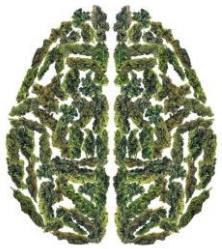


EFFECTS OF CANNABIS USE IN ADOLESCENTS

Selene Etches MD, FRCPC

DISCLOSURE

- No conflict of interest to declare
- No pharmaceutical industry support
- No support from cannabis producers

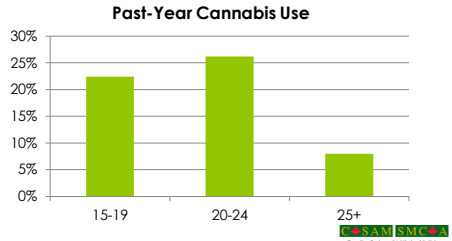
Canada's Lower-Risk Cannabis Use Guidelines (LRCUG)

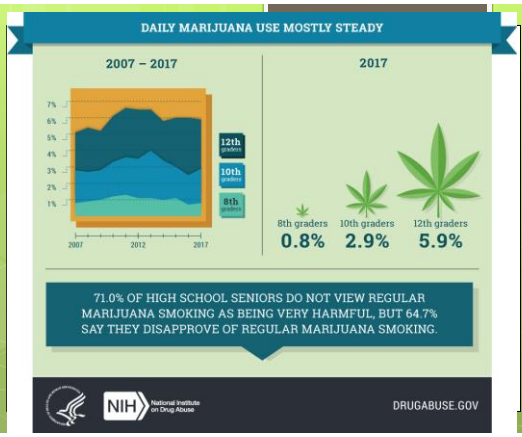
Recommendations

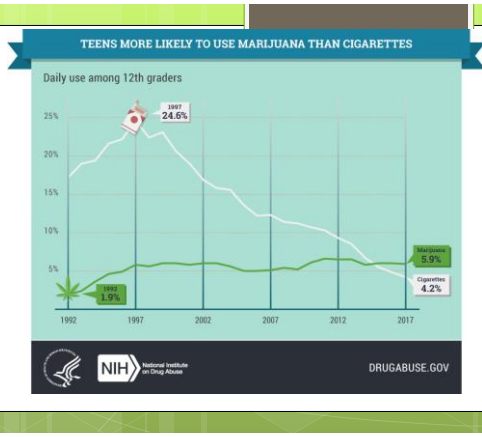
Cannabis use has health risks best avoided by abstaining	If you smoke cannabis, avoid harmful smoking practices
Delay taking up cannabis use until later in life	Limit and reduce how often you use cannabis
Identify and choose lower-risk cannabis products	Don't use and drive, or operate other machinery
Don't use synthetic cannabinoids	Avoid cannabis use altogether if you are at risk for mental health problems or are pregnant
Avoid smoking burnt cannabis—choose safer ways of using	Avoid combining these risks

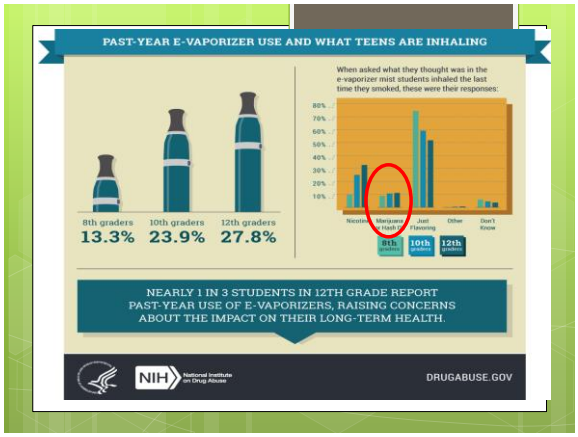
Cannabis is the most widely used illicit drug in Canada - 10.6% of Canadians aged 15+ years

