Up In Smoke
Part 2
Long-term Outcomes of Marijuana use

Marijuana Advocacy & Policy Summit
Columbus, OH
April 1, 2015

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved
Interests - Allan Barger, MSW

• Research Analyst employed by Prevention Research Institute™

• We develop and train others to implement Prime For Life® a motivational prevention/intervention program and Prime Solutions® a treatment program.

• No other competing interests.
What are the risks?

3. Dependence & Addiction
4. Other Outcomes & Risks
Increased Rates of Marijuana Use

Numbers in Millions

- Used Marijuana on 300 or More Days in the Past Year
- Used Marijuana on 20 or More Days in the Past Month

2002: 3.1
2003: 3.1
2004: 3.2
2005: 3.4
2006: 3.1
2007: 3.6
2008: 3.9
2009: 4.1
2010: 4.6
2011: 5.0
2012: 5.4
2013: 5.7
2014: 6.9
2015: 7.1
2016: 7.6
2017: 8.1
“Cannabis is not addictive” (or if it is, it’s so mild it doesn’t matter.

Why does this belief persist despite a lot of data to the contrary?

- Many people who smoked marijuana were not addicted and quit easily.
- Misunderstanding of “addiction.”
3. Dependence & Addiction

What we do know:

- Addiction is **not just defined by physiological dependence** characterized by withdrawal.
- Medical withdrawal does not lead to addictive behaviors.
- Withdrawal may play a role in continued use and relapse.
3. Dependence & Addiction

One View of Addiction: Same as DSM-5
Substance Use Disorders – 11 criteria

3 Biological Symptoms

1. Tolerance - need increased amounts or get diminished effect

2. Withdrawal
   A. Typical substance withdrawal syndrome or
   B. Substance or analog taken to relieve or avoid withdrawal

3. Craving – strong desire to use a particular substance
3. Dependence & Addiction

One View of Addiction: Same as DSM-V Dependence

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

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved
3. Dependence & Addiction

Addiction - A New Understanding from the Latest Brain Research

- specific 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
3. Dependence & Addiction

Neurobiological View of Addiction

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

Compulsive Drug Seeking/Using

Koob & Le Moal, 2008
3. Dependence & Addiction

Lingering Deficits in Executive Brain Functions

- Planning
- Organizing
- Focused attention
- Persistence to task
- Impulse Control
3. Dependence & Addiction

- Loss of Executive Control
- Chronic Elevation of Reward Threshold

Let’s explore the second brain change...
3. Dependence & Addiction

While “buzzed,” drunk or high, the brain’s reward threshold is lowered:

- Normal pleasures enhanced
- Friends feel friendlier
- Humor is funnier

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved
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**.
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.
3. Dependence & Addiction

Chronic Elevation of Reward Threshold

Recruitment of Anti-reward Systems

The second reason for reward rebound is activation of the anti-reward system.
3. Dependence & Addiction

Reward Rebound

➤ Many anti-reward chemicals help moderate and shut down the reward system.

➤ Loss of reward response leads to a:
  • Shift in values
  • Shift in behaviors

➤ Flip side of reward is stress.
3. Dependence & Addiction

Stress Threshold

• A point at which we are not stressed, moving to the point where we become stressed
3. Dependence & Addiction

• **Reward** – During the early “high,” the stress threshold is temporarily raised

• **Stress Threshold** - As a drug leaves the system, the brain’s stress set point is temporarily lowered.
3. Dependence & Addiction

Chronic Elevation of Reward Threshold

Recruitment of Anti-reward Systems

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

During and after the “high”

“High”

After the “High”

Stress & Reward Baseline

Reward Threshold

Stress Threshold

Reward Stimuli

Stress Stimuli

Stress Stimuli

Reward Stimuli

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved
3. Dependence & Addiction

The Brain: Our window on the world
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
3. Dependence & Addiction

Altered Reward & Stress Systems

- Leads to a shift in values and behaviors to
  - *avoid stress*
  - *seek reward*
Does marijuana use acutely LOWER reward threshold (more pleasure)?

- Lowered reward threshold by $\Delta^9$-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 opioid, 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”?

Several studies on cannabis abstinence syndrome report:

- Irritability (87%)
- Nervousness (80%)
- Depression (76%)
- Restlessness (76%)
- Anger (74%)
3. Cannabis Dependence & Addiction

A LOWER stress threshold after a marijuana “high”?

Other studies find:

- More aggressive responding during times of abstinence
3. Cannabis Dependence & Addiction

During and after the “high”

“High”

After the “High”

Stress Threshold

Stress & Reward Baseline

Reward Threshold

Reward Stimuli

Stress Stimuli

Stress Stimuli

Reward Stimuli

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved
3. Cannabis Dependence & Addiction

Recently I’ve been tryin’ to cut back, only 1 or two blunts a day but noticed jitteryness, anxiety, soreness all kinds of random effects I didn’t think was possible from some pot.

Anonymous, 20 years old
Chronic Elevation of Reward Threshold

Recruitment of Anti-reward Systems

Enhanced Stimulus-Response Links

Let’s explore the fourth and final criteria
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

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved
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

Compulsive Drug Seeking/Using

Copyright(C) 2015, Prevention Research Institute, All Rights Reserved

Koob & Le Moal, 2008
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%
Compared to Dependent Alcohol Users, Dependent Cannabis Users reported:

- Compulsive and out-of-control use more frequently
- Withdrawal similarly
- Tolerance considerably less often
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.
Summary

Marijuana has the ability to create:

- Social dependence
- Psychological dependence
- Physiological 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
An opinion piece published in the *Heart*, the journal of the American Heart Association specifically raised the issue of marijuana-related heart disease and death.

They recommended ED doctors inquire about drug use, including marijuana, as routinely as alcohol or tobacco. WHY?
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%)
Prospective research compared nonusers to users 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
Heart Disease and Death

- Among young users there are occasional sudden heart problems
  - Atrial fibrillation
  - Ventral fibrillation
- Three recent fatal heart attacks (2 men, 1 woman) where cannabis use was the only identifiable risk factor
The American Heart Association is concerned the problem may be under-recognized and under-reported, especially as marijuana use is legalized and as the population ages.

AHA calls for a national monitoring system.
Testicular Cancer

- Rates rising for several decades without a known cause
- Researchers explored many possible factors
- Marijuana use emerged as a possibility
We need more research, but...


Nonseminomous Germ Cell Tumor – a serious cancer requiring chemo and radiation therapies

- 2 – 3 times greater odds in
- Those starting use prior to age 18
- Those using weekly to daily
- Most common in men in their 30’s
Summary Risks

Well-established Risks

- Impaired Driving
- Cognitive Deficits
- Addiction / Mental Health

Areas of Concern

- Heart Disease
- Testicular cancer
- Psychosis