Mountain Plains ATTC (HHS Region 8)

ATTC Addiction Technology Transfer Center Network

Funded by Substance Abuse and Mental Health Services Administration

Cannabis Misuse & Cannabis Use Disorder (CUD)

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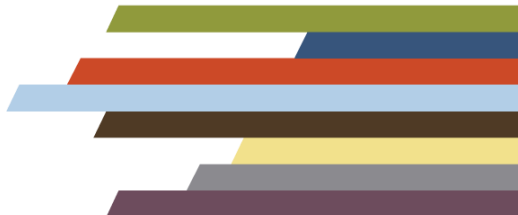

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Cannabis Misuse & Cannabis Use Disorder (CUD): Phenomenology, Intervention, Clinical Issues

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Mountain Plains Addiction Technology Transfer Center

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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

AGENDA

- Define cannabis and describe the evolving cannabis landscape
- Cannabis/marijuana (**THC-laden**) as an addictive substance
- Clinical Interventions for CUD and Cannabis Misuse

- Cannabis/marijuana as a therapeutic??

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.

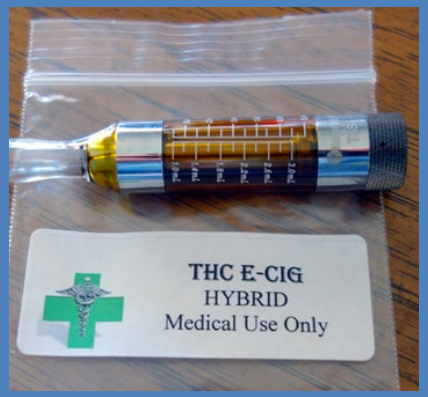
Rural Cannabis Use

	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

Legalization & New Products

THC-Laden Cannabis Products: Smoking / Vaping



High Potency (THC) Products - Concentrates

Edibles


GREEN HORNET

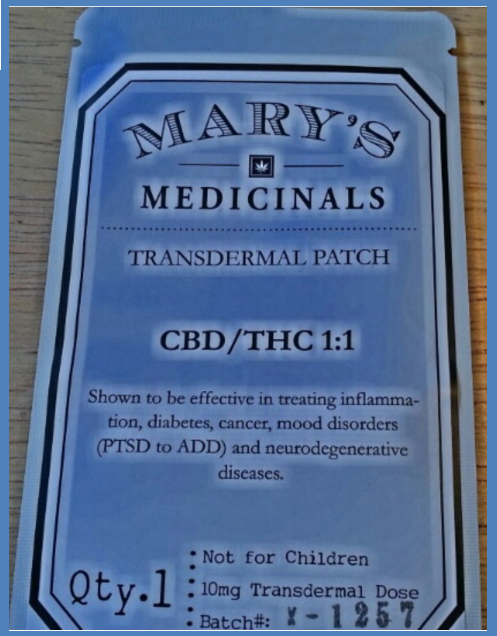

MEDICAL
CANNABIS
DARK CHOCOLATE
PURE INDICA
Minimum Cannabanoid Content 60 mg
NET WT. 1.6 oz / 45 g
The Marijuana Report.com


Edi-Pure
Sweet 'n Sour
25 X 10mg Value Pack
Net 62.5g / Not For Resale
250mg Active THC
450mg Trichome Oil Extract
For Medical Use Only
Keep From Children
Edi-Pure
Peach Tarts
10 X 25mg Value Pack
Net 57.1g / Not For Resale
250mg Active THC
450mg Trichome Oil Extract
For Medical Use Only
Keep From Children
Edi-Pure
Peanut Butter Sandwich
125mg THC 5 x 25mg Net 67.5
Not For Resale Medical Use Only
Keep Out of Reach of Children


105mg THC
PATTY'S PEPPERMINT


Edi-Pure
Fried Apple Pie
Edi-Pure
Crème Filled Cupcake
125mg THC Infusion
Edi-Pure
Crème Filled Cupcake
125mg THC Infusion
$12.00

Lotions / Cremes / Salves / Patches



CBD Products – Cannabis (no-THC)

What is Cannabis (Marijuana)?

- **PLANT: hemp — *Cannabis sativa, indica “strains”***

- **Contains over 100 compounds??**

What is in the Cannabis Plant?