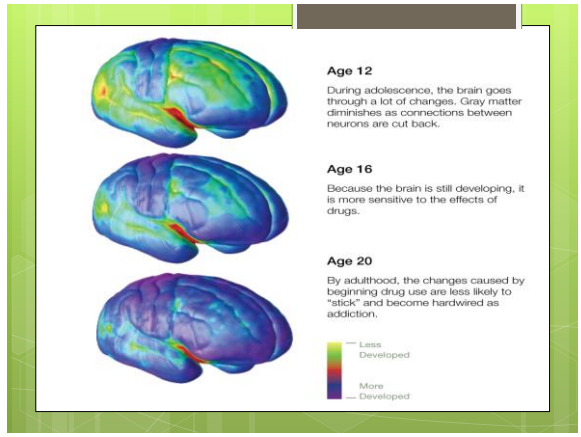
(CTADS, 2013)

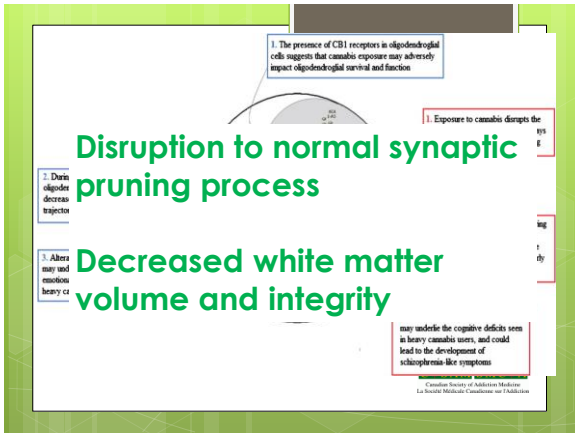







PAST-YEAR E-VAPORIZER USE AND WHAT TEENS ARE INHALING
When asked what they thought was in the e-vaporizer mist students inhaled the last time they smoked, these were their responses:
8th graders 13.3%
10th graders 23.9%
12th graders 27.8%
NEARLY 1 IN 3 STUDENTS IN 12TH GRADE REPORT PAST-YEAR USE OF E-VAPORIZERS, RAISING CONCERNS ABOUT THE IMPACT ON THEIR LONG-TERM HEALTH.
NIH National Institute on Drug Abuse
DRUGABUSE.GOV


Age 12
During adolescence, the brain goes through a lot of changes. Gray matter diminishes as connections between neurons are cut back.
Age 16
Because the brain is still developing, it is more sensitive to the effects of drugs.
Age 20
By adulthood, the changes caused by beginning drug use are less likely to "stick" and become hardwired as addiction.
Less Developed
More Developed


1. The presence of CB1 receptors in oligodendroglial cells suggests that cannabis exposure may adversely impact oligodendroglial survival and function
1. Exposure to cannabis disrupts the
Disruption to normal synaptic pruning process
Decreased white matter volume and integrity
may underlie the cognitive deficits seen in heavy cannabis users, and could lead to the development of schizophrenia-like symptoms
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https://www.youtube.com/watch?time_continue=5&v=FvszaF4vcNY
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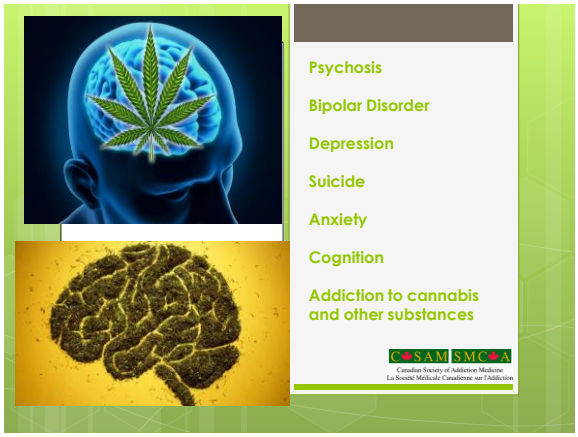
Psychosis
Bipolar Disorder
Depression
Suicide
Anxiety
Cognition
Addiction to cannabis and other substances
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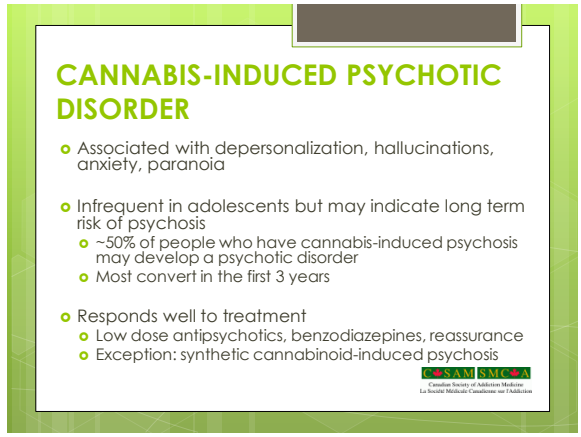
CANNABIS-INDUCED PSYCHOTIC DISORDER
Associated with depersonalization, hallucinations, anxiety, paranoia
Infrequent in adolescents but may indicate long term risk of psychosis
~50% of people who have cannabis-induced psychosis may develop a psychotic disorder
Most convert in the first 3 years
Responds well to treatment
Low dose antipsychotics, benzodiazepines, reassurance
Exception: synthetic cannabinoid-induced psychosis
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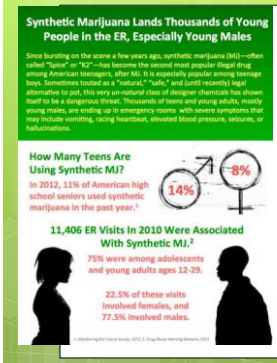
SYNTHETIC CANNABINOIDS

