



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

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WELCOME!

Today's Topic:

Treating my mental health problem with Cannabis

My patients swear by their use of Cannabis. Is that correct and how should I guide their ongoing use?

Robert Sise, MD, MBA, MPH

PANELISTS:

RICK RIES, MD, KARI STEPHENS, PHD, AND BARB MCCANN, PHD





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MY PATIENTS SWEAR BY THEIR USE OF CANNABIS. IS THAT CORRECT AND HOW SHOULD I GUIDE THEIR ONGOING USE?

BOB SISE, MD, MBA, MPH

ADDICTION PSYCHIATRY FELLOW

UNIVERSITY OF WASHINGTON



Or how I learned they should START worrying as cannabis use is comorbid with nearly all psychiatric diagnoses...

GENERAL DISCLOSURES

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GENERAL DISCLOSURES

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SPEAKER DISCLOSURES

- ✓ No conflicts of interest

PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose:

Mark Duncan MD

Barb McCann PhD

Anna Ratzliff MD PhD

Rick Ries MD

Kari Stephens PhD

Niambi Kanye

Betsy Payn

Diana Roll

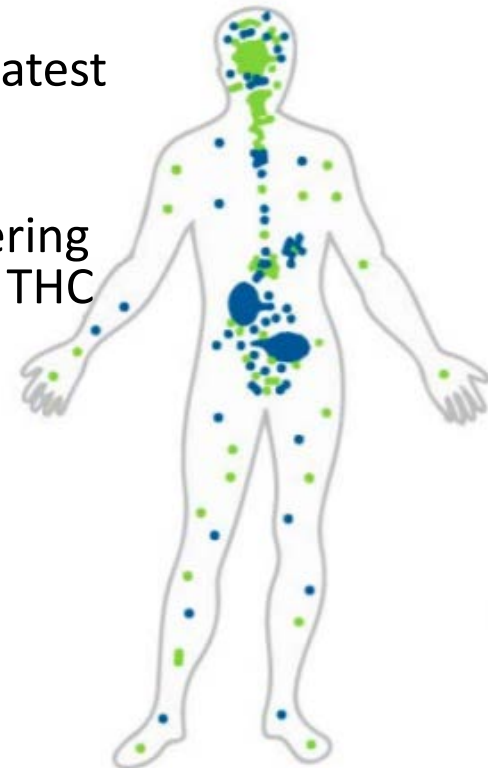
Cara Towle MSN RN

OBJECTIVES

- Overview of the substance - what type of cannabis?
- Review how cannabis use is related to:
 - Impaired Cognitive Function
 - Mood Disorders
 - Psychosis
 - Anxiety disorders
 - Other dx: PTSD, OCD, ADHD
 - Other forms of substance use
- Acknowledge evidence base for deleterious impact of cannabis use on mental health: *potential causal links*
- Discuss potential interventions and treatment for cannabis use

CANNABIS

- Wide variety of cannabis based products offering various concentrations of cannabinoids
 - 85 different cannabinoids have been isolated from the plant. (El-Alfy et al 2018)
 - The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and Δ^9 -tetrahydrocannabinol (THC)
 - Various different strains of cannabis exist, offering relatively different concentrations of CBD and THC
- THC: CB1 agonist
 - Psychoactive: altered mood, cognition
- CBD: Indirect CB1 and CB2 antagonist
 - Immunologic and anti-inflammatory effects
 - Antipsychotic?

