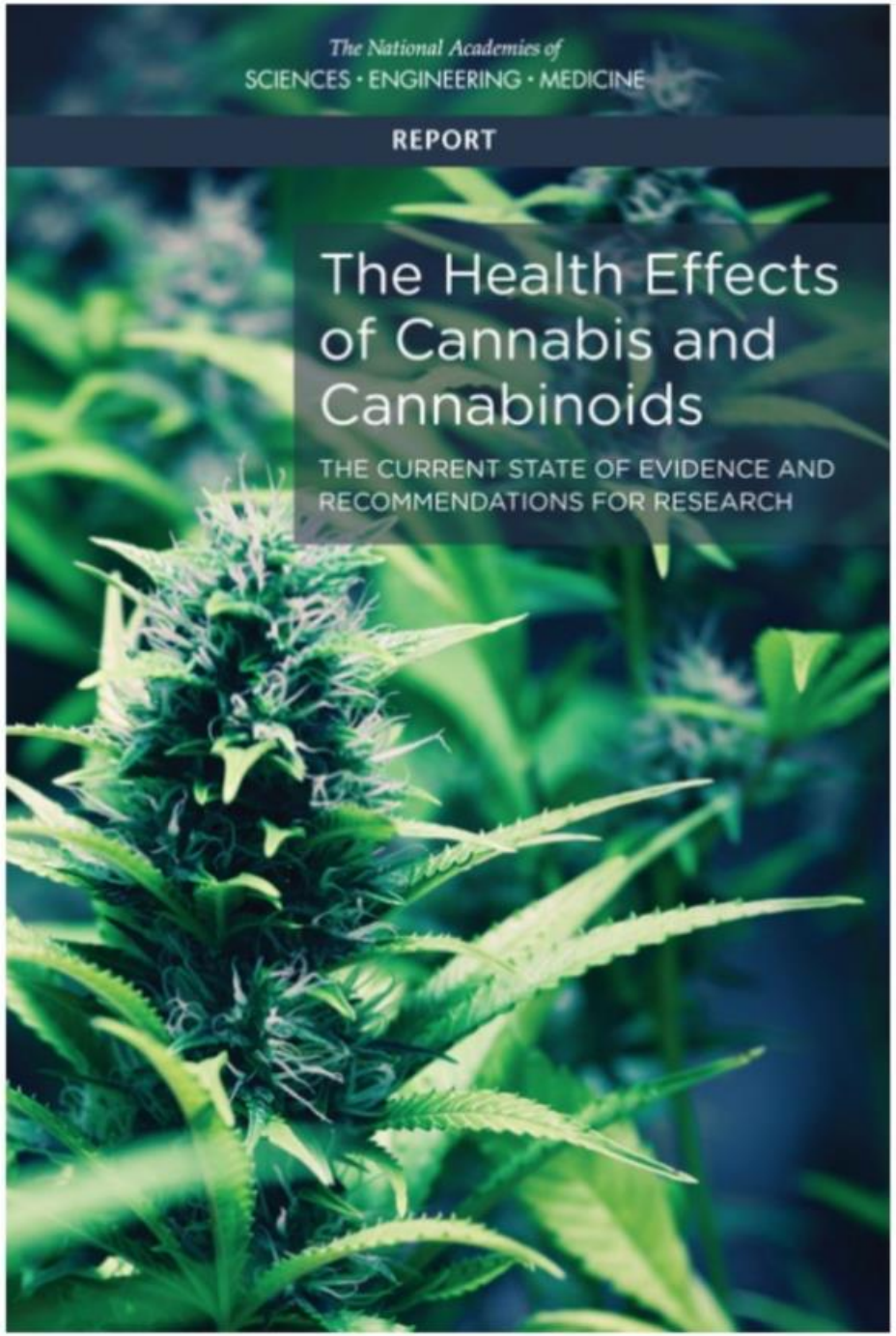
  There is no comparative clinical evidence to validate this claim.

