Clinical epidemiology, characteristics, services, and outcomes for youth with cannabis use disorders: Status of the problem and expectations for the future

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Disclosures

Funded by *National Institute on Drug Abuse (NIH)* to do clinical and laboratory research related to cannabis use and use disorders

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- Consultant / Participant: *Office of National Drug Control Policy’s* Marijuana and Kids Media Campaign (past)

- Scientific Review Board: *Center for Medical Cannabis Research*, State of California (past)

- Consultant to GW Pharmaceuticals/Otsuka on development of Nabiximols / Sativex (past)
Today’s Plan

1) Present a snapshot of cannabis and cannabinoid use among teens and how it has changed over time
   - Provide perspective relative to other substance use
   - Relation to medicalization / legalization?

2) Review clinical epidemiology related to cannabis use
   - use disorders, treatment “seeking”, co-occurring problems, vulnerable populations

3) Overview of the treatment literature
   - strengths and limitations

4) Special Issues
   - e-cigs, vaping, edibles, potency, creative chemistry
Marijuana/Cannabis / Cannabinoids

Over 100 compounds ; over 70 phytocannabinoids

Delta-9 THC psychoactive compound

Dose related effects:

- High, euphoria, relaxation
- Cognitive impairment (memory, learning, attention, time perspective)
- Anxiety, Panic, Hallucinations, Psychosis?
- Abuse/Dependence?
Marijuana / THC
Synthetic “Cannabis”

Sprayed on plant materials: potent CB1 agonists with effects similar to cannabis, but less reliable and more adverse effects…Why?
Synthetic Cannabinoids

- Do not contain THC
- Contain synthetic cannabinoid plus ??
- Misperceived as “synthetic marijuana”
- Advertised as “natural herbs,” “harmless incense,” “not for human consumption,” or “for aromatherapy only”
- Purchase via the internet, smoke shops and even gas stations.
DEA Cannabis Seizures (Potency)
Legal Marijuana and Potency

Strain Name: Loud
Grade: A
Smell: very potent and natural smell
Taste: orangish taste

**Potency:** 27.50% THC

Effects: head high with a body high but it’s not a hybrid
Reviewed by: Lungs n Green
Good Strain For: getting rid of stress and soreness and to feel good

Changing the Game: much of what we know is based on smoking marijuana with much lower doses of THC
A Take Home Message

Cannabis/Marijuana ≠ THC
Synthetic Cannabinoids ≠ THC/Marijuana

(a) Not all cannabinoids are the same
(b) Dose matters (how?)
# Top Drugs among 8th and 12th Graders, Past Year Use

## 8th Graders

<table>
<thead>
<tr>
<th>Drug</th>
<th>Illicit drugs</th>
<th>Pharmaceutical</th>
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</thead>
<tbody>
<tr>
<td>Marijuana/Hashish</td>
<td>12.7%</td>
<td></td>
</tr>
<tr>
<td>Inhalants</td>
<td>5.2%</td>
<td></td>
</tr>
<tr>
<td>Synthetic Marijuana</td>
<td>4.0%</td>
<td></td>
</tr>
<tr>
<td>Cough Medicine</td>
<td>2.9%</td>
<td></td>
</tr>
<tr>
<td>Tranquilizers</td>
<td>1.8%</td>
<td></td>
</tr>
<tr>
<td>Adderall</td>
<td>1.8%</td>
<td></td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>1.6%</td>
<td></td>
</tr>
<tr>
<td>OxyContin</td>
<td>2.0%</td>
<td></td>
</tr>
<tr>
<td>Salvia</td>
<td>1.2%</td>
<td></td>
</tr>
<tr>
<td>Vicodin</td>
<td>1.4%</td>
<td></td>
</tr>
<tr>
<td>Cocaine (any form)</td>
<td>1.0%</td>
<td></td>
</tr>
<tr>
<td>MDMA (Ecstasy)</td>
<td>1.1%</td>
<td></td>
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<tr>
<td>Ritalin</td>
<td>1.1%</td>
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## 12th Graders

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<tr>
<td>Marijuana/Hashish</td>
<td>7.9%</td>
<td>36.4%</td>
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<tr>
<td>Synthetic Marijuana</td>
<td>7.4%</td>
<td></td>
</tr>
<tr>
<td>Adderall</td>
<td>5.3%</td>
<td></td>
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<tr>
<td>Vicodin</td>
<td>5.0%</td>
<td></td>
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<tr>
<td>Cough Medicine</td>
<td>4.6%</td>
<td></td>
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<tr>
<td>Tranquilizers</td>
<td>4.5%</td>
<td></td>
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<tr>
<td>Hallucinogens</td>
<td>4.8%</td>
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<tr>
<td>Sedatives*</td>
<td>3.4%</td>
<td></td>
</tr>
<tr>
<td>Salvia</td>
<td>3.6%</td>
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<tr>
<td>OxyContin</td>
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<tr>
<td>Ritalin</td>
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</table>