- **THCA (Δ^9-tetrahydrocannabinolic acid)**
- **CBDA (Cannabidiolic acid)**
- CBGA (Cannabigerolic acid)
- CBCA (Cannabichromenenic acid)
- CBGVA (Cannabigerovarinic acid)
- THCVA (Tetrahydrocanabivarinic acid)
- CBDVA (Cannabidivarinic acid)
- CBCVA (Cannabichromevarinic acid)
- Terpenes: essential oils, smells, flavor

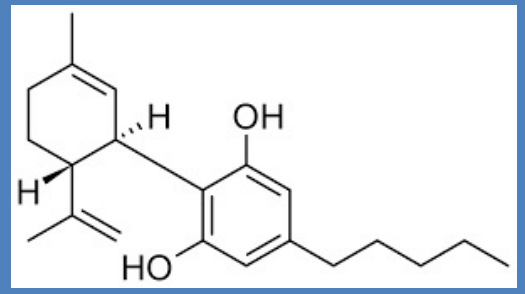
Delta-9 THC (tetrahydrocannabinol)

** Primary psychoactive constituent

Dose related effects:

- **High, euphoria**
- Cognitive impairment (memory, learning, attention, time perspective)
- Anxiety, Panic, Hallucinations, Psychosis?

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

THC DOSE MATTERS
AMOUNT x POTENCY

Potency (%THC) Plant Material / Flowers *

THC: 0.6% - 30.6%*

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

THC: 35.3% - 87.5%**

Potency (%THC) Edibles

THC: 20mg – 100mg**

Potency (%THC) Capsules

THC 5-50mg

Route of Administration Matters

SMOKE

VAPE

EDIBLE

OILS / TINCTURE

CREAM / PATCH

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

Cannabis (THC-laden) Addiction and Misuse

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

Scientific / Clinical evidence is strong and unambiguous

Evidence: Addictive Potential & Clinical Consequences
Biological, Behavioral, Epidemiological

- Endogenous cannabinoid system in the CNS
- 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

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

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."

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)

Cannabis and Mental Health/Illness

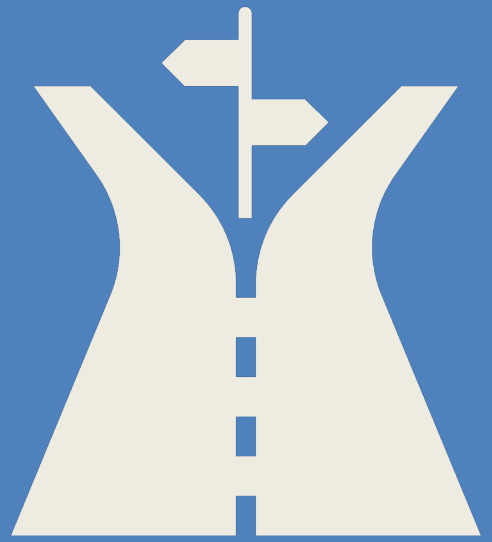
Cannabis use (thc-laden) is clearly associated with increased levels of mental illness; this relationship appears to be moderated by frequency of use and potency of the substance.

