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Cannabis Use and Addiction in Rural Populations: Phenomenology, Intervention, Policy

Alan J. Budney, PhD
Dartmouth College, Geisel School of Medicine
Center for Technology and Behavioral Health
alan.budney@dartmouth.edu

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This presentation is part of the Community Rounds Workshop Series

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Community Rounds
WORKSHOP SERIES

December 1, 2021

Social and Structural Determinants of Mental Health, Substance Use and Treatment

Brady Heward, MD

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Session Disclaimer

- The views, statements, and recommendations expressed during this activity represent those of the authors and speakers and do not necessarily represent the views of the University of Vermont.

- The speaker has financial relationships (consultant) with:
  - Canopy Growth, Inc.
  - Jazz Pharmaceuticals

- These relationships have been mitigated

- This activity did not receive any support from ineligible companies

- Speaker does not currently use cannabis recreationally or therapeutically
- Speaker discloses a strong bias against medical marijuana legislation and implementation

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Alternative Title:
Cannabis (Marijuana) Risk/Benefits?
Navigating the swamp

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Disclosures

Research supported by NIH-NIDA for > 30 yrs

- *Treatment Development for Substance Use Disorders*
- *Lab & Survey Studies: Withdrawal, Policy, Use Characteristics, Measuement of Use*

Scientific Review Board: *Center for Medical Cannabis Research*, *UCSD*

Consultant/Science Advisory Board: Canopy Growth, Inc; Jazz Pharmaceuticals

Don't Currently Use Cannabis: recreationally or therapeutically

Strong Bias: Against Medical Marijuana Legislation and Implementation

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Outline

- Define cannabis and describe the evolving cannabis landscape
- Cannabis/marijuana (THC-laden) as an addictive substance
- Clinical Interventions for CUD / Challenges for Rural Populations
- Cannabis/marijuana as a therapeutic

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Essential to Define Cannabis (Marijuana)

- Cannabis legalization (medical and recreational) has brought confusion

- We need to be on the same page if we hope to effectively:
  - Interpret and Communicate Research Findings
  - Have effective and meaningful conversations with friends and family
  - Communicate effectively with the Public, Patients, Youth, Healthcare Providers, Policy makers, etc.

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Rural Cannabis Use

Cannabis Across U.S. Geographic Regions

	Large Metro	Small Metro	NonMetro
Any past year cannabis use	16.08	14.80	12.07
Cannabis use disorder	1.50	1.45	1.12
Among Cannabis Users			
100 days or more	42.59	46.21	48.67
Uninsured	13.36	14.81	20.38
Living in poverty	16.25	22.35	27.06
College degree	31.61	20.98	12.72
Residence in MCL state	69.79	57.25	46.55
Nicotine dependence	19.81	27.14	36.11

NSDUH (2015-18) Moore et al. 2021

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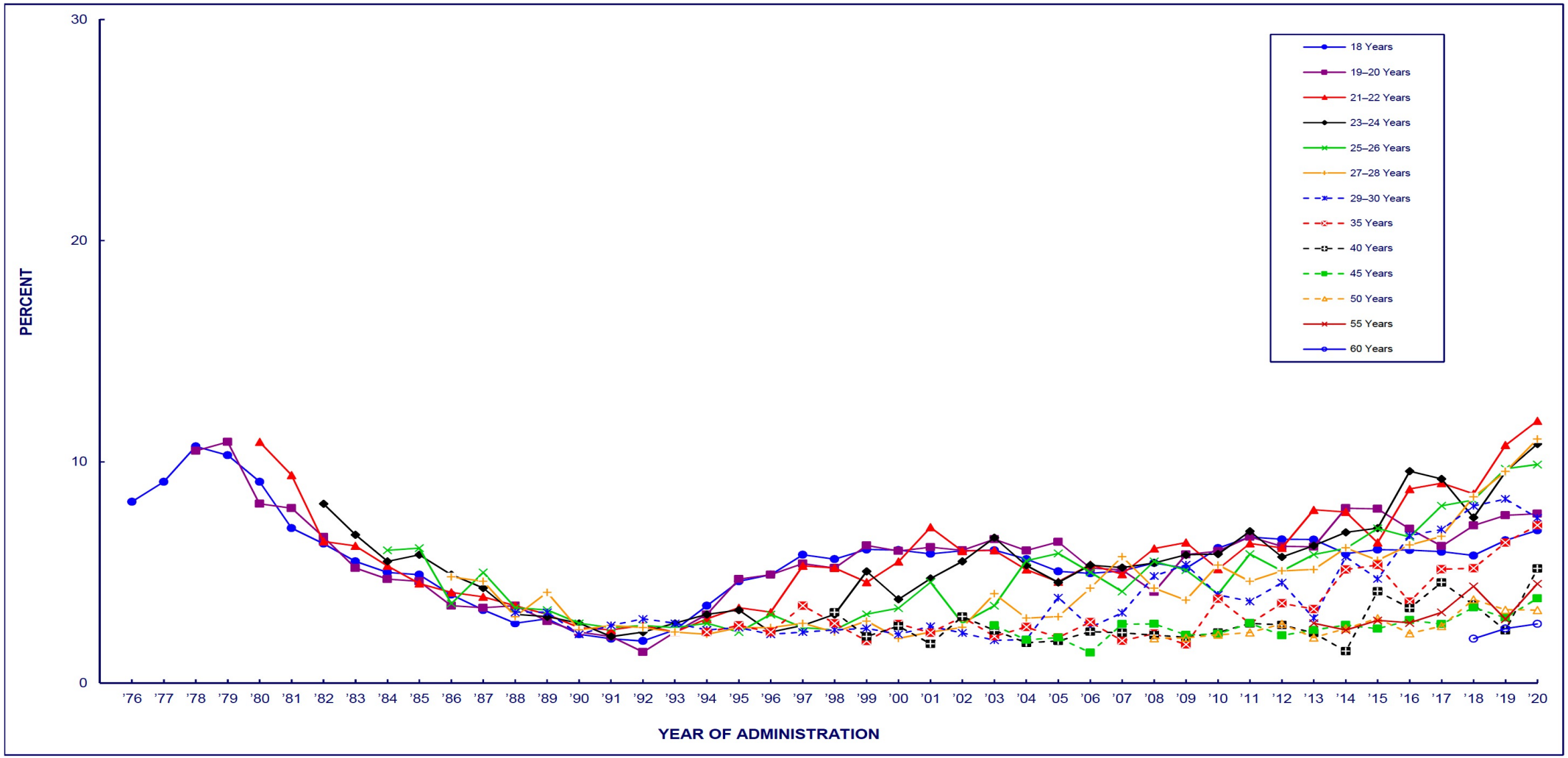
FIGURE 3-3c

MARIJUANA

Trends in 30-Day Prevalence of Daily Use
among Respondents of Modal Ages 18 through 60, by Age Group



