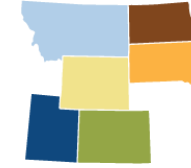




Mountain Plains ATTC (HHS Region 8)

ATTC

Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration



Cannabis and Physical and Mental Health- What do we (think we) know?

Andrew McLean, MD, MPH

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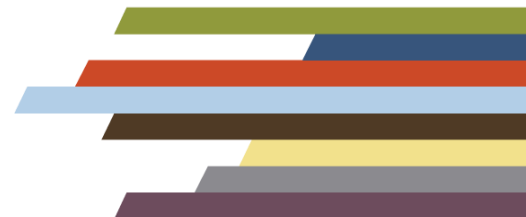


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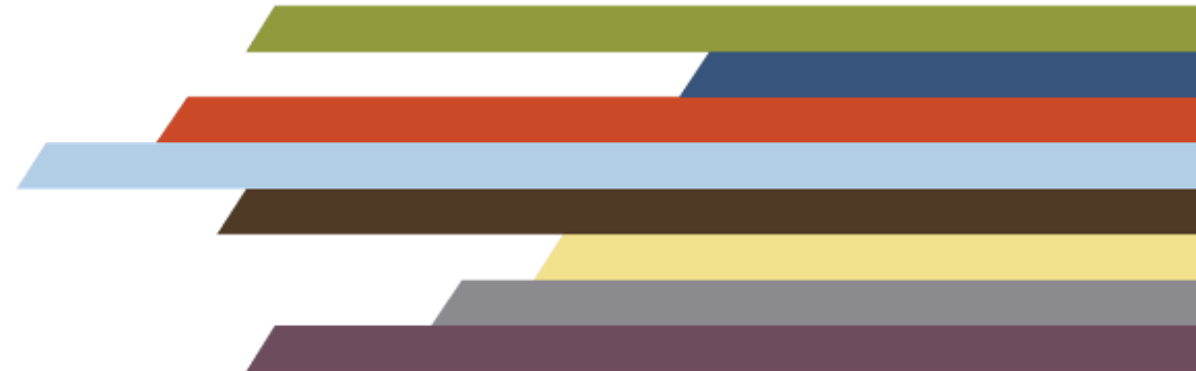
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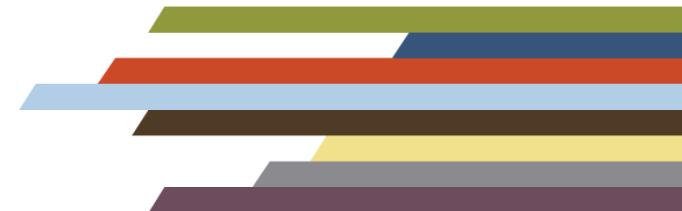
Cannabis and Physical and Mental Health- What do we (think we) know?

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Objectives:

- After the presentation, the participant:
 - 1) will have an understanding of the scientific evidence of risks and benefits of cannabis use in humans (with a focus on psychiatric issues)
 - 2) will have a general knowledge of the body's endocannabinoid system
 - 3) will have an understanding of THC potency

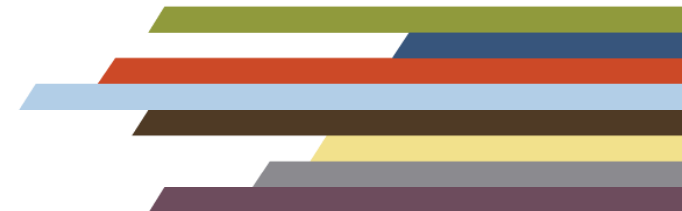


Cannabis

Marijuana refers to the dried leaves, flowers, stems, and seeds from the *Cannabis sativa* or *Cannabis indica* plant.