- 12% said, incorrectly, that both THC and CBD can elicit euphoric or intoxicating effects

  CBD does not

- 9% said, incorrectly, that CBD is side-effect free

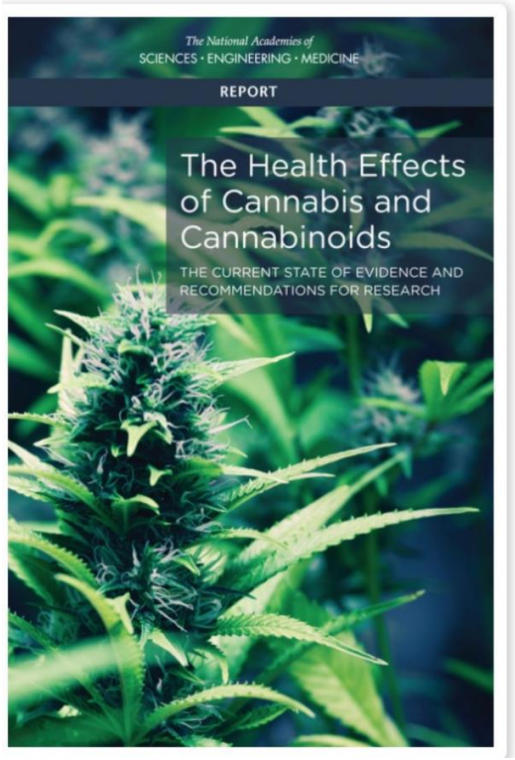
- https://www.neurologyreviews-digital.com/neurologyreviews/nord_march_2020/MobilePagedArticle.action?articleId=1566841#articleId1566841



National Academies Press (2017)

- Recently published 400-page document (US State Sponsored Data), systematic review of 10,700 publications, 2454 participants and all but 1 study was placebo-controlled
- Team made up of experts in mental health, epidemiology, public and population health, reproductive and fetal health, and cannabinoid biology
- Reviewed epidemiological, and clinical trial data on therapeutic effects of cannabis, including health outcomes, as well as data from systematic reviews and primary literature since 1999

CANNABIS: WHAT PROVIDERS NEED TO KNOW



Benefits of Medical Cannabis

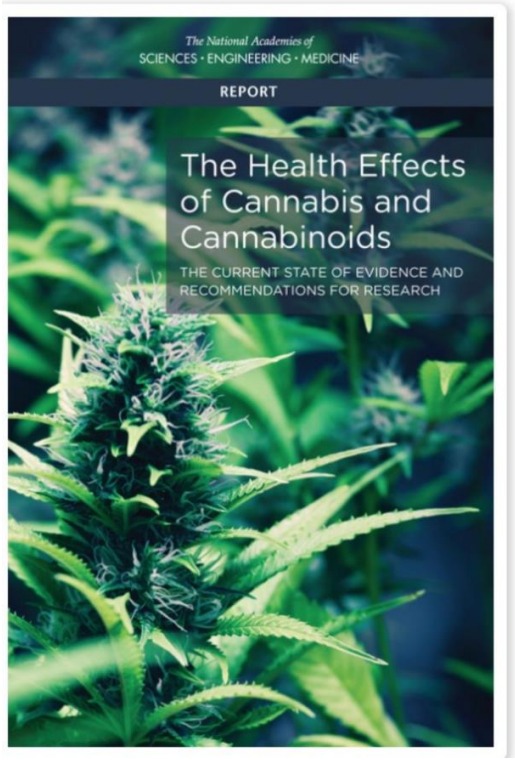
Chronic and Neuropathic Pain
Conclusive evidence to suggest modest to significant analgesic effects, which may be dose-dependent in some cases, have been observed in pain related to musculoskeletal issues, cancer and chemotherapy, and peripheral neuropathies

Nausea and Vomiting
Conclusive evidence to suggest cannabinoids can reduce acute or anticipatory nausea and vomiting associated with chemotherapy and radiotherapy