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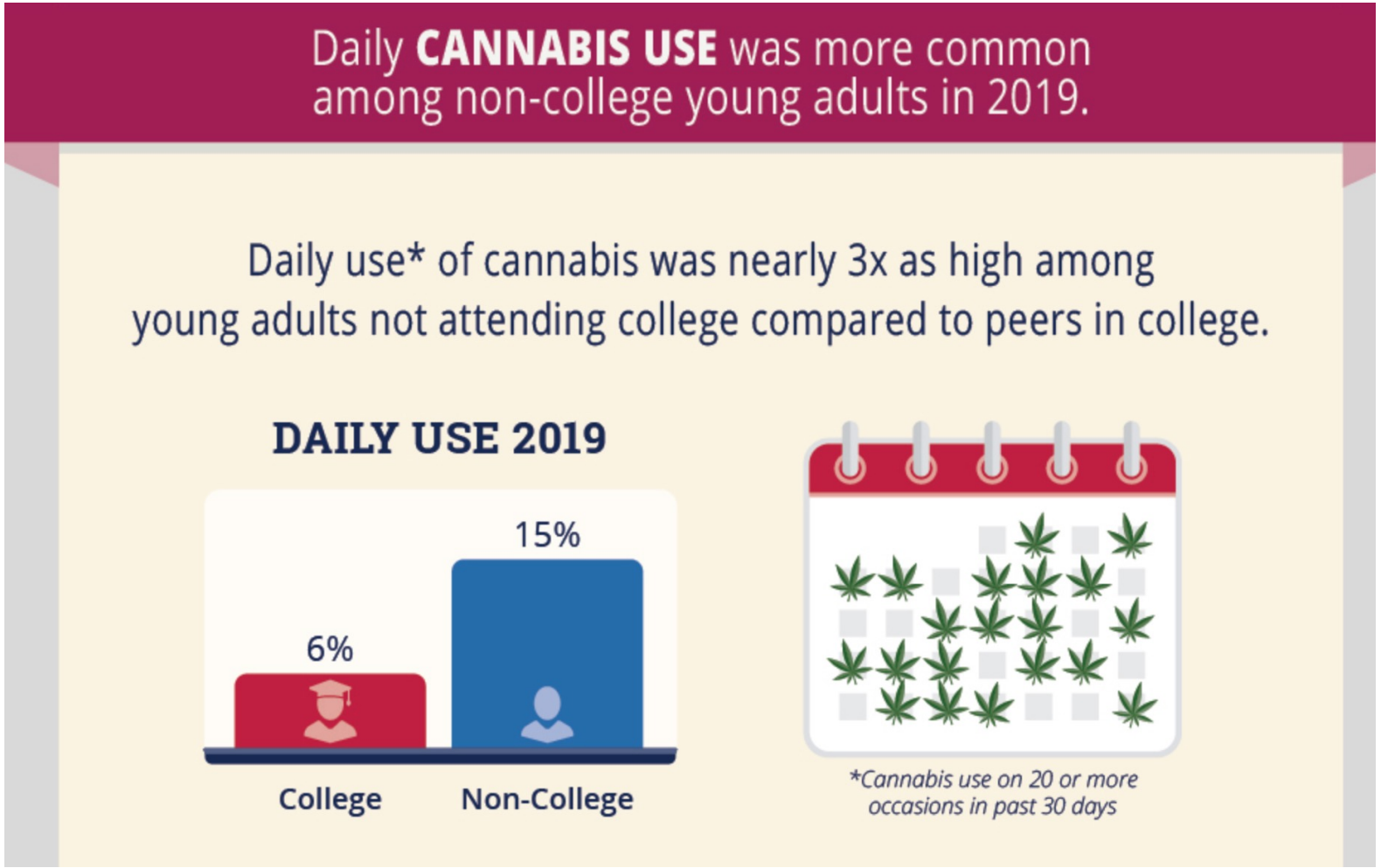
Monitoring the Future



NSDUH (2015-18) Moore et al. 2021

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Legalization & New Products

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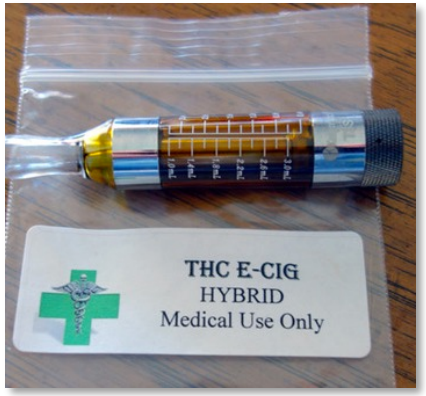
THC-Laden Cannabis Products:

Smoking / Vaping



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THC-Laden Cannabis Products:

Concentrates

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THC-Laden Cannabis Products:

Edibles

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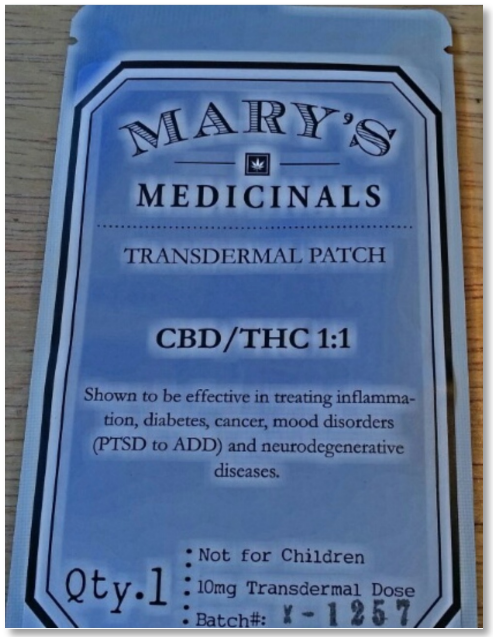
THC-Laden Cannabis Products:

Lotions / Cremes / Salves / Patches



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CBD Products – Cannabis (no-THC

90 Capsules
$90.00

1oz Tincture
$55.00

Tincture
$30.00

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Rural Cannabis (THC laden) Use

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NSDUH (2015-18) Moore et al. 2021

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The Cannabis Industry and Lobby

The Cannabis Trade Federation (CTF) has hired 15 lobbyists to push the Strengthening the Tenth Amendment Through Entrusting States Act

2019 ~ 4 Million Spent Lobbying for Marijuana Laws

Joint effort: cannabis lobby heads to Washington to woo US lawmakers

Industry leaders descended on the capital this week amid hopes the country at large is slowly embracing legalization

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What is Cannabis (Marijuana)?

- **PLANT: hemp — *Cannabis sativa, indica "strains"***

- **Contains over 100 compounds??**

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What is in the Cannabis Plant?

- CBGA (Cannabigerolic acid)
- **THCA (Δ9-tetrahydrocannabinolic acid)**
- CBDA (Cannabidiolic acid)
- CBCA (Cannabichromenenic acid)
- CBGVA (Cannabigerovarinic acid)
- THCVA (Tetrahydrocanabivarinic acid)
- **CBDVA (Cannabidivarinic acid)**
- CBCVA (Cannabichromevarinic acid)
- **THCA (Δ8-tetrahydrocannabinolic acid)**
- Terpenes: essential oils, smells, flavor

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Delta-9 THC (tetrahydrocannabinol)

** Primary psychoactive constituent

Dose related effects:

- **High, euphoria**
- Cognitive impairment (memory, learning, attention, time perspective)
- Anxiety, Panic, Hallucinations, Psychosis?
- FDA approved for:
    - nausea associated with cancer chemotherapy
    - treatment of anorexia associated with weight loss in AIDS patients

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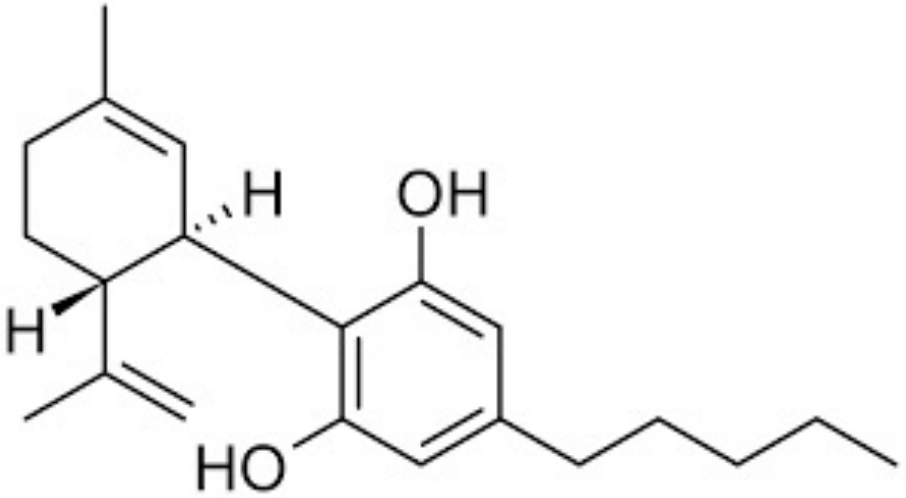
Cannabidiol (CBD)



- Cannabis plants have varying amounts of CBD
- Moderate the adverse effects of THC????
  - (anxiety, psychosis, and cognitive deficits)

** Demonstrated efficacy as an anti-epileptic (FDA approved pediatric epilepsy)

* Initial positive trial as an antipsychotic?