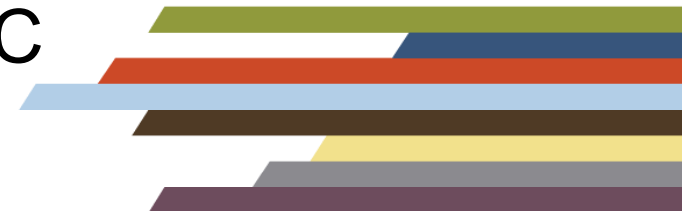


- There are hundreds of compounds in marijuana

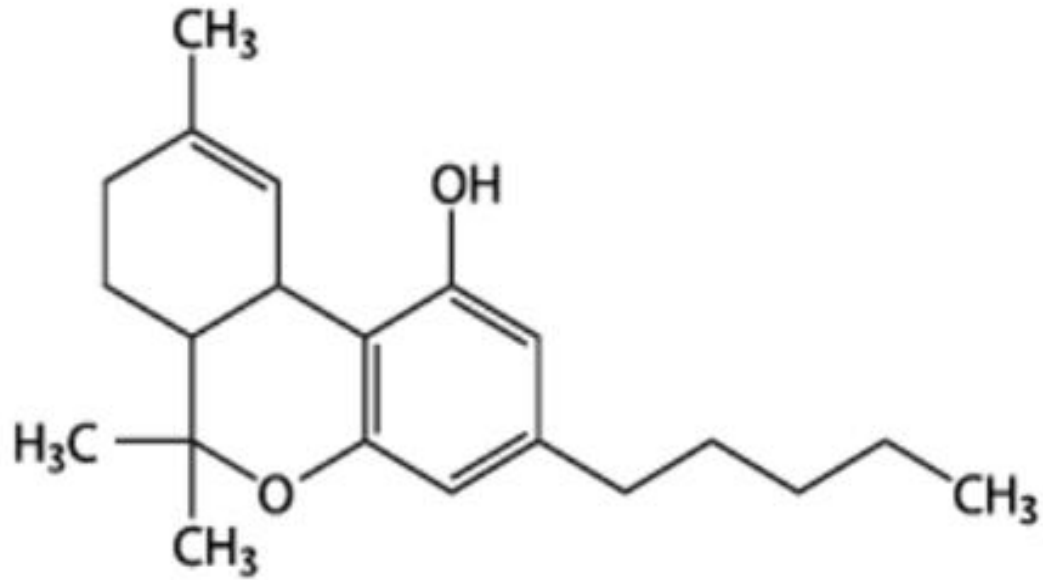


Cannabis Sativa

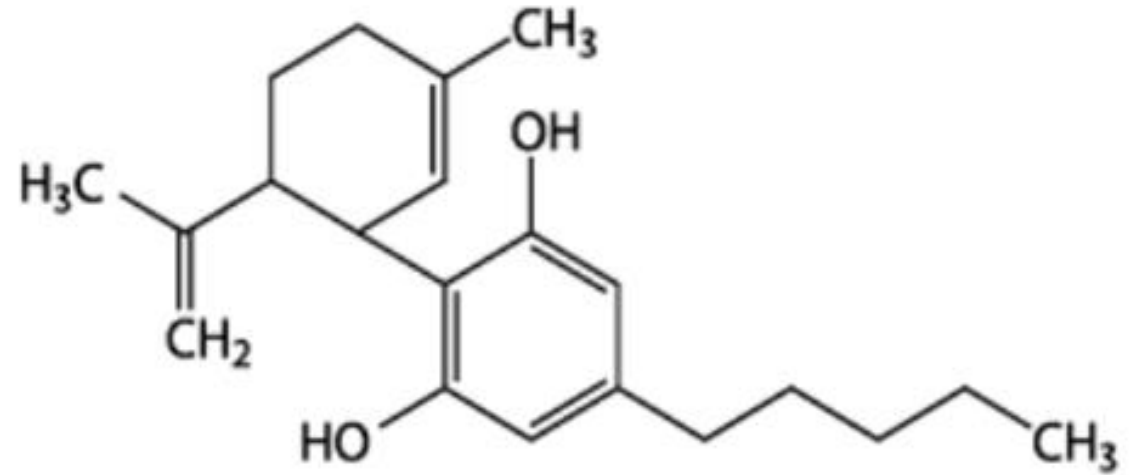
- Marijuana and hemp are cultivars of cannabis sativa.
- THC is derived from marijuana
- THC is the most psychoactive substance in marijuana
- CBD is typically derived from hemp
- Industrial hemp needs to contain less than 0.3% THC