* Only 12th graders surveyed about sedatives use

Source: University of Michigan, 2013 Monitoring the Future Study
Synthetic Cannabinoids

Use trending down!
Availability
% saying "fairly easy" or "very easy" to get

YEAR
'75 '77 '79 '81 '83 '85 '87 '89 '91 '93 '95 '97 '99 '01 '03 '05 '07 '09 '11 '13
PERCENT
100
80
60
40
20
0
Risk
% seeing "great risk" in using regularly

PERCENT

YEAR

'75  '77  '79  '81  '83  '85  '87  '89  '91  '93  '95  '97  '99  '01  '03  '05  '07  '09  '11  '13
Marijuana Perceived Risk vs. Past Year Use by 12th Graders

SOURCE: University of Michigan, 2013 Monitoring the Future Study
Adolescent Problematic Substance Use

Teen substance use / abuse is a major public health problem

- 90% of problematic substance use is initiated prior to age 18
- Average day: 71,000 are in outpt treatment; (SAHMSA, 2013)
  10,500 are in inpatient/residential
- 60-70 have co-occurring psychiatric dx (Dennis et al. 2007)

*** Need Better Prevention and Intervention Strategies
NSDUH 2012

MARIJUANA ABUSE OR DEPENDENCE – PAST YEAR BY AGE CATEGORY RECODE (5 LEVELS)

<table>
<thead>
<tr>
<th>Age Category</th>
<th>No/Unknown (ABUSEMRJ=0 and DEPNDMRJ=0)</th>
<th>Yes (ABUSEMRJ=1 or DEPNDMRJ=1)</th>
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<tbody>
<tr>
<td>12-17 Years Old</td>
<td>97</td>
<td>3</td>
</tr>
<tr>
<td>18-25 Years Old</td>
<td>94</td>
<td>6</td>
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</table>
NSDUH 2012

Marijuana Dependence or Abuse

% of Youth vs. AGE

AGE: 13, 14, 15, 16, 17, 18, 19, 20, 21
Adolescent Treatment Admissions
TEDS Data Set

Figure 19. Adolescent admissions aged 12 to 17, by primary substance: 2002-2012
Admissions x Criminal Justice Involvement TEDS Data Set

Figure 20. Adolescent admissions aged 12 to 17, by marijuana involvement and criminal justice/DUI source: 2002-2012

- Marijuana-Involved
  - Criminal justice referral
  - Non-criminal justice referral

- Not marijuana involved
  - Criminal justice referral
  - Non-criminal justice referral
Admissions x Race / Ethnicity
TEDS Data Set

Figure 12. Marijuana/hashish admissions, by gender, age, and race/ethnicity: 2012
ER Visits Increasing (Potency / Syntetics?)
DAWN Data Set

B Drug-Related Emergency Department Visits

<table>
<thead>
<tr>
<th>Year</th>
<th>Marijuana (in thousands)</th>
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<tbody>
<tr>
<td>2004</td>
<td>129</td>
</tr>
<tr>
<td>2005</td>
<td>100</td>
</tr>
<tr>
<td>2006</td>
<td>200</td>
</tr>
<tr>
<td>2007</td>
<td>300</td>
</tr>
<tr>
<td>2008</td>
<td>400</td>
</tr>
<tr>
<td>2009</td>
<td>500</td>
</tr>
<tr>
<td>2010</td>
<td>600</td>
</tr>
<tr>
<td>2011</td>
<td>456</td>
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</table>

No. of Emergency Department Visits (in thousands)
## Consequences

(Volkow et al., 2014)

<table>
<thead>
<tr>
<th>Effect</th>
<th>Overall Level of Confidence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addiction to marijuana and other substances</td>
<td>High</td>
</tr>
<tr>
<td>Abnormal brain development</td>
<td>Medium</td>
</tr>
<tr>
<td>Progression to use of other drugs</td>
<td>Medium</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Medium</td>
</tr>
<tr>
<td>Depression or anxiety</td>
<td>Medium</td>
</tr>
<tr>
<td>Diminished lifetime achievement</td>
<td>High</td>
</tr>
<tr>
<td>Motor vehicle accidents</td>
<td>High</td>
</tr>
<tr>
<td>Symptoms of chronic bronchitis</td>
<td>High</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>Low</td>
</tr>
</tbody>
</table>
Teen “Consequences / Associations”

- Poor academic performance
- Interferes with brain development
- Increased risk of accidents
- Relationship problems
- Health/mental health problems
- Delinquent behavior
- High risk sexual behavior
- Gateway / Associated with use of Multiple Substances

