RECREATIONAL AND MEDICAL MARIJUANA: POTENTIAL IMPLICATIONS FOR ADOLESCENT AND PSYCHIATRIC POPULATIONS

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Teen cannabis use is common.
**ILLEGAL DRUGS**

- **Past Year Use** among 12th graders
  - **Marijuana/Hashish**: 35.9%
  - **Synthetic Cannabinoids**: 3.8%
  - **LSD**: 3.2%
  - **Cocaine**: 2.3%
  - **MDMA (Ecstasy/Molly)**: 2.2%
  - **Hallucinogens**: 1.6%
  - **Heroin**: 0.4%

**Past Month Use** among 12th graders:

- **Marijuana/Hashish**: 22.3%
- **Cocaine**: 7.6%
- **Heroin**: 2.2%

**Daily Use**

- 8th graders: 0.7%
- 10th graders: 3.4%
- 12th graders: 5.8%

*Figures courtesy of NIH/NIDA*
Cannabis is far more potent than in prior decades.
Novel forms of THC delivery are the new norm, yet use is difficult to detect and we have very little information on long-term effects.
ONGOING BRAIN DEVELOPMENT MAY MAGNIFY CANNABIS’ EFFECTS

- Developmental changes in brain into 3rd decade of life
  - Connectivity
  - Chemistry
  - Morphology
- Prefrontal regions last to develop
  - Densely populated with cannabinoid receptors
  - Critically underlie higher order cognitive

Giedd et al., 1999; Gogtay et al., 2004; Sowell et al., 2001
ADDICTION LIABILITY

- 4M people aged 12+ have a past year CUD
- ~23% of people who received addiction treatment received treatment for CUDs
- Average adult entering tx for CUD has used daily for 10 years, tried to quit 6 times

Compton et al., 2004; NIDA, 2012a, 2012b; SAMHSA, 2012, 2017
RESIDUAL COGNITIVE EFFECTS OF CANNABIS

IQ decline
Memory
  Learning & retaining new information
Attention and concentration
  Response speed & variability
Executive functioning
  Working memory
  Verbal fluency
  Decision-making, risk-taking & inhibition
Abnormalities in brain structure and function
↓ Age of initiation → worse cognition

Schuster, Gilman & Evins, 2016; Crane, Schuster et al., 2015; Broyd et al., 2016; Lisdahl et al., 2013; Fontes et al., 2011
ARE COGNITIVE DEFICITS REVERSIBLE?

- Biological markers normalize after ~4 weeks
- Cannabinoid receptor density in brain
- Cortical blood volumes
- Especially in areas important for cognition
Users who Abstain for 30 Days

Users who continue to use cannabis

Ongoing Study on Neurocognitive Recovery with Cannabis Abstinence in High School Students

THC Concentrations in Urine

Attention

Memory

Schuster, et al., Journal of Clinical Psychiatry 2018
GREATER VULNERABILITY WITH PSYCHIATRIC DIAGNOSES?

**Total Words, Trials 1-5**

- **Group**: CON, MJ, MDD, MDD+MJ
- **Total # of Words Recalled**
  - CON: 65 ± 5
  - MJ: 60 ± 5
  - MDD: 55 ± 5
  - MDD+MJ: 50 ± 5

**Free Recall after Delay**

- **Group**: CON, MJ, MDD, MDD+MJ
- **% free recall**
  - Short Delay:
    - CON: 85 ± 5
    - MJ: 90 ± 5
    - MDD: 80 ± 5
    - MDD+MJ: 75 ± 5
  - Long Delay:
    - CON: 95 ± 5
    - MJ: 100 ± 5
    - MDD: 90 ± 5
    - MDD+MJ: 85 ± 5

Radoman et al., in press
Is MJ harmful? Yes for some:
• For kids, there are lasting detrimental cognitive effects of heavy use
• For some, high potency MJ exposure increases risk of psychotic illness
• On roadways and workplaces, MJ intoxication is a public safety risk

Is MJ medicine? Yes, components of MJ are medicine for some:
• CBD for children with some forms of epilepsy now FDA approved
• For some with spasticity due to MS, for some THC for severe weight loss.
• For ALL other indications, there are too few, poor quality data to know.
• Our group is poised to study epidiolex for chronic back pain in a clinical trial with PET imaging

Effective regulation using a public health framework is key to mitigating risk
Permitting cannabis use is one thing, Promoting it is another…
Those with adolescent cannabis use have greater severity of illness schizophrenia.