THC vs. CBD



Tetrahydrocannabinol

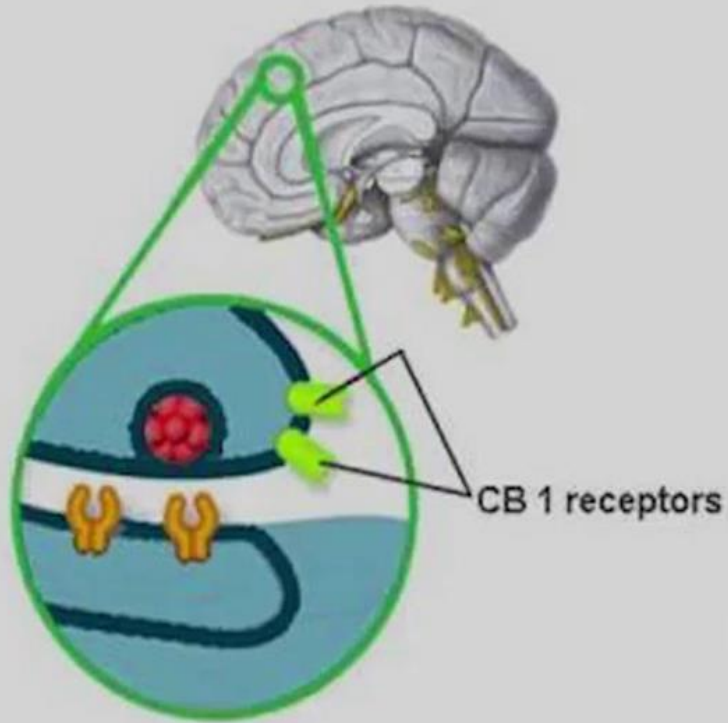


Cannabidiol

Cannabidiol Receptors

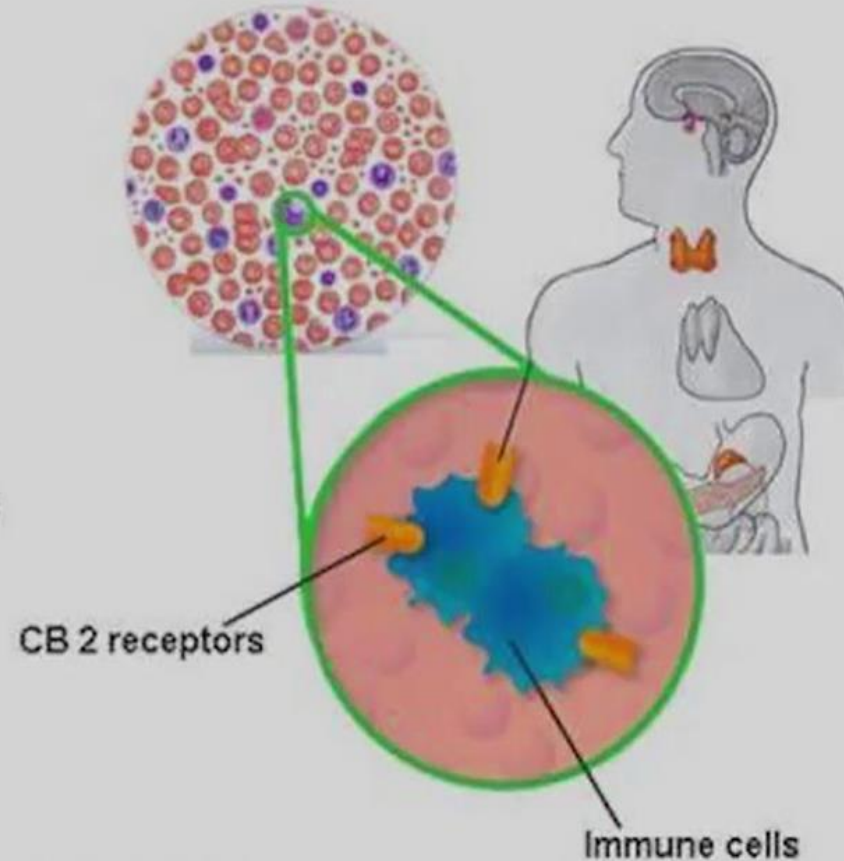
CB1 receptors

mainly localized in the brain
(hippocampus, cerebellum and cerebrum)



CB2 receptors

mainly situated in the periphery
(spleen, tonsillar and immune cells)



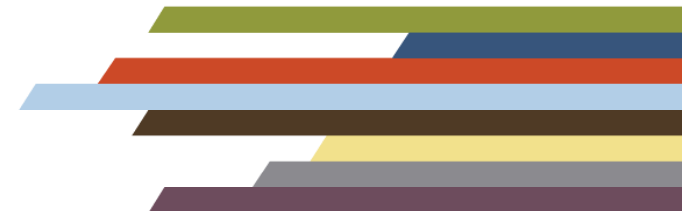
FDA Approvals...

THC

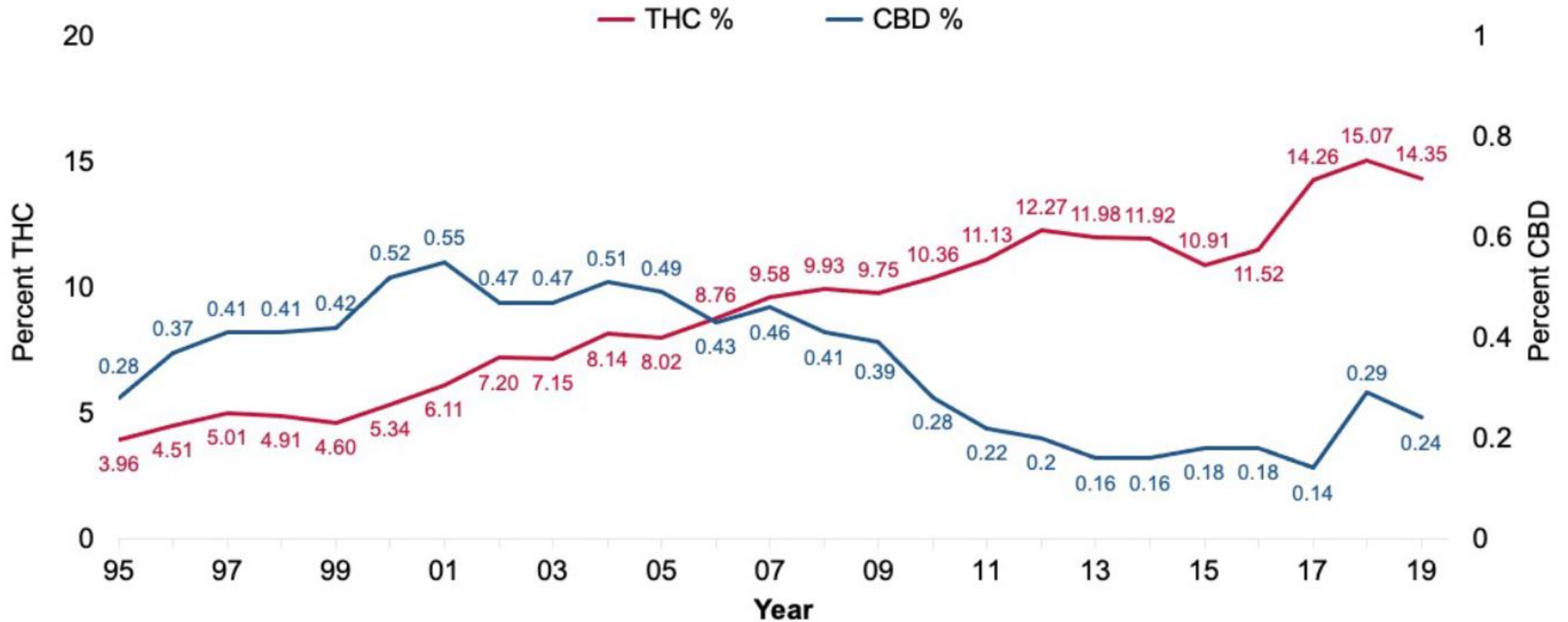
- Dronabinol as Marinol/Syndros
- Approved for AIDS associated anorexia or treatment-resistant nausea/vomiting secondary to cancer chemotherapy
- Nabilone as Cesamet is approved for the latter.