** Dose Dependent / Frequency / Acute vs. Chronic
Risk of being a Psychotic Case (Di Forti et al., 2014)

Frequent Use of High-Potency Cannabis, Drives the Increased Probability of Psychosis in Cannabis Users: (adjusted for gender, age, ethnicity, stimulants, level of Ed)
Daily Use, Especially of High-Potency Cannabis, Drives the Earlier Onset of Psychosis in Cannabis Users (Di Forti et al., 2014)
## Co-Morbidities with Cannabis Use Disorders

NESARC Data (Stinson et al. 2006);

<table>
<thead>
<tr>
<th></th>
<th>Past Year</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Axis I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MDE</td>
<td>11%</td>
<td>21%</td>
</tr>
<tr>
<td>Any Anxiety Dis</td>
<td>24%</td>
<td>30%</td>
</tr>
<tr>
<td>Bipolar I</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td><strong>Axis II</strong></td>
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<tr>
<td>Antisocial</td>
<td>30%</td>
<td>19%</td>
</tr>
<tr>
<td>Obsessive Comp.</td>
<td>19%</td>
<td>15%</td>
</tr>
<tr>
<td>Paranoid</td>
<td>18%</td>
<td>11%</td>
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</tbody>
</table>
Adolescent Co-Morbidity
CYT Study (Dennis et al. 2002)
Clinical Sample

Internalizing Disorders 33%
Anxiety, Depression, PTSD

Externalizing Disorders 61%
Conduct Disorder, ODD, ADHD
Impact of Cannabis Use on MDE at Age 29

Level of Cannabis Use at Different Ages

Degenhardt et al., 2012
Associations between frequency of cannabis use and depression scores at selected ages (15, 20, 25, 30 yrs) after adjustment for fixed sources of confounding

Horwood, et al., 2012: An integrative data analysis of four Australasian cohorts
Cannabis Use and Mental Illness (MI)

Cannabis use is associated with increased levels of MI; 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;
- age of onset of cannabis use, frequency and potency.
  Probability of occurrence is “low” in low risk samples

Cannabis use can probably be considered a risk factor for poor outcomes in functioning across mental illnesses

Data do not support the use of cannabis to treat any type of MI
AFTER HOURS OF THOUGHT ... OR MINUTES OF THOUGHT, WHICHEVER JUST OCCURRED, I THINK MARIJUANA IS NATURE'S WAY OF SAYING, "FORGET IT."
= Pharmacology (only one part)
= Availability
= Cost
= Genetics
= Intrapersonal Factors (emotional/behavioral)
= Environmental Factors / Alternatives
= Societal Norms and Attitudes
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
% Using Cannabis at Minimal Levels
(Waldron et al. 2001)

% pos. drug test: 84% 81% 76%
CYT Adolescent Study
Abstinence at Discharge

(Dennis et al., 2004)
MDFT vs. Group Treatment (CBT based)
Liddle et al. (2004)

< Weekly Marijuana Use

% of adolescents

MDFT

Intake

Group

6-Week

ETX
Days of Marijuana Use (month)
Carroll et al (2012)
MDFT vs CBT-Group Treatment (young teens)
Liddle et al. (2004, 2009)

% Abstinence

![Graph showing % Abstinence over time for MDFT and CBT Group.](image-url)
INCANT Trial (2013)

% Teens with Cannabis Dependence
Adding CM to CBT:
Adolescent Continuous Abstinence During Treatment (n = 69)

p = .06  p < .01
Abstinent During Treatment

Probation-referred Youth (M=21 yrs)

Carroll et al. (2006)
Post Treatment Abstinence

% Participants Abstinent

ETX 3 Months 6 Months 12 Months

MET/CBT MET/CBT/CM MET/CBT/CM/BPT
Brief Intervention Literature

General Settings

Reviews:

  Jensen et al., (2011)
  - 21 studies

School-based

  (Carney et al., 2014) Cochrane Review
  - 6 studies included
Meta analysis of BI for teens  
Jensen et al. (2011)
Cochrane Review of School-based BIs
(Carney et al., 2014)

Brief intervention versus information provision,
3 studies: 732 participants
(McCambridge 2008; Walker 2011; Werch 2005)

Brief intervention versus assessment only,
3 studies: 407 participants
(McCambridge 2004; Winters 2007b; Winters 2012)
Cochrane Review of School-based BIs

(Carney et al., 2014)

Moderate quality evidence that school-based brief interventions are no more effective than information provision for reducing substance use and other related problem behaviours.

When compared to assessment only, there is low quality evidence that BI performed more favourably.