Males with schizophrenia with v. without cannabis use before age 18-20 followed for 21 years had:

- Higher median duration of first hospital stay (59 vs. 30 days)
- Greater median number of hospitalizations (10 vs. 4)
- Greater total hospital days (547 vs. 184)
- Greater odds of having >20 hospitalizations OR=3.1 (1.3–7.3)
- Greater odds of hospital stay >2 years OR=2.4 (1.1–7.4)

Controlling for personality disorder, family SES, IQ, marital status, urban residence, risky use of alcohol, and other drug use

MARIJUANA RELATED PSYCHOTIC SYMPTOMS AMONG PRIMARY CARE PATIENTS

Routine pediatric visits, mean age 16.6

- Hallucinations (27%)
- Paranoia/Anxiety (33.6%)
- Any psychotic symptom (42.9%)

Significantly higher rates among youth with depressive sx, CUD


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• committee considered more than 10,000 scientific abstracts
• arrived at nearly 100 different research conclusions related to cannabis and health, organizing these into 5 categories:
  • conclusive,
  • substantial,
  • moderate,
  • limited,
  • no/insufficient evidence
There is **NO or insufficient evidence** to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for:

- Cancers, including glioma (cannabinoids)
- Anorexia nervosa (cannabinoids)
- Irritable bowel syndrome (dronabinol)
- Epilepsy (cannabinoids)
- Spasticity in patients with paralysis due to spinal cord injury (cannabinoids)
- Amyotrophic lateral sclerosis (cannabinoids)
- Chorea and neuropsychiatric symptoms associated with Huntington’s disease (oral cannabinoids)
- Parkinson’s disease (cannabinoids)
- Dystonia (nabilone and dronabinol)
- Achieving abstinence in the use of addictive substances (cannabinoids)
- Mental health outcomes in individuals with schizophrenia or psychosis (cannabidiol)

There is **conclusive or substantial evidence** that cannabis or cannabinoids are effective:

- For the treatment for **chronic pain** in adults (cannabis)*
- Antiemetics in the treatment of chemotherapy-induced **nausea and vomiting** (oral cannabinoids)
- For improving patient-reported **multiple sclerosis spasticity symptoms** (oral cannabinoids)
CONCLUSIONS FOR: CARDIOMETABOLIC RISK

There is limited evidence of a statistical association between cannabis use and:
- The triggering of acute myocardial infarction (cannabis smoking)
- Ischemic stroke or subarachnoid hemorrhage
- Decreased risk of metabolic syndrome and diabetes
- Increased risk of prediabetes

CONCLUSIONS FOR: RESPIRATORY DISEASE

There is substantial evidence of a statistical association between cannabis smoking and:
- Worse respiratory symptoms and more frequent chronic bronchitis episodes (long-term cannabis smoking)

CONCLUSIONS FOR: INJURY AND DEATH

There is substantial evidence of a statistical association between cannabis use and:
- Increased risk of motor vehicle crashes

There is moderate evidence of a statistical association between cannabis use and:
- Increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal
WHAT ABOUT RISK OF HARM?

CONCLUSIONS FOR: PSYCHOSOCIAL

There is moderate evidence of a statistical association between cannabis use and:
• Impairment in cognitive domains of learning, memory, and attention (acute cannabis use)

There is limited evidence of a statistical association between cannabis use and:
• Impaired academic achievement and education outcomes
• Increased rates of unemployment and/or low income
• Impaired social functioning or engagement in developmentally appropriate social roles

CONCLUSIONS FOR: ABUSE OF OTHER SUBSTANCES

There is moderate evidence of a statistical association between cannabis use and:
• The development of substance dependence and/or substance abuse disorder for substances including alcohol, tobacco, and other illicit drugs

There is limited evidence of a statistical association between cannabis use and:
• The initiation of tobacco use
CONCLUSIONS FOR: MENTAL HEALTH

There is substantial evidence of a statistical association between cannabis use and:
• The development of schizophrenia or other psychoses, with the highest risk among the most frequent users

There is moderate evidence of a statistical association between cannabis use and:
• Better cognitive performance among individuals with psychotic disorders and a history of cannabis use
• Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use)
• Increased risk for the development of depressive disorders
• Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users
• Increased incidence of suicide completion
• Increased incidence of social anxiety disorder (regular cannabis use)

WHAT ABOUT RISK OF HARM?
CONCLUSIONS FOR: PROBLEM CANNABIS USE (CUD)