*** Anxiolytic, anti-depressant, stress reduction, pain relief, anti-inflammatory, anti-cancer agent, Type 1 diabetes, rheumatoid arthritis, etc. :

No clinical data demonstrating efficacy for any of these

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Entourage Effect: Mixture or Ratio of Compounds

- Cannabis plants / products have varying amounts of each of the aforementioned; **Entrourage Effect/hypothesis** is that the whole plant (compound interactions) are important to observed effects
- How much does each contribute to various effects?
- Logically / pharmacologically, combinations should have some effect, **but these have not been studied clinically.**

- **Russo (2016)**

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Dose Matters

Amount x Potency

Potency (%THC) Plant Material / Flowers *

THC: 0.6% - 30.6%*

CBD: 0.04% - 14.6%*

Potency (%THC) Concentrates (Oils, Tinctures, Wax, Patches)

THC: 35.3% - 87.5%**

CBD: 0.01% - 40.3%**

Potency (%THC) Edibles

THC: 20mg – 100mg**

CBD: 20mg

Potency (%THC) Capsules

THC 5-50mg

CBD 5-25mg

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Route of Administration Matters

SMOKE

VAPE

EDIBLE

OILS / TINCTURE

CREAM / PATCH

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Summary: Part I:

To make sense of cannabis research findings -

To have an intelligent conversation about cannabis -

To be smart about what you choose to use or recommend –

Requires that you are aware and understand:

All Cannabinoids are not the same!!

- THC ≠ CBD
- Dose / strength of THC and CBD matters
- Their combination and mixture of other cannabinoids and terpenes may matter, but we have little to no idea about if or how much they matter

Do not believe everything you hear or read!!!

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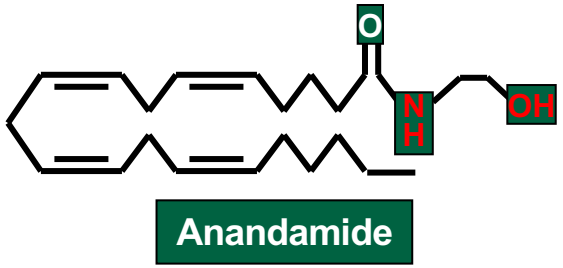
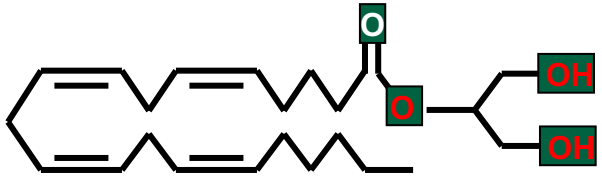
Biological Plausibility for Addiction and Therapeutics

Endogenous Cannabinoid System (eCB)



Anandamide



2-Arachidonoylglycerol (2-AG)

Cannabinoid Receptors

CB1

CB2

Endogenous Cannabinoid Ligands

Anandamide

2-Arachidonoylglycerol

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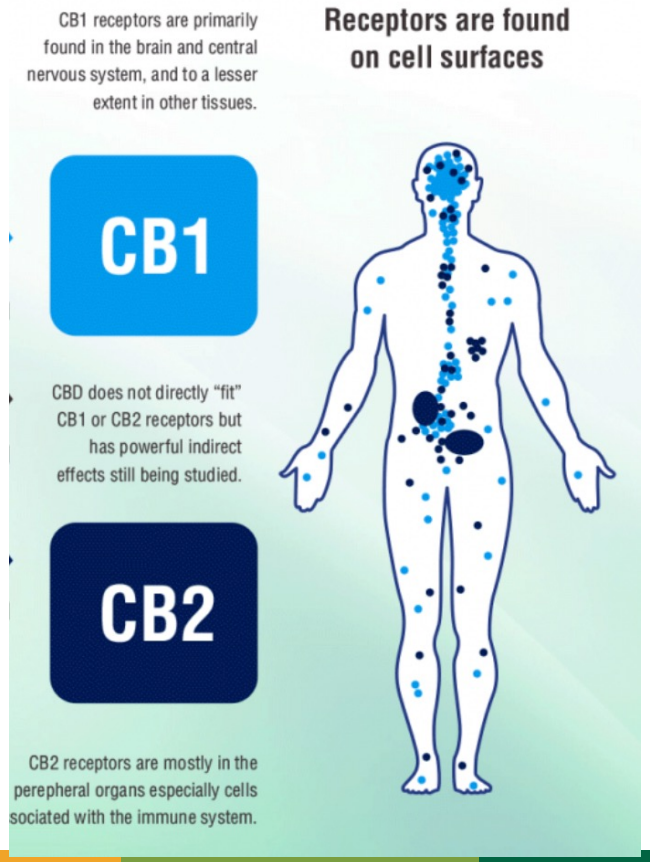
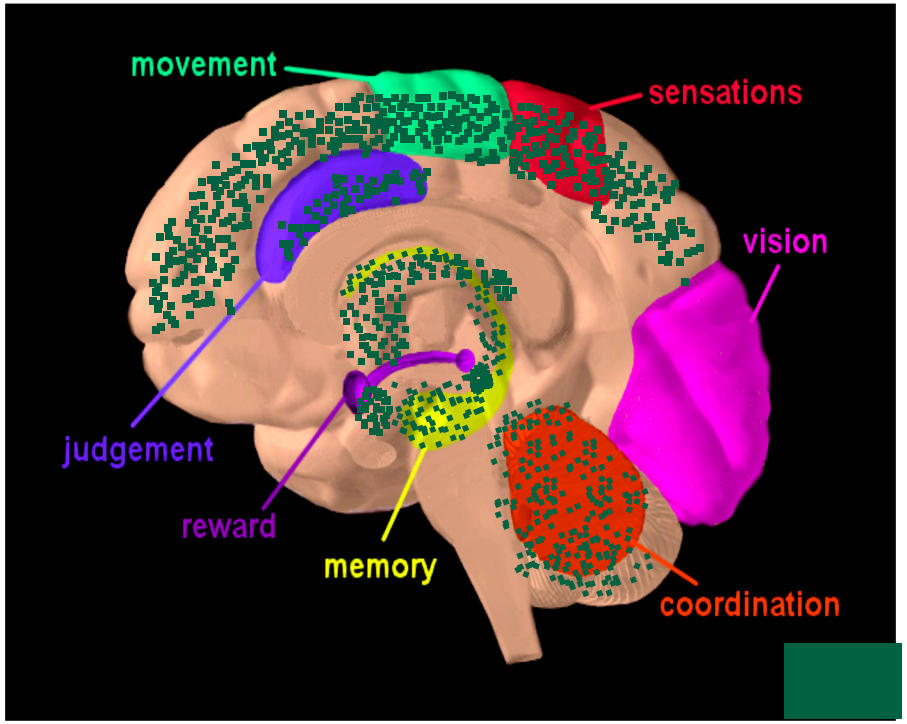
Biological Plausibility

