Slide 1

Marijuana
Sailing the Rhetorical Seas Pt. 2

KSAODS, July 2014

Sponsored by Prevention Research Institute

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What are the risks?
1. Impairment
2. Cognitive deficits
3. Addiction
4. Diminished Life Outcomes
5. Not typical, but real:
   A. Cardiac problems
   B. Heart attacks & fatalities
6. Rare but devastating:
   A. Schizophrenia
   B. Cancer

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Risk 1. Impairment

“Getting high is just harmless fun and a great way to relax.”

Seed of Truth:
Marijuana can be fun and relaxing.
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**Risk 1. Impairment**

Cannabis is the most commonly used illegal substance in DUI.

- DUI reports on adults 18 and older:
  - 17,876,000 DUIs - with alcohol
  - 13,124,000 DUIs - with cannabis (drugs of all kind other than alcohol)
  - 2,900,000 DUIs - with cocaine (drugs of all kind other than alcohol)

NOTE: Cocaine is the 2nd largest drug using/driving group (Source: NSDUH, 2006)

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**Risk 1. Impairment**

Research on Cannabis and Driving

- Past use of THC (24 hours earlier) – no effect on crash risks
- Recent use of THC (past 2-4 hours) - increases risks for motor vehicle accidents
- THC alone increases risk
- Synergistic effect of alcohol & THC - greater impairment than either alone

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**Risk 1. Impairment**

Marijuana users do attempt to adjust for impairment
- Slower speeds
- Greater following distance

Marijuana impairs mostly automated driving skills
- Weaving
- Time estimation
- Impaired ability to shift attention
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**Risk 1. Impairment**

**Effects of Cannabis and Alcohol Combined**
- THC & alcohol vs. same-BAL alcohol only
  - 2.5 increased odds of causing fatal crash
- When both alcohol and THC was present in fatally injured drivers, 95% of those drivers caused the fatal crash
- THC and alcohol combined results in:
  - Severe driving impairment
  - Sharp increase in the risk of accidents and culpability

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**Risk 1. Impairment**

**Impact of THC Impairment on Fatal Crashes**
- Any level THC – 2.7 increased odds of causing a fatal crash
- > 5 ng/ml THC – 6.6 increased odds of causing a fatal crash

THC mostly impairs automated driving skills.

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**Risk 1. Impairment**

**State Per Se THC Impairment Levels**
- None
- Any illegal substance or metabolite in the blood (defined in state code)
- Per se THC levels ranging from 1 ng/ml – 10 ng/ml
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**Risk 1. Impairment**

- Pennsylvania has a 1 ng/ml per se THC law
- Ohio and Nevada have 2 ng/ml in blood per se THC laws
- Three states have per se THC laws at 5 ng/ml in blood
  - Colorado
  - Washington
  - Montana

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**Risk 1. Impairment - Are they impaired?**

**Why Measuring THC Impairment is Complex**

- Not like alcohol in its effects
- Unlike alcohol, impairment does not follow blood levels
- We need to know what we're measuring
  - THC, Hydroxy-THC, Carboxy-THC

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**Risk 1. Impairment - Are they impaired?**

**Why Measuring THC Impairment is Complex**

- $\Delta^9$-THC (THC) – psychoactive, persists in blood 1-4 hours
- 11-Hydroxy-$\Delta^9$-THC (hydroxy) psychoactive, persists in blood 2-6 hours
- 11-Nor-9-Carboxy-THC (carboxy) non-psychoactive, persists in blood for a number of days
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**What are the risks?**

1. Impaired Driving
   - 2.7 increased odds of causing a fatal crash with any THC blood level
   - 6.6 increased odds of causing a fatal crash with ≥5 ng/ml blood level

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**Executive Brain Functions -**

- Attention
- Concentration/Persistence to Task
- Decision Making (especially with new information)
- Impulsivity/Inhibition

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**Executive Brain Functions -**