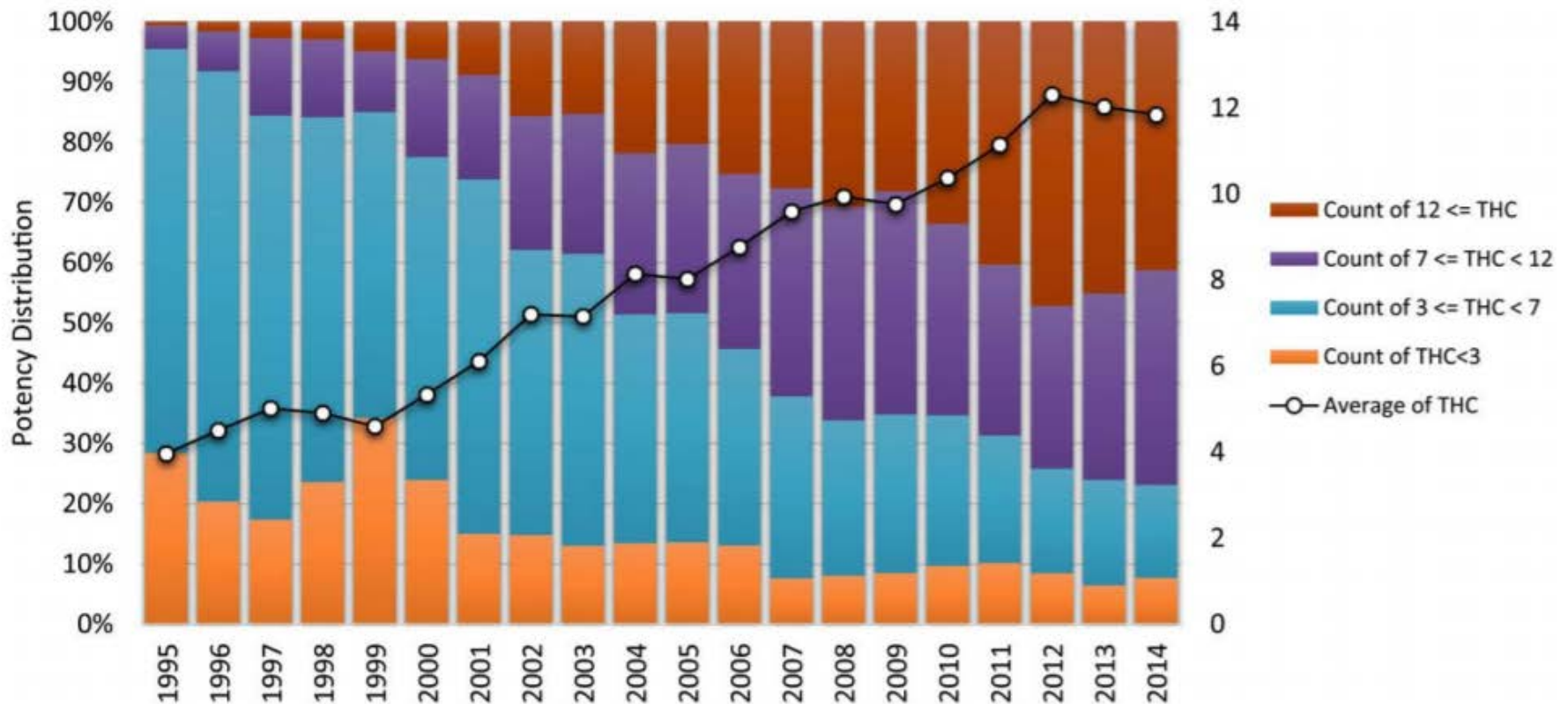


CB1

CB2

THC CONCENTRATION

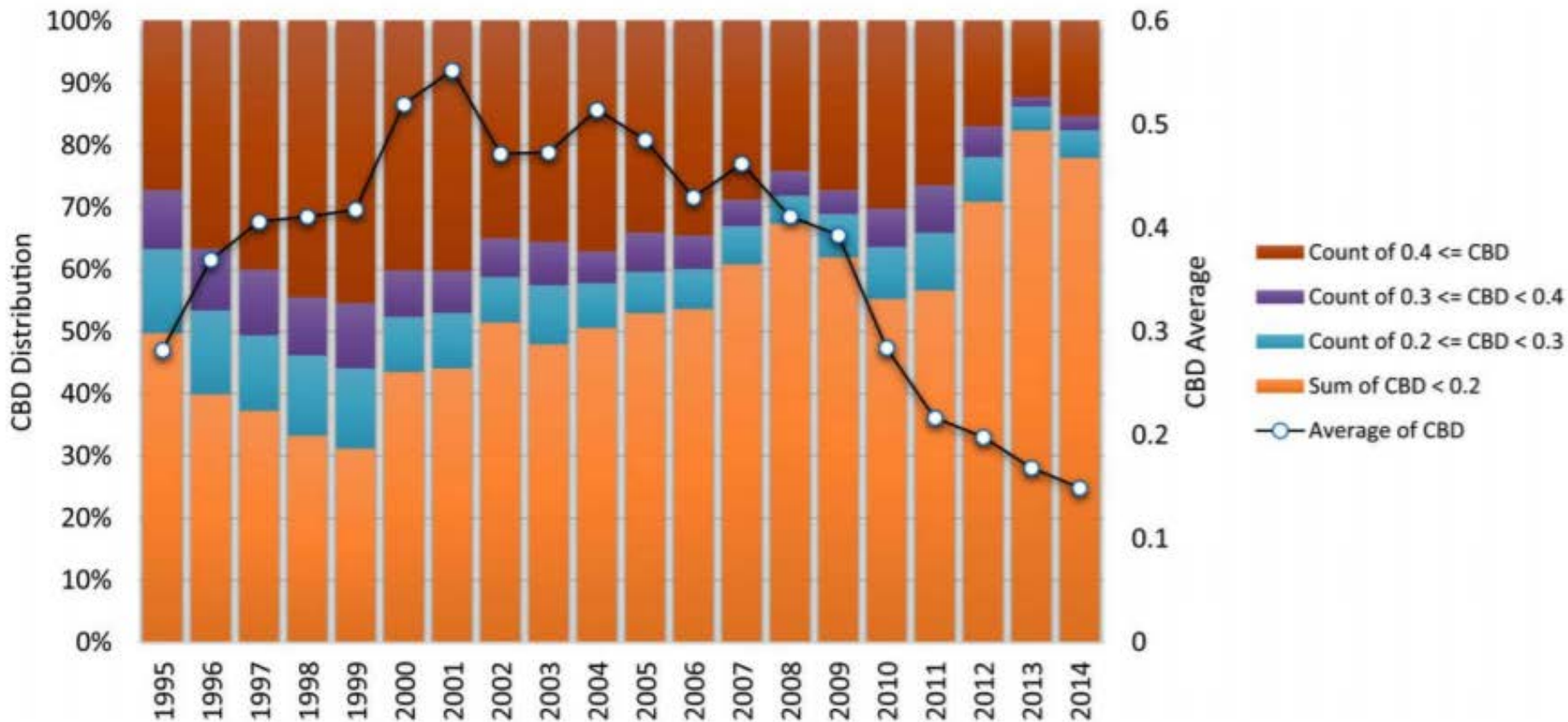
COURTESY- DR. KATE REAN



ElSohly et al. Biological Psychiatry (2016) 79(7):613-619

CBD CONCENTRATION

COURTESY- DR. KATE REAN



ElSohly et al. Biological Psychiatry (2016) 79(7):613-619

METHODS OF USE

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- Smoking
 - Pipe, bong, blunt, joint, vaporizer
 - Often mixed with tobacco
- Edibles
 - Delayed effects
- Concentrates
 - Butane hash oil, dabs, wax, shatter
 - Up to 80-90% THC



CANNABIS USE & COGNITIVE FUNCTION

Significant evidence of acute and long-term impairment

- In a dose-dependent manner, cannabis acutely impairs:
 - Attention
 - Concentration
 - episodic memory
 - associative learning (Scott et al 2018)
- Long-term cannabis use is associated with impaired
 - verbal memory
 - cognitive processing speed

*both generally resolve after >1 month of abstinence (Schulte et al 2014 and Auer et al 2016)

CANNABIS USE & MOOD DISORDERS

Significant association

- In 2011, 2ndary analysis of 43,000 US adults:
 - 2-3 times higher rates of lifetime cannabis use among patients with depression or bipolar disorder (vs. patients w/o mood disorder dx) (Martins et al 2011)
- 2018 systematic review found that recent cannabis use (over prior 6 month period) was associated with higher intensity of mood symptoms during subsequent follow-up (2.5 months to 5 years) (Mammen et al 2018)

CANNABIS USE & DEPRESSION

Significant association- causal link?

- In 2014 meta-analysis: heavy cannabis users had a significantly higher rate of MDE vs. light or nonusers – OR: 1.62 (95% CI 1.21-2.16 (Lev-Ran et al 2014)
- Unclear evidence regarding casual link
 - twin study findings supports hypothesis that comorbidity of cannabis use disorder and depression: due to genetic and environmental factors that predispose to both disorders (Lynskey MT et al 2014).

CANNABIS USE & BIPOLAR DISORDER

Significant association- causal link?