Cannabinoid Receptors Are Located Throughout the Brain and Body





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Cannabinoid System Receptor Location and Function

- Cerebellum - movement/coordination
- Hippocampus - learning, memory
- Cerebral Cortex - executive function
- Nucleus Accumbens - reward (dopamine system)
- Basal Ganglia - movement
- Hypothalamus - body regulation
- Amygdala - emotional responses
- Spinal Cord - sensation (pain)
- Brain Stem - sleep, arousal, motor
- Central Gray Matter - analgesia
- Nucleus solitary tract - visceral sensation, nausea/vomiting

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Cannabis (THC-laden) Addiction

Cannabis (THC-laden) is addictive in every accepted scientific and clinical meaning of that concept

Scientific / Clinical evidence is strong and unambiguous

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Evidence: Addictive Potential & Clinical Consequences

Biological, Behavioral, Epidemiological

- Effects of administration and cessation on brain reward centers are similar to other drugs with addictive potential (CB1R)
- THC functions as a reinforcer in the human lab
- Clinically meaningful withdrawal syndrome
- Clinical Epidemiology: People meet CUD criteria
- Treatment seeking for CUD is prevalent
- Treatment response is modest; difficult to quit; high rate of relapse

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Cannabis (thc-laden) is more similar than dissimilar to other substances that are considered “substances of abuse”

Like other substances, cannabis is used primarily for its positive (and negative) reinforcing effects

A subset of those who use cannabis (conditional probability = 10-30%) will develop problems

Problems will range from mild to severe

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Vulnerable Populations
Highest Rates of CUD / Cannabis Consequences

Poverty --- Disadvantaged, underserved minorities, low SES

reduction/deprivation of prosocial reward, increased stress

Psychiatric Disorders

- perceived benefits, symptom relief

Physical Disorders

- perceived benefits, symptom relief

Teens

- impulsivity, developing neuro-system, lack of established roles and responsibilies, peer influence

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Rural Populations
Risk for Consequences May Be Increased?

Generally Fewer Services for those who are Disadvantaged:

- Fewer Support Services for those living in Poverty
- Mental Health/Psychiatric Care: less access, lower quality, fewer options
- Healthcare/Specialty Care: less access, lower quality, fewer options

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Rural Populations
Access to Quality Care for CUD is Limited?

Generally Fewer Services for those who are Disadvantaged:

- Fewer Professional SUD Treatment Services available
- Less access, perhaps lower quality, fewer options, greater burden

Why is this important?

- CUD is not rare
- People seek treatment for CUD
- We have efficacious treatments, but as with other SUDs, outcomes are limited

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Interventions for CUD and Misuse

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Pharmacotherapy / Medications

Potential Targets:

- Withdrawal : mood, sleep, anxiety, GI symptoms
- CB1 receptor agonist substitution
- CB1 antagonists
- Opioid antagonists
- GABA and Glutamate
- Enzymatic targets (FAAH)

**** No robust findings to date, no FDA approved medications!**

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Interventions for CUD and Misuse

Adolescents

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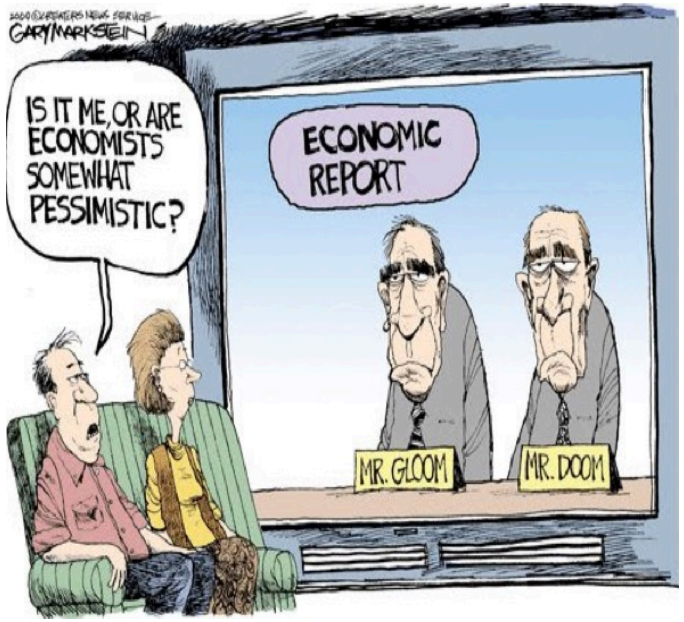
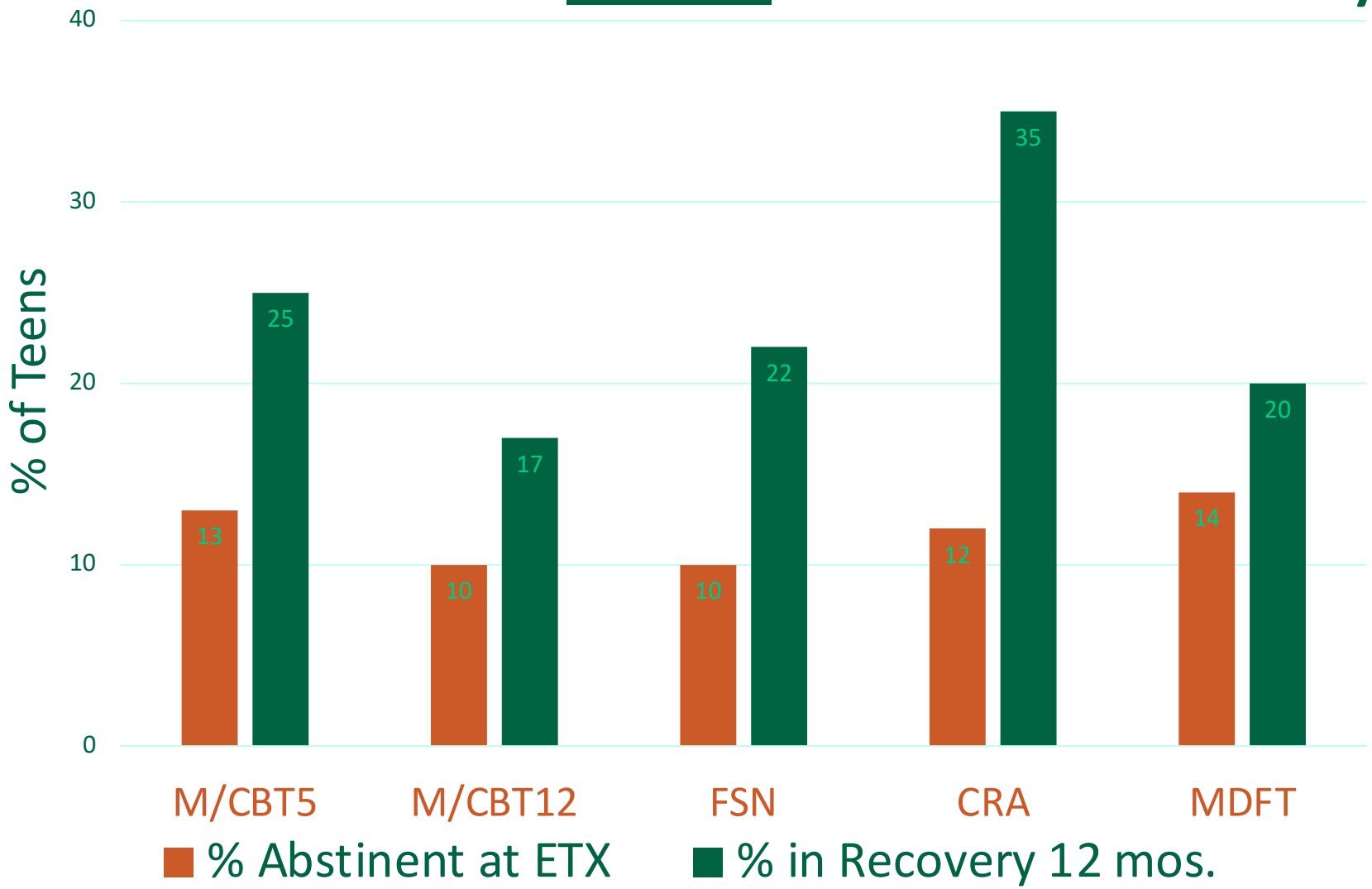
Adolescent Intervention Literature