- Reaction Time
- Risk Taking
- Verbal fluency
- Working (or Short-term) Memory
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**Risk 1. Impairment**

While IMPAIRED, multiple studies find deficits in:
- Attention (in light but not heavy users)
- Concentration
- Inhibition
- Impulsivity
- Increased Risk-taking

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**Risk I: Acute Impairment & Injury**

Does Cannabis Protect from Overall Injury?
- Two studies found an inverse relationship between injury and marijuana use.
- Results widely promoted by NORML

Does this make what we teach wrong? **No**
- Marijuana users are more likely to do nothing – reducing their risk for injury.
- When they drive or do other activities, they are **MORE** likely to be injured.

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**Risk I: Acute Impairment & Injury**

- Marijuana use linked to increased rates of injury requiring hospitalization
- Increased risk for cannabis users vs. nonusers:

<table>
<thead>
<tr>
<th></th>
<th>Any Injury</th>
<th>Vehicular Injury</th>
<th>Assault Injury</th>
<th>Self-inflicted Injury</th>
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<tbody>
<tr>
<td><strong>Males</strong></td>
<td>1.5 Increased Odds</td>
<td>2.3 Increased Odds</td>
<td>2.6 Increased Odds</td>
<td>3.4 Increased Odds</td>
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<tr>
<td><strong>Females</strong></td>
<td>2.1 Increased Odds</td>
<td>2.5 Increased Odds</td>
<td>2.3 Increased Odds</td>
<td>2.9 Increased Odds</td>
</tr>
</tbody>
</table>
Risk 1 – Impairment

Do cannabis users do better at school or work while using? They may!

- Acute effect is decreased ability to shift attention, i.e. more focus on one thing.
- Rebound effect is decreased ability to focus on one thing while not using, increasing the felt need to use to function.
- Rebound effect may increases with duration of use.

What are the risks?

2. Cognitive deficits
   a) lowered IQ in heavy using adolescents
   b) attentional deficits
   c) Impaired executive brain functions

The New View

- Those using cannabis do injure themselves and others.
- Cannabis use decreases the ability to shift attention among multiple tasks.
- Impairs impulse control with more impulsive behavior
- Impairs working memory
- Increases risky decision-making
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Risk 2 – Lingering Effects

“It’s better than alcohol. I don’t have a hangover; I get high, I come down. Everything is fine.”

Seed of Truth:
• People don’t have obvious hangovers from using marijuana.

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Risk 2 – Lingering Effects

Deficits in:
• Short-term memory
• Attention
• Decision making / Risk Taking
• Verbal Fluency
• Reduced IQ (in those starting in adolescence)

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Risk 2 – Lingering Effects

Executive Brain Functions help us:
• Plan
• Organize new information
• Integrate the info into new approaches
• Persistence to task
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**Risk 2 – Lingering Effects - Psychosis**

Subthreshold psychosis can also be a problem:

- Becoming more asocial
- Loss of motivation/energy/concentration
- Drop in functioning
- Increased suspicion and/or exaggerated beliefs
- Odd behaviors

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**Risk 2 – Lingering Effects Summary**

**The New View**

- Cannabis users over time can develop subtle, but significant, cognitive problems including impaired:
  - Decision-making,
  - Integration and use of new information,
  - Problem solving, and
  - With early onset, a potentially lower IQ

Marijuana is different from alcohol; but that doesn’t make it “safe.”

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**Risk 2 – Lingering Effects Summary**

**The New View**

- Most people using marijuana will not develop a psychosis disorder, but risk is there for some.
- Predictors of psychosis disorders:
  - Family history of psychosis,
  - Daily use in adolescence
  - Episodes of toxic psychosis.
- Long-term or high-potency use may cause subthreshold psychosis symptoms.
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Risk 3 – Dependence & Addiction

“Cannabis is not addictive. Or if it is, it’s so mild it doesn’t matter.”

Seed of Truth:

• Many people who smoked marijuana were not addicted and quit easily.