- Lifetime rate of cannabis use disorder in Bipolar Disorder ~ 30% (vs. 1.5% in gen pop) (Bally et al 2014)
- Significant association between cannabis use and both:
 - earlier age of onset of first manic episode
 - more frequent mood episode (ibid)
- Cannabis use associated with a 3X increased risk (odds ratio = 2.97, 95% CI 1.80-4.90) for new onset of manic symptoms (Gibbs et al 2015)

CANNABIS USE & PSYCHOSIS

Significant association

- Cross-sectional study indicates regular cannabis use associated with 2-3 X higher lifetime prevalence of schizophrenia compared with nonusers (Gage et al 2016)
 - Strongly associated with:
 - earlier age of onset of use,
 - higher frequency of use/amount used
 - Use of products with high THC/CBD ratios
- In systematic review including 53 studies of patients with schizophrenia-spectrum disorders (Green et al 2005)
 - 23.1% prevalence of cannabis use over the past 6 months
 - 42.2% prevalence of lifetime use

CANNABIS-INDUCED PSYCHOSIS

Associated with higher THC concentrations

- Case studies demonstrate general association between use of high dose THC products (e.g. wax) and cannabis-induced psychosis. (Volkow et al 2016 and Di Forti et al 2015)
 - Acute THC administration causes increased dopamine release
 - increased activation of dopamine pathway: more marked with higher frequency of use/THC doses
- Unclear whether this acute effect is related to the development of schizophrenia associated with chronic cannabis use.
 - Danish study using national registry (~1500 patients who received a diagnosis of cannabis-induced psychosis from 1994 and 2014, and followed them through August 2014) found:
 - 41.2% conversion rate to schizophrenia (Starzer 2018)

CANNABIS USE & SCHIZOPHRENIA

Strong Association

- Systematic review of 35 longitudinal studies (Moore et al 2007) found:
 - increased risk of psychosis associated with any lifetime use (OR 1.41, 95% CI 1.20-1.65)
 - Dose-response relationship: 2X increase in risk among highest frequency users (OR 2.09, 95% CI 1.54-2.84).
- Finnish Prospective Longitudinal study (Mustonen 2018): significantly increased risk of psychosis among subjects who used cannabis >4 times by age 16 y/o vs. those who had never used:
 - ~6500 individuals born in northern Finland in 1986
 - Evaluated at age 15 to 16 years
 - Evaluated again at age 30 years
 - adjusted HR ratio 3.02, 95% CI 1.14-7.98

CANNABIS USE & SCHIZOPHRENIA

Causation vs. mutual association with third factor?

- A cross-sectional study ~7K adults in the Netherlands Twin Registry: risk score for schizophrenia derived from a large genome-wide association meta-analysis accounted for no more than 0.5% of the variance in:
 - Lifetime use
 - Frequency of use
 - Quantity of use
 - Age at initiation of use (Verweij et al 2017)
- Authors concluded the increased prevalence of cannabis use by people with schizophrenia is not likely explained by a shared genetic liability

CANNABIS USE AMONG PSYCHOTIC PTS

Worsens positive symptoms

- In their 2016 systematic review/meta-analysis of 24 longitudinal studies (> 16.5k participants), Schoeler T, Monk and coauthors found:
 - cannabis use was associated with increased relapse, rehospitalization, and positive symptoms (but not negative symptoms)
 - As well as poorer overall level of functioning
- 2-year-long prospective longitudinal study of 220 adults with first-episode psychosis found:
 - increased risk of relapse with hospitalization during periods of cannabis use (OR 1.13) (Schoeler T, Petros N et al 2016)

CANNABIS USE & ANXIETY DISORDERS

Significant Association

- In 2011 secondary analyses of 43,000 US adults (US sample):
 - Similar to case for pts with mood disorders: 2-3 times higher rates of lifetime cannabis use among patients with anxiety disorders (vs. those w/o) (Martins et al 2011)
- Survey of 36,309 adults in the US found that among those meeting dx criteria for cannabis use d/o:
 - 23.4% had a current anxiety disorder (note: adjusted odds ratios were not significant (1.2, 95% CI 0.88-1.56 for men; 0.8, 95% CI 0.58-1.23)
 - Among women w/ cannabis use d/o:
 - Specific phobia- 9.9%
 - GAD: 19.9%
 - Social phobia: 7.2%
 - Panic Disorder: 15.2%
 - Among men w/ cannabis use d/o:
 - Specific phobia- 8.6%
 - GAD: 12.2%
 - Social phobia: 7.1%
 - Panic Disorder: 7.4%