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



Interventions for CUD and Misuse

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!**

Interventions for CUD and Misuse

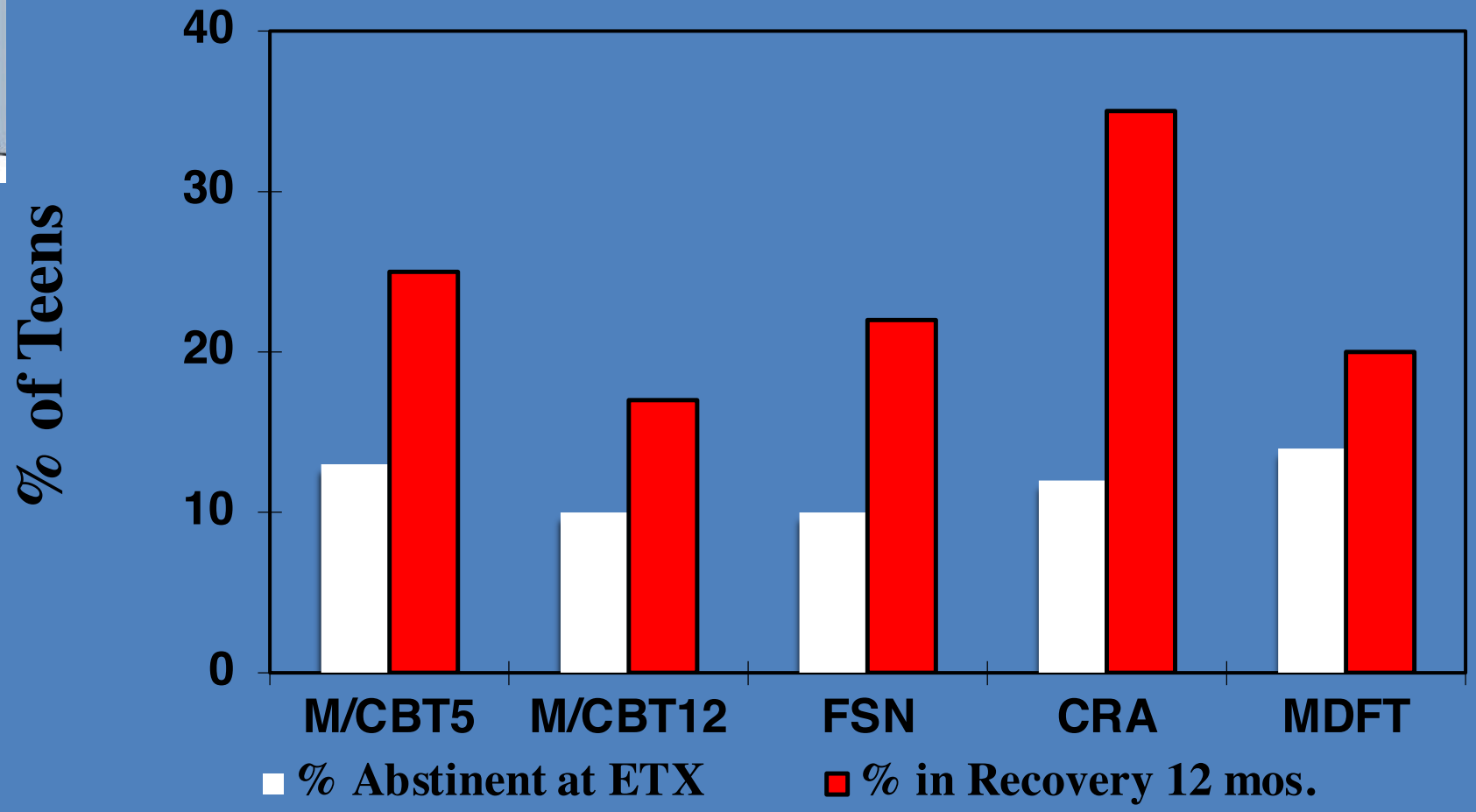
Adolescents

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)