Cannabidiol

- FDA Approved as Epidiolex for:
- Lennox-Gastaut Syndrome and
- Dravet Syndrome

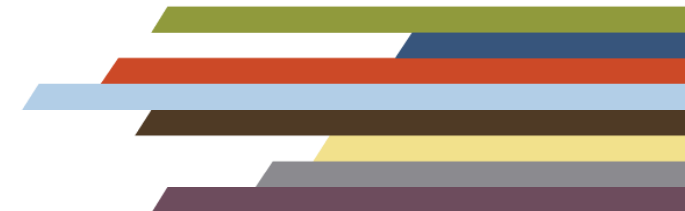


Percentage of THC and CBD in cannabis samples seized by the DEA from 1995-2019



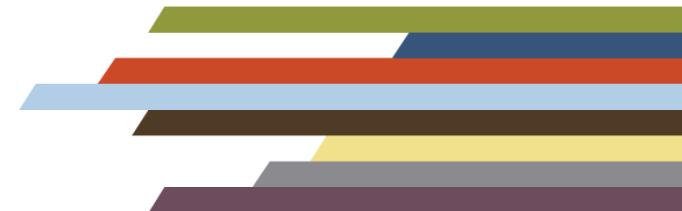
Absorption and bio-availability

- **Smoking or vaporizing** allows for pulmonary first-pass metabolism with direct systemic blood stream absorption across lung lining. THC bio-availability ~ 30%
- Similarly, **sublingual** (i.e., use of oils, etc...) absorption also avoids first-pass metabolism, with slightly less rapid absorption than above. Bio-availability~20%?
- **Edible** use-absorbed via intestinal mucosa and transported to the liver and metabolized prior to reaching other organs, such as the brain. THC bio-availability ~10%
- Only about 1% of administered THC dose reaches the brain.
- **However**-THC variability in marijuana plants can range from 0.3-30% or higher



Marijuana

- Can have both stimulant and sedative properties.
- Antiemetic properties*
- Anticonvulsant effects
- Muscle-relaxing effects
- Reduction of intraocular pressure



THERAPEUTIC EFFECTS

In adults with chemotherapy-induced nausea and vomiting, oral cannabinoids are effective antiemetics.

In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms.

In adults with multiple sclerosis (MS)-related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.

For these conditions, the effects of cannabinoids are modest; for all other conditions evaluated, there is inadequate information to assess their effects.

CANCER

The evidence suggests that smoking cannabis does not increase the risk for certain cancers (i.e., lung, head, and neck) in adults.

There is modest evidence that cannabis use is associated with one subtype of testicular cancer.

There is minimal evidence that parental cannabis use during pregnancy is associated with greater cancer risk in offspring.

CARDIOMETABOLIC RISK

The evidence is unclear as to whether and how cannabis use is associated with heart attack, stroke, and diabetes.

RESPIRATORY DISEASE

Smoking cannabis on a regular basis is associated with chronic cough and phlegm production.

Quitting cannabis smoking is likely to reduce chronic cough and phlegm production.

It is unclear whether cannabis use is associated with COPD, asthma, or worsened lung function.

Some Psychoactive effects of THC

Acute effects:

Usually temporary and reversible, and do not present a risk of harm (outside of risk of activities when intoxicated).

Pleasant: Euphoria and relaxation; transient sensory experiences, enhanced perception of experiences

Noted: Deficits in processing speed, attention, working memory, motivation; craving of sweet and salty foods; sleepiness; tachycardia

Unpleasant:

Anxiety

Paranoia/Psychotic symptoms, depending on genetic/vulnerability characteristics

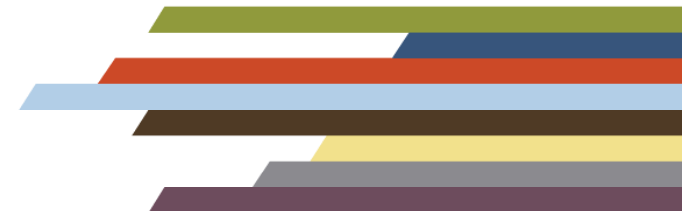


Re: Acute stress relief and cannabis use

- In general, THC at low doses *might* reduce anxiety, at high doses, may increase anxiety, negative mood, subjective distress.