Multiple types of family-based and group / individual behavioral efficacious interventions for SUD / CUD

Waldron et al.	FFT, CBT, combo
Liddle et al.	MDFT
Henggeler et al.	MST
Dennis et al./Godley et al.	MET/CBT, ACRA, FSN
Szapocznik et al.	BSFT
Stanger, Budney et al.	CM
Walker et al.	TMCU
Dennis et al. and others	Technology / Smartphone Delivery



Cannabis Youth Treatment Study



(Dennis et al., 2004)

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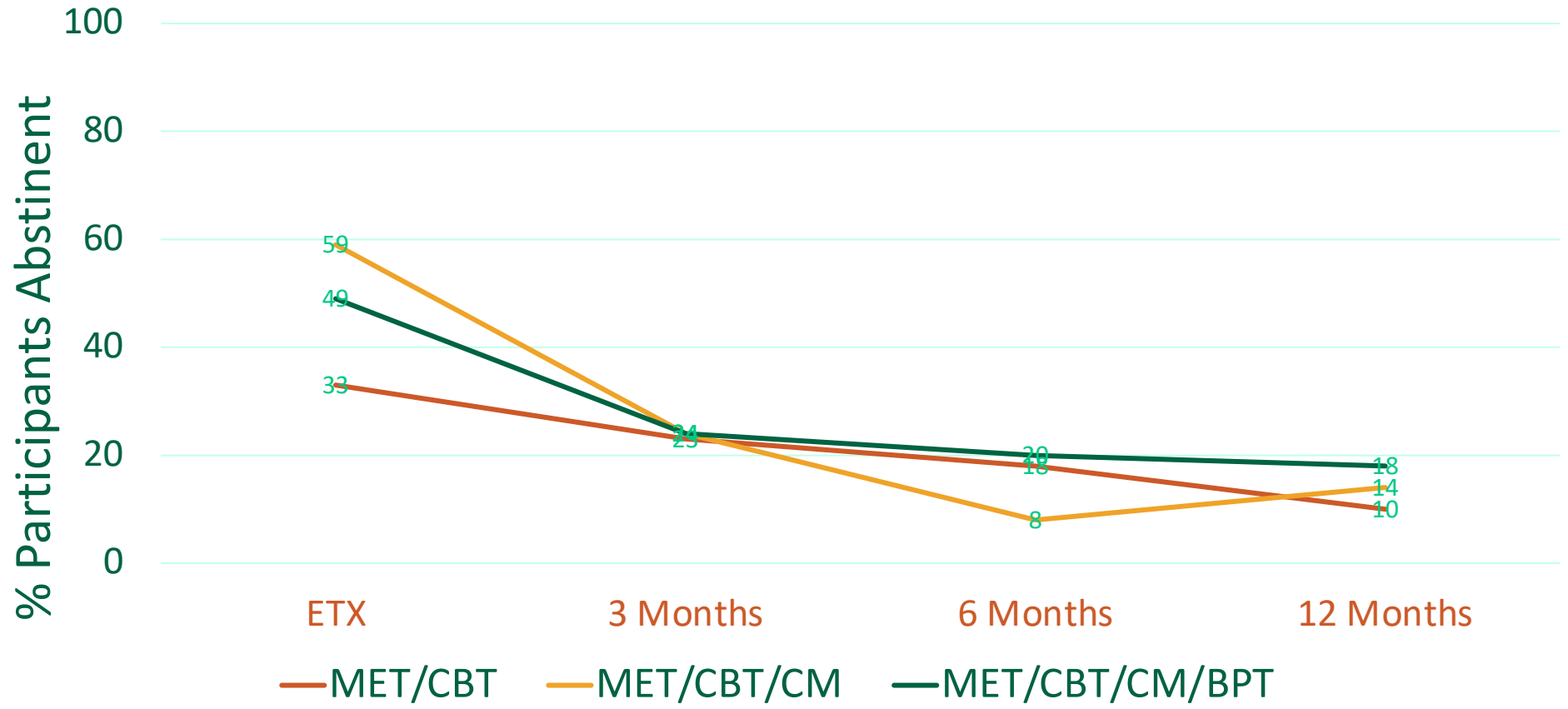
CM for Adolescents:

Replication and Extension

CM enhances outcomes, but did not maintain



(Stanger et al., 2015)

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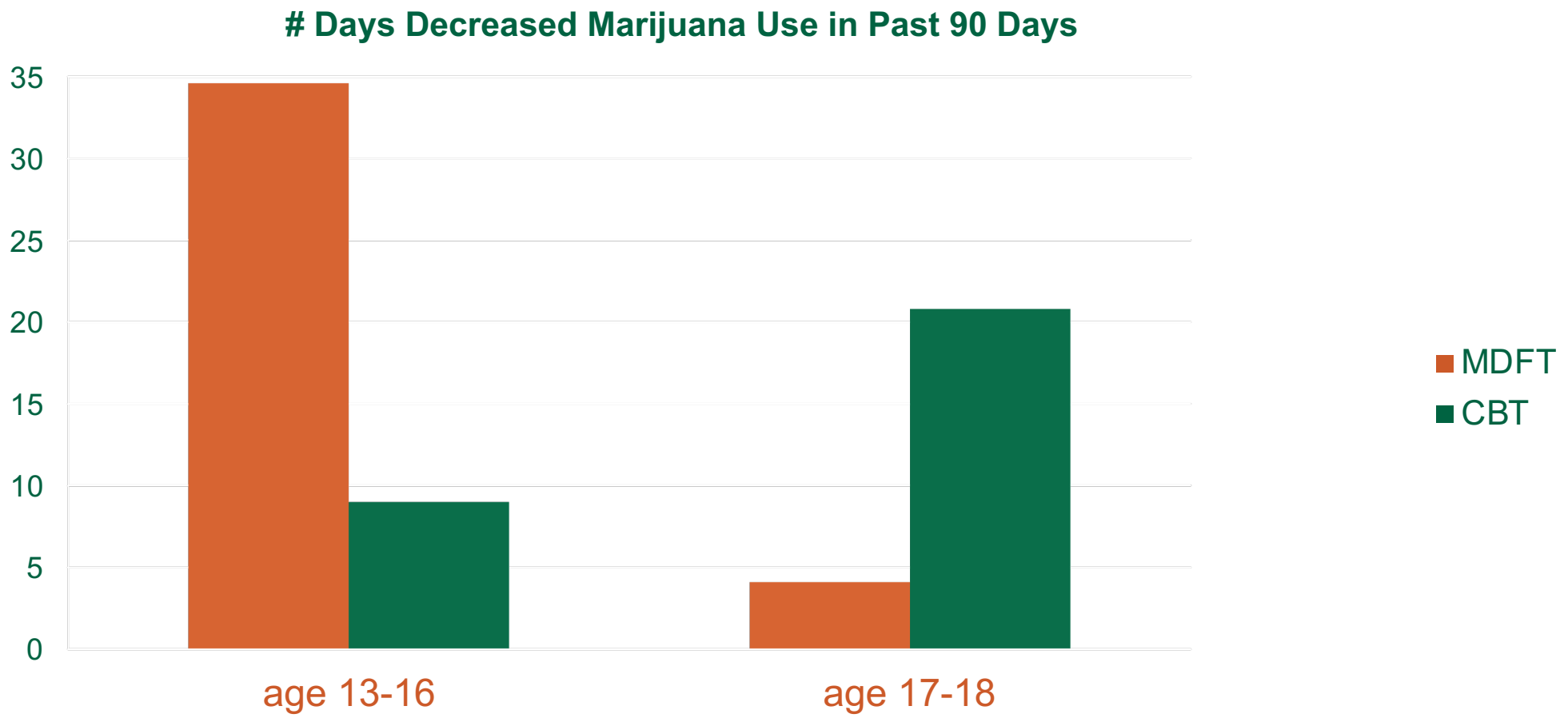
Multidimensional Family Therapy (MDFT) vs. Group Treatment (CBT based)