Contingency Management for Teens with CUD

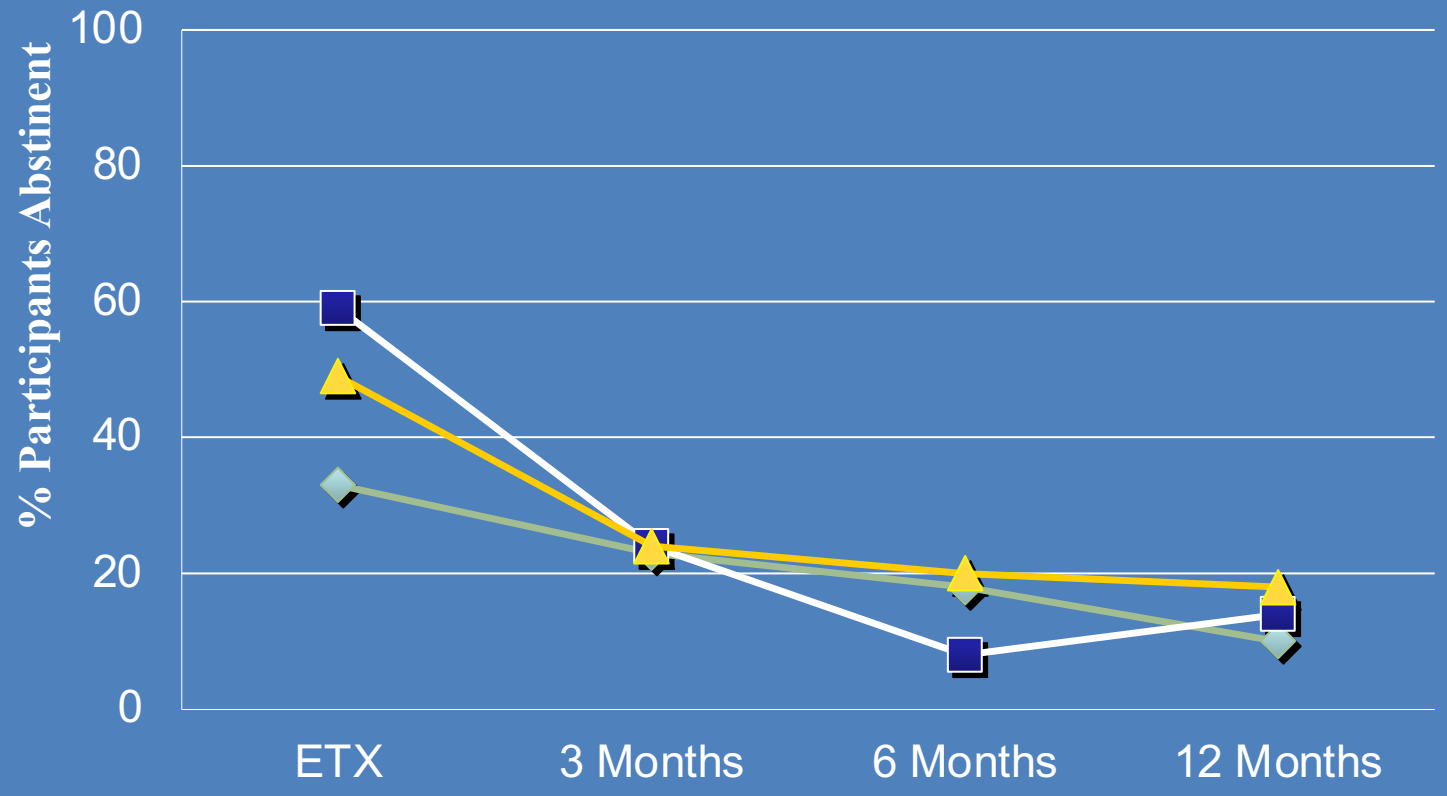
Clinic-based Incentive Program

- *Incentives*: escalating schedule; bonuses; reset for use (Weeks 3-14)
- *Magnitude of Reinforcement:* $590 over 14 weeks

Home-based CM Program - Substance Monitoring Contract