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Risk 3 - Dependence & Addiction

Is Marijuana Addictive?

➢ A New Understanding – Addiction is centered in brain
➢ Can marijuana use meet criteria for dependence and addiction?
  • Withdrawal
  • Loss of control

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Risk 3 - Dependence & Addiction

What we do know:

• Addiction is not just defined by physical dependence leading to withdrawal.
• Medical withdrawal does not lead to loss of control.
• Withdrawal may play a role in continued use and relapse.
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**Risk 3 - Dependence & Addiction**

One View of Addiction: Same as the eleven DSM-V Substance Use Disorders

- **3 Biological Symptoms**
  1. **Tolerance** - need increased amounts or get diminished effect
  2. **Withdrawal**
     1. Typical substance withdrawal syndrome or
     2. Substance or analog taken to relieve or avoid withdrawal
  3. **Craving** - strong desire to use a particular substance

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**Risk 3 - Dependence & Addiction**

One View of Addiction: Same as DSM-V Dependence

- **Eight Behavioral Symptoms**
  1. Recurrent use with failure to engage in life roles
  2. Recurrent use despite social or interpersonal problems
  3. Recurrent use in physically hazardous situations
  4. Using more or longer than intended
  5. Desire or have unsuccessful efforts to cut down/control use
  6. Spend a lot of time obtaining, using, or recovering
  7. Decrease or give up important activities due to drug
  8. Recurrent use despite knowledge of physical or psychological problems caused or made worse

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**Risk 3 - Dependence & Addiction**

Another View of Addiction: Homeostasis to Allostasis

- High blood pressure is an allostatic state.
- Drug-driven brain changes lead to addiction as the brain tries to maintain stability in the brain’s reward systems.
- Persistent vulnerability to relapse and addiction
- **Addiction is an allostatic state characterized by the**
  - Compulsion to seek and take drug
  - Loss of control in limiting intake
  - Emergence of a negative emotional state when access is blocked

*Source: Koob & Le Moal, 2008*
Risk 3 - Dependence & Addiction

Addiction - A New Understanding from the Latest Brain Research

- group of behaviors arising from an altered brain
- characterized by
  - A compulsion to seek and take drug
  - The loss of control in limiting intake
  - The emergence of a negative emotional state when access to the drug is blocked

Koob & Le Moal, 2008

Neurobiological View of Addiction

- Chronic Elevation of Reward Threshold
- Recruitment of Anti-reward Systems
- Enhanced Stimulus-Response Links
- Loss of Executive Control

Compulsive Drug Seeking/Using

Lingering Deficits in Executive brain functions
  - Planning
  - Organizing
  - Focused attention
  - Persistence to task

Koob & Le Moal, 2008
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Risk 3 - Dependence & Addiction

- Loss of Executive Control
- Chronic Elevation of Reward Threshold

Let’s explore the second brain change...

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Risk 3 - Dependence & Addiction

**Reward Rebound**

- While “buzzed,” drunk or high, the brain’s reward threshold is temporarily lowered.
- Following the “high,” the reward threshold is temporarily raised.

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Risk 3 - Dependence & Addiction

**Reward Rebound**

What we experience as *euphoria*, the brain and its neurons experience as a *threat*.

- The brain responds to protect itself by making its reward system less sensitive to all reward.
- This is the first reason we have a reward rebound – the brain is acting to protect itself.
The second reason for reward rebound is activation of the anti-reward system.

Reward Rebound
- Many anti-reward chemicals help moderate and shut down the reward system.
- Loss of reward response leads to:
  - Shift in values
  - Shift in behaviors
- Flip side of reward is stress.

Let’s see the outcomes of these two chronic brain changes.
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Risk 3 – Dependence & Addiction

Altered Reward & Stress Systems

➢ Loss of reward leads to a shift in values and behaviors
  • Less rewarding = less valuable,
  • Less rewarding = less time & energy invested

➢ Small stressors:
  • have more power to trigger our stress responses

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Risk 3 – Dependence & Addiction

Altered Reward & Stress Systems

➢ Leads to a shift in values and behaviors to
  • avoid stress
  • seek reward

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Risk 3 – Cannabis Dependence & Addiction

Does marijuana use acutely LOWER reward threshold (more pleasure)?