Spasticity
Moderate evidence to suggest benefits in certain spastic conditions

Sleep Dysfunction
Moderate evidence to suggest benefits in insomnia

CANNABIS: WHAT PROVIDERS NEED TO KNOW



Harms of Medical Cannabis

Lung Disease
Substantial evidence of statistical association between cannabis smoking and worsening respiratory symptoms and more frequency chronic bronchitis episodes (chronic smokers)

Injury and Death
Substantial evidence of a statistical association between cannabis use and increased risk of motor vehicle crashes.
Moderate evidence of overdose injuries including respiratory distress among pediatric populations in legal US states

Perinatal Exposure
Substantial evidence of statistical association between maternal cannabis smoking and lower birth weight of offspring

Mental Health
Substantial evidence of a statistical association between cannabis use and the development of schizophrenia/psychoses, with highest risk in frequent users

RESEARCHERS ARE STUDYING WHETHER MEDICAL MARIJUANA CAN HELP TREAT SEVERAL CONDITIONS INCLUDING:

- Alzheimer's disease
- Appetite loss
- Cancer
- Crohn’s Disease
- Diseases effecting the immune system:
  HIV/AIDS or MS
- Eating disorders such as anorexia
- Epilepsy
- Glaucoma
- Mental health conditions:
  Schizophrenia and PTSD
- Multiple sclerosis
- Muscle Spasms
- Nausea
- Pain
- Seizures
- Wasting syndrome (cachexia)

https://www.ncbi.nlm.nih.gov/books/NBK425767/

CANNABIS: WHAT PROVIDERS NEED TO KNOW

SO WHAT IS HAPPENING?

- Dosing Guidelines
- Federal Law
- State Law
- County Law
- Research
- Not my patients

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- https://www.fda.gov/news-events/public-health-focus/fda-and-cannabis-research-and-drug-approval-process
- https://www.healthline.com/health/cbd-vs-thc#drug-testing
- https://jcannabisresearch.biomedcentral.com/?gclid=CjwKCAjwkvWKBhB4EiwA-GHjFtA9ilgyLt2ba9-ZpzE_fI98NLOpVh1jzU7WtLWiCBnAErQtwR5SHxoCIhYQAvD_BwE
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- https://www.pharmacytoday.org/article/S1042-0991(20)30965-8/fulltext
- https://www.usnews.com/news/best-states/articles/where-is-marijuana-legal-a-guide-to-marijuana-legalization

HALLUCINOGEN USE:

- Use had been relatively stable over the past few decades until 2020, when reports of use started to increase dramatically.
- In 2021, 8% of young adults reported past-year hallucinogen use, representing an all-time high since the category was first surveyed in 1988.
- By comparison, in 2016, 5% of young adults reported past-year hallucinogen use, and in 2011, only 3% reported use. Types of hallucinogens reported by participants included LSD, MDMA, mescaline, peyote, “shrooms” or psilocybin, and PCP.
- The only hallucinogen measured that significantly decreased in use was MDMA (also called ecstasy or Molly), showing statistically significant decreases within one year as well as the past five years – from 5% in both 2016 and 2020 to 3% in 2021.

ALCOHOL

- Alcohol remains the most used substance among adults
- Daily drinking have been decreasing over the past decade
- Binge drinking (five or more drinks in a row in the past two weeks) rebounded in 202.
- High-intensity drinking (having 10 or more drinks in a row in the past two weeks) has been steadily increasing over the past decade and in 2021 reached its highest level ever recorded since first measured in 2005.