CANNABIS USE & ANXIETY DISORDERS

Acute use often worsens anxiety, unclear regarding impact of long-term use

- Cannabis intake causes transient acute anxiety in many.
- Less clear regarding impact of long-term use:
 - Prospective longitudinal community-based study of ~35K US adults found:
 - no increased risk of developing an anxiety disorder among cannabis users (OR 1.0, 95% CI 0.8-1.3) (Blanco 2016)
 - Australian, 15-year prospective longitudinal study of ~2K adolescents found daily cannabis use during adolescence:
 - associated with a 2.5-fold increased risk of anxiety disorder at age 29 years (Degenhardt et al 2013)

CANNABIS USE & PTSD

Significant association, potentially worsens severity

- National epidemiologic studies found comorbidity rates of PTSD and cannabis use d/o: ~10%
 - Kerridge et al 2018
 - Hasin et al 2016
- Systematic review of 4 prospective longitudinal cohort studies of adults with PTSD at baseline found:
 - current (prior month) cannabis use was associated with higher levels of PTSD symptoms over time (vs. in individuals with no or little use) (Mammen 2018)

CANNABIS USE &...OCD... ADHD

Sig. associations for OCD and ADHD but weak study designs

- OCD: In household survey of ~9K Australians:
 - 19.9% prevalence of OCD among pts with cannabis use d/o vs. 2.4% among patients who are abstinent. (Teesson 2012)
- ADHD
 - 20-30% comorbidity between ADHD and cannabis use d/o based on community surveys: (De Alwis et al 2014 and Vogel et al 2016)
 - Of note, self-medication hypothesis (Cooper 2017)

CANNABIS USE & OTHER SUBSTANCE USE

Sig. associations but weak study designs- all community surveys

- Alcohol:
 - community survey of 36K US adults found- EtOH use disorder had higher risk of cannabis use disorder (adjusted OR 6.0, 95% CI 5.10-6.97) (Kerridge 2018)
- Similar for Stimulants, tobacco and most other psychoactive substances (meth, MDMA):
 - 6-16X more likely as per community survey data
 - Note, sig. risk for OUD but not as remarkable: 4X

TAKEAWAYS FROM THE EVIDENCE



*or how I learned to help my patients START worrying
and avoid/minimize cannabis use*

TAKEAWAYS RE CANNABIS USE

- Overwhelming evidence of acute & long-term impairment in cognitive function associated with use
- Significant association between cannabis use and mood disorders
 - Use associated with worsened severity of mood episodes
 - Unclear re causal link
- High THC consumption associated with both acute psychosis and increased life-time risk of psychotic disorder
 - Associated with worse positive sx
 - Evidence suggestive of casual link: change in dopamine pathways

TAKEAWAYS RE CANNABIS USE

- Significant association between cannabis use and anxiety disorders
 - Unclear re causal link
 - Acute use worsens anxiety, unclear re impact of chronic use
- Significant association between PTSD and cannabis use
 - Cannabis use potentially worsens sx severity
- Significant associations between cannabis use and OCD, ADHD and other substance use disorders
 - Note: weak study designs

HOW TO COMMUNICATE THIS TO PATIENTS?



TREATMENT

- Psychosocial interventions
 - Contingency Management
 - Motivational Enhancement Therapy
 - Cognitive Behavioral Therapy
- Pharmacology
 - Gabapentin decreased cannabis use and withdrawal symptoms in one study at 300 mg-300 mg-600 mg dose *12 weeks (Mason et al 2012)
 - N-Acetyl cysteine decreased cannabis use and cravings in adolescents (2400 mg daily for eight weeks) but not replicated in larger, adult study (Gray et al 2012 and 2017)

HARM REDUCTION STRATEGIES

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- Specific populations at high risk
 - Adolescents
 - Mental health diagnoses
 - Family history of psychosis
- Decrease overall use
 - Both frequency and amount consumed
 - Limiting time of day
 - Limit amount purchased at a time
- Decrease THC potency
 - No synthetics
 - No concentrates

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