One study:

- “Low dose” THC = 7.5mg
- “High dose” THC = 12.5mg



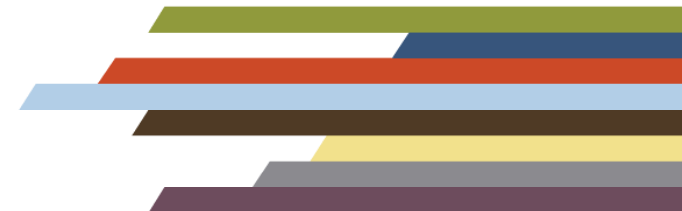
Amounts

So, for example:

Let's say a sample of cannabis has 12.5% THC

1 gm would provide 125mg of THC

If an individual smoked a bowl (roughly 0.25gm), they would be smoking 31.25mg of THC

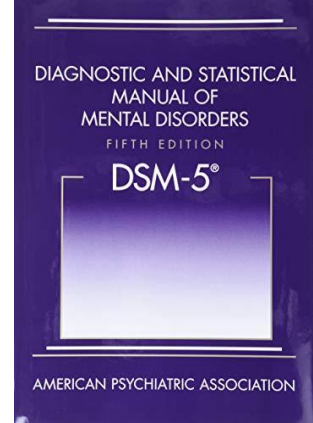


Edible vs. inhaled and ER visits

- Colorado study-approx. 10,000 patients
- While cannabinoid hyperemesis syndrome was twice as likely with inhaled vs. ingested cannabis, the opposite was true for acute psychiatric symptoms, intoxication and cardiovascular symptoms.
- Cannabis-attributed presentations involving edible use-10%
- Edible Products as percent representation of state total cannabis sales:
 - 0.32%

Example-Substance X

Pattern of use, number of concerns (>2), time-frame (within a 12-month period), length of remission/maintenance



1. Larger amounts used, or for longer than intended
2. Can't cut down/control use
3. Focus/time spent on obtaining drug or recovering
4. Craving
5. Recurrent issue with fulfilling obligations/roles due to use
6. Using despite ongoing problems re: above
7. Important activities are given up/reduced (social, occupational, etc...)
8. Recurrent use despite physical hazards
9. Recurrent use despite medical/psychological impact from use
10. Tolerance
11. Withdrawal

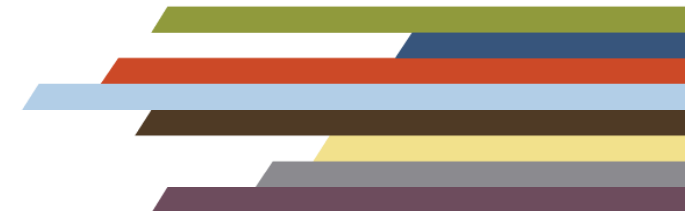
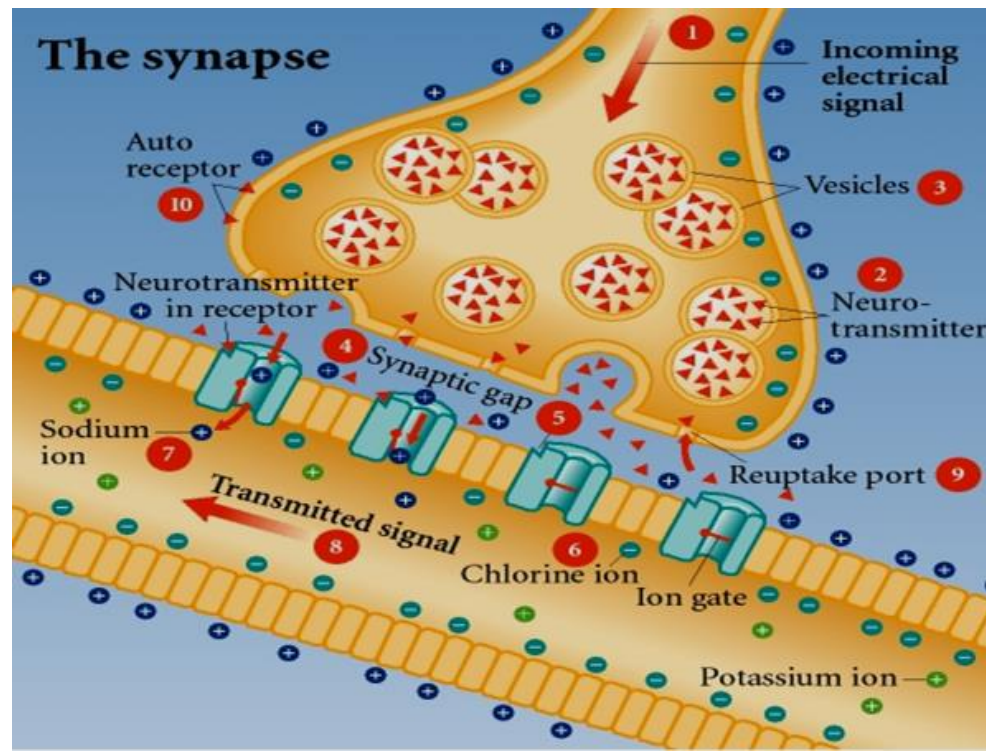
Tolerance and Dependence

Tolerance

Changes in receptors in the body (including the brain), changes in metabolism, etc... can result in the drug no longer having the same initial response, thus requiring more drug to obtain the same effect.