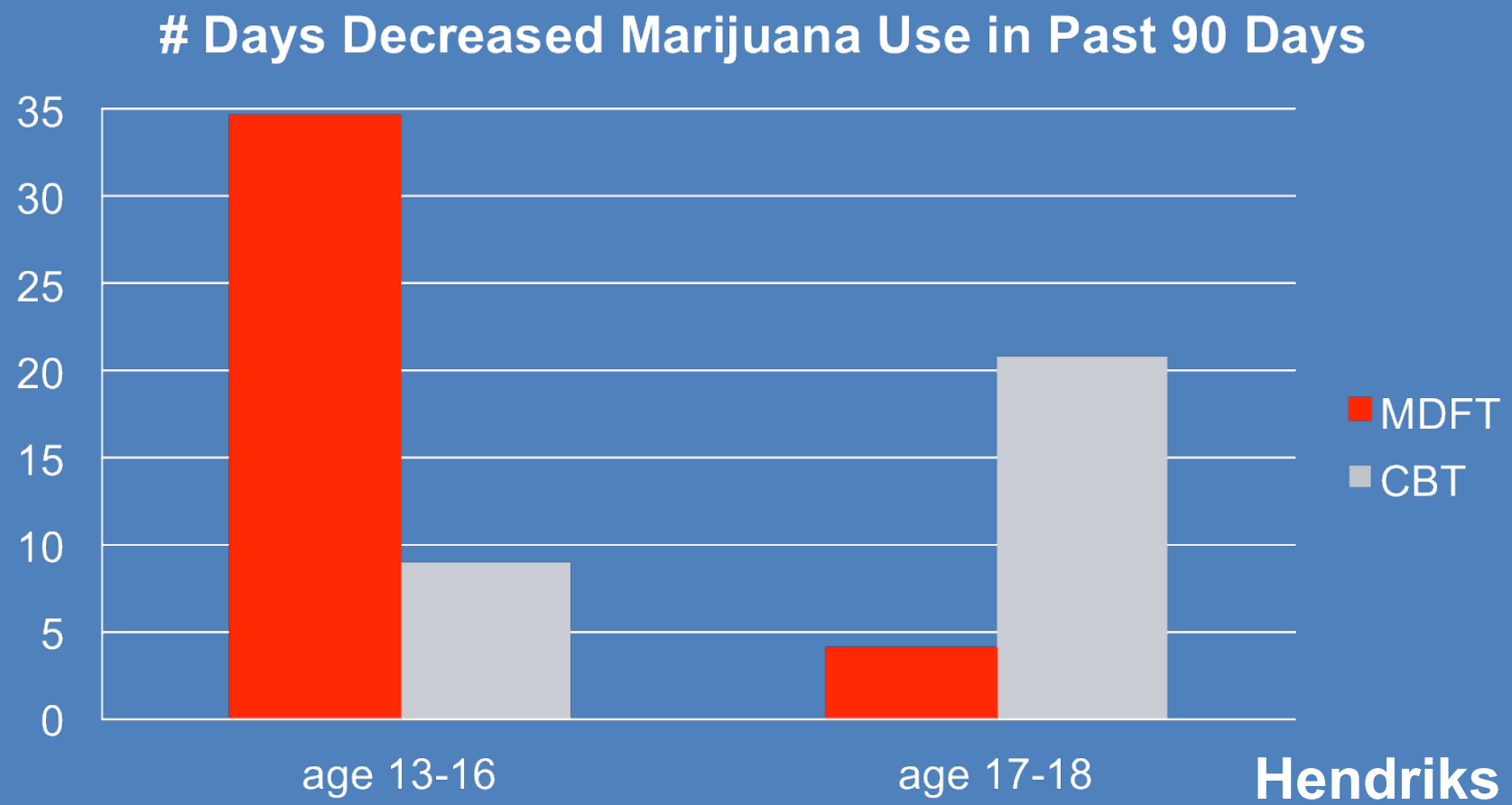
- reward for abstinence; punishment for use
- use same monitoring procedures to determine abstinence
- individualized magnitude and type of reward/consequence
- weekly ~15 min. parent sessions (incentives for adherence)