There is **substantial evidence** that:
• Stimulant treatment of ADHD during adolescence is *not* a risk factor for the development of CUD
• Being male and smoking cigarettes are risk factors for CUD
• Initiating cannabis use at an earlier age is a risk factor for CUD

There is **substantial evidence** of a statistical association between:
• Increases in cannabis use frequency and the progression to developing CUD
• Being male and the severity of CUD, but recurrence does not differ between males and females

**There is moderate evidence** that:
• Anxiety, personality disorders, and bipolar disorders are *not* risk factors for CUD
• Major depressive disorder is a risk factor for CUD
• Adolescent ADHD is *not* a risk factor for CUD
• Exposure to the combined use of abused drugs is a risk factor for CUD
• Neither alcohol nor nicotine dependence are risk factors for CUD
• During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for CUD

WHAT ABOUT RISK OF HARM?
RANDOMIZED TRIAL OF MEDICAL MARIJUANA CARDS VS. WAITLIST

Assessing adults, aged 18-55, seeking medical marijuana cards for:
• Pain,
• Insomnia,
• Depression, or
• Anxiety

Funded by
• MGH ECOR
• ROIDA042043

Active Study Group
- Baseline
- 2 week
- 1 month
- 3 month
- 6 month follow-up
- 12 month follow-up

Waitlist Control Group
- Baseline
- 2 week
- 1 month
- 3 month
- 6 month follow-up
- 12 month follow-up
MM CARDHOLDERS DOUBLE THEIR USE AFTER GETTING THEIR MM CARDS, BEGIN TO OBTAIN CANNABIS PRODUCTS AT DISPENSARIES

• Preliminary results
• for an ongoing trial.
• n = 52 MM
• n = 31 WLC
NO DETECTABLE CBD IN 1/3 OF MED MJ PATIENTS PURCHASING CBD PRODUCTS AT DISPENSARIES

86 Participants:
Reported use of Medical MJ products with CBD only or CBD + THC

67.4%: Had at least one urine that contained CBD metabolites

32.6%: Of participants had no CBD detected in urine
TO DATE, MM USERS REPORT MINIMAL TO NO EFFECT ON PAIN...

Preliminary results for an ongoing trial
n = 52 MM
n = 31 WLC
LITTLE EFFECT ON SLEEP...

Preliminary results for an ongoing trial

n = 52 MM
n = 31 WLC
AND LITTLE TO NO BENEFIT FOR ANXIETY AND DEPRESSION...

Preliminary results for an ongoing trial

n = 52 MM
n = 31 WLC
WHILE MEDICAL MJ PURCHASED AT MA DISPENSARIES HAD NO CBD FOR 1/3 OF PATIENTS AND LITTLE EFFICACY, THERE WERE SIDE EFFECTS CONSISTENT WITH HIGH THC PRODUCTS...

45 Psychiatric AEs
- 18 Psychotic
- 20 Worsening of Depression
- 7 Anxiety

27 Gastrointestinal
- 20 Nausea/vomiting/abdominal pain

17 Other CNS
- Headache, migraines or cluster headache
'I was taking what I thought was CBD oil, and apparently it wasn't what I thought it was. I started feeling the effects when I was driving, which was really scary. I got home as quickly as I could. I felt so high I didn't know where I was and couldn't focus, and the only way I got home was the noises from GPS. I was paranoid that I might have hit someone or something, but I checked my car and there was no damage.'
• MJ use in adolescence is associated with mental health disorders, cannabis use disorder, and cognitive decline that is potentially reversible.

• Substantial epidemiologic evidence suggests some of these relationships are causal.

• New high potency THC oils, dabs, vapes, and edibles are driving up THC exposure and changing the clinical picture, probably increasing the risk for psychosis.

• American Acad Peds recommends counseling all adolescents: ‘Non-use is best for health.’ First Episode Psychosis programs advising sibs not to use.

• ‘Medical’ marijuana in MA is not reliably tested or labeled

• Aside from pediatric epilepsy and MS, there is little rigorous data to support ANY medical claims
Dozens of doctors, scientists warn Mass. marijuana is ripe for ‘regulatory failure’

By Naomi Martin Globe Staff, May 30, 2019, 2:08 p.m.

• Physicians and scientists, from every major medical school and hospital in Massachusetts, are signing onto a call for MA to regulate marijuana using a public health framework, putting public health ahead of commercial interests.

• Permitting cannabis use is one thing, Promoting it is another…