Dependence*

Physiologic changes with ongoing drug use can result in symptoms of withdrawal if the drug is not present



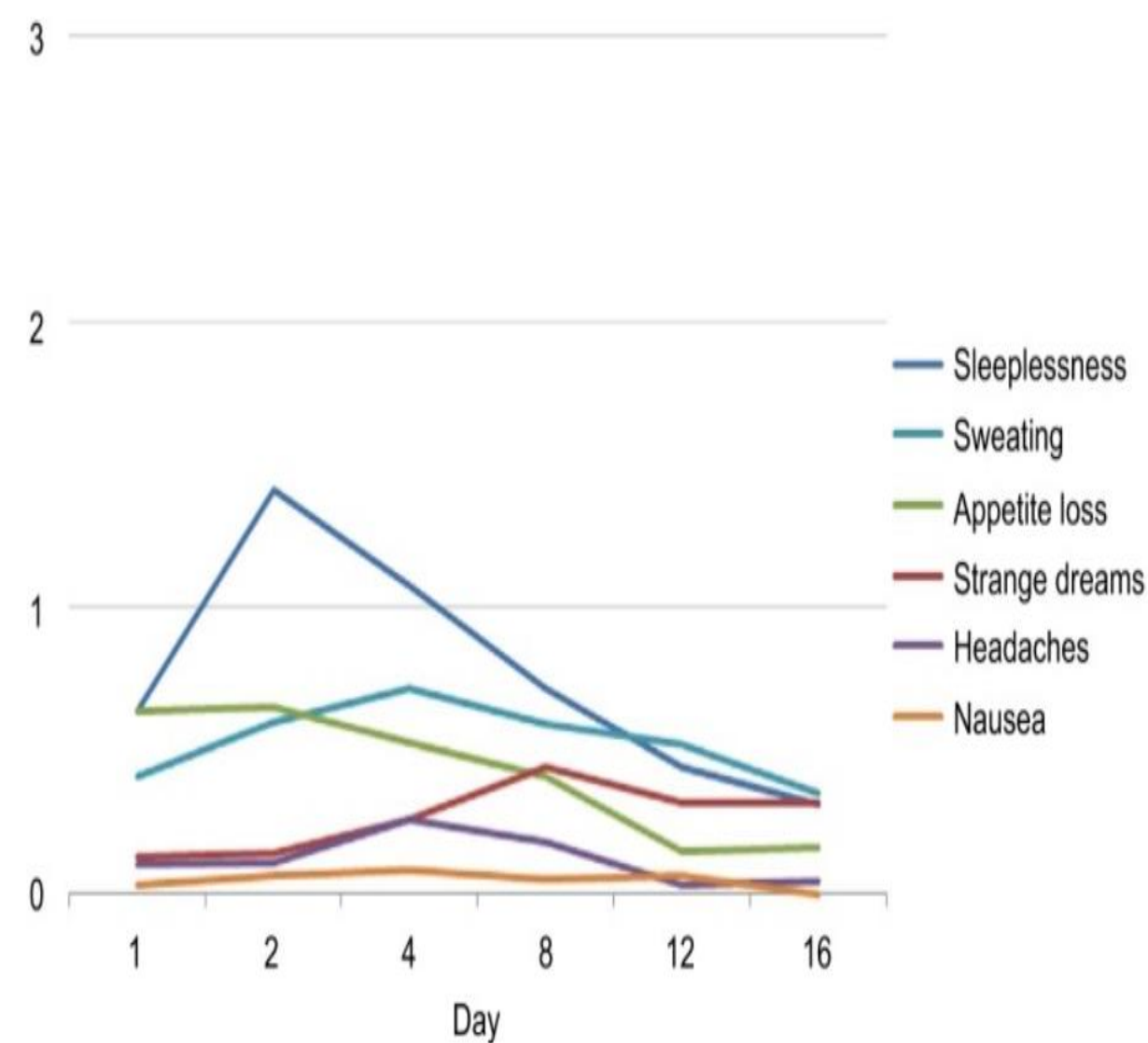
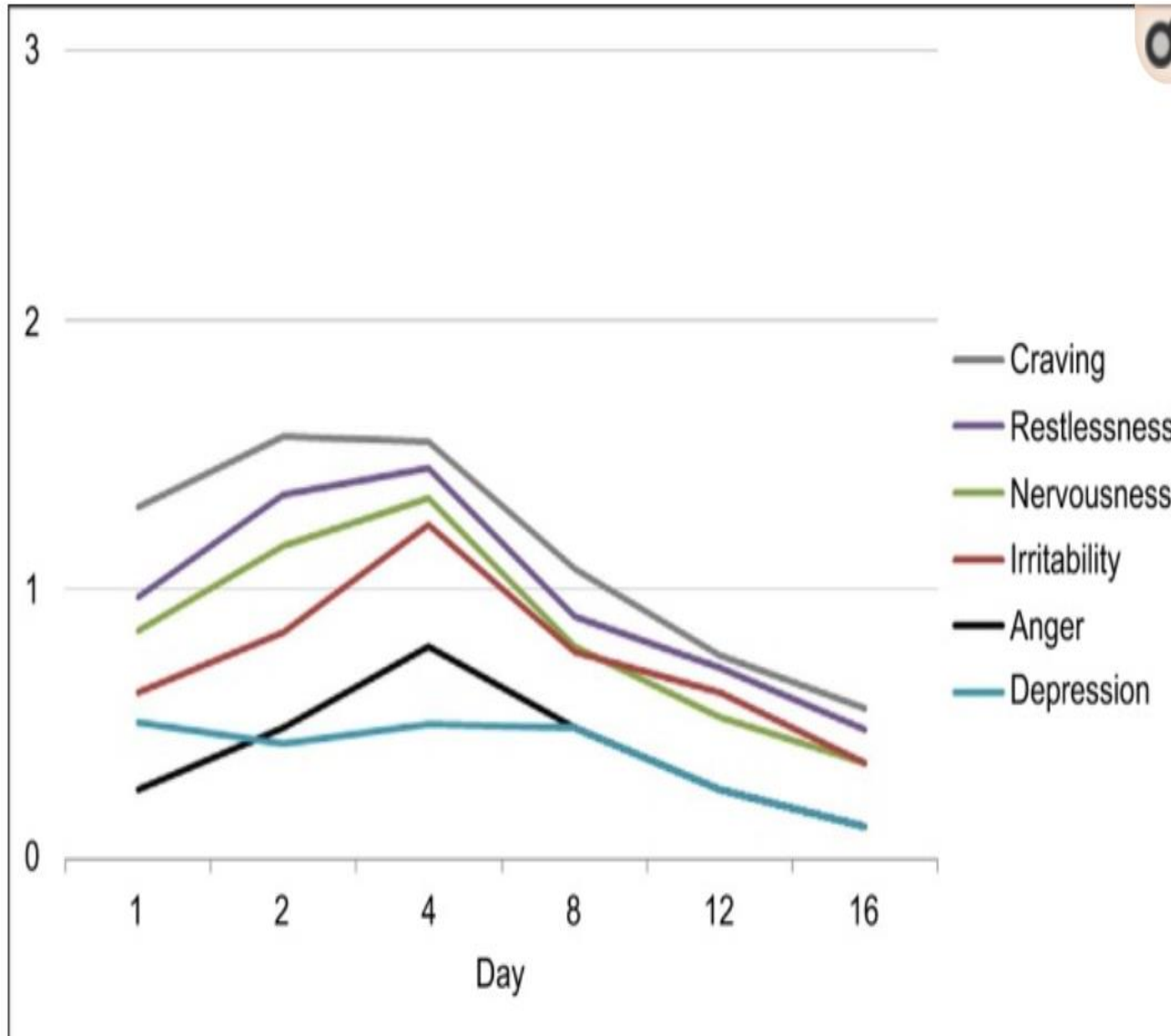
Cannabis Use Disorder (CUD)