Contingency Management for Adolescents:
Replication and Extension
CM enhances outcomes, but did not maintain
(Stanger et al., 2015)



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

Age Effects



Hendriks et al. (2012)

Teen Marijuana Check-UP

Walker et al. (multiple studies)

MI/MET Intervention

Two individual sessions (30-60 minutes)

Motivational Interviewing

Review of Personal Feedback Report

Personal Feedback Report included:

- Normative data
- Recent use patterns
- Use Disorder symptoms
- Goals, Social supports, Potential Benefits of Quitting

Interventions for Cannabis Use Disorder (CUD) and Misuse

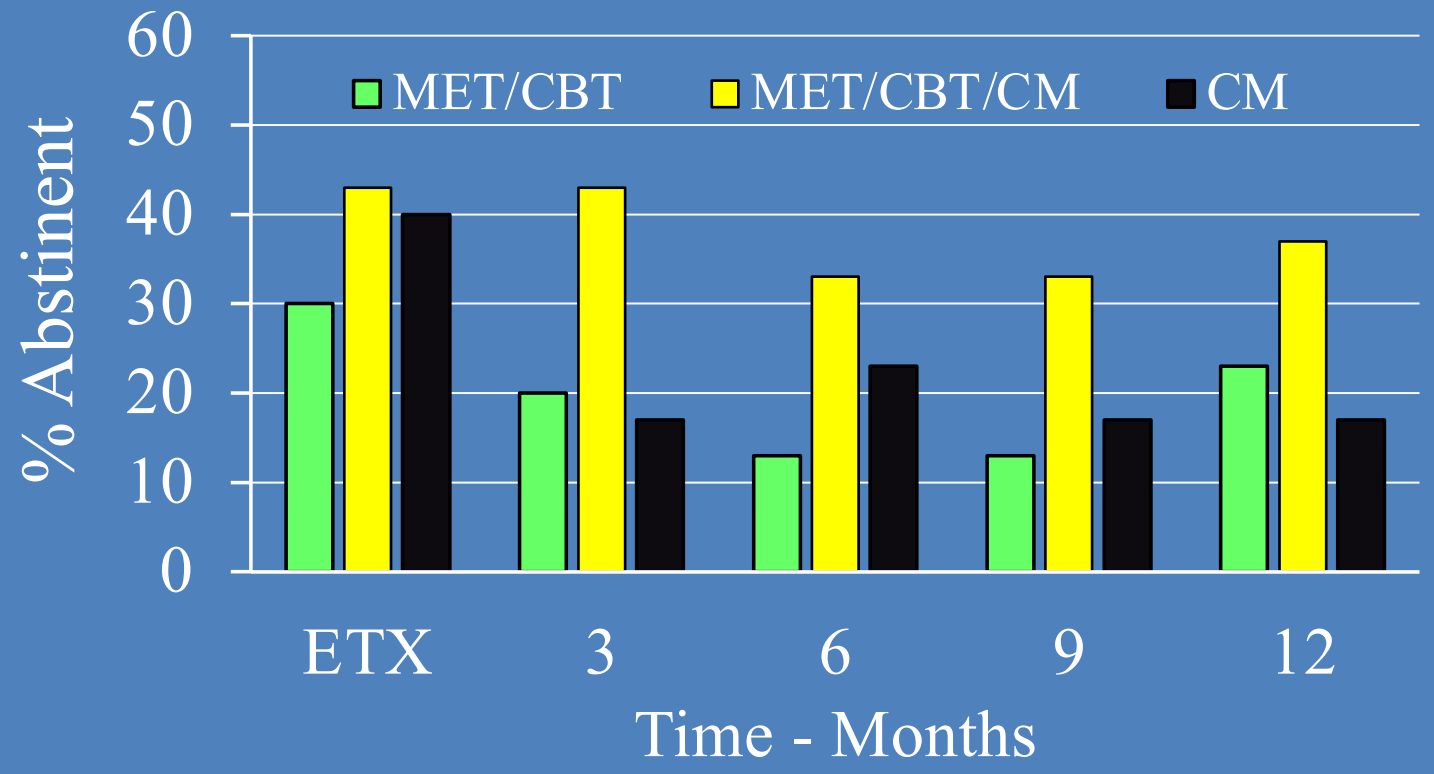
Adults

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

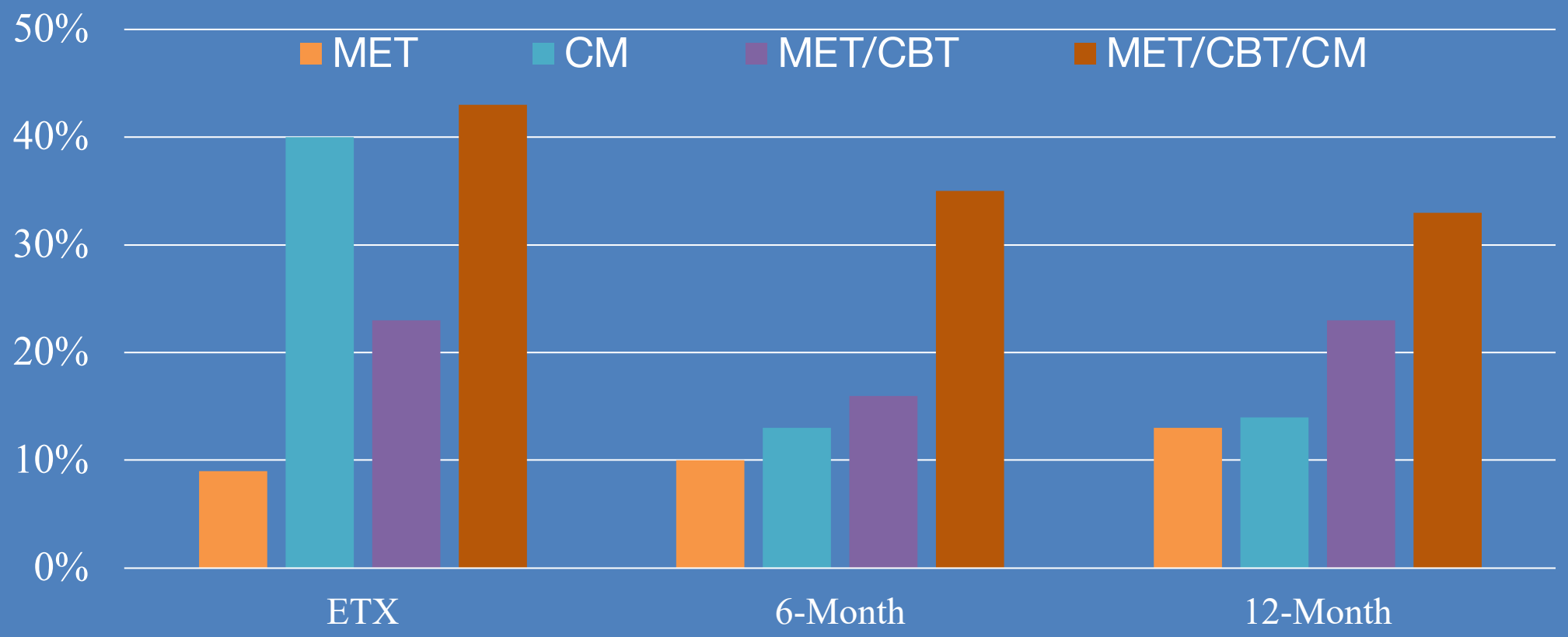
CM Improves Abstinence Outcomes
MET/CBT Maintains Abstinence

Replication and Extension (Budney et al. 2006)



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

CUD Treatment Abstinence Outcomes Across Multiple Studies



Treatment Development Challenges

1) Non-responders / Improve initial treatment response

2) Maintenance of effects: Challenge for all interventions

3) Reduced use / Harm reduction

4) Transportability / Dissemination / Access

Digital Therapeutics Technology – Value Added

Promise of Applying Technology (related to Rural Population disparities)

Research has demonstrated that technology tools can:

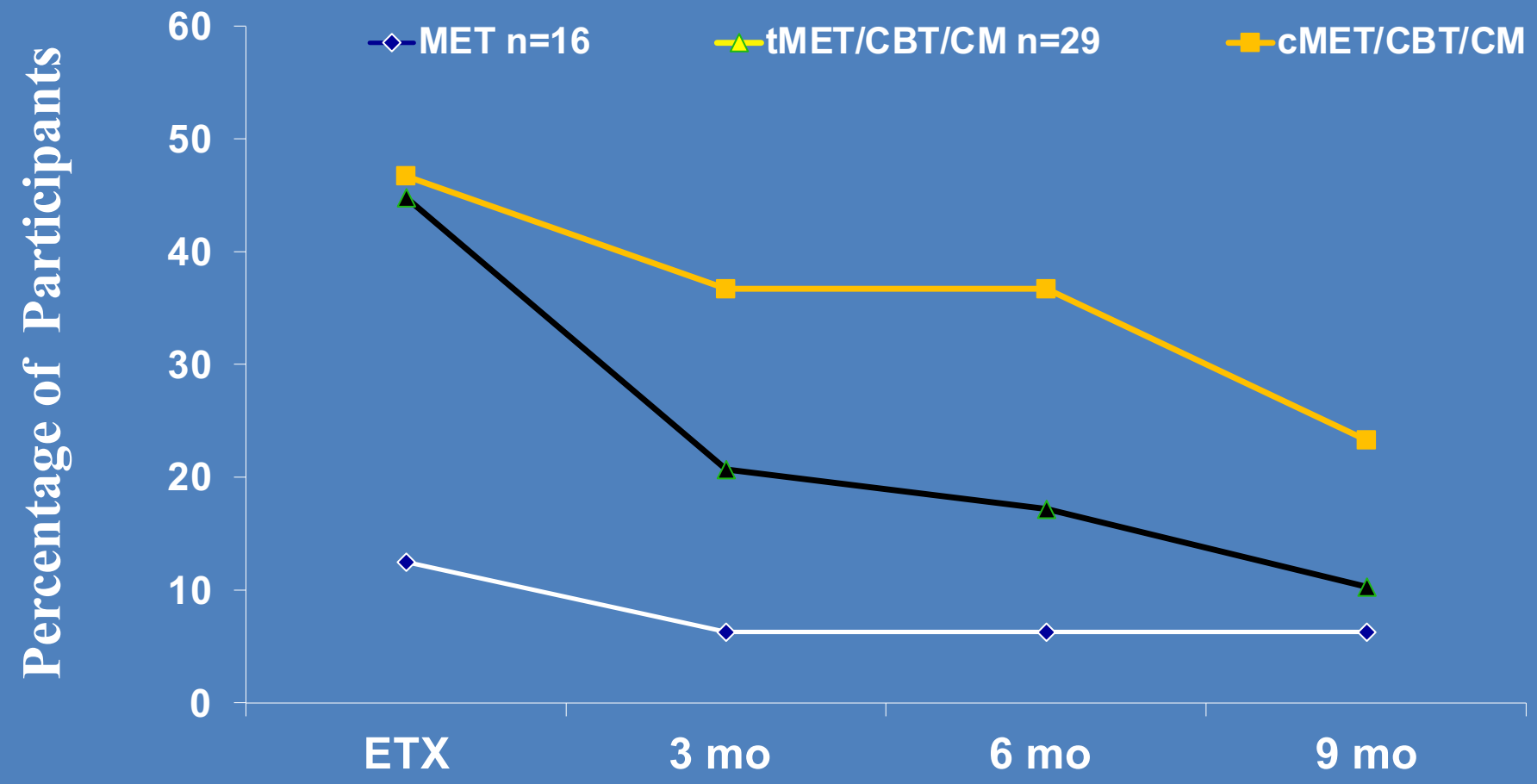
- be highly useful and acceptable to diverse populations
- have a large impact on health behavior and outcomes
- produce outcomes comparable to, or better than, clinicians
- **enhance dissemination / fidelity / reduce patient and therapist burden**
- **increase quality, reach, and personalization of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

ADULT CUD RCT

⇧ Access and ⇩ Cost

(Budney et al. 2015, 2011)

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



Availability of Digital Therapeutics - Limited

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

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

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

Recent Advances Under Study
Transdiagnostic Vulnerability Targets

- **Temporal Discounting**: **Devaluing the future**
  - Future Focus / Enhance Valuation of the Future
    - **Episodic Future Thinking (EFT):** guides creation of hypothetical, personal future events which putatively enhance attention to and valuation of the future
    - **Substance-Free Activity Session (SFAS)**: integrated with brief motivational interventions in college students: focus on career goals, relation to college performance, what it takes, benefits

- **Distress Tolerance**: capacity to withstand negative emotional states
  - Distress Tolerance Training
    - Mindfulness, Crisis Skills, Sensory awareness, Distraction
    - ACT: acceptance and change therapy