➢ Lowered reward threshold by ∆9-THC has been demonstrated by:
  • Rate-frequency paradigm
  • Reward-threshold paradigm

➢ Similar to all other abused drugs
➢ Cannabis produces conditioned place preference in lab animals.
➢ Self-administration studies find both animals and humans will self-administer cannabis.
Does marijuana use acutely RAISE stress threshold (reduce stress)?

Multiple studies report:
- Cannabis stimulates the production and release of opioids, calming the brain and reducing pain (emotional or physical).
- Marijuana users state enhanced relaxation as the #1 reason they use.

A LOWER stress threshold after a marijuana “high”? Multiple studies report:
- Irritability (87%)
- Nervousness (80%)
- Depression (76%)
- Restlessness (76%)
- Anger (74%)

A LOWER stress threshold after a marijuana “high”? Multiple studies find:
- More aggressive responses during times of abstinence
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**Risk 3 – Cannabis Dependence & Addiction**

**During and after the “high”**

<table>
<thead>
<tr>
<th>Stress</th>
<th>Reward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold</td>
<td>Threshold</td>
</tr>
</tbody>
</table>

**“High”**

**After the “High”**

<table>
<thead>
<tr>
<th>Stress</th>
<th>Reward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Threshold</td>
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</tbody>
</table>

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**Risk 3 – Cannabis Dependence & Addiction**

Let’s explore the fourth and final criteria

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**Risk 3 – Cannabis Dependence & Addiction**

**Enhance Stimulus Response**

- Compared to non-users, cannabis users:
  - More quickly focused on cannabis cues
  - Spent more time looking at those cues
  - Rated the cues as more pleasurable
  - Increased craving increased the stimulus response
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Risk 3 – Cannabis Dependence & Addiction

Neurobiological View of Addiction

- Loss of Executive Control
- Chronic Elevation of Reward Threshold
- Recruitment of Anti-reward Systems
- Enhanced Stimulus-Response Links

Koob & Le Moal, 2008

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Risk 3 – Cannabis Dependence & Addiction

Symptom prevalence in dependent cannabis users:

- Persistent desire 91%
- Unintentional use 84%
- Withdrawal 74%
- Excessive time obtaining/using 74%
- Continued use despite health problems 63%
- Tolerance 21%
- Social consequences 18%

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Risk 3 – Cannabis Dependence & Addiction

Compared to Dependent Alcohol Users, Dependent Cannabis Users reported:

- Compulsive and out-of-control use more frequently
- Withdrawal similarly
- Tolerance considerably less often
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Most Powerful Predictive Risk Factor of Dependency at Age 21
- Frequency of cannabis use at age 18
  - Even after controlling for pre-existing psychological or social factors
- Nonusers who began use - 1.8 odds
- Odds nearly double at each level of use.

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Summary
Marijuana has the ability to create:
- Social dependence
- Psychological dependence
- Physical dependence
- Behavioral Loss of Control

Marijuana is addictive, characterized by:
- A compulsion to seek & take drug
- Loss of control in limiting intake
- The emergence of a negative emotional state when access to the drug is blocked

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“People smoking marijuana do just as well in life as those who don’t.”

Seed of Truth:
- Many people who use marijuana have functional lives.
Life Outcomes of Cannabis Users Ages 24-37

- Multiple studies of users vs. non-using peers found among cannabis users:
  - More with only a high school education or less
  - More who are unemployed
  - More with lower income
  - More episodes of use predict greater risk of these outcomes

Life Outcomes of Cannabis Users Ages 24-37

- Multiple studies of users vs. non-using peers found among cannabis users:
  - More who never married or are divorced
  - More who are disabled
  - More who use alcohol, tobacco, or other drugs.