Age Effects



Hendriks et al. (2012)

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Interventions for CUD and Misuse

Adults

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Behavioral Treatments Literature (Adults)

Stephens, et al. (1994)	SS, CBT
Stephens, et al. (2000)	MET, CBT
Budney et al. (2000)	MET, MET/CBT, MET/CBT/CM
Copeland et al. (2001)	MET/CBT
MTPG (2004)	MET, MET/CBT
Budney et al. (2006)	MET/CBT, CM, MET/CBT/CM
Carroll et al. (2006)	MET/CBT, DC, MET/CBT/CM, DC/CM
Kadden et al. (2007)	MET/CBT, CM, MET/CBT/CM
Kay-Lambkin (2009, 2011)	MET/CBT (computerized)
Budney et al (2011, 2015)	MET/CBT/CM (computerized)
Carroll et al (2012, 2013)	CBT, CM, CBT/CMabst, CBT/CMhmk
Litt et al. (2013, 2020)	CaseM, CBT/CMabst, CBT/CMhmk, IAPT
Hoch et al (2014)	CANDIS (MET/CBT/Problem Solving)
Others	Brief Interventions College Students

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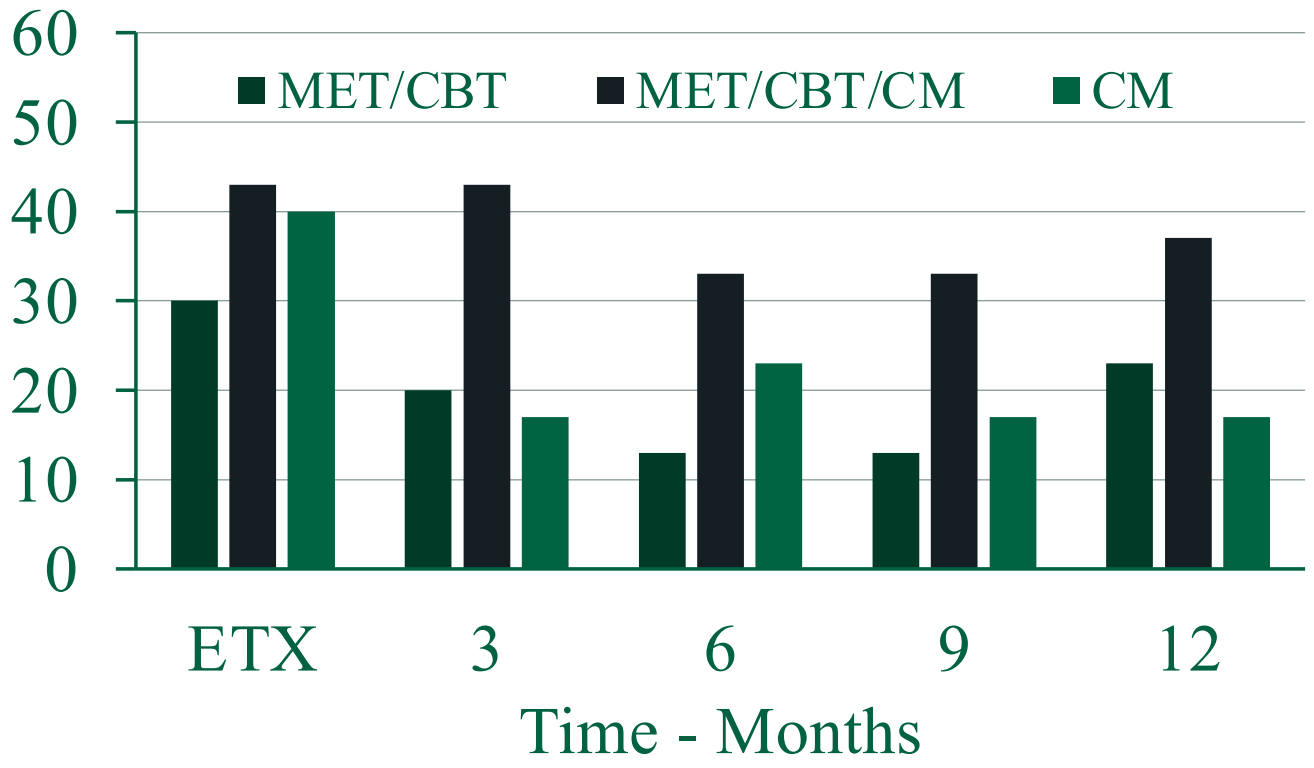
CM Improves Abstinence Outcomes
MET/CBT Maintains Abstinence

Replication and Extension (Budney et al. 2006)



MET/CBT/CM: gold standard - replicated in Carroll et al, 2006 and Kadden et al., 2007

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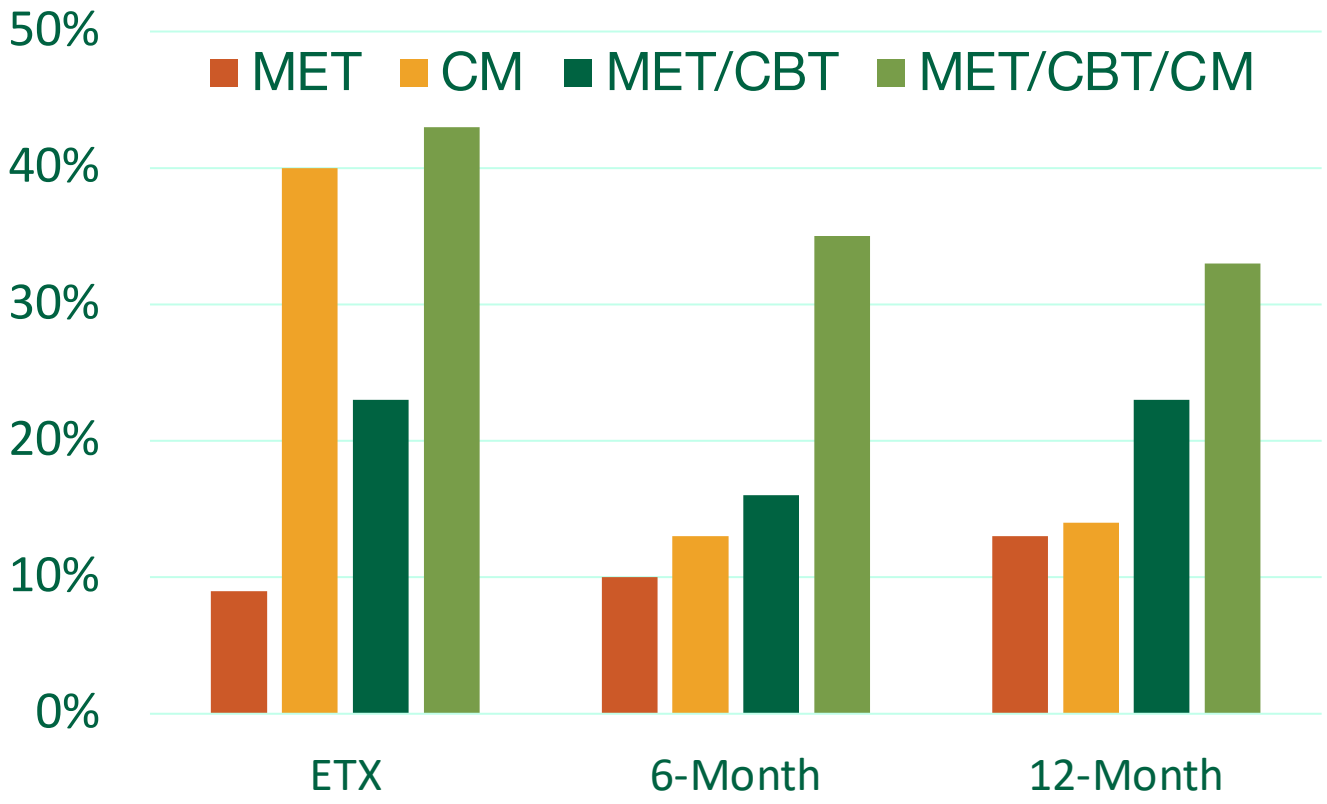
CUD Treatment Abstinence Outcomes Across Multiple Studies