Summary: Treatments for CUD

Multiple interventions are “efficacious”, but CUD is not easy to treat, i.e., rates of success do not appear much different than for other SUDs

Integrating CM (abstinence-based incentives) can improve outcomes

% of teens improved appears **lower** than that observed with adults

Rates of success in disadvantaged populations are low

**** Still much, much room for Improvement**

Working with Cannabis Users

Diverse Clinical Population

- "High" Functioning
- Granola Crowd
- Disadvantaged, Multiple Problems
- Co-occurring Disorders

Types of Interventions

Not much difference than other substances

Clinical "counseling" strategies are similar

Clinical Issues Related to Changing Landscape

Legality / Alcohol comparisons

- Millions of people enjoy a drink. What's so different about mellowing out with pot?
- It's clearly not as harmful as alcohol?
- I'd rather have her (my daughter) smoke a little marijuana than get drunk and wreck the car
- I'd probably drink a lot more and get into trouble; with marijuana I don't bother anybody.

Clinical Issues Related to Changing Landscape

I know I get high too much, but some is medically necessary

I think marijuana helps his ADHD; seems less harmful than prescribed medications (stimulants)

It really helps my PTSD symptoms

I need it for sleep, and I know they say it helps with sleep

Keeping a stash around for medical purposes makes it impossible for me to avoid using too much.

Clinical Issues Related to Changing Landscape

Lack of perceived adverse effects

- Isn't there something really bad about marijuana you can tell me about so I'll get motivated? Everything I hear is that it is good for you.
- My life isn't so bad the way it is, so it's hard to really commit to quitting getting high.

Reduction rather than abstinence

- I don't think I'll ever want to quit; cutting back would be good.
- I'd like to reduce from 5 times per day to just twice per day.

How To Respond?

Motivational Interviewing; Socratic Reasoning

- Diffuse and deflect, don’t argue
- Nonjudgmental, empathic
- Maintain professionalism: empirical knowledge
- Don’t need to take a stand on legalization
- Ask if interested in what the current research offers
- You can agree that alcohol seems more harmful
- Gently remind / explore marijuana-related problems
- Refocus: acknowledge / explore personal dilemmas

Harm Reduction

- Abstinence does not need to be “the goal”
- Personalize goals!

Consider Strategies from Approaches with Problem Drinkers or Tobacco Smokers

- Tolerate non-abstinence goals
- Review track record of quitting or reducing
- Conduct personal experiments
- Expect lapses or relapses
- Expect flip-flopping of goals and use patterns
- Conceptualize as helping with a series of attempts, not a single episode, learn from set backs

Legalization may change openness to this framework

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

Public Heath Challenges

1) De-Medicalize Cannabis Use (THC-laden)
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

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

Research Priorities

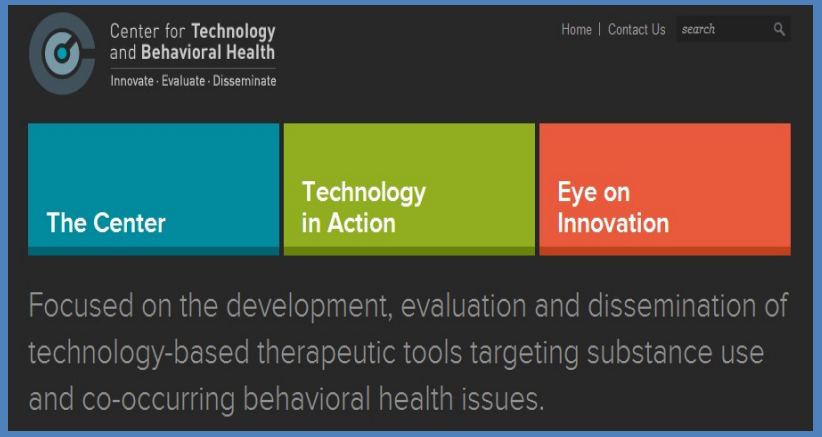
- Regulatory Science: mitigate harm
  - Industry/marketing, dose/content control, access
- Protect those Vulnerable to Addiction and Consequences
  - disadvantaged/poor, mental and physical health disorders, youth
- Communication Science
  - How do we best communicate about potential positive effects and potential harmful effects?
- Develop Cannabis Use Guidelines
  - What level of use is low risk (safe)? High risk?
  - Help everyone make informed and safe choices

Science and Common Sense

Champion Innovation:

Develop More Effective and Available Programs for Your Community

Acknowledgements



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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)

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Questions & Discussion

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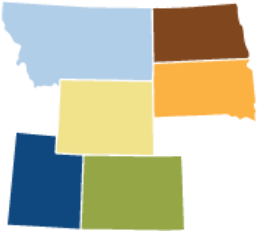

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