- Pharmacological research tools to study endocannabinoid system
- Synthetic cannabinoids sprayed on herbal plants
- No cannabidiol
- Super agonist at CB_1 receptor
- Can cause acute renal failure, hypertension, myocardial infarction, seizures, psychosis, death
- Not detected in standard urine drug screens



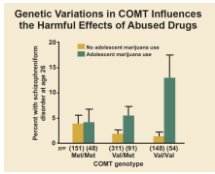
- Severe agitation and anxiety
- Muscle spasms
- Severe tachycardia and hypertension
- Fever
- Hypoglycemia and hypokalemia
- Chest pain
- Acidosis
- Tremors and seizures
- Intense hallucinations and psychotic episodes
  - Can last weeks
- Suicidal thoughts and actions

CANNABIS USE AND PSYCHOSIS

- Increased risk of developing psychotic symptoms or schizophrenia-like psychotic disorder especially if preexisting risks for psychosis
- Earlier first episode
- Stronger association with:
  - Early age at first cannabis use
  - Frequent daily use
  - Use of high potency cannabis (high THC, low CBD)

CANNABIS AND PSYCHOSIS

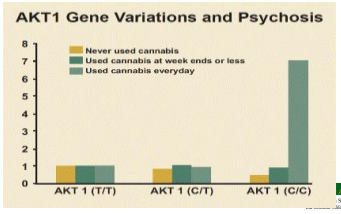
- Link between poor outcomes when cannabis used in adolescence (not adulthood) and Val variant of catechol-O-methyltransferase (COMT) gene



Exponentially increased risk if have Val allele(s), cannabis use, and childhood trauma

CANNABIS AND PSYCHOSIS

- 7x increased risk of developing psychosis



CANNABIS USE AFTER ONSET OF PSYCHOTIC DISORDER

- Cannabis is the most commonly used illicit substance in patients with schizophrenia
  - Increased number of hospitalizations
  - Increased length of hospital stays
- Stopping cannabis after onset of psychosis:
  - Decreased positive symptoms
  - Improved mood and anxiety
  - Improved global functioning
  - Increased medication adherence
  - Decreased relapse

OPPOSING ARGUMENT: EPIDEMIOLOGY DATA

- Lifetime prevalence of psychotic disorders remains consistent (~3%) across regions with differences in cannabis consumption, even in regions where consumption has increased

ANIMAL STUDIES

- Down-regulation of GABAergic activity
- Prefrontal cortex network disinhibition
  - Associated with schizophrenia in humans

BIPOLAR DISORDER AND CANNABIS

- Earlier age of onset of bipolar disorder
- Greater length and number of affective and manic episodes
- More rapid cycling
- More suicide attempts
- Increased overall disability
- More hospitalizations
- More severe course of illness

- Patients with bipolar disorder who stopped using cannabis had similar outcomes after 2 years to those who did not use cannabis

BOTTOM LINE

- Advise siblings of those with psychosis not to use cannabis
- Advise those with a family history of psychosis not to use cannabis
- Stopping cannabis use after diagnosis of psychotic disorder or bipolar disorder, improves prognosis of the mental health disorder

DEPRESSION AND CANNABIS

- People who use cannabis, particularly early, regular and heavy use are more likely to have an adolescent and/or adult depression
  - Causality in question
    - Is this a direct consequence of early cannabis use?
    - Are individuals self-medicating symptoms?
    - Is it an interaction between the two variables?