Replication and Extension (Budney et al. 2006)



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Treatment Development Challenges

1) Non-responders / Improve initial treatment response

2) Maintenance of effects: Challenge for all interventions

3) Reduced use / Harm reduction – do not have a good measure

4) Transportability / Dissemination / Access

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Digital Therapeutics Technology – Value Added

Promise of Applying Technology (address Rural Population disparities)

Research has demonstrated that technology tools can:

- be highly useful and acceptable to diverse populations
- have a large impact on health behavior and outcomes
- produce outcomes comparable to, or better than, clinicians
- **enhance dissemination / fidelity / reduce patient and therapist burden**
- **increase quality, reach, and personalization of care**
- **be cost-effective**

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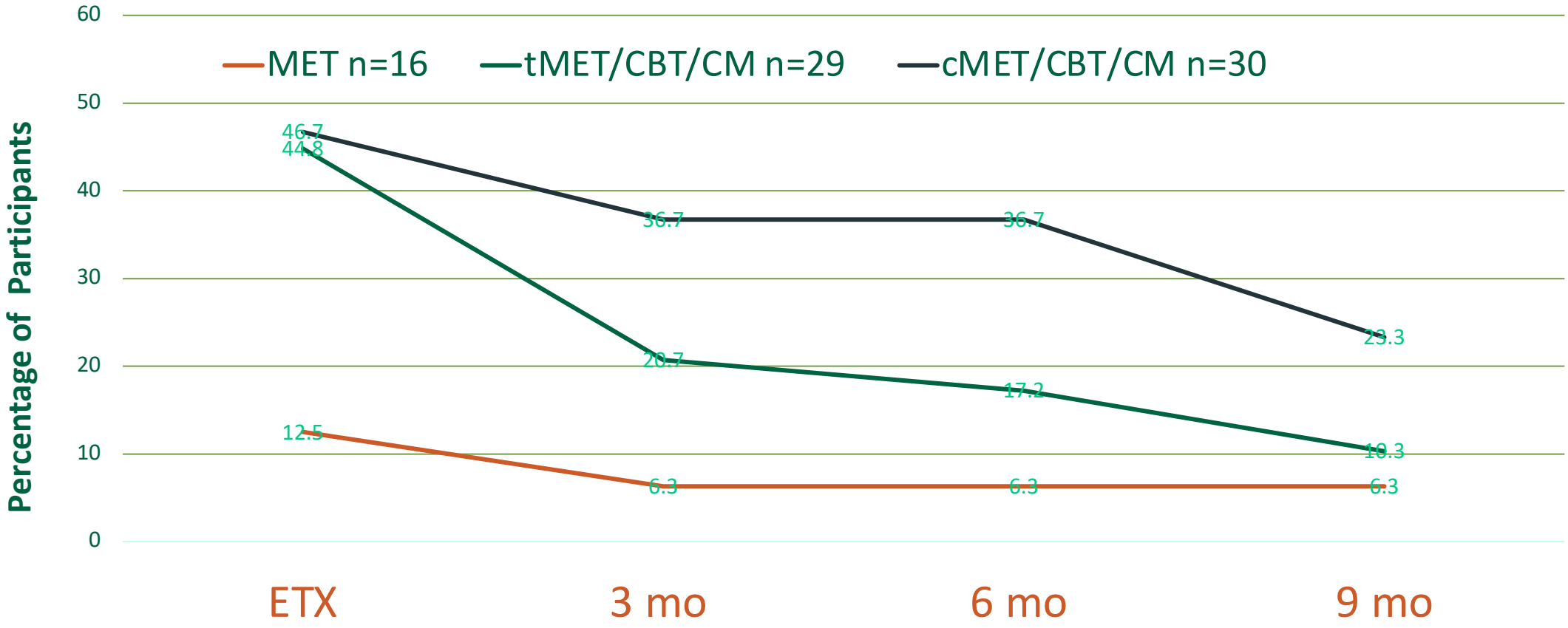
ADULT CUD RCT

⇧ Access and ⇩ Cost

MET/CBT/CM: computer-assisted vs. therapist-delivered



(Budney et al. 2015, 2011)

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Availability of Digital Therapeutics - Limited

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E-toke – Online Cannabis Intervention (e-Check-Up to Go)

- Online self-assessment
- Motivational enhancement
- Coping skills training
- Used across the country – mostly with young adults in college

echeckup TO GO

http://www.echeckuptogo.com/programs/cannabis

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Other Commercially Available DTs

- ReSet/ReSet-O: https://www.resetforrecovery.com/ (FDA authorized)
- Dynamicare: https://www.dynamicarehealth.com/
- CBT4CBT: https://cbt4cbt.com/
- ACHESS: https://www.chess.health/