- Interpretation of research is somewhat difficult given the change in criteria/nomenclature
- In the past, there was “abuse” and “dependence”, the latter referring to more severe symptoms/impact
- DSM 5 now uses “mild” (2-3 symptoms), “moderate” (4-5 symptoms) and “severe” (6 or more symptoms)

Cannabis Withdrawal Syndrome

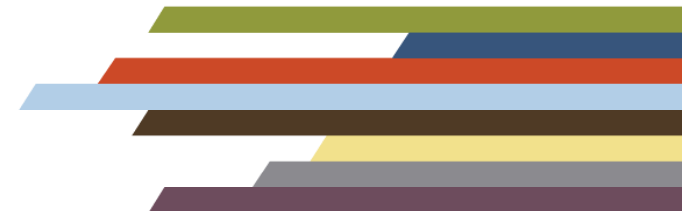
Bonnet and Preuss, [Subst Abuse Rehabil.](#) 2017; 8: 9–37

0= none, 1=mild, 2=moderate, 3=heavy

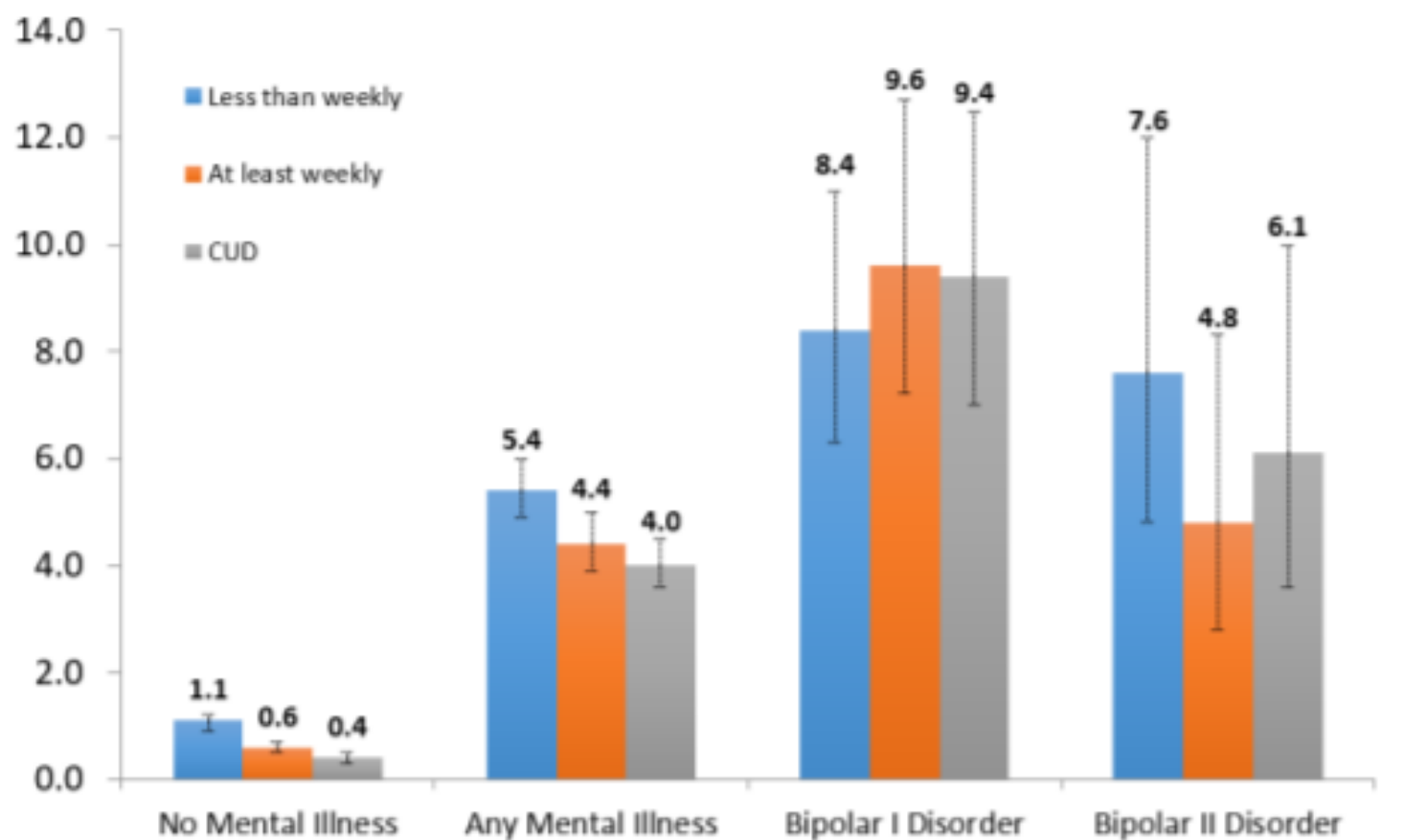


Comorbidities

- Literature appears to support that:
- Those with daily or weekly cannabis use are more likely to meet criteria for-
 - Severe cannabis use disorder (CUD)
 - Other substance use disorders (SUD)
- Those with CUD were more likely to have risk of an associated anxiety or mood disorder, PTSD or personality disorder.



Rates of marijuana use and CUD in past year by Diagnosis



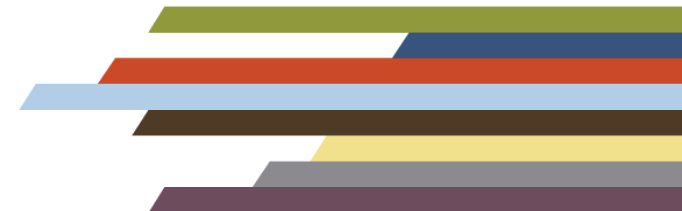
Source: Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Cannabis use and cannabis use disorders among individuals with mental illness. *Comprehensive Psychiatry*. 2013 Aug 31;54(6):589-98.

Regular use, generalities:

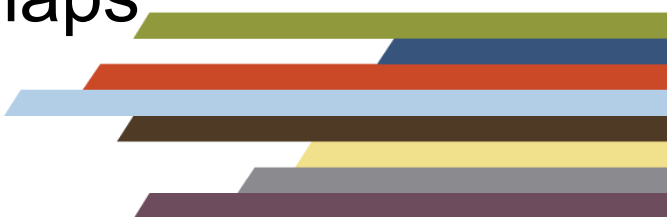
Condition/Disorder	THC	CBD
Anxiety	An association with social anxiety disorder and use.	Appears to decrease anxiety
Mood disorders	Studies have shown initial subjective improvement in depression with longer term decline in benefit and later negative subjective mood.	Further studies needed
Psychosis/Schizophrenia	Increased risk of disorders in subgroup of early users with genetic pre-disposition	Further studies needed