DEPRESSION AND CANNABIS

- CB1 receptor antagonist rimonabant
  - High number of cases of anxiety and depression
- Mice that lack CB1 receptors have increased depressive symptoms
- Rodents that have impaired CB1 signaling have depressive symptoms

SUICIDE AND CANNABIS

- Appears to be an increased risk of suicidal ideation and suicide attempts although evidence is mixed
- Risk factor (OR = 2-3) may be heavy use under age 15

ANXIETY AND CANNABIS

- Endocannabinoid system mediates HPA axis stress responsiveness
- HPA system and cannabinoid system undergo extensive changes in adolescence
- Does appear clear correlation between early, regular cannabis use and adolescent anxiety disorders
  - Difficult to establish causation

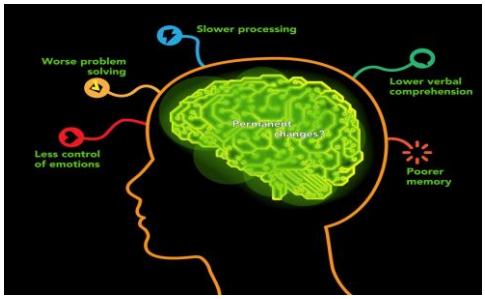
ANXIETY AND CANNABIS

- Social anxiety disorder is associated with 6.5 x increased risk of developing a cannabis use disorder
- THC, especially at doses >5%, can induce fear, panic attacks
- Formulations with high THC:CBD increase anxiety scores
- Formulations with low THC:CBD may decrease anxiety scores

ANIMAL STUDIES

- Decreased CB1 receptor density
- Decreased G-protein coupling in nucleus accumbens
- Increased CREB activity in hippocampus and prefrontal cortex
- Adult rats exposed to chronic high dose THC in adolescence show lowered motivation and anhedonia

COGNITIVE EFFECTS OF CANNABIS USE IN ADOLESCENCE



BRAIN IMAGING

- Increased cortical activity when engaging in cognitive tasks
  - Poorer reaction times and more errors on tasks involving executive functioning
- Problem: retrospective studies
- Deficits in working memory may be reversible after 4-6 weeks of abstinence

PERMANENCE OF IQ DECLINE?

- One study showed IQ decline (full scale and verbal) among persistent cannabis use in adolescence
  - Drop from 50th% to 29th% (5-8 points)
  - Didn't control for SES and personality traits
- Twin studies
  - One study: no difference in IQ
  - Another study: significant decrease in IQ

ANIMAL STUDIES

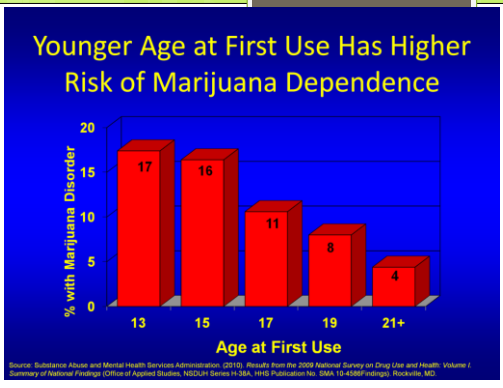
- Rats exposed to cannabis in adolescence display altered structural maturation in prefrontal cortex
  - Impairments in adult cognition
- Memory impairments associated with changes in the hippocampus

COGNITIVE EFFECTS OF CANNABIS USE IN ADOLESCENCE

- More frequent, earlier and persistent cannabis use correlated with increased impairment
- ABCD study – started fall 2015
  - 11,000+ youth ages 9-10
  - Will follow into early adulthood
  - Integrating brain imaging with genetics, neuropsychological, behavioral, and other health assessments