Overall, BI did not seem to have a significant effect on alcohol or tobacco use; however, BIs seemed to reduce cannabis use in comparison to the assessment-only control condition **

** Quality of the evidence rated as low
Making Excellent Progress, but

1) Cannabis Use Disorders not “easy” to treat
2) We have well-specified efficacious interventions that work better than others in decreasing use and engendering abstinence
3) Innovations in behavioral approaches continued to provide incremental increases in outcomes
4) We need to keep working along this path, as there remains much room for improvement in the rate of “success”
5) Dissemination/translation of most efficacious interventions should become a priority.
E-cig (vaping) Use Rapidly Increasing (MMWR 2013)
Vaping of Cannabis Rapidly Increasing
No Data!!!!

• Concerns
  – Perceived as less harmful
  – Vaping other flavors / substances may ease transition to cannabis
  – May lead to use of other forms of cannabis
  – Increase mixing of cannabis and tobacco or nicotine
  – Cool to vape / smoke?
Clinical Issues and Challenges in Working with Youth Marijuana Users

Diverse Clinical Population
- High Functioning
- Disadvantaged, Multiple Problems
- Co-occurring Disorders

Not much difference than other substances, particularly alcohol
Clinical “counseling” strategies are similar
“Medicinal” use somewhat unique
Challenges

1) Maintenance .... Challenge for all interventions
   - establish meaningful lifestyle change to compete with substance use
2) Non-responders
3) Reduced use / Harm reduction
4) Individual / cultural differences impact interventions
5) Transportability / Dissemination
Cannabis: Reasons for Concern

Sneaky drug with relatively subtle effects… can function under the influence

Has many seemingly positive “functions” (like other drugs)

More potent than it used to be

Kids develop dependence more quickly than adults

Adolescents like adults don’t believe it is “addictive” or “harmful”

Regular use likely impacts neurodevelopment

May increase probability of mental illnesses

Increases probability of exposure to other substances
Cannabis is more similar than dissimilar to other substances that are considered “drugs of abuse”

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

a small subset of persons who use cannabis go on to have problems...some serious, some moderate, and some not so serious

like other substances, it is not legal or recommended for those under 18 (or 21)
Cannabis has great importance to Addiction Science and Medicine

How to define or operationalize:

– addiction
– dependence (physiological and psychological)
– medical use (relevant to scheduling a substance)

Think hard about Policy, Laws, Regulations, and Attitudes about potentially harmful substances

- Seems like Groundhog Day…
Is Cannabis Use, Misuse, Abuse, Dependence a Public Health Issue?

- Consequences of Clinical Importance
- Relatively large numbers seek treatment
- Impacts a significant proportion of youth and adults
- Multiple consequences associated with abuse
If You Answer Yes

• does not mean:
  - you can’t investigate potential benefits
  - you can’t explore harm reduction strategies
  - you believe it is worse than alcohol or tobacco
  - you believe it is the same as cocaine and heroin
  - you believe it should or should not be legalized or decriminalized
Conclusions

- Cannabis / cannabinoid use increasing, likely to continue to increase among youth (legal status, price decrease, reduced perception of risk, enticing products, vaping)

- Might be on a trajectory towards becoming a more dangerous class of substances with legalization movement leading to enticing products including edibles, increased potency in those products, and surely other modifications that will increase its allure
Conclusions

- Youth may be particularly vulnerable to development of problematic / excessive use or use disorders
- Consequences of moderate to heavy use appears substantial
- Interventions have efficacy, but are fairly weak
- Much work to be done in areas of regulation and treatment and prevention development and implementation
THANKS!!!!

<table>
<thead>
<tr>
<th>Faculty/Trainees</th>
<th>Staff / Therapists</th>
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<tbody>
<tr>
<td>Cathy Stanger</td>
<td>Patty Costello</td>
</tr>
<tr>
<td>Stephanie Fearer</td>
<td>Eliza Wessinger</td>
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<tr>
<td>Brent Moore</td>
<td>Gray Norton</td>
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<tr>
<td>Ryan Vandrey</td>
<td>Leanna Delhey</td>
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<td>John Hughes</td>
<td>Lee Whetstone</td>
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<td>Doris Ogden</td>
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<td>Warren Bickel</td>
<td>Jonathan Young</td>
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<td>Denise Walker</td>
<td>Heath Rocha</td>
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<td>Roger Roffman</td>
<td>Andrea Meier</td>
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<td>Bob Stephens</td>
<td>Merrie Vannucci</td>
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<td>Pam Brown</td>
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<td>Stacy Ryan</td>
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<td>Sarah Clark</td>
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<tr>
<td>Jen VanScoyoc</td>
<td>Stanley See, Hao Yang</td>
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<tr>
<td>Dustin Lee, Valerie Noel</td>
<td>Nick Tacke</td>
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NIDA, NIAAA for research support