Are other drugs the real problem?

- Cannabis-only dependent users in treatment vs. other drug-dependent users in treatment
  - Cannabis users had more:
    - Depression
    - Personality disorders
    - Psychosis/schizophreniform disorders
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**Risk 4 – Life Outcomes Summary**

**The New View** - As a group, marijuana users report

- Poorer quality of life than nonusers, even after controlling for many background factors and other drug use
  - Lower educational levels
  - Less employment / lower income
  - More never married or divorced
  - Less overall life satisfaction
- Marijuana does not contribute to improved quality of life.

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**Risk 5 – Health Problems**

1. Acute Cardiac Problems & Heart Attack
2. Schizophrenia or Other Psychosis Disorder
3. Testicular Cancer - nonseminomous germ cell cancer

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**Risk 5 – Heart Disease and Death**

The research says:

- Marijuana use increases heart rate by 30-100% of normal (up to 160 beats per minute)
- Supine hypertension, orthostatic hypotension & fainting
- 4.8x increased risk of myocardial infarction (heart attack) in the first hour after smoking
- Reduced experience of angina (12% vs 25%)
Among young users there are occasional sudden heart problems
- Atrial fibrillation
- Ventral fibrillation (more serious)

There were two recent fatalities reported in young men using cannabis
Concern that the problem is under-recognized and reported, especially as the population ages

Comparing marijuana users to nonusers in those with known heart disease:
- Doubled (1.9x) increased risk of fatal heart attack in 4 years with any use
- 2.5x increased risk for less than weekly users
- 4.9x increased risk for weekly or more users

The research says:

The prospective research says:
Researchers share concerns:
• The problem is seldom recognized and may be unreported
• Physicians should inquire about marijuana use particularly in heart problems in young adults
• As the population ages, use the marijuana may be contraindicated in those with heart disease

Studies show cannabis use linked to development of schizophrenia

<table>
<thead>
<tr>
<th>Cannabis Use</th>
<th>Dose-Response Curve and % Developing Schizophrenia</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-10 times</td>
<td>11% Developed Schizophrenia</td>
<td>1.1 increased odds</td>
</tr>
<tr>
<td>11-50 times</td>
<td>19% Developed Schizophrenia</td>
<td>2.2 increased odds</td>
</tr>
<tr>
<td>&gt; 50 times</td>
<td>38% Developed Schizophrenia</td>
<td>3.3 increased odds</td>
</tr>
</tbody>
</table>

Similar findings from other research

Most people using marijuana will not develop a psychosis disorder, but risk is there for some.
Long-term or high-potency use may cause subthreshold psychosis symptoms.
Predictors of psychosis disorders:
• family history of psychosis,
• daily use in adolescence
• personal history of high-potency marijuana use
• episodes of toxic psychosis
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- Risk 7 – Cancer
  - It is suggested the marijuana cures cancer.
  - This implies that smoked or inhaled marijuana will cure cancer, which is not true.
  - Pure THC and some other cannabinoids applied to some tumors reduce the size of the tumors.
  - This is a promising area that should be pursued.
  - Other evidence suggests marijuana may impair immune response to tumors.

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- Risk 7 – Testicular Cancer (rare but devastating)
  - Three independent studies implicate marijuana use as a risk factor for a particular form of testicular cancer (Testicular germ cell tumor or TGCT).
  - Most commonly occurring in young adults aged 18 to 45.
  - Doubled the risk (1.7 to 2.2 increased odds).

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- Overall Research Conclusions
  1. Acute impairment is hazardous.
  2. Lingering effects do happen.
  3. Dependence and addiction happen and quantity/frequency of use predict it.
  4. Life outcomes are not improved by the use of cannabis.
Overall Research Conclusions
5. There is increased risk for heart disease for some
6. Marijuana seems to be an environmental risk factor for schizophrenia
7. Marijuana use, particularly daily use, may increase risk for testicular cancer in young men