EPIDEMIOLOGY – CANNABIS USE DISORDERS

- 1/10 who ever use
- 1/6 who start in adolescence
- ¼ - ½ who use daily
- Large proportion self-discontinue



TRANSITION TO OTHER SUBSTANCE USE

- Longitudinal and cross-sectional studies
- Link between early cannabis use and increased likelihood of developing a substance use disorder
- Substance use is multifactorial and risks that predispose to early cannabis use may also predispose to substance use disorder risk

RISK FACTORS	PROTECTIVE FACTORS
Chaotic home environment	Strong family bonds
Ineffective parenting	Parental engagement in child's life
Little mutual attachment and nurturing	Clear parental expectations and consequences
Inappropriate, shy, or aggressive classroom behavior	Academic success
Academic failure	Strong bonds with pro-social institutions (school, community, church)
Low academic aspirations	Conventional norms about drugs and alcohol
Poor social coping skills	
Affiliations with deviant peers	
Perceived external approval of drug use (peer, family, community)	
Parental substance abuse or mental illness	

SOURCE: US Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse, (1997) Preventing drug use among children and adolescents: A research-based guide. NIH Publication No. 97 - 4212.

ANIMAL STUDIES

- Exposure to cannabis in adolescence alters the maturation of the endogenous opioid system
  - Adult rats exposed to cannabis in adolescence, showed increased response to reinforcing properties of opioids
  - Seems this is true for other substances as well

LIMITATIONS TO ANIMAL STUDIES

- Reliance on synthetic cannabinoids which are usually full agonists at CB1 and CB2 receptors
- Typically use intraperitoneal or intravenous routes of drug administration
- Models typically approximate daily, high dose cannabis users

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., Editor

Adverse Health Effects of Marijuana Use

Nora D. Volkow, M.D., Ruben D. Baler, Ph.D., Wilson M. Compton, M.D., and Susan R.B. Weiss, Ph.D.

Table 2. Level of Confidence in the Evidence for Adverse Effects of Marijuana on Health and Well-Being.

Effect	Overall Level of Confidence*
Addiction to marijuana and other substances	High
Abnormal brain development	Medium
Progression to use of other drugs	Medium
Schizophrenia	Medium
Depression or anxiety	Medium
Diminished lifetime achievement	High
Motor vehicle accidents	High
Symptoms of chronic bronchitis	High
Lung cancer	Low

* The indicated overall level of confidence in the association between marijuana use and the listed effects represents an attempt to rank the strength of the current evidence, especially with regard to heavy or long-term use and use that starts in adolescence.

PSYCHOSOCIAL TREATMENTS

- Motivational Enhancement Therapy
- Cognitive Behavioural Therapy
- Contingency Management
- Family-based Programs
- Exercise
- Internet assisted therapy/telephone assisted therapy
  - Apps
  - Computer-delivered CBT/MET/CM

RELAPSE PREVENTION: MEDICATION ADJUNCTS

- **Gabapentin**
  - 12 week RCT of 1200 mg daily (divided doses)
  - Decreased use, decreased withdrawal, decreased craving, improved sleep
- **N- acetyl-cysteine**
  - 1200 mg BID + contingency management
  - Decreased cannabis use

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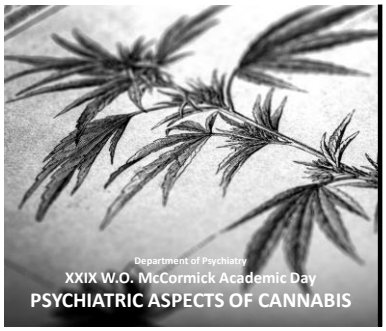
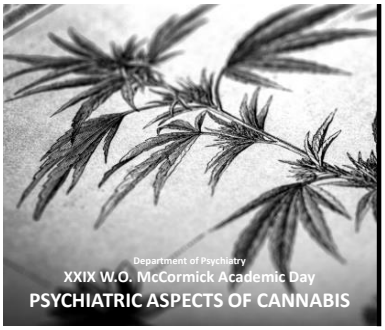


Q&A

Please line up behind the microphones

evaluation:
https://surveys.dal.ca/opinio/s?s=41941



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Return your name badge at the 2:15 break to enter a draw for a door prize