Cognitive Issues	Association with early use and educational underachievement	Further studies needed

Synthetic Cannabinoids

- Most well known: JWH-18
- Developed for research on cannabinoids
- “K2”, “Spice”, etc...
- Binds much more strongly to CB1 receptors than THC
- Compared to THC, tachycardia, agitation, hallucinations, and hypertension more frequently associated with the use of synthetic cannabinoids.
- The scientist who developed JWH-18 was quoted as saying,
“People who use it are idiots.”

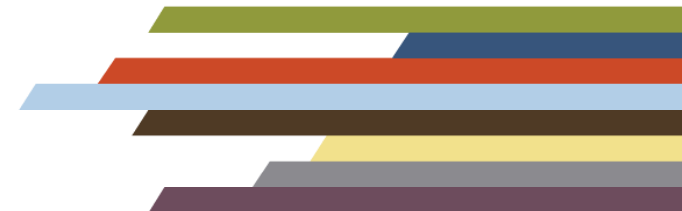


So...

- The majority of individuals who use cannabis do not suffer significant problems
 - The most robust evidence for benefit of THC is for nausea/vomiting post-chemo; spasticity and neuropathic pain (not psychiatric disorders)
 - Those with higher dose and frequency use have higher risks of negative side effects, CUD and co-morbidities
 - Better studies are needed in differentiating association from causation in cannabis use and psychiatric disorders.
 - A subset of individuals who use THC early and have genetic predisposition are at significantly higher risk for psychotic disorders.
 - CBD *appears* to have some benefit re: anxiety and perhaps mitigates some THC side effects.
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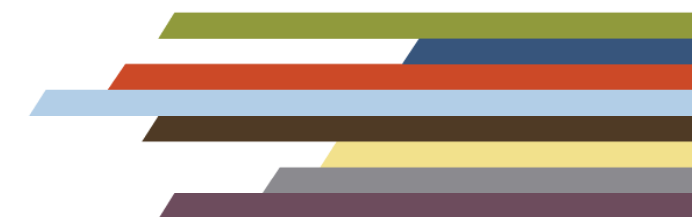
Factors- The “Hows”

- How early you started (before 17?)
- How much you use (amount)
- How often you use (less than weekly?)
- How potent the THC is you use (%)
- How you take it (smoke, eat, etc...)
- How you picked your parents (genetics)



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Questions/Comments?