ALCOHOL

- **What is considered 1 drink?**
- The National Institute on Alcohol Abuse and Alcoholism defines one standard drink as any one of these:
- 12 ounces (355 milliliters) of regular beer (about 5% alcohol)
- 8 to 9 ounces (237 to 266 milliliters) of malt liquor (about 7% alcohol)
- 5 ounces (148 milliliters) of wine (about 12% alcohol)
- 1.5 ounces (44 milliliters) of hard liquor or distilled spirits (about 40% alcohol)

Alcohol use disorder - Symptoms and causes - Mayo Clinic

DSM-5 CRITERIA: ALCOHOL USE DISORDER

- **A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least two of the following, occurring within a 12 month period:**
- Alcohol is often taken in larger amounts or over a longer period of time than intended.
- There is a persistent desire or unsuccessful efforts to cut down or control alcohol use.
- A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects.
- Craving, or a strong desire or urge to use alcohol.
- Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home.
- Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol.
- Important social, occupational, or recreational activities are given up or reduced because of alcohol use.
- Recurrent alcohol use in situations where it is physically dangerous.
- Alcohol use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol.
- Tolerance.
- Withdrawal.
- **Severity:**
- Mild: 2-3 symptoms.
- Moderate: 4-5 symptoms.
- Severe: 6 or more symptoms.

TYPES OF TREATMENTS

- Several evidence-based treatment approaches are available for AUD. One size does not fit all and a treatment approach that may work for one person may not work for another.
- Treatment can be outpatient and/or inpatient and be provided by specialty programs, therapists, and doctors.
- Medications Three medications are currently approved by the U.S. Food and Drug Administration to help people stop or reduce their drinking and prevent relapse: naltrexone (oral and long-acting injectable), acamprosate, and disulfiram. All these medications are non-addictive, and they may be used alone or combined with behavioral treatments or mutual-support groups.
- Behavioral Treatments Behavioral treatments, also known as alcohol counseling or "talk therapy," provided by licensed therapists are aimed at changing drinking behavior. Examples of behavioral treatments are brief interventions and reinforcement approaches, treatments that build motivation and teach skills for coping and preventing relapse, and mindfulness-based therapies. Mutual-Support Groups Mutual-support groups provide peer support for stopping or reducing drinking. Group meetings are available in most communities, at low or no cost, at convenient times and locations—including an increasing presence online. This means they can be especially helpful to individuals at risk for relapse to drinking. Combined with medications and behavioral treatment provided by health professionals, mutual support groups can offer a valuable added layer of support. Please note: People with severe AUD may need medical help to avoid alcohol withdrawal if they decide to stop drinking. Alcohol withdrawal is a potentially life-threatening process that can occur when someone who has been drinking heavily for a prolonged period of time suddenly stops drinking. Doctors can prescribe medications to address these symptoms and make the process safer and less distressing.

NARCAN

- Opioid receptor Agonist
- Naloxone is a medicine that rapidly reverses overdose
- This means that it attaches to opioid receptors and reverses and blocks the effects of other opioids.
- Naloxone can quickly restore normal breathing to a person if their breathing has slowed or stopped because of an opioid overdose. But, naloxone has no effect on someone who does not have opioids in their system, and it is not a treatment for opioid use disorder.


RECOVERY
Expectations
Reality

NEWS LINKS

- Fentanyl overdose survivor shares her story | Nightline (youtube.com)
- Intervention: MULTIPLE Overdoses Can't Stop Peter's EXTREME Fentanyl Addiction | A&E (youtube.com)
- Heartbreaking photo shows dangers of fentanyl (youtube.com)
- Crisis Next Door - The Fentanyl Epidemic (youtube.com)
- Carfentanil: the next deadly street drug? (youtube.com)
- Jason "Jelly Roll" DeFord Opening Statement – YouTube

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- Buprenorphine - StatPearls - NCBI Bookshelf (nih.gov)
- www.sublocadehcp.com/?&msclkid=c68f3ed7eb3f14ce47be58705fc253e3&utm_source=bing&utm_medium=cpc&utm_campaign=BR%20%7C%20HCP%20%7C%20Sublocade&utm_term=sublocade&utm_content=Sublocade&gclid=c68f3ed7eb3f14ce47be58705fc253e3&gclsrc=3p.ds
- Status Report on Missouri's Substance Use and Mental Health | dmh.mo.gov
- VIVITROL® for Alcohol Dependence and Opioid Dependence
- Why are Drugs so Hard to Quit? (youtube.com)