** For use as Blended Care – integrate with other programs

** Not tested directly in controlled trials for CUD or Misuse

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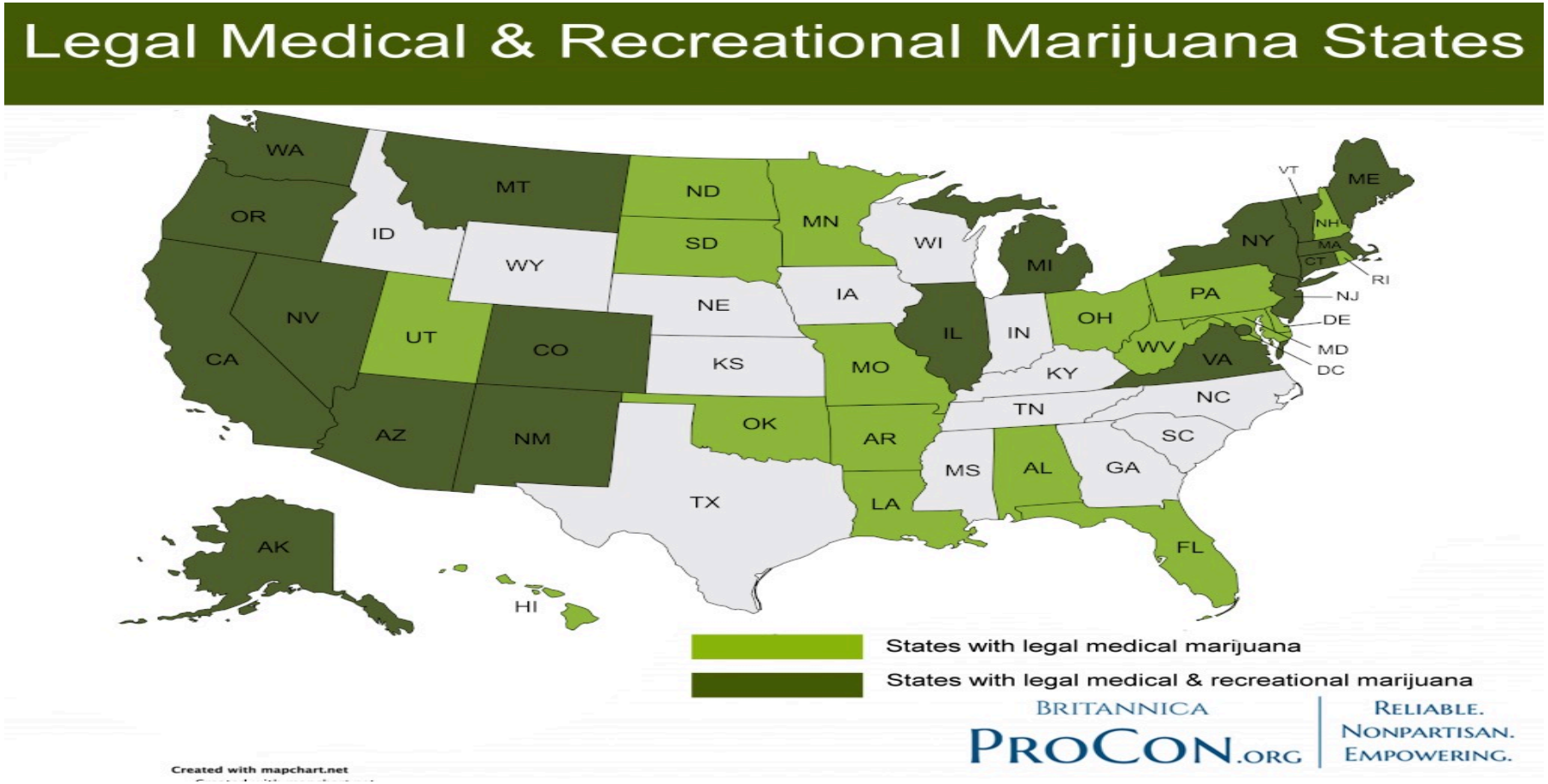
Cannabis / Marijuana as “Medicine”?

19 Recreational Cannabis Law States 37 Medical Cannabis Law States



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Cannabis / Marijuana as “Medicine”?

Politicians / Congresspersons / State Regulators have informed the public that Marijuana/Cannabis is a medicine that is effective for a host of medical and psychological disorders

Those dispensing / selling / promoting these products (**Cannabis Industry**) inform the public / consumer which compounds are effective for what condition, provide “education”, recommendations, and sell the product

Physicians / Medical Societies generally do not support Medical Marijuana Laws, although some say they would support Legalization with Regulation

Booming Cannabis Industry looking to make money!

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Cannabis and Mental Health / Illness

Scarce to no clinical evidence to suggest that cannabinoids improve depressive disorders or symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, or psychosis (CBD perhaps a little).

Very low-quality clinical evidence that pharmaceutical THC (with or without CBD) leads **to a small improvement in symptoms of anxiety among individuals with other medical conditions**

Remains **insufficient evidence** to provide guidance on the use of cannabinoids for treating mental disorders within a regulatory framework

(Black et al. 2019: The Lancet)

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Cannabis and Mental Health/Illness Summary

Cannabis use (thc-laden) is clearly associated with increased levels of mental illness; this relationship appears to be moderated by frequency of use and potency of the substance.

Growing evidence that cannabis use may have causal impact on lowering of the age of onset of Psychotic Disorders; related to age of onset of cannabis use, frequency and potency.

Cannabis use should be considered a risk factor for poor outcomes in functioning across most all mental disorders (IMHO).

Data do not support the use of cannabis (of any type) to treat any type of mental disorder

Preclinical research indicates reason to further investigate the potential of cannabinoids on varying types of mental illness

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Cannabis (thc-laden) is **more similar than dissimilar to other substances that are considered "substances of abuse"**

Like other substances, cannabis is used primarily for its positive (and negative) reinforcing effects

NEGATIVE REINFORCEMENT: REMOVAL OF AVERSIVE CONDITIONS (FEELINGS, THOUGHTS, PAIN)

*** Alcohol, opiates, cocaine, sedatives, nicotine ….. All provide similar types of "relief" from unwanted or undesirable states


AFTER HOURS OF THOUGHT ...
OR MINUTES OF THOUGHT,
WHICHEVER JUST OCCURRED,
I THINK MARIJUANA IS
NATURE'S WAY OF SAYING,
"FORGET IT."

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Rural Populations and Cannabis Therapeutics

Poorer Access to Cannabis Dispensaries / Increased Burden

Less Access to Healthcare Services ----

cannabis as medicine even more attractive?

IMHO: THIS IS ONE DISPARITY THAT MAY BE BENEFICIAL

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Public Heath Challenges

1) De-Medicalize Cannabis Use (THC-laden) – sending the wrong message
2) Change Positive Public Perception
3) Adopt Harm Reduction Perspective and Policies
4) Reduce Impact of Burgeoning Industry
5) Increase access to quality prevention and intervention programs
6) Develop Cannabis Use Guidelines
   - What level of use is low risk (safe)? High risk?
   - Help everyone make informed and safe choices

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Science & Common Sense

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Champion Innovation:

Develop More Effective and Available Programs for Your Community

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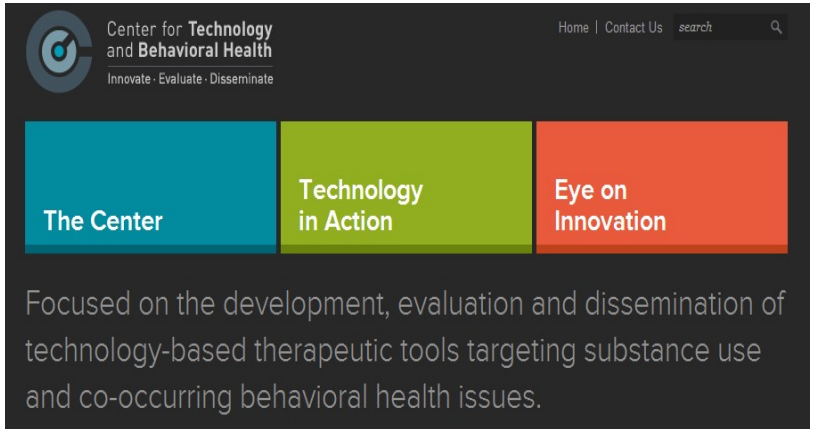
Acknowledgements



Support from NIDA

T32-DA037202 Training in Science of Co-Occurring Disorders

P30-DA029926 (Center for Technology and Behavioral Health)

R01-DA015186 (Behavioral Treatments for Adolescent Cannabis Use)

R01-DA023526 (Development of Computerized Treatment for Marijuana Use Disorders)

R01-DA050032 (Leveraging Social Media to Develop a Cannabis Exposure Index)

Copy of Slides, Articles, or Other:

alan.j.budney@dartmouth.edu

www.c4tbh.org

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Questions & Discussion

Email us your questions at cora@uvm.edu

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Thank you participating in this
UVM CORA Community Rounds Workshop Series

Our next session will be held on
Wednesday, December 1, 12-1pm ET

Social and Structural Determinants of Mental Health, Substance Use and Treatment
Brady Heward, MD

Register Now at go.uvm.edu/SDoH

Contact us at CORA@uvm.edu // Center on Rural Addiction: https://uvmcora.org/
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